

Overview and Governance



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Governance Team

Institutional Steering Committee (ISC)
Internal Advisory Board (IAB)
External Advisory Board (EAB)
Executive Oversight Committee (EOC)
Committee on Maternal, Child and Adolescent Health (CMCAH)

Abbreviations: ACRIN / NLST – American College of Radiology Imaging Network / National Lung Screening Trial; BIP – Biomedical Informatics Program; BIRN – Biomedical Informatics Research Network; BSD-CDM – Biostatistics, Study Design, and Clinical Data Management Program; CAP – Community-Academic Partnership Council; CC-HEATRs – Community Centers in Health Education and Translational Research; CCRR – Clinical and Community Research Resources Program; CDU – Charles Drew University of Medicine and Science; Cedars-Sinai – Cedars-Sinai Medical Center; CER – Comparative Effectiveness Research; CERP – Community Engagement in Research Program; CNSI – California NanoSystems Institute; CTSI-ED – Research Education, Training and Career Development; CTT – Center for Translational Technologies; E/T – Evaluation & Tracking; EAB – External Advisory Board; EOC – Executive Oversight Committee; ETU – Evaluation & Tracking Unit; GCRCF – General Clinical Research Center; HAAF – Healthy African American Families; Harbor-LA BioMed – Los Angeles Biomedical Institute at Harbor UCLA Medical Center; HIPAA – Health Insurance Portability and Accountability Act; HSR – Health Services Research; i² – Institute for Informatics; IAB – Internal Advisory Board; IMED – Institute for Molecular Medicine; Internal Advisory Board – IAB; IOM – Institute of Medicine; ISC – Institutional Steering Committee; JCCC – Jonsson Comprehensive Cancer Center; LONI – Laboratory of Neuro Imaging; LS-MSMS – liquid chromatography-tandem mass spectrometry; MALDI-TOF – matrix-assisted laser desorption/ionization-time-of-flight; MCBH – Maternal and Child Health Bureau; MSCR – Master of Science in Clinical Research; NCS – National Children’s Study; OIA – Office of Industry Alliances; OIS – Office of Investigator Services; PCORI – Patient-Centered Outcomes Research Institute; PD – Program Director; PET – Positron Emission Tomography; Program Pilot/ Collaborative Program – Pilot and Collaborative Translational and Clinical Studies; RCMI – Research Centers in Minority Institutions; Regulatory Program – Regulatory Support and Knowledge, Research Ethics and Industry Alliances Program; SPH – UCLA School of Public Health; STAR – Specialty Training and Advanced Research; TRCs – Translational Research Clusters; TTTRP – Translational Therapeutics and Technologies Research Program; UC – University of California; UCSF – UC San Francisco; WHI – Wireless Health Institute.

1. **APPROACH:** THE INTENT OF THE UCLA-CTSI INITIATIVE

1.1. Introduction and Goals

The UCLA CTSI is an academic-clinical-community partnership designed to accelerate scientific discoveries and clinical breakthroughs to improve health in the most populous and diverse county in the United States. Our **mission** is to create a borderless clinical and translational research institute that brings UCLA innovations and resources to bear on the greatest health needs of Los Angeles.

The national Clinical and Translational Science Awards program is designed to speed translation of laboratory discoveries into treatments for patients, to engage communities in research, and to train the next generation of clinical and translational science investigators. How will the UCLA CTSI continue to make progress toward these objectives? We are aligning our strengths to support clinical and translational science that is in full partnership with and responsive to the needs of our community. Our UCLA CTSI is bridging disciplinary and institutional boundaries to create transdisciplinary teams focused on the greatest opportunities as well as the greatest needs in our region. CTSA funding will accelerate our progress in achieving our transformative mission and allow the UCLA CTSI to make significant contributions to the goals of the national CTSA consortium.

Please note that this section has been completely revised. Therefore, changes are not marked in the document.

To accomplish our mission the UCLA CTSI has established five goals.

Goal 1: Create an academic home for clinical and translational science that integrates and builds on the many strengths of UCLA and its partners. We are developing an adaptive infrastructure that transcends barriers and provides resources to promote transdisciplinary clinical and translational research. Our leadership is empowered to promote collaborative, translational research across institutional and departmental boundaries.

Goal 2: Build transdisciplinary research teams to accelerate and translate discovery to improve health. We are assembling transdisciplinary Translational Research Clusters focused on the diseases and risk factors of highest priority in our community. We are streamlining regulatory processes and access to core resources to increase efficiency and support the widest range of research.

Goal 3: Transform educational and career development programs to promote the next generation of clinician investigators and translational scientists. We are designing our programs to transcend the training silos that impede transdisciplinary team-based research. We are infusing substantive community input into all levels of training. We have added CTSA K12 and T32 components; recruited leading mentors; and implemented mentoring programs for junior faculty from underrepresented groups.

Goal 4: Advance and expand strong bi-directional academic-community partnerships to ensure that new scientific discovery is relevant to community needs. We are integrating and redeploying our resources and using emerging technologies to support effective application, scaling and spread of co-developed knowledge to improve health. We are leveraging well-recognized expertise in health services research to build cost-effectiveness and outcomes analysis into early-stage research.

Goal 5: Serve as a national resource for collaborative research through regional, statewide and national CTSA consortia. We are transcending institutional barriers and collaborating in education, training and clinical trial recruitment through our membership in the Greater Los Angeles CTSA Coalition and West Coast CTSA Consortium. We are committed to sharing our innovations and resources as members of the national CTSA.

1.2. The UCLA CTSI: Our response to the needs of Los Angeles and the nation

The UCLA CTSI partner institutions serve Los Angeles County, the most populous and diverse county in the United States. An ethnic, economic and cultural mosaic, Los Angeles County provides challenges for health and disease research that few counties replicate. The county's population is larger than that of 42 states. Three-quarters of the county's nearly 10 million residents are non-white and one-third of residents were born outside the US. Ninety languages are spoken here. There is no ethnic majority.

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Residents of Los Angeles County are disproportionately young, poor and sick. Nearly one in three is under age 18 and one in five is below the federal poverty line. One in four lacks health insurance. Rates of premature death and disability related to heart disease, diabetes, stroke, AIDS, depression, violence and other preventable conditions far exceed national averages. The disease burden is magnified by language barriers, cultural beliefs, poverty and disparities in access to care. A 15-year life expectancy gap separates our healthiest and sickest populations. Though the life-expectancy gap between African Americans and whites has narrowed nationally, it has not done so in Los Angeles. Addressing health disparities is a special focus of our UCLA CTSI, which in the pre-award period has organized Translational Research Clusters focused on the greatest causes of disability and early death in LA County. Our purpose is to address the major causes of premature death and significant morbidities in Los Angeles County. Because our current translational/clinical research programs and health care systems so inadequately impact these causes of death and quality of life issues, we propose a transformative mission. As the US population becomes more diverse in the 21st Century, our experiences and successes will offer a model for health improvement nationwide.

1.3 Our tradition of excellence in clinical and translational science makes UCLA an outstanding academic home for our CTSI. UCLA is home to exceptional advances in clinical and translational science that impact today's practice of medicine. For example, UCLA professor Dr. Dennis Slamon and his colleagues conducted the laboratory and clinical research that led to the development of the widely used breast cancer drug Herceptin, which targets a specific genetic alteration found in more than 25 percent of breast cancer patients. Another example is the major impact of the original invention of Positron Emission Tomography (PET) by UCLA Professor Dr. Michael Phelps. PET is used routinely for important clinical assessments in cancer, neurological disorders and cardiovascular disease. (Both Drs. Phelps and Slamon serve on our CTSI IAB. Please refer to letters on pages 1540 and 1550). We are now training a generation of investigators whom we expect to continue to make major scientific contributions that impact health. How will they accomplish effective translational investigation? Our CTSI proposes to create a collaborative culture in which practice-changing innovation is not the exception but the rule.

1.4. THE UCLA CTSI: The key to our transformation

The complex problems of medical science today cut across disciplinary lines. Disis and Slattery recently summarized the necessity of multidisciplinary team science in translational investigation.¹ Disis noted, however, that academic research centers are not organized to encourage diverse teams to coalesce in an effort to discover and apply research findings in clinical and translational investigation. Börner et al. observed that in order to take advantage of the opportunities offered by team science, we must develop new ways to retain, recruit and empower scientists to work together across disciplines, departments, institutions and geography.² At UCLA, our CTSI is the key to transforming our environment to establish transdisciplinary team science as our operating principle in clinical and translational investigation.

Our strategic planning identified our specific strengths, weaknesses and opportunities to transform. Our strengths include a long history of collaboration among investigators at our four partner institutions. In addition, we have longstanding relationships with leaders in our Los Angeles community that we can leverage to expand our ties to our large, diverse population. We have outstanding educational and training resources in basic sciences, dentistry, engineering, health services research, medicine, nursing and public health.

We also identified deficiencies that require CTSI-mediated transformation. We have limited central mechanisms to match investigators by research interest, project knowledge or complementary skills. Similarly, there is a pressing need for incorporating the needs and desires of our community into our research enterprise. In a 2010 survey, faculty said our organizational structure was too large and compartmentalized, and that regulatory requirements and burdensome paperwork deterred inter-institutional team science research. Training in translational team science is limited.

To address the health needs of Los Angeles and the nation, we must act. The UCLA CTSI offers us an unprecedented opportunity to address these barriers and re-engineer our clinical and translational research environment.

1.5. In transforming our research enterprise, the UCLA-CTSI is guided by three core principles

1) **Team science:** We are facilitating transdisciplinary teams to address the key impediments to health in our community. We anticipate that team science training in our education programs will lead to a new generation of

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creative investigators who seek solutions to major problems by exploiting the synergy of their collaborations. We are working with our Chancellor, Deans, Department Chairs and promotion committees to structure academic rewards that recognize the critical nature of team science in effective clinical/translational investigation. We are creating new team-based funding mechanisms including Translational Research Cluster grants which support investigator-initiated, transdisciplinary, team-based research with preferences given to projects that address major health problems in our community. We have started transdisciplinary team-based training programs including the UCLA Society of the CTSI. We have institutional commitment to invest more than \$30 million in new team-based science and faculty recruitment during the next five years.

2) **Flexible Research Infrastructures:** We are shaping research services to fit requirements for effective investigation in all environments. Examples include mobile research units that bring studies to community clinics, access to a full array of support services via our online Virtual Home and Office of Investigator Services, and Catalyst funding mechanisms for stimulating pilot research. We are using GPS equipment to collect a range of real-time data from research subjects to help us understand the impact of behaviors and experiences in patients' lives. Our CTSI is using this technology in the community to monitor breast cancer survivors, health behaviors in people with HIV, and exercise and stress levels in new mothers.

3) **Community Engagement:** We are emphasizing solutions for the major health problems in Los Angeles County and focusing on the multiple determinants of both health and disease. This is being accomplished by facilitating collaborative, equitable, bi-directional partnerships in all phases of our translational and clinical research. We are partnering to build on the resources and strengths within the community. Community leaders are represented at the highest organizational levels of the CTSI.

2. PARTICIPATING INSTITUTIONS

The CTSI is well-constituted to drive innovations that will transform health in Los Angeles. Clinicians and scientists at our four partner institutions have faculty appointments at UCLA.

UCLA and Charles Drew University of Medicine and Science (CDU) provide the full range of education, research and clinical care for adult and pediatric diseases, and a unique commitment to underrepresented populations. Faculty from ten UCLA schools – Medicine, Business, Dentistry, Education and Information Studies, Public Affairs, Engineering and Applied Sciences, Law, Nursing, Public Health, and the College of Arts and Letters – bring transdisciplinary strength to enrich clinical and translational research.

Los Angeles Biomedical Institute at Harbor UCLA Medical Center (Harbor-LA BioMed) and the Burns and Allen Research Institute at Cedars-Sinai Medical Center (Cedars-Sinai) bring outstanding expertise in clinical research and health care delivery. They are a large public (Harbor-LA BioMed) and non-profit academic (Cedars-Sinai) medical centers with culturally, economically and ethnically diverse patient populations. Each has a rich network of community partners, service delivery platforms and extensive experience in community-based vaccine and drug trials.

We have partnered with 28 leading community service organizations, advocacy groups, health delivery networks, churches and schools that are already activated and attuned to issues of health care access, affordability and quality (please refer to letters on pages 1399-1427). Our partners include ■ the Community Clinic Association of Los Angeles County, an association of 44 community and free clinics with more than 130 clinical sites; ■ the Magnolia Community Initiative, a network of 70 health and community organizations working to meet the health needs of 100,000 residents and 35,000 children in underserved communities near downtown Los Angeles; ■ the Healthy African America Families, an advocacy group focused on health improvement among African Americans and Latinos in South Los Angeles; and ■ the Los Angeles Urban League, which is focused on reducing racial disparities in education, employment, safety, housing and health.

For more details on our academic partners, refer to section 6 below. A full listing of our community partners is found in the narrative of our **Community Engagement in Research Program (CERP)**.

2.1. The UCLA CTSI is built on a strong foundation of success in discovery, translational science, community engagement and health services research

Our **discoveries** have transformed adult and pediatric medicine and improved health worldwide. Outstanding contributions include: ■ discovery of the roles of nitric oxide (Ignarro) in human disease ■ invention of the nicotine patch (Jarvick and Rose) and the pulmonary-artery catheter (Swan and Ganz) ■ major advances in

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brain mapping (Mazziotta and Toga) and solid organ transplants in children and adults (Busuttill) ■ development of limb-salvage techniques for cancer patients (Eilber) and ■ the first identification of AIDS (Gottlieb).

Our clinical and basic sciences facilities provide an exceptional environment in which to pursue **transdisciplinary translational research** to improve the health of children and adults. Medical researchers are working with engineers, chemists and other disciplines to ■ develop point-of-care salivary diagnostics for cancer (Wong) ■ create a thin-film Nitinol neurovascular stent to reduce strokes in children with neurovascular aneurysms and arteriovenous fistulas (Levi) ■ adapt cell phone technology to study care and quality-of-life outcomes for pediatric cancer survivors (Casillas and Estrin) ■ test new exercise interventions to prevent childhood obesity in minority children (Yancey).

We have a longstanding commitment to **population and community-based research** involving adults and children. The African American Study of Kidney Disease and Hypertension Trial is studying high risk residents of South Los Angeles to identify genetic predictors of responsiveness to angiotensin-converting enzyme (ACE) inhibitors, beta blockers and the calcium channel blockers (Norris). As the largest center in the National Children's Study, we are tracking 5,000 children in our community from before birth to age 21 to examine the biological, chemical, physical, social, psychological and behavioral influences on childhood development and long-term health (please refer to letter on page 1526). UCLA is home to the Federal Life Course Research Network, which advances research on the epidemiology, origins and impact of factors that influence health and disparities over the life course (Halfon).

We have world-leading expertise in **health services research** (HSR). Particular UCLA strengths in HSR include ■ leading experts in comparative effectiveness research (CER), enabling scientists to identify potentially cost-effective treatments at earlier stages of translation ■ design of quality and outcome measures for clinical trials ■ multiple transdisciplinary research centers that incorporate discovery into community interventions for patient behavior and practice change locally, nationally and globally ■ expertise in methods for increasing fidelity to clinical protocols once adopted in practice ■ health care reform and care redesign.

The UCLA CTSI brings a unique set of strengths to bear on the health disparities in Los Angeles County. A CTSA will enable us to leverage our talents and resources to effect transformative change in our community. In achieving our five overarching goals, the UCLA CTSI will drive innovations to improve health in Los Angeles, and in doing so, become an important resource to the national CTSA for health improvement throughout the US.

2.2. Unique resources of the UCLA CTSI

The UCLA CTSI has close collaborations with world-leading centers, institutes, schools and programs with which we will co-fund and conduct our clinical and translational science.

The California NanoSystems Institute (CNSI) promotes rapid translation of discoveries at the intersection of biology and engineering, including robotics, neuro-engineering, biomaterials, and biosensors.

The Wireless Health Institute (WHI) unites innovators from computer science, engineering, business management, medicine, nursing, theatre, film and television to develop cutting-edge devices for health improvement and disease prevention.

Our internationally renowned Jonsson Comprehensive Cancer Center is a leader in innovative research, diagnosis, treatment and prevention.

The Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research leads basic scientific inquiry of adult and human embryonic stem cell biology and early pathways to clinical translation.

The UCLA AIDS Institute unites experts from multiple disciplines to discover and test new approaches to containing, and ultimately, conquering HIV.

The Institute for Molecular Medicine is a recognized leader in multidisciplinary team science focused on problem-solving in patient care.

The UCLA School of Public Health brings recognized strengths in community and environmental health, adolescent health, nutrition, and health policy research.

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The UCLA Anderson School of Management brings world-class expertise in managing biomedical innovation and technology transfer.

The Henry Samueli School of Engineering and Applied Science is a leader in development of novel materials for medical devices and drug delivery, microelectronics and telemedicine.

Our Specialty Training and Advanced Research (STAR) Program is recognized for excellence in training physician-scientists.

More detail on intra-UCLA collaborations can be found in our letters of support (pages 1437 – 1476).

2.3. The UCLA CTSI: Recent Progress

With local funds in the pre-award period, the UCLA CTSI has taken substantial strides to transform its approach to clinical and translational biomedical research. These advances encompass progress in:

Organization: Established new ■ University Institute level status for the UCLA CTSI ■ **Leadership** of CTSI Principal Investigator, Dr. Steven M. Dubinett, Associate Vice Chancellor for Translational Science ■ Executive Oversight Committee (EOC) including all program leaders and partner institutions in ongoing weekly meetings ■ **CTSI Virtual Home**, an internet portal that facilitates communication across the entire CTSI community and directs members to resources and expertise ■ CTSI-wide **Harmonization Initiative**, already resulting in conforming memorandums of understanding and a demonstration project for facilitated inter-institutional IRB review.

Initiatives in team science: ■ the **70 Block Project**, a new model for community-based participatory research in South Los Angeles in partnership with the LA Urban League ■ the **UCLA CTSI Committee on Maternal, Child and Adolescent Health (CMCAH)** bringing investigators together from Pediatrics, Family Medicine, the Schools of Public Health and Engineering, the National Children's Study investigators and partner institutions to address new transdisciplinary collaborations ■ **Translational Research Clusters (TRCs)** leverage local funds to support transdisciplinary research addressing the most pressing health needs in Los Angeles County; six new team-based research programs initiated in mental health, cardiovascular disease/stroke, cancer, HIV, addiction and diabetes/obesity ■ **Team Science Translational Research Retreat** with presentations by leaders of TRCs and representatives of the Los Angeles County Health Department.

Education and Training: ■ With institutional funds, established the successful **Society of the CTSI**, a junior faculty award that provides transdisciplinary mentorship ■ received a K30 supplement to develop curriculum to teach state-of-the-art methods of **comparative effectiveness research (CER)** ■ new curricula focused on **leadership in science training** and communication of science skills. ■ opened the **UCLA Master of Science in Clinical Research (MSCR)** program to physicians at all four CTSI institutions via distance learning.

Inter-CTSA collaborations: ■ Membership in the **Greater Los Angeles CTSA Coalition** with University of Southern California and University of California, Irvine CTSA's. Together, we have identified four key areas in which to create infrastructure to support collaboration: **distance learning** and Web-based training; sharing **core services** and expertise; **community outreach and engagement**, including recruitment of community groups in areas of overlap; and developing a **pediatric clinical trials network** to foster childhood and adolescent health collaborations. ■ We are working with the **West Coast CTSA Consortium** to establish priorities for collaboration (please refer to letters on pages 1477–1489).

Receipt of a CTSA will allow us to not only sustain, but accelerate, this transformative work.

3. INSTITUTIONAL COMMITMENT

Our partner institutions have committed significant resources to ensure the success of the UCLA CTSI. The financial and space commitments are summarized here. Greater detail is found in letters from Drs. Baker, Block, Economou, Feinberg, Melmed, Meyer and Washington on pages 1375–1389 in this application.

Financial commitments: New institutional support from ■ UCLA Ronald Reagan Medical Center including \$15 million for direct support of inpatient and outpatient clinical research ■ UCLA Chancellor's commitment of \$14 million for support of CTSI faculty and Office of Investigator Services (OIS) ■ collaborating UCLA institutes' and partners' support of \$3.2 million per year for pilot and collaborative studies ■ David Geffen School of Medicine of \$12 million for recruitment of new CTSI faculty ■ Cedars Sinai commitment of \$10.5 million in

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support of faculty, bio-banking, and research imaging ■ CDU commitment of \$3 million in support of faculty development and informatics infrastructure ■ Harbor-LA BioMed commitment of \$8.25 million for support of clinical trials infrastructure and research pilot funding

Table 1. Institutional financial commitment to the UCLA CTSI

Source and Purpose of Commitment	Commitment Amounts
UCLA Chancellor: Team-Based Research, Staff and Faculty Support	\$14,000,000
UCLA Vice Chancellor for Research: Research Data Repository Commitment	\$5,000,000
David Geffen School of Medicine: CTSI Faculty Recruitment, Office of Investigator Services, Clinical Trials Management System Implementation	\$17,500,000
UCLA Healthcare System: Commitment for Clinical Research	\$15,000,000
Cedars-Sinai: Commitment of \$10.5 million in support of faculty, bio-banking and research imaging	\$10,500,000
LA Bio-Med: Commitment of \$8.25 million for support of clinical trials infrastructure and research pilot funding	\$8,250,000
Drew: CDU commitment of \$3 million in support of faculty development and informatics infrastructure	\$3,000,000
Total Institutional Commitments	\$73,250,000
Additional CTSI Space Commitments from all 4 Partner Institutions	\$202,200,000

Space: Our four partner institutions are committing a total of 56,000 square feet of space for the **CTSI Home**. Sixty thousand square feet of additional space is allocated outside the Home. Thus, dedicated new Home space for the CTSI exists at Harbor-LA BioMed (8,700 square feet), Cedars-Sinai (11,280 square feet), CDU (8,000 square feet) and UCLA-Westwood (28,000 square feet).

Ambulatory Clinical Research Facilities: The new UCLA Westwood ambulatory CCRR facility (to open in January 2011) occupies 20,200 square feet, includes outpatient areas, a service center including pharmacy and sample processing/triaging resources, and conference rooms. ■ The outpatient unit at Harbor-LA BioMed (4,300 square feet with 11 examination/consultation rooms) is located in a research building adjacent to conference rooms and is the telemedicine hub at Harbor-LA BioMed. ■ The outpatient unit and research cores at Cedars-Sinai occupy 5,500 square feet, with 5 examination rooms, a bionutrition consultation room and an onsite sample processing laboratory. ■ The CDU outpatient clinical research resource occupies an 8,000-square-foot clinical research suite in the new 62,000-square-foot Research and Nursing facility, with support for community-based participatory research to address community health disparities.

Inpatient Clinical Research Facilities: The CTSI has two inpatient units located approximately 25 miles apart, providing investigators and our diverse research participants the option of selecting the most conveniently located inpatient site. The inpatient units include: The new cutting-edge inpatient unit at the Ronald Reagan UCLA Medical Center (Westwood) contains 6 beds (3 are institutionally supported). Additional beds can be accessed from the adjacent Telemetry Unit when research bed demands are high. The inpatient unit at Harbor-LA BioMed contains 6 research beds plus 6 beds supported by Los Angeles County. This is a flexible unit that transforms from a research unit to a medical surgical unit, dependent on research usage, thus providing an efficient, economical means to support research requiring intensive monitoring or care that can only be provided in an inpatient setting.

4. INNOVATION: HOW THE UCLA CTSI WORKS

4.1. Key Function Program Areas

The CTSI is organized into nine program areas, which are briefly described here. These program areas are the vehicles through which we achieve the overall goals of our CTSI. In concert with the Office of the Institute, all programs work to achieve Goal 5 — **Serve as a national resource for collaborative research through regional, statewide and national CTSA consortia**. More information about individual program missions, leadership and operations is available in their respective program narratives elsewhere in this application.

Pilot and Collaborative Translational and Clinical Studies Program (Pilot/Collaborative Program) drives research within the UCLA CTSI. It assembles new transdisciplinary teams among senior and junior investigators; provides seed funding; fosters collaborations among basic, clinical and community researchers;

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provides funding for development of novel methodologies and assists the transition of research from preclinical to Phase I clinical trials; recruits new translational faculty. *Goal 2 — Build transdisciplinary research teams to accelerate and translate discovery to improve health.*

Community Engagement in Research Program (CERP) is the primary link to our diverse Los Angeles community. It strengthens and builds strong bi-directional partnerships that help CTSI scientists identify research relevant to community needs. CERP builds community capacity to engage in research; communicates research findings; serves as a point of contact for community health care providers and facilitates opportunities for health services and comparative effectiveness research. *Goal 4 — Build and expand strong bi-directional academic-community partnerships to ensure that new scientific discovery is relevant to community needs.*

Center for Translational Technologies (CTT) links scientific teams with core technologies. It provides online access to and supervises the use of a diverse array of existing cores; supports development of new technologies; provides personalized counseling to help investigators select and use cores; and facilitates multidisciplinary collaborations and networking. *Goal 2 — Build transdisciplinary research teams to accelerate and translate discovery to improve health.*

Clinical and Community Research Resources Program (CCRR) supports and supervises human studies and clinical trials. It builds on our highly successful GCRCs to include flexible, mobile research units that bring scientific teams to our population. It provides bio-nutrition services, clinical research management, and clinical education and training opportunities. *Goal 4 — Build and expand strong bi-directional academic-community partnerships to ensure that new scientific discovery is relevant to community needs.*

Regulatory Support and Knowledge, Research Ethics and Industry Alliances Program (Regulatory Program) ensures that our research is in full regulatory compliance and meets the highest quality assurance standards. Through its Office of Investigator Services, it functions as a gateway to CTSI investigator resources and provides a one-stop shop for protocol submissions. It actively seeks and encourages industry alliances and offers ethics counseling and research. *Goal 1— Create an academic home for clinical and translational science that integrates and builds on the many strengths of UCLA and its partners.*

Biomedical Informatics Program (BIP) leverages our expertise and resources in data management to provide databases, tools, resources and infrastructure for the acquisition, storage and analysis of data. It provides the online infrastructure and support for the Office of Investigator Services. *Goal 1— Create an academic home for clinical and translational science that integrates and builds on the many strengths of UCLA and its partners.*

Biostatistics, Study Design, and Clinical Data Management Program (BSD-CDM) leverages our existing strengths and resources to provide one-stop biostatistical design and data management services to CTSI research teams. It fosters development of novel clinical trial designs and biostatistical methodologies; operates a secure, user-friendly CDM system; and offers expanded translational science courses in clinical trials methodology and new methods in biostatistics and modeling. *Goal 2 — Build transdisciplinary research teams to accelerate and translate discovery to improve health.*

Research Education, Training and Career Development (CTSI-ED) houses most of our education and training activities. It builds on collaborations with other CTSI programs to identify training and education needs and opportunities. It ensures CTSI trainees acquire the core competencies needed to conduct multidisciplinary research, and to integrate community priorities and input into research across the T1 to T4 spectrum. *Goal 3— Transform educational and career development programs to promote the next generation of clinician investigators and translational scientists.*

Evaluation & Tracking (E/T) helps CTSI leaders set goals, measure outcomes, inform leadership decision-making, and identify opportunities for improvement. Its Center for Evaluation and Health Services Research (HSR) facilitates and conducts studies to improve the science of evaluations, and collaborates with other CTSI researchers to evaluate strategies to boost the speed and efficiency of translation. *Goal 1— Create an academic home for clinical and translational science that integrates and builds on the many strengths of UCLA and its partners.*

4.2. Activities to Achieve the Goals of the CTSI

4.2.1. Goal 1: Create an academic home for clinical and translational science that integrates and builds on the many strengths of UCLA and its partners.

The traditional culture of science and discovery presents challenges to transdisciplinary research. Administrative requirements, disciplinary pathways and systems of rewards and incentives are everyday barriers to formation of well-functioning scientific teams. These constraints have prevented us from making the greatest use of our outstanding people and resources to meet the complex demands of medical science.

Our CTSI is meeting these challenges in two ways. First, we have new leaders with extensive experience in translational science and the authority to elevate the value of team science within our research enterprise. Second, we are creating the infrastructure and support to facilitate the formation of teams to accelerate clinical and translational research. Joined in unity of purpose, the CTSI leadership embraces innovation and the diversity of thought inherent in transdisciplinary collaboration. We strive to foster an environment in which the only impediments to translational investigation are the limits of our imagination.

Our leadership:

Steven M. Dubinett, MD, Associate Vice Chancellor for Translational Science, is Director of our CTSI. Building on original discoveries relevant to inflammation in the pathogenesis of lung cancer, Dr. Dubinett has developed a translational research program that utilizes these laboratory-based discoveries in the translational research and clinical environment. Changes in the distribution of Dr. Dubinett's effort and activities to allow sufficient time to direct the UCLA CTSI are described in the budget description. This includes an eight-point plan outlining specific details that will allow for this important transition. Dr. Dubinett reports to UCLA Chancellor Gene Block (please refer to **Administrative Core** budget justification page 186).

A. Eugene Washington, MD, MSc, chairs our CTSI IAB. He was appointed Vice Chancellor for UCLA Health Sciences and Dean, David Geffen School of Medicine in February, 2010. Dr. Washington is an internationally renowned clinical investigator and health-policy scholar whose wide-ranging research has been instrumental in shaping national health policy and practice guidelines.

James S. Economou, MD, PhD, chairs our IAB with Dr. Washington. Dr. Economou was recently appointed Vice Chancellor for Research at UCLA and maintains a referral-based clinical practice in surgical oncology and translational cancer gene therapy research.

More details on our leadership can be found in Governance (section 5) below.

Our supportive infrastructure:

Our new **Office of Investigator Services** (OIS) provides investigators with efficient, one-stop access to information and research support. Research Facilitators, personnel with experience in project coordination, provide investigators with expert assistance with proposal development and help navigate them through regulatory requirements. They also provide referrals to Domain Experts who can provide help with technical cores, biostatistics and study design, biomedical informatics services, and clinical and community resources (refer to **Regulatory Program** for more detail).

Investigators contact Research Facilitators in person, by telephone or through the **Virtual Home**, an internet portal that provides information and access to all CTSI services. The Virtual Home maintains a database that includes investigators, facilities, laboratories, community research locations, services, consultants (e.g. biostatistics, ethics), regulatory documents and tips for successful grant applications including templates of successful submissions. Another core element of the Virtual Home is the Research Action Planner, which provides support for creating initial plans for research projects, explores potential collaborators and identifies CTSI resources. The Research Action Planner also links investigators to IRB and other oversight committees and facilitates entry of studies into clinical trials registries. The Virtual Home is also a community resource that provides news and notice of events (see **BIP** for more details). The review processes for requests for CTSI resources are described in the appropriate program areas (refer to **CTT**, **BSD-CDM**, **BIP**, **CCRR**, **Regulatory Program** and **Pilot/Collaborative Program** for details).

We are also streamlining and accelerating preparation and approval of CTSI-sponsored protocols and accompanying IRB applications and research contracts. We have crafted a facilitated **IRB review** process for

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research throughout the CTSI, and are working toward achieving full reciprocity to improve efficiency. In addition, we have developed processes for faculty to have research privileges throughout the CTSI, enabling investigators to do studies and access resources in the most appropriate settings (refer to **Regulatory Program** and **CCRR** section 4. for more detail).

4.2.2. Goal 2: Build transdisciplinary research teams to accelerate and translate discovery to improve health.

UCLA invests significantly in pilot projects and technologies each year. However, no existing campus-wide mechanism is dedicated to translational team science.

To correct this deficiency, our CTSI has instituted a transforming funding mechanism —the **Translational Research Grant Program** – which leverages local funds to support transdisciplinary research addressing the most pressing health needs in Los Angeles County. This program consists of five innovative mechanisms through which we will annually award 30 to 40 grants with a total value of up to \$3.6 million – 150 to 200 grants totaling \$18 million during the next five years. We will match the annual CTSI contribution of \$425,000 by more than 7 to 1 with philanthropic, corporate and other institutional funds. These grant mechanisms will drive our transformation by supporting team science, new faculty research, development of novel methodologies and technologies, seminars and retreats to foster collaboration and prototype development.

Specific features of our program include:

Catalyst Grants: 10-15 awards annually of \$1,000 to \$25,000 each to support seminars and day-long symposia with experts both within and outside UCLA.

New Technology Transfer and Prototype Grants: at least one grant annually of \$800,000, dispersed over three years to support preclinical studies and phase-1 clinical trials. Scientist-inventors interested in developing business plans or industry collaborations may do so through the CTSI Office of Industry Alliances (OIA) (see **Regulatory Program**).

Novel Translational Technologies and Methodologies Grants: up to three awards annually of up to \$100,000 each for development of any research tool, technique, or resource with the potential of bridging critical gaps in the conduct of translational biomedical science.

The cornerstone of our program is our new **Translational Research Cluster Grant**, which unites our best minds from across a range of disciplines against our most challenging health problems. In the pre-award period, we sponsored a retreat at which six transdisciplinary teams proposed innovative approaches for addressing addiction, HIV infection, cancer, cardiovascular disease and stroke, diabetes and obesity, and mental illness, all of which rank among the top causes of death and disability in Los Angeles. Based upon interactions and discussions at the retreat and a survey that followed, planning is now in process for an additional retreat and funding of the Translational Research Cluster program. We provided these teams with Catalyst funds to develop research plans.

The outstanding results of a translational science seed grant program we recently pilot-tested indicate our new CTSI mechanisms will be a resounding success. During the last three years with local funds, we awarded 35 one-year seed grants of \$30,000 for clinical and translational research. These awards, which totaled \$1.05 million, led to publication of 137 papers and \$39 million in new funding from NIH and other sources, including \$13 million for which seed grant recipients were named as PI or Co-PI (refer to **Pilot/Collaborative Program** for more details about our awards programs).

In addition to these transformative mechanisms, we are expanding the successful **UCLA Society of the CTSI Scholars Program** that we pilot-tested with local funds in the pre-award period. This program brings promising young investigators together with teams of interdisciplinary mentors focused on research that spans the laboratory, clinic and community. We plan to award eight to 12 awards of \$25,000 to \$50,000 annually. Our four scholars who received annual grants of \$30,000 in the pre-award period have since obtained an additional \$1.5 million in new funding from NIH and other sources.

Our CTSI grants are awarded through peer-review mechanisms described in detail in the **Pilot/Collaborative Program** portion of this application. More than 65 experienced faculty have volunteered to serve as ad-hoc reviewers and their letters of commitment (pages 1563–1607) and biosketches are included in the application.

4.2.3. Goal 3: Transform educational and career development programs to promote the next generation of clinician investigators and translational scientists.

UCLA has an outstanding record of advanced training in translational and clinical sciences. Our numerous successful NIH-funded and institutionally supported programs annually train over 1,200 pre-and post-doctoral scholars. However, traditional training environments tend to isolate community researchers and clinical and basic scientists, impeding interdisciplinary team-based translational investigation.

Thus, we are transcending our education and training silos. First, we have transformed our approach to ensure our trainees acquire the skills necessary to conduct community-partnered research. We have assembled a **cadre of community mentors for our trainees** and have partnered with Los Angeles Urban League's 70 Block Project. This demonstration project, designed to enhance health and wellness by mobilizing residents in a high-risk 70-block urban setting to implement evidence-based health promotion and disease prevention strategies, will provide trainees with vibrant settings to design and implement collaborative, partnered community interventions (refer to **CTSI-ED** and **CERP** for details).

Second, we are providing course and training materials on the Virtual Home so that our scholars have easy access to educational and training resources. The Virtual Home will maintain a suite of research tools so that our trainees may gain experience using these tools and provide information on faculty and community mentors, trainee opportunities within the four CTSI partner institutions, and select community organizations.

Third, we are expanding highly successful training programs and launching new ones. For example, we are expanding our highly successful, institutionally supported **Subspecialty Training and Advanced Research (STAR) Program** to include trainees from all four CTSI partners. Our new programs address community needs by adding community mentors to virtually all CTIS trainees' interdisciplinary teams and by creating innovative educational programs for pre- and postdoctoral trainees in clinical and translational, health services, and community-based research. Four new programs are proposed: ■ the K12 Mentored Interdisciplinary Translational Therapeutics and Technologies Research Program (TTTRP) ■ T32 PhD Training Program in **Clinical, Comparative Effectiveness, and Community-Partnered Translational Research** ■ PhD Track of Molecular Medicine with an emphasis in Translational Systems Biology and ■ new Executive Master's of Public Health (EMPH) in Community Research (refer to **CTSI-ED** for more detail).

4.2.4. Goal 4: Advance and expand strong bi-directional academic-community partnerships to ensure that new scientific discovery is relevant to community needs.

Los Angeles County offers an ideal environment for developing effective translational strategies. It encompasses the full spectrum of best-to-worst in health care services, delivery capacity, and outcomes. Los Angeles faces challenges common to the national CTSA network including sizable subpopulations who are underrepresented in all phases of translational research, and fragmented and often low-performing health care systems that require implementation, dissemination and diffusion research for scientific discovery to have a large social impact.

At the same time, Los Angeles has assets for increasing translational research. UCLA has national leaders in the concepts and practice of community-partnered research, cutting-edge biomedical and clinical researchers, strong community leaders who value translational research and are dedicated to the CTSA mission, and a virtually unlimited source of potential community partners and populations. True community partnership requires community and academia to share fully and equitably in input on project selection, study design, implementation, assessment and dissemination, decision making and in resources (both dollars and opportunities). We have achieved a level of shared purpose and collaboration that brings CTSI and Los Angeles to the leading edge of transformation.

We have designed our structures and processes to incorporate bi-directional community participation throughout the research process. Loretta Jones, Chief Executive Officer of Healthy African American Families, one of our community partners, is an Associate Director of the CTSI. Ms. Jones, who also is a Co-leader of **CERP** and a **CCR** Program investigator, will ensure that community needs and concerns are well represented. Our **Community-Academic Partnership Council (CAP)** assists in identifying key community priority areas for community-engaged research and its members serve as ambassadors and educators in bi-directional knowledge transfer programs (e.g., symposia, workshops, and journal clubs). For more information, please refer to **CERP** section 6.5.1.

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We propose several groundbreaking projects to meet this goal. With the Los Angeles Urban League, we are spearheading the aforementioned **Healthy Community Neighborhood Initiative**. In partnership with community clinics, we are establishing **Community Centers in Health Education and Translational Research** (CC-HEATRs). They provide a functional repository of studies of interest to communities, computers/kiosks to access local health resources and learn about ongoing clinical trials, and access to archived tutorials and community symposia. In addition, we are maintaining and broadening bi-directional communication with our community through social networking, community liaisons and promotoras (refer to **CERP** for details).

We have initiated a **mobile “chaperone” services** to link the CTSI partners and communities. To capitalize on Los Angeles County’s size and diversity in our research efforts, the **CCRR** must enhance integration of research across the CTSI partner institutions and effectively reach out to our community with the ability to bring research capabilities to the doorstep and facilitate bringing research participants more easily to the research center when that is safer and more appropriate. As part of its institutional commitment to the CTSI, the UCLA DGSOM Dean’s Office has donated three vans, support for their maintenance and three full-time drivers. These mobile units transport investigators, trainees, staff, research subject advocates and research resources (such as meals prepared by the research dietitians) into the community to conduct research and collect feedback from community leaders and participants to direct our future research agendas. The vans also bring scientists, students, promotoras, and study participants to the various institutional sites to engage in training by teleconferencing or in person, in-house clinical and translational research projects, investigator team meetings, and for specialized research interventions that cannot be conducted in the field (e.g., body composition, radiological imaging *in vivo*). These mobile teams give the CTSI another way of obtaining feedback from community leaders and participants to direct our future research agendas (See **CCRR** for details.)

A distinctive feature of our CTSI is the integration of key concepts and methods of **health services research** (HSR) with community-engaged research. UCLA is a recognized leader in HSR and comparative effectiveness research. Our HSR investigators participate in agenda-setting symposia and town halls about the science of risk and disease, behavioral patterns and health care responses to priority conditions for communities. This helps communities pose and answer questions about how health care systems can best achieve their goals. HSR develops measures and comparisons that show which interventions are working, where they fall short of expectations and why and how effective interventions can spread (see **CERP** for more details about our community engagement in research initiatives).

4.2.5. Goal 5: Serve as a national resource for collaborative research through regional, statewide and national CTSA consortia.

The complexities of biomedical research and translation require transdisciplinary teams that span institutional boundaries. The mission of the UCLA CTSI is to transform our partnership into a borderless institute that supports collaborative teams throughout our region, state and nation. We are full participants in the **Greater Los Angeles CTSA Coalition** with the University of Southern California and the University of California, Irvine. Collectively, we form the backbone of one of the most productive networks for clinical investigation and translational science in the nation. Our group has outlined four initial areas for inter-institutional collaboration to accelerate innovations to improve health and health care in our region. As noted above in section 2.3, those areas are: distance learning and online training; sharing core services and expertise; community outreach and engagement, including recruitment of community groups in areas of overlap; and developing a pediatric clinical trials network to foster childhood and adolescent health collaborations [refer to letter from Drs. Thomas Buchanan (USC), Dan Cooper (UCI) and Steven Dubinett (UCLA) pages 1477-1478].

Program leaders of our CTSI are well on the road to achieving these priorities. ■ Drs. Kathy Sakamoto (UCLA), Cooper (UCI) and Edward Gomperts (USC) have started developing a **pediatric clinical trials network** that leverages a program within the UCI CTSI. ■ Dr. John Brekke (USC) and longtime collaborator Dr. Joel Braslow (UCLA) are investigators for UCLA Translational Research Cluster focused on mental illness (see **Pilot/Collaborative Program**). ■ Drs. Carol Mangione (UCLA) and Jonathan Samet (USC) have met during the preparation phase of this application and will use **teleconferencing for sharing curricular opportunities for trainees** at both of our institutions. ■ Drs. Mangione and Arthur Toga (UCLA) have close research collaborations with Dr. Carl Kesselman (USC) on AHRQ funded research designed to create a federated data system for the State of California and NCCR-funded **databasing and distributed computing**, respectively. ■

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Dr. Toga (UCLA) and Dr. Steven Potkin (UCI) collaborate on functional brain-mapping in the NCRF-funded **Biomedical Informatics Research Network (BIRN)** ■ and Leaders of our **CCRR** have been holding monthly teleconferences with their counterparts at USC and UCI in advance of a face-to-face retreat scheduled for January 2011.

We are active participants in the **West Coast CTSA Consortium** and collaborative groups whose members and goals overlap with the national CTSA. For example, in October 2010, we participated in the **University of California-wide Biomedical Research Acceleration Initiative** Retreat to identify areas of collaboration to accelerate biomedical research across UC biomedical campuses. Our group identified **contracting, IRBs and recruitment to studies** as areas for initial attention. We are now in the process of identifying policy changes, new infrastructure or processes that will reduce barriers to clinical and translational research for our institutions, researchers and external partners. University of California campuses with CTSA include UC San Diego, UC Irvine, UC Davis and UC San Francisco.

In the coming year UCLA CTSA leaders and investigators are scheduled to participate in **national CTSA meetings** related to ethics and sleep medicine. To prepare this application, we sought the advice of leaders from 20 different CTSA to ensure our proposal was aligned with the national consortium's needs and goals.

5. GOVERNANCE STRUCTURE OF THE UCLA CTSA

5.1. Background

The development of this proposal was originally initiated by our former UCLA Vice Chancellor for Medical Sciences and Dean of the DGSOM, Gerald Levey. Following Dr. Levey's retirement in 2009, Dr. A. Eugene Washington was recruited to be UCLA Vice Chancellor for Medical Sciences and Dean of the DGSOM. Vice Chancellor Washington has launched the revision of the previous application, recruiting Dr. Steven M. Dubinett as the CTSA Program Director. Along with the leadership of Drs. Washington and Dubinett, in 2010, UCLA announced the appointment of Dr. James S. Economou as Vice Chancellor for Research. This set in motion a leadership team with extensive experience in translational investigation and academic research administration to guide the clinical and translational research mission at UCLA.

The UCLA CTSA governance structure includes representatives from all the CTSA partner institutions, ensuring that administrative and academic research services are highly coordinated and responsive to investigator and community needs. In designing our governance structure, we have benefitted by consultation with more than 20 funded CTSA sites across the country. We have also been guided by the task force on clinical research of the American Association of Medical Colleges and by the recent Institute of Medicine report on cooperative clinical trials groups. The CTSA's own consortium governance manual also served as a guide. Utilizing the governance structure outlined below, we took the structures used by others and adapted them to the UCLA environment in order to begin to transcend important obstacles by implementation of key strategies.

With the guidance of our new leadership, the implementation of our governance structure has already achieved accomplishments enumerated above (refer to section 2.3). For example, we have initiated a new transdisciplinary **Committee on Maternal, Child and Adolescent Health (CMCAH)** to guide new integrated research strategies, provide advice to the EOC and develop new transdisciplinary training opportunities (described in section 5.4.4 below).

5.2 Overall Organization

The size and complexity of the UCLA CTSA requires a flexible and responsive administrative organization with clear roles and responsibilities. We have established a key managing committee, the Executive Oversight Committee (EOC), and three oversight and advisory committees: Institutional Steering Committee (ISC), IAB, and External Advisory Board EAB. **Figure 1** provides the organizational chart for the UCLA CTSA. In brief, the EOC is chaired by and reports to the CTSA Program Director (Steven M. Dubinett), who in turn directly reports to the Chancellor of UCLA (Gene Block). During the past year the EOC has been meeting weekly to plan implementation of UCLA CTSA programs. The EOC will receive counsel from and provide reports to the IAB and EAB. The IAB will be co-chaired by Vice Chancellors A. Eugene Washington and James S. Economou. The ISC includes the leadership of the four CTSA partner institutions. The ISC is responsible for overseeing and providing guidance for coordination and prioritization of UCLA CTSA operations with institutional agendas, strategic investments, and resource sharing to best advance the CTSA mission. It will report to the Chancellor

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 and interact with the Program Director. Operational matters will be handled by the staff of the CTSI Office of the Institute.

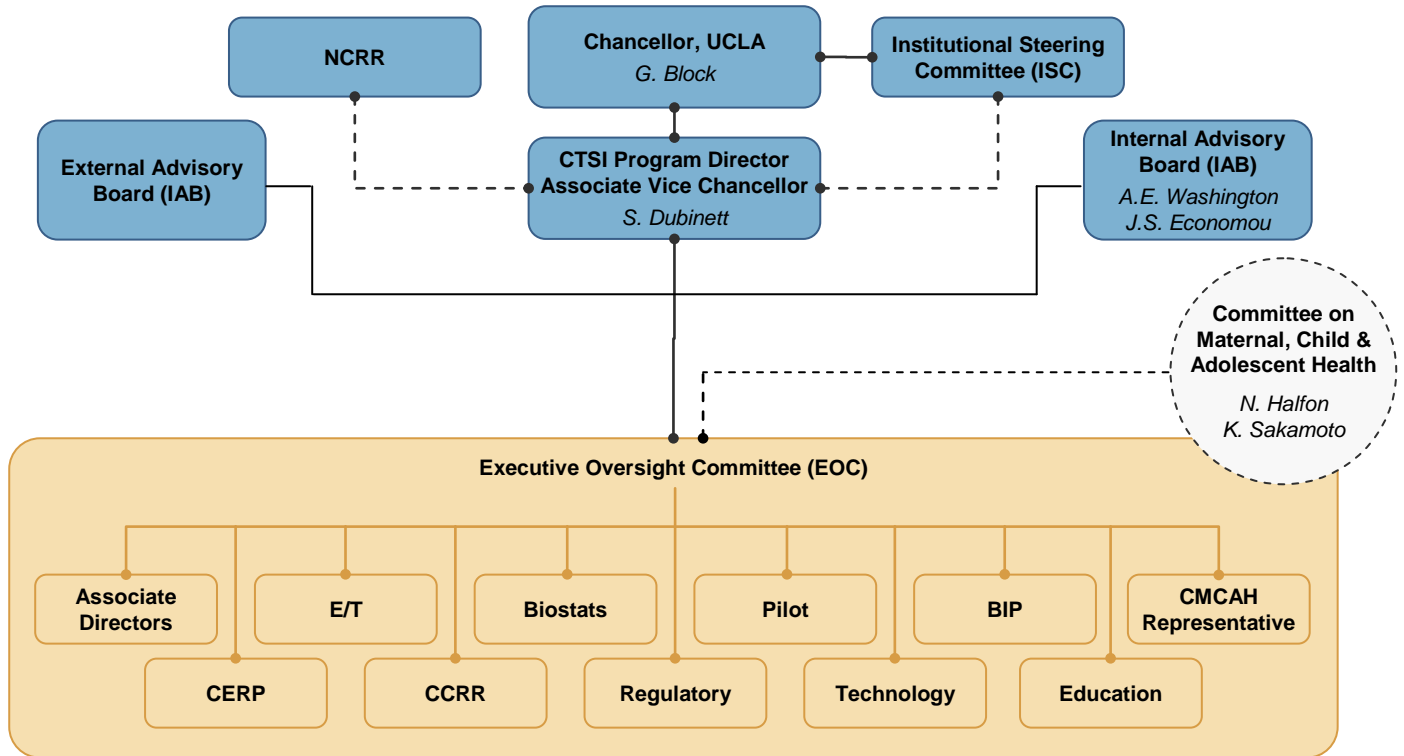


Figure 1. UCLA CTSI Governance Structure. The CTSI Program Director has the necessary authority to achieve the mission of the CTSI. He chairs the EOC, whose members include the nine Program Leaders. The dotted lines refer to advisory functions provided by the National Center for Research Resources (NCRR) and ISC directly to the Program Director and to the EOC from the Committee on Maternal, Child & Adolescent Health (CMCAH).

5.3. Executive Oversight Committee

Chaired by and reporting to the CTSI Program Director, the EOC has direct responsibility for overseeing resources and strategies, and the structure, function, and budget of the CTSI. It prioritizes UCLA CTSI activities, allocates resources, sets decision-making policies and procedures, assists in conflict resolution, reviews and sets investigator recharge mechanisms and inter-institutional resource sharing, and reviews reports from the Evaluation & Tracking Unit (ETU). One of the guiding principles of our CTSI governance is that it be consensus-driven. If consensus is not achieved, a two-thirds majority vote of all the EOC members will be required for passage of any significant action. If action is required that cannot be remedied by EOC vote, the Program Director has authority for final decision and action after consultation with the Chancellor. **The EOC is comprised of the Program Area Leaders and Associate Directors, all of whom are voting members.** In cases where Programs Areas have more than one Leader, Leaders will participate as voting EOC members on a rotating basis. A member of the Committee on Maternal, Child and Adolescent Health (CMCAH) will also participate as a voting member of the EOC on a rotating basis. (The CMCAH will always have representation on the EOC). The EOC meets weekly. Starting in January 2011, all EOC meetings will have videoconferencing capacity at all sites. On a quarterly and rotating basis, the EOC members will visit each partner institution for town hall meetings with investigators to receive feedback and facilitate bi-directional communication. These town hall meetings will supplement our regular online needs assessment surveys. These EOC partner institution town hall meetings will serve as another pathway to facilitate UCLA CTSI integration.

An important purpose of the EOC is to serve as a clearinghouse for information from the IAB and external sources (the NIH and the EAB). The EOC thus serves as a node for dissemination of data and information important to ensure smooth functioning of each of the programs. The EOC will operate with regular input from the EAB and IAB, E/T (see **Evaluation & Tracking**), and each of the Programs. The EOC provides regular reports to the ISC and through the Program Director, to the Chancellor.

5.4. Leadership

The EOC includes the Program Director, Associate Directors including a representative from each of the four participating institutions and other leaders. All members of the EOC have extensive applied experience in clinical and translational research, the education of young investigators, the promotion of interdisciplinary research, the development of community health programs, and the management of large-scale research and research infrastructure programs:

Steven M. Dubinett, MD, CTSI Program Director, Associate Vice Chancellor for Translational Science, is Chief of the Division of Pulmonary and Critical Care Medicine and Director of the Jonsson Comprehensive Cancer Center (JCCC) Lung Cancer Research Program. He has extensive experience in translational investigation, academic administration, mentorship and peer review. He is jointly appointed as Professor in three departments: Medicine; Pathology and Laboratory Medicine; and Molecular and Medical Pharmacology. At UCLA since 1988, he is a member of the Institute of Molecular Medicine, the Molecular Biology Institute and the California NanoSystems Institute. Building on original discoveries relevant to inflammation in the pathogenesis of lung cancer, he has developed a translational research program which now utilizes these laboratory-based discoveries in the translational research and clinical environment. Dr. Dubinett has received uninterrupted peer-reviewed federal funding for translational lung cancer research for more than 20 years. As a member of NCI's Translational Research Working Group, Dr. Dubinett participated in designing pathways to clinical goals: developmental pathways that characterize the transformation of scientific discoveries into new clinical modalities for oncology. Dr. Dubinett serves as the Director for Biomarker Development for the American College of Surgeons Oncology Group and oversees biospecimen utilization in the context of clinical trials. He currently serves as the Chair of the Research Evaluation Panel for biospecimen utilization for the American College of Radiology Imaging Network / National Lung Screening Trial (ACRIN / NLST). He also is a member of the FDA Cellular, Tissue & Gene Therapies Advisory Committee.

Changes in the distribution of Dr. Dubinett's effort and activities to allow sufficient time to direct the UCLA CTSI are described in the budget description. This includes **an eight-point plan** outlining specific details that will allow for this important transition (please refer to **Administrative Core** budget justification on page 186).

Authority of the Institute Director: The Program Director and EOC will have full authority to develop CTSI-wide policies, procedures, and best practices, and to garner higher administrative assistance as needed, to ensure the optimal and most effective functioning of the CTSI across the partner institutions (see Letters of Support from institutional officials on pages 1375 – 1389). The CTSI Program Director Steven Dubinett reports to Dr. Gene Block, the Chancellor of UCLA.

A. Eugene Washington, MD, MSc, IAB Chair, was appointed Vice Chancellor for UCLA Health Sciences and Dean, DGSOM in February, 2010. He is an internationally renowned clinical investigator and health-policy scholar whose wide-ranging research has been instrumental in shaping national health policy and practice guidelines. Prior to coming to UCLA, Dr. Washington served as Executive Vice Chancellor and Provost for UC San Francisco (UCSF), where he co-founded the Medical Effectiveness Research Center for Diverse Populations. He also co-founded the UCSF-Stanford Evidence-based Practice Center and, from 1996 to 2004, chaired the Department of Obstetrics, Gynecology, and Reproductive Sciences. He was recently appointed Chair of the Board of Governors of the Patient-Centered Outcomes Research Institute (PCORI). The Patient-Centered Outcomes Research Institute was mandated by the health reform legislation — the Patient Protection and Affordable Care Act — to "assist patients, clinicians, purchasers and policy-makers in making informed health decisions."

James S. Economou, MD, PhD, Vice Chancellor for Research at UCLA will chair the IAB with Dr. Washington. He received all of his education from the Johns Hopkins University, completed his general surgical training at the University of California, San Francisco and joined the UCLA faculty in 1986. He is the Beaumont Professor of Surgery and Chief of the Division of Surgical Oncology. He has joint appointments in the Departments of Microbiology, Immunology and Molecular Genetics, and Molecular and Medical Pharmacology. A tumor immunologist, Dr. Economou has been continuously funded by the NIH since joining the faculty and has chaired two NIH study sections. Dr. Economou is President-Elect of the Society of Surgical Oncology and the recipient of its James Ewing Medal. As Vice Chancellor for Research, Dr. Economou maintains a referral-based clinical practice in surgical oncology and translational cancer gene therapy research.

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Gene Block, PhD, Chancellor, will Chair the ISC. He was appointed Chancellor of UCLA in 2007 and holds faculty appointments in Physiological Science in the College of Letters and Science, and Psychiatry and Bio-behavioral Sciences at DGSOM. He is an active PI on an NIH-funded research program in circadian biology. Dr. Block's career spanned Stanford University and the University of Oregon in Psychology before joining the faculty at the University of Virginia in 1978, where he eventually served as Vice President and Provost.

5.4.1. Functions of the Associate Directors

Our Associate Directors are thought leaders from a wide range of fields. Their collective experience spans the full range of biomedical to community-engaged translational research. They bring a diversity of thought necessary to support successful transdisciplinary science and all have embraced innovation in successful investigation. The Associate Directors have been chosen in consultation with Vice Chancellors Washington and Economou and following extensive discussions with other academic and community leaders. The selection of the Associate Directors was also discussed at the EOC. The Associate Directors are all nationally recognized leaders in their respective fields and have had success in leading multidisciplinary research teams in translational investigation. It is anticipated that their participation in ongoing consultation with the PD will enhance the transformative mission of the CTSI. Several additional specific responsibilities are described below. All of the Associate Directors will participate on the EOC as voting members. They will meet with the Program Director (PD) at least monthly.

The Associate Directors at each of the partner institutions have Dean-level appointments within the DGSOM. To ensure their ability to address faculty issues readily, Drs. Norris, Wang and Raffel are Assistant Deans for Clinical and Translational Sciences. These Associate Directors will be responsible as site directors at the partner institutions and in a matrix fashion, to the Program Director (Dubinett) and to the local institutional leadership. Ms. Jones represents the community perspective. They share important internal and external oversight responsibilities in four key areas: communications, development, inter-CTSA partnerships and intra-UCLA CTSI partnerships.

Some examples of their activities include: ■ representing the UCLA CTSI in the National CTSA Consortium, ■ strengthening our partnership with the West Coast CTSA Consortium, including expanding videoconferencing with a broad array of collaborators, ■ participating in Greater Los Angeles CTSA Coalition activities, ■ interfacing with the Los Angeles County Health Department and local academic collaborators, including RAND, Caltech and the Greater Los Angeles VA, ■ overseeing content of the CTSI annual report and the annual retreat, ■ interfacing with CTSI Advisory Boards, ■ managing personnel conflicts within the CTSI, and ■ seeking opportunities for support, including foundations, corporate philanthropies and other private funding sources.

5.4.2. Associate Directors

John Adams, MD, CTSI Associate Director, is Vice Chair for Research, Department of Orthopaedic Surgery, DGSOM at UCLA. He is also founding director of the Orthopaedic Hospital Research Center and a member of the senior advisory committee in the Department of Molecular, Cell and Developmental Biology and Life Science Faculty Executive Committee in the UCLA College of Letters and Science. He formerly was founding program director for the General Clinical Research Center (GCRC) at Cedars-Sinai Medical Center for 13 years and, a founding co-director of the UCLA K30 clinical research curriculum grant, and director of the Bone Center and Division of Endocrinology at Cedars-Sinai Medical Center for 10 years. His translational and clinical research efforts in the area of vitamin D synthesis, metabolism and action as well as in human metabolic disease, including metabolic bone diseases such as hypercalcemia and osteoporosis have been continuously funded by the NIH for the last 30 years.

Neal Halfon, MD, MPH, CTSI Associate Director and Chair, Committee on Maternal, Child and Adolescent Health, is Professor, Departments of Pediatrics, Health Sciences, and Policy Studies and Director, Center for Healthier Children, Families and Communities: an interdisciplinary cross-campus research, training and policy institute with faculty membership spanning five schools and 15 academic departments. He directs the Department of Health and Human Services Maternal and Child Health Bureau (MCHB) funded Child and Family Health Training Program, responsible for training doctoral students and advancing leadership of health professionals in MCH research, program development and systems improvement. He is the PI for the UCLA based Los Angeles and Ventura Study Center for the NICHD funded National Children's Study (NCS).

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Loretta Jones, MA, Associate Director and Co-leader of the Community Engagement Program, is the founder and executive director of Healthy African American Families (HAAF), a nonprofit, community serving organization whose mission is to improve the health outcomes, quality of care, and social progress of the African American and Latino communities in Los Angeles County through education, training, and collaborative partnering with community, academia, researchers, and government. Her work is featured in a 2007 *JAMA* article, "Strategies for Academic and Clinician Engagement in Community-Participatory Partnered Research,"³ and a 2009 *JAMA* article, "'Research' in Community-Partnered Participatory Research."

Carol Mangione, MD, MSPH, CTSI Associate Director and Leader of Research, Education, Training and Career Development Program, is a professor and Barbara A. Levey MD & Gerald S. Levey MD Endowed Chair in Medicine DGSOM at UCLA. She is a Professor in the School of Public Health and consultant in the RAND Health Program. Dr. Mangione is Director of the NIA-funded UCLA Resource Center for Minority Aging Research/Center for Health Improvement of Minority Elderly and Co-Director of the UCLA Robert Wood Johnson Clinical Scholars Program. Currently she is a PI for the Centers for Disease Control and Prevention-funded study of the quality of care for persons with diabetes in managed-care setting. She also is conducting an NIDDK-funded project focused on community-based empowerment intervention among older Latinos and African Americans with diabetes to improve their self-care skills.

Keith Norris, MD, CTSI Associate Director, CDU Site Director and Leader of Community Engagement Research Program (CERP), is Professor of Medicine and Assistant Dean for Clinical and Translational Sciences, DGSOM at UCLA; Executive Vice President for Research and Health Affairs at CDU, Director of the Research Centers in Minority Institutions (RCMI). He is PI for the RCMI Translational Research Network, a major NIH initiative complementary to the CTSA, supporting multi-site clinical translational research among minority and other collaborating institutions throughout the nation. He will also serve as a mentor for the K12.

Leslie Raffel, MD, CTSI Associate Director, Cedars-Sinai Site Director and Leader of Clinical and Community Research Resources (CCRR), is Professor of Pediatrics and Assistant Dean for Clinical and Translational Sciences, DGSOM, and Associate Director of the Common Disease Genetics Program in the Cedars-Sinai Medical Genetics Institute, where she has been involved in the design and implementation of studies of hypertension, type 1 diabetes, type 2 diabetes, insulin resistance, and subclinical cardiovascular phenotypes using family-based, case-control, and cohort designs in multiple ethnic groups. Since 2008, she has been the Associate Program Director for the Cedars-Sinai GCRC satellite, having served as the GCRC Assistant Program Director for the previous 12 years.

Arthur Toga, PhD, CTSI Associate Director and Leader of Biomedical Informatics, is Associate Vice Provost for Informatics at UCLA and Professor of Neurology, founder and Director of the Laboratory of Neuro Imaging (LONI), and Director of the Institute for Informatics (i²) and Associate Dean for Informatics, DGSOM. Dr. Toga is well known for his contributions to computational neuroscience, biomedical data management, and numerous informatics initiatives, and he has extensive experience in managing large interdisciplinary projects, including P20, P41, T32, and U54 grants. Dr. Toga directs the Informatics Cores for the Alzheimer's Disease Neuroimaging Initiative, Huntington's Disease Neuroimaging Initiative, Parkinson's Progression Markers Initiative, and International Consortium for Brain Mapping, and is one of four executive directors of the Biomedical Informatics Research Network. Dr. Toga will also serve as a mentor for the K12.

Christina Wang, MD, CTSI Associate Director, Harbor-LA BioMed Site Director, and Leader of Clinical and Community Research Resources, is Professor of Medicine and Assistant Dean of Clinical and Translational Research, DGSOM. An internationally recognized investigator in male reproductive endocrinology and biology, she is Co-Director of a Male NICHD Contraceptive Clinical Network Center that designs and conducts phase 1 to 3 studies for NICHD. She is Program Director of the GCRC at Harbor-LA BioMed and the satellite GCRC at Cedars Sinai and has extensive experience in implementing joint programs, collaborative research, unified policies and procedures for use in the Harbor-LA BioMed, Cedars-Sinai and Drew GCRCs.

Antronette K. Yancey, MD, MPH, CTSI Associate Director, is a professor in the Department of Health Services, UCLA School of Public Health and is the co-director of the UCLA Kaiser Permanente Center for Health Equity. Dr. Yancey's primary research interests are in chronic disease prevention and adolescent health promotion. She returned to academia full-time in 2001 after five years in public health practice, first as Director of Public Health for the city of Richmond, VA, and as Director of Chronic Disease Prevention and Health

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Promotion, Los Angeles County Department of Health Services. She serves on the Institute of Medicine (IOM) Standing Committee on Childhood Obesity Prevention and Health Literacy Roundtable and National Physical Activity Plan Steering Committee. She chairs the Board of Directors of the Oakland, CA-based Public Health Institute.

5.4.3. Administrative Support for EOC

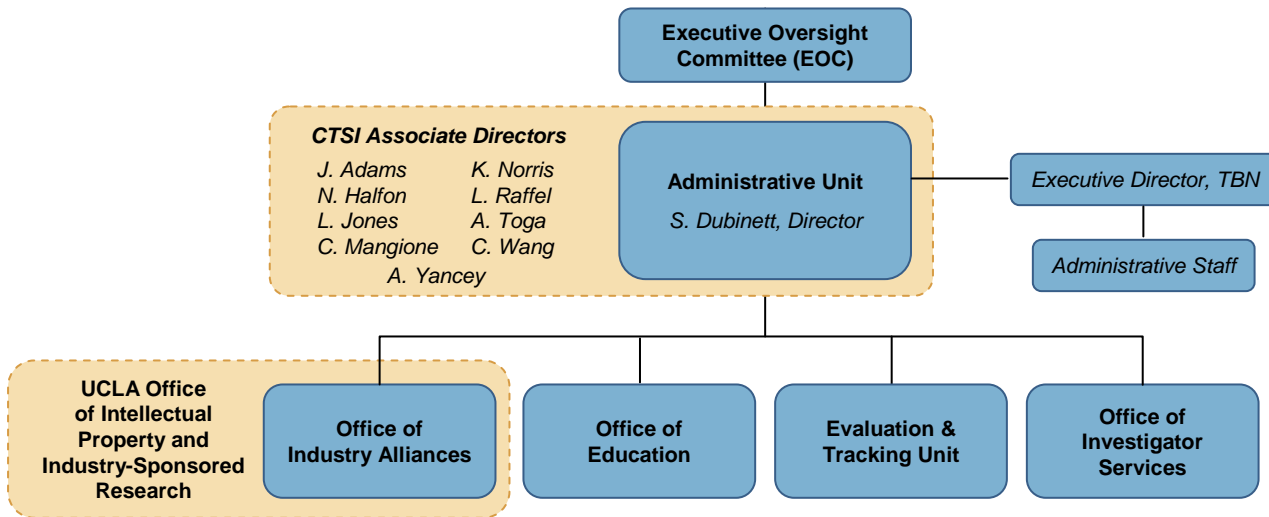


Figure 2. UCLA CTSI Office of the Institute. The CTSI Program Director leads the Office of the Institute. An Executive Director manages day-to-day operations. Four cross-cutting functions are housed here. The shaded areas within dotted lines depict input of the CTSI Associate Directors to the Director and the UCLA Office of Intellectual Property and Industry-Sponsored Research to the CTSI Office of Industry Alliances.

5.4.3.1. Office of the Institute. Support for the EOC is provided by the CTSI Office of the Institute. The Office of the Institute provides programmatic structure and administrative, analytical, IT, financial, and logistical support, along with facilitation of the Institute’s interactions with staff of the key program functions. **(Figure 2).**

Located adjacent to the new ambulatory clinical research center in Westwood, the Office of the Institute also has direct oversight over application, selection, funding and evaluation process for the CTSI pilot grant program discussed above. In addition, the Office of the Institute coordinates proposals for specific applications of health services research to community-partnered research conducted by the CTSI.

The Office will be managed by an Executive Director who will be responsible for the daily operation of the administrative functions and oversight of all staff in the Office of the Institute, including communications and finance. (The full descriptions of the fund management and administrative team’s responsibilities are detailed in the budget justification of the **Administrative Core.**)

Two Program Managers will provide assistance with collaborations and resources, proposal development, expert referrals and regulatory approvals for Translational Research Cluster Groups (refer to section 4.2.2 above and **Pilot/Collaborative Program** section 6.1.1.1). In addition, the faculty Program (key function) Leaders will be supported in their duties by an Executive Assistant. The Program Managers and Executive Assistants will be responsible for tracking resources for proposal development and report to the Executive Director.

A Comparative Effectiveness Research Coordinator will help coordinate collaborations in comparative effectiveness research, communication of research findings, and facilitation of opportunities for health services research. This coordinator will serve as project manager for teams to respond to Comparative Effectiveness Research-related RFAs and work closely with Health Services Research investigators involved in the **CERP**.

Partner sites will communicate and obtain resources and information through our Virtual Home, a website that provides comprehensive access to education and training materials and research resources, including a catalog of technical cores, regulatory advice and IRB applications (refer to section 4.2.1 above and **Regulatory Program**). This resource and other forms of technological communication, such as videoconferencing and webcasts, will reduce the requirements for administrative staff. **Integration meeting:** There will be weekly

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administrative integration videoconference meetings chaired by the Executive Director with partner site administrators and the chief Research Facilitator. This will be a continuation of current administrative meetings already underway in unifying all CTSI partner institutions. The site-specific Associate Directors will participate in these meetings on a biweekly basis. The Executive Director will make regular reports on site integration to the PD and the EOC (please refer to figure 2 above).

Four cross-cutting activities are housed in the Office of the Institute: the Education Office, the Office of Investigator Services, the Office of Industry Alliances and the Evaluation and Tracking Unit.

5.4.3.2. Role of Other UCLA Partner Entities. The CTSI has partnered with and receives support from several key entities at all of the partner institutions, including Research Policy and Compliance, Conflict of Interest Review Committee, Biomedical Affairs/BioSafety Committee, Office of Research Administration, Office of Intellectual Property, Office of Contracts and Grants, Intellectual Property and Technology Transfer, Office for the Protection for Research Subjects, and Budget and Administration.

5.4.4. Committees and Boards

Committee on Maternal, Child and Adolescent Health (CMCAH). The CTSI formed the Committee on Maternal Child and Adolescent Health (CMCAH) to drive innovation and stimulate translational research using life course concepts. Genetic and other biomedical breakthrough discoveries have outstanding potential to save and improve children's lives, and to reduce preventable adult deaths from diabetes and cardiovascular disease that have origins in pregnancy and childhood. MCAH investigators offered this expertise in multiple team science research clusters in the 2010 retreat. CTSI's transformative vision for pediatric biomedical science supports our investigators who drive major scientific breakthroughs. We are **forging the transdisciplinary team environment** for these biomedical scientists by synergistic connections with investigators who take bench knowledge directly to practice communities and policymakers. This will transform systems and policies that are artifacts of outdated biomedical concepts.

Under the leadership of **Kathleen Sakamoto, MD** (Vice Chair of Research, Department of Pediatrics) and **Neal Halfon, MD** (Associate Director of the CTSI and Director of the Center for Healthier Children, Families and Communities) **this group of leading investigators combines expertise across the translational continuum** from bench to bedside to community, drawing from partner institutions in multiple departments and disciplines including obstetrics and gynecology, neonatology, general pediatrics, adolescent medicine, family medicine, pediatric subspecialties, and health services research. Committee roles include ■ defining the MCAH strategic plan for the CTSI, ■ advising on ways to address the unique biomedical issues for children such as life course implications of fetal and environmental exposures, unique technology and industry partnerships, and research participation, ■ launching new transdisciplinary initiatives that lead to novel, transforming areas of investigation, ■ connecting investigators with local community partners to experiment with novel interventions and transformative health care redesign, ■ linking UCLA with other CTSA's and national translational agendas, and ■ encouraging novel MCAH studies through **recognition awards for junior investigators, including eight this year** for investigators pursuing a broad range of studies ranging from therapeutic interventions for specific medical conditions to pediatric health care redesign. The Committee will convene quarterly and as needed to review and respond to CTSI progress, milestones and processes. A Committee representative serves on the EOC of the CTSI. For a full listing of committee membership, please refer to page 195 in the Administrative Core Budget Justification.

Institutional Steering Committee (ISC). The ISC will be composed of the leaders of all four partner institutions, and will oversee coordination and prioritization of UCLA CTSI operations with inter-institutional agendas, strategic investments, and resource sharing to best advance the CTSI mission. This Committee will provide counsel and direction to the PD, and through him to the EOC. This committee will be chaired by the UCLA Chancellor, and includes the UCLA Vice-Chancellor of Medical Sciences and Dean, DGSOM (A. E. Washington, MD), the President of the Los Angeles Biomedical Research Institute at Harbor UCLA Medical Center (David I. Meyer, PhD), the Senior Vice-President for Academic Affairs for Cedars-Sinai (Shlomo Melmed, MD), and the Dean of the College of Medicine for CDU (Richard Baker, MD), or their designees. The Committee will meet bimonthly. Minutes will be maintained and transmitted to Dr. Dubinett.

External Advisory Board (EAB). The EAB functions as an interface with the scientific community and an outside perspective to the management of the UCLA CTSI. The EAB will include academic leadership from

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other CTSAs, leaders from industry and foundations. The EAB will be available to provide recommendations to the EOC. The EAB will provide such input on a regular basis, although no less than twice yearly, once in person on campus and once through videoconferencing. One of the Committee's two annual meetings will coincide with the UCLA CTSI Annual Retreat. The EAB's impact will be direct and change will be effected via their reports to the PD and EOC.

Internal Advisory Board (IAB). The primary mission of the IAB is to provide advice to the EOC. The IAB provides an interface with the professional Schools at UCLA and CDU as well as partner institutions and community members. The IAB includes broad representation in expertise and includes successful academicians and community representatives. The IAB will be co-chaired by Vice Chancellors A. Eugene Washington and James S. Economou. The IAB will be focused on providing advice specific to the overall goals of the CTSI. The members have been selected based on their expertise in providing guidance with the intent of harmonizing CTSI activities involving relevant faculty recruitment, educational initiatives, collaborative research funding, technology core development, community engagement, interactions with other CTSAs and strategic investments among the schools and institutions working toward the CTSI mission. The IAB will meet at least twice each year. The IAB will have 30 members including the Dean from the College of Science and Health at CDU, representatives from UCLA Schools (College of Letters & Sciences, Dentistry, Engineering and Applied Science, Law, Management, Nursing, Public Health), and one community member from the CTSI CAP Council (see [UCLA CTSI Community Program](#)). IAB members have been selected by the PD and EOC in consultation with Vice Chancellors Washington and Economou. In the IAB meetings members will focus on specific goals relevant to their expertise. This will assure that the IAB is effective and focused. The IAB will be able to effect change through the institutional authority of its chairs and members. The counsel of the IAB will also facilitate the goals of the CTSI via bi-directional communication with the PD and EOC. Please refer to page 1147 for the complete listing of IAB membership.

5.5. Procedures for Minimizing and Resolving Conflicts

We will address conflict by first attempting to minimize its occurrence, through the implementation of procedures and protocols. Secondly, we will create impartial procedures to address conflict resolution in key areas, including publication and authorship. These procedures will rely heavily on the advice and counsel of the IAB. The aim of these policies is to oversee the resolution of any conflicts that may arise within the CTSI, through consultation with the IAB, and the implementation of protocols. For example, these conflicts may include: budgetary or funding issues, assignment of resources and conflicts between individual investigators.

Processes for Minimization and Avoiding Conflict: Avoiding conflict will be facilitated by implementation of the following CTSI-wide procedures instituted by the EOC:

- **Processes for Resolving Conflict:** Resolution of conflicts will be attempted at the Program level first. For those issues not resolvable at that level, several alternatives, either informal or formal, will be available.
- **Informal Process:** An informal discussion will occur with the Program Leader and PD. If necessary these discussions will involve the Chairs of the IAB (Vice Chancellors Washington and Economou). If required this may also involve the staff of the NCCR. If these informal processes are not successful in resolving the issues within a reasonable period of time, an individual may enter into the formal process briefly outlined below.
- **Formal Process:** The first step of the formal process involves the EOC, which will attempt to resolve the problem to the satisfaction of the involved parties. The final step will be handled by a panel comprised of select members of the IAB, EAB, and relevant NCCR staff (the Appeals Committee); there will be no appeal beyond this step.
- **General principles to consider during the formal process include:** (a) all parties must agree to maintain absolute confidentiality with regard to any information or documents obtained as a result of this process; (b) all parties, including non-key personnel, are expected to cooperate fully and promptly with the formal process; and (c) any individual with potential or perceived conflict of interest with the dispute or the disputants will not be involved in the resolution of the conflict nor in any related discussion. If necessary, the Director or Appeals Committee will rule on the presence of such a conflict.

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- **Disagreements between Awardee and NCR Staff:** As stated in the RFA, this U54 application will follow the general NIH principles of arbitration such that *“an Arbitration Panel composed of three members will be convened... This special arbitration procedure in no way affects the awardee's right to appeal an adverse action that is otherwise appealable in accordance with PHS regulations 42 CFR Part 50, Subpart D and HHS regulations 45 CFR Part 16.”*

5.6. Community Participation in Governance

As noted above, the UCLA CTSI is committed to advancing and expanding strong bi-directional academic-community partnerships to ensure that new scientific discovery is relevant to community needs. The UCLA CTSI will be interactive and accountable to the communities we serve and strongly supportive of CTSI investigators with longstanding and successful involvement in community engagement. Consequently, we have taken the approach of including one or more community advocates on each of our key steering committees within the UCLA CTSI. These individuals will be drawn from members of the CERP CAP Council, which reflects the broad constituency of our community partners. They will provide key input to convey community concerns and priorities in formulating ideas for investigation.

Monitoring, Responding to, and Anticipating Investigator and Community Partner Needs. A critical function of the leadership of the UCLA CTSI is to monitor individual investigator and community partner's needs and concerns, and to attempt to anticipate these. This important function will be accomplished using a number of approaches. First, the Office of the Institute will perform an annual satisfaction and needs assessment of the entire investigator and community partner groups. Second, a complaint/compliment hot-line will be established (telephone, fax and web-based) within the entire UCLA system and all UCLA CTSI institutions for investigator and community comments, with appropriate and regular announcements as to the existence of this avenue of communication. The query/comment will be referred to the appropriate leader within the UCLA CTSI structure by the staff of the Office of the Institute, after consultation with the Program Director for consideration and reply. Third, the Research Facilitators of the Office of Investigator Services (OIS) and the Technology Officers of the **CTT** will directly engage the CTSI investigator community to identify nascent or development needs and problems with the utilization of core resources.

5.7. UCLA CTSI Annual Retreat

The Annual Retreat is a forum whereby the UCLA CTSI community and its stakeholders can communicate and review strategic initiatives and goals. The annual retreat will serve three functions: i) sharing of information and progress; ii) receiving feedback; and iii) providing information and seeking guidance from the External Advisory Board (EAB). The entirety of the CTSI research community, including CTSI investigators, trainees, core managers, clinical coordinators and partnered community organizations will be invited. In addition, UCLA's Chancellor and members of the ISC, EOC, IAB, and EAB will be attending. Each Program will be responsible for providing progress reports and preliminary scientific reports to attendees. Selected posters, oral presentations from both senior and junior investigators to promote cross talk, mentoring, and collaboration will be included. Following the retreat the EAB will review the UCLA CTSI's structure, utilization, and productivity, with an exit meeting with the EOC at the end of the retreat in an effort to provide critical, stimulating, and thoughtful advice to CTSI directors that promotes transformation, integration, innovation, and continuous improvement of the overall Institute and its key functions and scientific agendas. At our retreat in September 2010 we heard presentations from the first six Translational Research Cluster groups presenting plans for transdisciplinary projects including those from HIV, Addiction, Stroke/Cardiovascular Disease, Breast Cancer, Diabetes/Obesity and Mental Health/Cognition.

5.8. Procedures for Periodic Evaluation of the UCLA CTSI Leadership

All faculty within the UCLA system are subject to formal academic review within the UCLA system, monitored by the Office of Academic Personnel. Likewise all employment and Human Resources issues will be dealt with along the procedures outlined by the individual UCLA CTSI institution's rules and regulations. However, as the UCLA CTSI has specific performance and productivity needs that may be distinct from those of the general faculty and employees, a separate UCLA CTSI-relevant periodic evaluation of the CTSI leadership will be performed.

The Institutional Steering Committee (ISC), through the Office of the Institute, will monitor the results of this once yearly assessment of the UCLA CTSI leadership. The yearly assessment will gather, to the extent

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possible, 360° evaluations of the performance of these UCLA CTSI leaders using a standardized uniform assessment tool surveying superiors (e.g., institutional leaders), peers (e.g., Internal Advisory Board, External Advisory Board, other Program Directors), subordinates (e.g., research staff), and clients (at-large investigator and lay community). The ISC will review all materials gathered and generate an assessment of each leader. As needed, education, skills training, or other remediation tools, or replacement, may be recommended. In the event that concerns about the performance of a UCLA CTSI leader are raised prior to the scheduled review, an early review can be requested by the ISC.

5.9. Appointments and Promotions of Faculty Members of the UCLA CTSI

Similar to the vast majority of institutions, all faculty operating within an Institute or Center, such as the CTSI, have a primary Department and School for their appointments and promotions. However, any promotion or recruitment involving faculty funded in whole or in part by the UCLA CTSI will require agreement of the CTSI Program Director and appropriate Chair and/or Dean. Of particular note is the commitment of \$12,000,000 from Vice Chancellor A. Eugene Washington for joint recruitment of faculty, which will be co-recruited by the CTSI and selected interdisciplinary institutes of UCLA.

Similarly, the Program Director and Associate Directors will work with the Deans of the respective schools to ensure that at the time of a search or promotion the interests of clinical and translational research and the UCLA CTSI are represented. To promote recruitment and protect faculty time for interdisciplinary research, we highlight three CTSI-supported initiatives, further described in the **Pilot/Collaborative Program**: ■ UCLA/CDU Partnership grants, to support faculty establishing inter-institutional research partnerships ■ UCLA/CDU Faculty Innovation Program, for recruitment of new CDU translational research faculty ■ Recruitment and retention initiative for faculty from disadvantaged backgrounds. Finally, to promote interdisciplinary team research, the new UCLA and CDU academic policy prioritizes contribution rather than the number or position of authorship for academic promotion and advancement.

6. RESOURCES AND ENVIRONMENT

The David Geffen School of Medicine at UCLA (DGSOM) is one of the top ten medical schools in the country. DGSOM engages the efforts of more than 6,000 clinical faculty, 2,000 full-time faculty and 1,000 active investigators, many recognized with the highest national and international awards and honors. Constituting a critical mass of outstanding research in all areas of basic, clinical, translational, and population-based research, UCLA is ranked seventh in the United States in research funding from the NIH, with over 800 active research awards totaling more than \$360 million, and has the fourth highest total research dollars from all sources, over \$1 billion annually. The School of Medicine education and training currently encompasses 1,800 residents, 700 medical students, and 500 graduate students working toward PhD degrees in health-related sciences, with 240 active D-, F-, K-, R-, and T-series training and career development programs and single-awardee fellowship projects. In addition to its commitments to the CTSI, DGSOM has greatly expanded its capacity to accommodate clinical and translational science in the last two years with the opening of: a \$70-million, 130,000-square-foot Neuroscience Research Building; a \$74-million, 130,000-square-foot Biomedical Sciences Research Building; and a \$45-million, 95,000-square-foot Orthopaedic Hospital Research Building. The Institute of Molecular Medicine (IMED; 23,248-square-feet, wet labs, technology cores) is undergoing a \$5.4-million renovation.

The UCLA Health System is comprised of four hospitals: the Ronald Reagan UCLA Medical Center (520 beds), the Mattel Children's Hospital (520 beds) UCLA and Stewart and Lynda Resnick Neuropsychiatric Hospital (75 beds) and the Santa Monica-UCLA Medical Center and Orthopaedic Hospital (271 beds). The Westwood campus also includes the Jules Stein Eye Institute and Doris Stein Eye Research Center, the Semel Institute for Neuroscience and Human Behavior Neuropsychiatric Institute, and the UCLA Jonsson Comprehensive Cancer Center, one of 39 NCI-designated comprehensive cancer centers. Outpatient facilities include: a six-story, 380,000-square-foot ambulatory care center housing the Family Health Center for primary care for routine illnesses, the Children's Health Center, Internal Medicine clinics, and a Surgery Center; and a 104,000-square-foot building housing the outpatient, training and research programs of the Stewart and Lynda Resnick Neuropsychiatric Hospital and the Jane and Terry Semel Institute for Neuroscience and Human Behavior. This building also houses the UCLA Medical Center rehabilitation program. The UCLA Health System has a staff of more than 2,000 physicians, including 1,500 full time physicians employed at Ronald

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Regan UCLA Medical Center. The Ronald Regan UCLA Medical Center employs 2,500 support staff. UCLA Health System hospitals and clinics have over 1 million annual patient visits and 80,000 hospital admissions annually.

The UCLA School of Public Health (SPH) consistently ranks among the top 10 schools of public health in the country by U.S. News & World Report. Its distinguished faculty includes 12 members of the Institute of Medicine, and 10 recognized by Academy Health over the last two decades with the Distinguished Investigator Award or outstanding scientific paper of the year. The School houses five academic departments including Biostatistics, Community Health Services, Environmental Health Sciences, Epidemiology and Health Sciences. SPH also houses several highly productive interdisciplinary research centers and numerous NIH-funded scientists who will participate in CTSI transdisciplinary team-based research. SPH centers include: the UCLA Kaiser Permanente Center for Health Policy Equity, the Center for Occupational and Environmental Health, the Center for Health Policy Research, the Center for Adolescent Health Promotion, the Center for Environmental Genomics, the Center for Healthier Children, Families and Communities, the Center for Global and Immigrant Health, the Center for Public Health and Disasters, the Center for Metabolic Disease Prevention and the Division of Cancer Prevention and Control Research.

The Burns and Allen Research Institute at Cedars-Sinai Medical Center (Cedars-Sinai). Cedars-Sinai is the largest non-profit, academic medical center in the western United States. This tertiary care facility has over 2,200 medical staff members, 9,000 employees serving the Los Angeles area. Cedars-Sinai is located in the densely populated city of West Hollywood and serves a diverse catchment area. Biomedical education is an integral function of the Cedars-Sinai commitment to developing excellent patient care. Cedars-Sinai is a major teaching facility of the DGSOM, with over 240 full-time faculty members in ten different departments who participate in the training of medical students, interns, residents, and fellows. In addition to contributing to the teaching of DGSOM medical students, Cedars-Sinai faculty teach 450 residents and fellows in over 60 graduate medical education programs on site. Cedars-Sinai ranks among the top 10 non-university hospitals nationwide receiving research funding from the NIH. In the past 5 years, the Research Institute has doubled the amount of extramural research expenditures to almost \$60 million/year,

Cedars-Sinai has one of the largest state-of-the-art clinical research facilities of any private institution in the nation, under the purview and oversight of the Burns and Allen Research Institute. It includes over 270,000 square feet of laboratory and laboratory support space, including the seven-story, 216,000 square foot, state-of-the-art Barbara and Marvin Davis Research Building, adjacent to the main hospital. This facility has a vivarium and operating rooms solely for research purposes. The Advanced Health Sciences Pavilion, scheduled for occupancy in early 2013, will add an additional 150,000 square feet of clinical research and laboratory space. Cedars-Sinai has an active clinical and translational research program embodied by the NIH-funded GCRC, established in 1994 as a satellite of the Harbor-LA BioMed GCRC. The GCRC provides clinical research infrastructure for investigators who receive their main research support from federal and other national, as well as international, agencies.

Charles Drew University of Medicine and Science (CDU). CDU is one of the premier minority academic institutions in the nation, is a private, non-profit school founded in 1966 in response to inadequate medical facilities within the Watts region of Los Angeles. It is the only academic health sciences center in an area of 1.6 million people—the largest underserved urban area in the United States. The university is also the nation's only dually designated Historically Black Graduate Institution and Hispanic Serving Health Professions School. The CDU community catchment area, approximately 40% African American and 60% Hispanic, with 35% of residents living below the federal poverty level, has been historically isolated from participation in clinical and translational research.

Grounded in new partnerships over the last 10 years with Harbor-LA BioMed and UCLA-Westwood, the growth in research activity at CDU has translated into a high level of productivity. CDU ranks in the top 7% of over 3,400 institutions funded by NIH (FY05), with over \$20 million per year in NIH funding and \$11 million in non-NIH funding (FY07). CDU was recently ranked in the top 50 private research universities as rated by the Center for Measuring University Performance at Arizona State University. It is noteworthy that a 2007 NSF-funded analysis reported that U.S. scientific publishing was flat from 1992 to 2001 despite increased research

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funding, but that the Number 1 institution in the country over this period of time in terms of publication growth, among the top 200 institutions by level of NIH funding, was CDU.³ Of substantial relevance to the UCLA CTSI mission, in July 2007 the NCRP awarded a \$9.5 million, 3-year grant to CDU (PI Keith Norris, MD) to launch the Research Centers in Minority Institutions (RCMI) Translational Research Network. This network is designed to increase the opportunity for multi-site clinical and translational research among minority and other collaborating institutions throughout the United States. As the RCMI activities are integrated into the NIH Roadmap and the national CTSA infrastructure, one of the most important and direct linkages will be the proposed UCLA CTSI. These activities will be enhanced by the recent completion of a \$43-million facility for clinical and basic research (45,000 square feet) and nursing education (15,000 square feet). As a CTSI partner, CDU will critically contribute to bridge the translational gap from basic science to medical care through its exceptional network of community partnerships, and through its leadership in refining and disseminating community-partnered participatory research principles.

Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center (Harbor-LA BioMed).

Harbor-LA BioMed is affiliated with both the DGSOM and the Harbor-UCLA Medical Center. It draws on a catchment area of about 3 million residents, 0.55 million below the poverty level. It is actively involved in teaching 50% of all DGSOM medical students. The Research Institute has an annual budget of over \$73 million (\$65 million from research grants and contracts) and supports more than 1,000 research studies from 142 active investigators in emerging infections, cancer, women's health, male reproductive health, vaccine research, neonatology, autoimmune diseases, cardiology, neurosurgery, and genetics. For 52 years, physician-scientists at Harbor-LA BioMed have made major contributions to the advancement of medicine, including the modern cholesterol test, the newborn thyroid deficiency screening test (now used for every U.S. newborn), a screening procedure for Tay-Sachs disease that has dramatically diminished the incidence rates nationwide and worldwide, and a genetically engineered enzyme replacement for mucopolysaccharidosis.

The GCRC at the Harbor-LA BioMed has been continuously funded for 40 years and supports the multidisciplinary research of a large cadre of well-funded and productive investigators (total NIH support for 2008-2009 was \$27 million). Their publication rate is one of the highest among GCRCs. In 2002, the outpatient clinical research unit opened an additional 5,500 square feet for research, with an adjoining 2,000 square feet conference room for research education-related activities. Campus-wide centers have been funded with their administrative home at Harbor-LA BioMed, creating an expanded support base for promoting clinical and translational research. Current centers include the Emerging Infection Center, Perinatal Research Center, Cancer Prevention Clinical Trials Center, Liu Center of Pulmonary Hypertension Research, Rehabilitation Clinical Trials Center, CT Reading Center, HIV Medicine Research Center, UCLA Center for Vaccine Research, and the Male Reproductive Center, which is a World Health Organization-collaborating Center for Research in Reproduction and a NICHD-funded Contraceptive Clinical Trial Network Center.

The total clinical research space available at Harbor-LA BioMed is 25,000 square feet. In the past 3 years, LA BioMed has acquired major equipment (real-time PCR, laser capture microdissector, two liquid chromatography-tandem mass spectrometry [LS-MSMS] machines, matrix-assisted laser desorption/ionization-time-of-flight [MALDI-TOF] mass spectrometer) and provided scientific and technical support to meet the needs of Harbor-LA BioMed investigators. Over the past 8 years, Harbor-LA BioMed, in partnership with California State University Dominguez Hills, has trained underrepresented students in biomedical research. These NIGMS-funded programs pair underrepresented undergraduate and master's-level students in biology with well-funded mentors at Harbor-LA BioMed. Many of these students have since applied and been admitted to PhD programs throughout the country.

7. NATIONAL COLLABORATION, DATA SHARING AND DISSEMINATION PLAN

The UCLA CTSI leadership will identify barriers and set priorities for developing collaborative solutions and standard approaches to address the challenges in CTSA-based research according to operational, educational, and clinical/therapeutic goals. In addition, committee members will recommend strategies in clinical and translational research that can be implemented across this Institute as well as the national CTSA consortium in an effort to work toward identifying, adopting, and implementing policies and best practices to ■ advance clinical and translational research as a discipline ■ share policies, practices, and resources ■ Discuss opportunities and overcome impediments ■ identify and address issues impeding clinical research, government policies and practices, and other appropriate topics, and ■ facilitate collaboration and sharing

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among partners in clinical and translational research, e.g., community partners, laboratories, hospitals, and industry

7.1. Intellectual Property and Resource Sharing

Intellectual property and data generated under this project will be administered in accordance with both university and/or CTSI institution, and NIH policies, including the NIH Data Sharing Policy and Implementation Guidance of March 5, 2003. Ownership of sole or joint inventions developed under the project will be owned by the institution(s) employing the inventor(s). Inventors shall be determined by U.S. Patent law, Title 35 SC. University and participating investigators/institutions will disclose any inventions developed under the project, and such inventions will be reported and managed as provided by NIH policies. Sole inventions will be administered by the institution employing the inventor. Joint inventions shall be administered based on mutual consultation between the parties. Similar procedures will be followed for copyrights.

Materials generated will be disseminated in accordance with university/participating institution and NIH policies. Depending on such policies, materials may be transferred to others under the terms of a material transfer agreement. Access to databases and associated software tools generated under the project will be available for educational, research, and nonprofit purposes. Publication of data shall occur during the project, if appropriate, or at the end of the project, consistent with standard scientific practices. Research data that document, support, and validate research findings will be made available after the main findings from the final research data set have been accepted for publication. Additional details of Intellectual Property sharing are also discussed in **Regulatory Program**.

7.2. Sharing Research Data and Software

The UCLA CTSI is committed to open and timely dissemination of results from investigations using the resources of the Institute. Investigators presenting research protocols for support by the UCLA CTSI will describe their data-sharing plans in the protocol. The policy of the UCLA CTSI is that appropriately anonymous or consented data will be shared in a timely fashion, e.g., after the first publication emanating from the research study. All researchers will receive training and will adhere to all provisions of the Health Insurance Portability and Accountability Act (HIPAA) to ensure rights and privacy of participants in any research protocol.

The UCLA CTSI is committed to the growth of an open source community. To that end, software supported by resources of the UCLA CTSI will be developed in open source and made freely available to biomedical researchers, educators, and other nonprofit institutions such as education facilities, research institutions, and government laboratories. The terms of software availability will permit commercialization directly or of enhanced or customized versions of the software, and incorporation of the software or elements into other software packages. Research institutions outside the UCLA CTSI may modify source code and share modifications with other colleagues, or other recipients from NIH for awards under the CTSA program.

7.3. National Cooperation

Investigators at the UCLA CTSI have a broad range of collaborations with investigators at other CTSA institutions. We have been actively engaged in seeking advice from each of the members of the West Coast CTSA Consortium (letters enclosed on pages 1477-1489). In total we have sought the advice of leaders from 20 different CTSA. In addition to those of the West Coast Consortium we have had visits from CTSA investigators from Iowa, Pittsburgh and the University of Washington. We have had phone or video conference calls with investigators from Colorado, Cornell, Boston University, Columbia, UCSF, UCI, UCSD, USC, Scripps, UC Davis, Stanford, University of Oregon, Vanderbilt and UT Southwestern. In addition, we have participated in the University of California (UC) Biomedical Research Acceleration Initiative which includes the Program Directors from the UC CTSA jointly working on issues related to IRB harmonization, joint contracting and bioinformatics. Together with the investigators at USC and UCI CTSA we have formed the Greater Los Angeles CTSA Coalition (letter enclosed describing these activities signed jointly by Drs. Dubinett, Dan Cooper and Tom Buchanan). **Specific inter-institutional collaborations ongoing with investigators from CTSA institutions are noted throughout this application. We have joint interests and collaborations with other centers in laboratory based, translational and clinical studies as well as imaging, informatics, ethics, training and community engagement research.** The UCLA CTSI looks forward to formally working with the CTSA Consortium in a variety of areas. For example, the program director and the director of the Program for Biomedical Informatics will have full authority to speak on behalf of

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the UCLA CTSI and to communicate concepts for incorporation into the structures and functions of the UCLA Institute. Individual schools that are members of the CTSA Consortium may develop new pharmacologic therapies, procedures, and devices that are developed in their institutions but, for reasons of conflict of interest, these should be evaluated and tested in a third-party institution. We will support the notion that members of the CTSA, including ourselves, are available to participate in the testing of those agents, procedures, or devices.

INTERNAL ADVISORY BOARD (IAB) MEMBERSHIP:

IAB Chairs: James S. Economou, MD, PhD (Vice Chancellor for Research, UCLA) **A. Eugene Washington, MD, MSc** (Vice Chancellor for Medical Sciences and Dean of the DGSOM)

Board Members:

Goal 1: Richard Baker, MD (CDU College of Medicine); **Jonathan Braun, MD, PhD** (Pathology and Laboratory Medicine); **Judith Gasson, PhD** (Jonsson Comprehensive Cancer Center); **No-Hee Park, PhD, DMD** (Dentistry); **David Rimoin, MD, PhD** (Cedars-Sinai Pediatrics- Medicine & Human Genetics); **Ronald Swerdloff, MD** (Harbor Endocrinology); and **Peter Whybrow, MD** (Psychiatry and Behavioral Science).

Goal 2: Vijay Dhir, PhD (Henry Samueli School of Engineering and Applied Science); **Michael Phelps, PhD** (Molecular and Medical Pharmacology); **Jerome Rotter, MD** (Cedars-Sinai Human Genetics); **Dennis Slamon, MD** (Medicine-Hematology and Oncology); **Jayduut Vadgama, PhD** (CDU Medicine); and **Paul Weiss** (California NanoSystems Institute).

Goal 3: Aimée Dorr, PhD (Graduate School of Education and Information Studies); **Noel Bairey Merz, MD** (Cedars-Sinai Heart Institute); **Ronald Edelstein, EdD** (CDU College of Medicine); **Alan Fogelman, MD** (Medicine); **Alfred Osborne, PhD, MBA, MA, BS** (Anderson School of Management); **Victoria Sork, PhD, MS** (College of Letters and Sciences- Ecology and Evolutionary Biology); and **Owen Witte, MD** (Microbiology, Immunology, and Molecular Genetics).

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Pilot and Collaborative Translational and Clinical Studies Program



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Abbreviations: AHRQ – Agency for Healthcare Research and Quality, ASAP – Adult Survivorship Action Plan, BIP – Biomedical Informatics Program; BSD-CDM – Biostatistics, Study Design and Clinical Data Management Program, CCRR – UCLA CTSI Clinical and Community Research Resources, CDU – Charles Drew University, CFAR – Center for AIDS Research; CNSI – California NanoSystems Institute; CTSI-ED – UCLA CTSI Research Education, Training and Career Development Program, CTT – UCLA CTSI Center for Translational Technologies, DGSOM – David Geffen School of Medicine; DMH – Department of Mental Health; EOC – UCLA CTSI Executive Oversight Committee, E/T – UCLA CTSI Evaluation and Tracking Program, HSA – Health Services Academy, IMED – Institute for Molecular Medicine, JCCC – Jonsson Comprehensive Cancer Center; JCTM – Joint Center for Translational Medicine, NLM – National Library of Medicine, NTTM – Novel Translational Technologies and Methodologies; ORU – Organized Research Units, RAID – Rapid Access to Interventional Development; RCMAR – Resource Centers for Minority Aging Research; SMI – Severe Mental Illness; T2DM – Type 2 diabetes mellitus; STAR – Specialty Training and Advanced Research, TRC – Translational Research Cluster; TRWG – Translational Research Working Group; UCI – University of California, Irvine; USC – University of Southern California; WHI – Wireless Health Institute

1. OVERVIEW

Our **Pilot and Collaborative Clinical and Translational Studies Program** (Pilot Program) is the research engine of the UCLA CTSI. It delivers two key functions: First, it supports Pilot and Collaborative Translational and Clinical Studies among basic, clinical, community and population-based scientists. Second, it supports the development of the Novel Clinical and Translational Methodologies needed to sustain an environment of intellectual exploration. *Our mission is to offer the only campus-wide translational team science grants available at UCLA.* Our collaborators in the Los Angeles area include the University of Southern California (USC) and the University of California, Irvine (UCI), which participate with us in the Greater Los Angeles CTSA Coalition. In our prior review, our Pilot Program was reviewed with our Center for Translational Technologies (Translational Technologies and Resources key function) and received an aggregate score of 2. Reviewers praised the experience of our leadership; the variety of available seed funding; and our grant application review process.

In the current application, we highlight a new transforming funding mechanism —the **Translational Research Cluster (TRC) Grant Program**— which leverages local funds to support transdisciplinary research addressing the most pressing health needs in Los Angeles County. This program is one of five innovative mechanisms through which we will annually award 30 to 40 grants with a total value of up to \$3.6 million – 150 to 200 grants totaling \$18 million during the next five years. We will match the annual CTSI contribution of \$425,000 by more than 7 to 1 with philanthropic, corporate and other institutional funds (see **Table 1**). These grant mechanisms will drive our transformation by supporting team science, new faculty research, development of novel methodologies and technologies, seminars and retreats to foster collaboration and prototype development.

The Pilot Program team serves as a Parent Grant Review Committee overseeing a CTSI study section of internal and external reviewers. Sixty experienced faculty reviewers with a diverse range of expertise have volunteered to serve as ad hoc reviewers (see **Letters** and **Budget Justification**). Our program includes an institutional commitment of \$2 million a year -- \$12 million over the next five years – for faculty recruitment. We have assembled more than \$30 million in new institutional and other commitments to support the transformative approaches in this program. Substantive revisions since our last submission are indicated in the left margin.

2. SPECIFIC AIMS

The UCLA CTSI provides the operations and governance necessary to facilitate successful transdisciplinary clinical and translational research. The overarching *mission* of the UCLA CTSI is to *transform our academic-clinical-community partnership into a borderless institute that brings our combined innovations and resources to bear on the most pressing health needs in our diverse Los Angeles community.*

The Pilot Program is central to achieving the mission of the UCLA CTSI. Its comprehensive Translational Research Grant Program provides pilot funds to ■ support interdisciplinary translational research collaborations; ■ assist in early-stage product development; and ■ catalyze new interactions and collaborations among basic, clinical and community researchers. Additional mechanisms support the development of ■ novel methods and technologies and ■ new translational faculty. The cornerstone of our transformative initiative is our new Translational Research Cluster (TRC) Grant Program, which unites our best minds from across a range of disciplines against the most challenging health problems. We designed these mechanisms to address **a major deficit that requires CTSI-mediated transformation: the need to expand and elevate our research focus to the transdisciplinary team science level.**

UCLA and its partners are at the forefront of clinical and translational discoveries that have made major contributions to healthcare. To address the health care needs of the 21st Century, however, we must move away from research conducted in isolated disciplinary silos. Although UCLA invests significantly in pilot projects and technologies each year, *no existing campus-wide mechanism is dedicated to transdisciplinary translational team science.* Addressing the complexities of modern translational research requires multidisciplinary teams that partner with communities to prioritize research and disseminate best practices. The UCLA CTSI offers us an unprecedented opportunity to re-engineer our clinical and translational research environment.

Specific Aim 1: Advance transformative collaborative translational research through broad-ranging

funding mechanisms. We will expand and implement our comprehensive Translational Research Grant Program to support the full range of translational team science. The mechanisms of support include:

- Translational Research Cluster Grants: (six to eight awards annually of up to \$200,000 each). These awards support investigator-initiated, transdisciplinary, team-based research with preferences given to projects that address major health problems in our community.
- Catalyst Grants: (10-15 awards annually of \$1,000 to \$25,000 each). These awards have been initiated with local funding; they support seminars and day-long symposia with experts both within and outside UCLA to drive novel team science initiatives.
- New Technology Transfer and Prototype Grants: (at least one grant annually of \$800,000, dispersed over three years). This award supports preclinical studies and phase-1 clinical trials.

Specific Aim 2: Develop novel clinical and translational technologies and methodologies. We are instituting Novel Translational Technologies and Methodologies Grants (up to three awards annually of up to \$100,000 each). These awards foster the development of any research tool, technique, or resource with the potential of bridging critical gaps in the conduct of translational biomedical science.

Specific Aim 3: Attract and enable the next generation of faculty to establish careers in team-based clinical-translational research through the Society of the CTSI. The Society of the CTSI consists of CTSI Scholars and their multidisciplinary mentorship team. Our pilot program awarded four recently appointed faculty \$25,000 a year for three years to conduct pilot studies considered highly probable to lead to federally funded translational research. Our plans are to increase the number of CTSI Scholars and the size of awards. We will annually award 12 senior postdoctoral or recently appointed faculty up to \$50,000 per year for three years to conduct studies under a team of transdisciplinary mentors.

Specific Aim 4: Using a multidimensional recruitment strategy, recruit at least 25 new CTSI translational research faculty over the next five years to ensure that the UCLA CTSI fulfills its academic research and teaching mission.

3. PROGRESS TO DATE

The Pilot Program has begun the process of transforming translational and clinical research at UCLA CTSI partner institutions to focus on team-based science critical to our diverse Los Angeles community. Below, we highlight examples of recent accomplishments achieved with local support. Receipt of a CTSA will enable us to accelerate our transformation and fully accomplish.

- With Catalyst Grant funding, we organized a series of think tanks in 2010 with teams of basic, clinical, community and population scientists; comparative effectiveness researchers; health advocates; business and industry experts; public policy experts, and government leaders to develop research objectives for our initial TRC. These think tanks produced six outstanding abstracts targeting ■ mental health ■ cardiovascular disease and stroke ■ cancer ■ HIV ■ addiction and ■ diabetes and obesity (see **section 6.1.1.1.** for more detail). These six proposals were presented at a UCLA CTSI-wide Translational Cluster Retreat in September 2010. Based on extensive discussions at the retreat these proposals are now being modified for consideration as the initial Translational Research Cluster Grants.
- We selected four CTSI Scholars. This pilot program, a collaboration with the **CTSI Research Education, Training and Career Development Program (CTSI-ED)**, allowed us to develop and electronically circulate an RFA among all four UCLA CTSI partners. A distinct feature of this program is that scholars receive mentoring in two disciplines. Within three weeks, we had 44 letters of intent from highly qualified candidates from an array of disciplines and from all four institutions. As indicated above, we plan to include up to 12 Scholars per year (see **section 6.2.1.**). Current scholars are:
 - Tamara Horwich, MD, Assistant Professor of Medicine, UCLA: *Management of Diabetes with Metformin in Patients with Chronic Heart Failure.* ■ Progress to date: Six publications and \$30,000 in new funding.
 - Xiao Hu, PhD, Assistant Professor of Medicine, UCLA: *Development of Noninvasive continuous Monitoring of Brain Physiology in NICU Patients.* ■ Progress to date: 12 publications and \$875,000 in new funding.

Program Director/Principal Investigator (Last, First, Middle): Dubinett, Steven, MD

- Mina Patel-Chamberlin, MD, Division of Nephrology Fellow, Harbor-UCLA Medical Center: *Identification of Biomarkers to Predict Progression of Renal Disease*. ■ Progress to date: two publications
 - Christine S. Walsh, MD, MS, Assistant Professor of Obstetrics and Gynecology, Cedars-Sinai Medical Center: *Role of Cyclin E in Ovarian Cancer*. ■ Progress to date: 11 publications and \$637,000 in additional funding.
- With local funds, we awarded 35 one-year seed grants of \$30,000 for clinical and translational research during the last three years. These awards led to publication of 137 papers and \$39 million in new funding from NIH and other sources, including \$13 million for which faculty were named as PI or Co-PI.

4. SIGNIFICANCE: PILOT PROGRAM RATIONALE

UCLA is home to outstanding achievements in scientific discovery and translational investigation that have influenced medical care around the world. But the research model that produced many of them — that of a lone investigator developing a hypothesis, testing it in a laboratory and bringing that discovery to human benefit — is no longer tenable. The complexity of challenges facing society requires collaboration¹. The major benefits of collaboration include: the enhanced capacity for creativity, team-based learning, better use of scarce resources and more effective outcomes. Diverse, multidisciplinary teams are the most successful collaborations in accelerating innovation². Disis and Slattery recently summarized the necessity of multidisciplinary team science in translational investigation³. Disis noted, however, that academic research centers are not organized to encourage diverse teams to coalesce in an effort to discover and apply research findings in clinical and translational investigation. *Our CTSI is the key to transforming our environment to establish transdisciplinary team science as UCLA's operating principle in clinical and translational investigation.*

The UCLA plan places the CTSI at the heart of a high priority initiative to expand and elevate transdisciplinary, team-based investigation. We believe a full spectrum of transdisciplinary teams is required to address the increasingly complex biological, environmental, social and cultural determinants of health in our diverse Los Angeles community. How do we create and sustain these teams? Our Pilot Program is focused on creating the environment requisite for effective team science. The thought diversity inherent in our transdisciplinary teams provides expertise, knowledge and problem-solving styles that can be combined in novel approaches to produce transformative innovation.

Our greatest challenge but also our greatest opportunity is to foster collaborative clinical and translational research across the full spectrum of expertise within this large-scale, multi-institutional scientific enterprise. Through the Pilot Program, the UCLA CTSI has begun to address this challenge by: ■ retaining and creating opportunities for current faculty in translational medical sciences ■ recruiting new faculty ■ stimulating team-based translational research through our Translational Research Cluster Grant program and ■ leveraging our resources through partnerships with institutional and disease-specific peer-reviewed seed grant programs. Parallel to this, the UCLA CTSI has instituted programs to inspire and recruit high school students, undergraduates, and graduate students to the exciting world of translational science (see **CTSI-ED**, the Community Engagement and Research Program [**CERP**], and the Clinical and Community Research Resources Program [**CCRR**]).

These activities will ■ seed the education and research of a promising new generation of investigators who learn team science approaches at an early stage of their career development ■ promote new interdisciplinary translational research collaborations among a broad spectrum of disciplines ■ assist in the translation of research from preclinical to phase I clinical trials ■ catalyze new collaborations.

5. INNOVATION AND ENVIRONMENT

The existing strength of clinical and translational research at UCLA is facilitated by significant intramural institutional investment. We have recently demonstrated that we can enhance these investments by emphasizing team science funding to influence the direction and selection of research that is funded in existing programs. For example, in the pre-award period, we altered the direction of an established, centrally-administered seed grant program in the David Geffen School of Medicine (DGSOM) and spread the program throughout UCLA and its partner institutions. Utilizing this local funding the CTSI leadership created a new category within the Stein-Oppenheimer Program emphasizing team science called the Stein-Oppenheimer

Clinical-Translational Seed Grant Initiative. This category provided three grants of \$30,000 each specifically for translational research from the clinic to the community. In addition to changing the yearly invitation for proposals, members of the CTSI leadership team joined the Stein-Oppenheimer Seed Grant Program Selection Committee to ignite the initiative. The number and quality of grant proposals in this category has steadily increased. Consequently, this year we began funding more clinical-translational seed grants. We have a commitment from the DGSOM to now apply these funds toward expanding our CTSI Scholars Program. In our new program, junior investigators will conduct translational investigations under the joint mentorship of at least two mentors from different disciplines.

We have already seen significant returns on our investments. A grant to Dr. Michael Ong in 2007 for “Explaining Care Variation for Translation into Hospital Care Process Change,” allowed him to develop the preliminary data for understanding variation among six California academic medical centers. This work led to several publications and a \$10 million award from the Agency for Healthcare Research and Quality (AHRQ) for comparative effectiveness research. His study, “Variations in Care: Comparing Heart Failure Care Transition Intervention Effects,” compares the effectiveness of two adaptations of existing care transition programs to reduce hospital readmissions among heart failure patients.

We also strategically utilized our local funding for disease-specific programs to seed new transdisciplinary projects with a high likelihood of ultimately receiving federal support. For example, the Jonsson Comprehensive Cancer Center (JCCC), in collaboration with the CTSI, awarded a \$25,000 seed grant to pediatric oncologist Dr. Jackie Casillas in early 2010. The grant allowed her to develop preliminary data on the use of cell phone technology for providing personalized health messages to pediatric cancer survivors. This work resulted in a \$216,000 grant in September, 2010 from the National Cancer Institute for “A Community Academic Partnership to Develop an Adolescent and Young Adult Survivorship Action Plan (ASAP).” Dr. Casillas also received a recognition award from the UCLA CTSI for her innovative work.

The expected outcome of her study is the development of a reusable text-messaging software tool. This tool will then be tested nationally for its effectiveness in increasing survivors’ awareness of the need for survivorship-care planning and access to care. She is developing the tool in collaboration with Deborah Estrin, PhD, a UCLA professor of computer science and engineering, who is an investigator in the UCLA CTSI CCRR.

Table 1. Summary of CTSI Grant Program and Funding

Opportunity Funds	Number per Year	Grant Amount	Duration of Award (Years)	Annual Support from CTSI	Annual Institutional Support
Team Cluster Seed Grants	6-8	Up to \$200,000	1 (up to 3)	\$200,000	\$1,400,000
CTSI Scholars	8 to 12	\$25,000 to \$50,000	1 (up to 3)	\$50,000	\$350,000
Technology Transfer & Prototype Grants	1	Up to \$800,000	1 (up to 3)	\$50,000	\$750,000
	2	\$50,000	1	\$0	\$100,000
Catalyst Grants	~11-15	\$1,000 to \$25,000	~1	\$50,000	\$350,000
NTTM Development Awards	1-3	Up to \$100,000	1 (up to 2)	\$75,000	\$225,000
Funding Totals				\$425,000	\$3,175,000

*Partners include Institutional resources, donors, and industry.

6. APPROACH

6.1. Specific Aim 1: Advance transformative collaborative translational research through broad-ranging funding mechanisms.

6.1.1. Our comprehensive Translational Research Grant Program supports the full range of translational team science.

The UCLA CTSI Translational Research Grant Program (see **Table 1**) has been initiated with local funding. Examples of these funded programs are shown in section 3 above as well as section 6 below. We will be expanding the program over the next two years to include: Translational Research Cluster Seed Grants;

Technology Transfer and Prototype Grants; and Novel Translational Technologies and Methodologies Grants. In addition to serving the entire spectrum of CTSI partner faculty members, these four programs will be critical for the development of projects by CTSI Institute Scholars (see **Specific Aim 3**) and new faculty recruits (see **Specific Aim 4**). The program is designed to serve as a tangible integrating resource that activates and binds translational research collaborations. In keeping with the intended purpose of facilitating and advancing translational medicine, investigators will have the opportunity to minimize additional costs in project implementation by utilizing all of the key CTSI functions. When fully implemented, the grant application and review process is designed to be all-electronic, thus streamlining operations.

6.1.1.1. Translational Research Cluster Grants. These grants support multidisciplinary team-based research addressing major health problems in our community. Translational Research Cluster Grant supported investigators will generate ideas and interventions that will lead to improved health. Teams will include members from multiple disciplines and may include clinical, basic or translational scientists, trainees, university or community-based medical practitioners, patient advocates, health services and clinical effectiveness researchers and industry representatives. The teams will be encouraged to include faculty from a variety of schools such as law, business, engineering and education. Each TRC will include investigators from all partner institutions. During the first year of the CTSA grant, the program will award as many as eight one-year grants of up to \$200,000 each. Funding for subsequent years, up to a total of 3 years, will be subject to annual competitive renewal. By leveraging institutional and industry funding we anticipate expanding this program substantially in years 3–5. The TRCs will make use of the resources of CTSI program areas such as CERP, Biomedical Informatics Program (BIP), Biostatistics, Study Design and Clinical Data Management Program (BSD-CDM) and the Center for Translational Technologies (CTT). Importantly, each TRC will be assigned a CTSI Research Program Manager who will act in the capacity of a professional project manager to assist the team in achieving milestones. The inclusion of project managers as part of the TRC mechanism is based upon 1) NIH based advisory panel recommendations such as the “Translational Research Working Group (TRWG) — Harnessing Discovery for Patient and Public Benefit” and 2) UCLA faculty surveys on priorities for stimulating clinical and translational research. As described above (see **section 3**) we awarded our first Catalyst Grants in 2010 to support development of Translational Cluster Grant proposals. Summaries of the abstracts presented at our daylong Translational Cluster Retreat are provided below. Based on the overwhelmingly favorable response of faculty at the Retreat, we plan to hold quarterly symposia on topics relevant to team science and our translational clusters. Our initial cluster teams in mental health, diabetes and obesity, cardiovascular disease and stroke, cancer, addiction and HIV are receiving additional Catalyst funding from local resources to further develop their team-based research proposals

Mental Health TRC

This Cluster proposes two complementary core projects that span from basic to social science, and a third project that creates the infrastructure needed to accomplish the core projects. The first project, “Foundations of Mental illness,” will examine the pathways by which genetic, clinical, and sociocultural factors interact in the expression of severe mental illness (SMI) and metabolic disorders within SMI populations, and how these factors moderate outcomes. This project will focus on public mental health clients in Los Angeles County and will include investigators from Los Angeles County Department of Mental Health (DMH) and the UCLA and USC CTSIs. The second project, “Managing Risk,” looks specifically at the metabolic side effects and risk factors associated with psychotropic drugs. It is hypothesized that some component of the genetic variants from Project 1 will substantially modify the risks of serious side effects. At the service level, this project will allow for the Mental Health Cluster to collaborate with the Los Angeles County DMH as they endeavor to construct an integrated system of care for mental and physical health including the adaption of the medical home. The third project will harmonize Los Angeles County DMH’s disparate data bases to create a crucial data infrastructure for both projects and for future translational projects. This third project will interface with the BIP in collaboration with Dr. Douglas Bell. (Cluster Co-Leaders: P. Arns, J. Braslow, J. Brekke [USC-CTSI], N. Freimer, S. Marder, G. Ryan)

Diabetes and Obesity TRC

This proposed Cluster will conduct pilot studies to test the efficacy of melatonin for prevention of Type 2 Diabetes Mellitus (T2DM) in high-risk African-American and Pacific Rim immigrants. This study will build on basic research from the USC and UCLA CTSIs that suggests a relationship between the melatonin receptor,

diabetes and sleep. In addition, qualitative research conducted by investigators at UCLA in partnership with residents of low income neighborhoods suggests that sleep disturbance is common across the age spectrum in these communities, which are also disproportionately affected by diabetes and obesity. The diabetes-obesity cluster will work concurrently with community partners to engage communities in Los Angeles County through forums or symposia to raise awareness of the impact of sleep on obesity and diabetes; discuss community perspectives on sleep hygiene / sleep disorders and mutable factors that deter or promote adequate sleep; and review evidence-based and novel therapies, including melatonin, for improving sleep and potentially reducing the T2DM risk. (Cluster Co-Leaders: A. Brown, P. Butler, R. Jackson, C. Mangione)

Cardiovascular Disease and Stroke TRC

This Cluster seeks to improve cardiovascular health and dramatically reduce death and disability among Angelinos from heart failure, myocardial infarction, or stroke. The CTSA Cardiovascular Disease and Stroke Cluster will facilitate: 1) development of personal activity monitors to measure and promote physical activity; 2) creation of a coronary heart disease simulation model to estimate the absolute and relative impact of various risk factors and cardiovascular treatments on racial differences in life expectancy; 3) testing of atherosclerosis management interventions; 4) completion of preclinical development through phase 2 trials of myocardial stem cells for heart failure and neuronal precursor stem cells for recovery from post-stroke disability; 5) broader participation of diverse communities in cardiovascular research; 6) community-level intervention trials in well-defined community samples to develop scalable and sustainable interventions to improve chronic cardiovascular risk factor management and to improve positive health behaviors in children that reduce risk over the life course; and 7) development, testing, and dissemination of a portfolio of smart phone apps and websites that increase accessibility, local applicability, and desirability of healthy cardiovascular behaviors. (Cluster Co-Leaders: J. Saver, K. Watson, A. Yancey)

Breast Cancer TRC

This proposed Cluster will test the hypothesis that disparities in breast cancer incidence and outcome are due to 1) disparities in access to quality screening, diagnostic and treatment resources and 2) to differences in breast cancer biology arising from lifestyle and/or genetic factors. Through collaborations with engineers in the California NanoSystems Institute, we will use high throughput array and next-generation sequencing strategies to develop and compare molecular signatures across different stages of breast cancer. In collaboration with our research partners spanning multiple and diverse Los Angeles County communities, molecular signatures of tumors from different racial and ethnic populations can be compared and contrasted. With UC Cancer Centers and CTSA's, our cluster will investigate host factors, such as aging, behavior, stress, cytokine profiles and co-morbid conditions such as hypertension, diabetes and obesity that interact with the tumor phenotype to generate clinical outcomes. Based upon analysis of both the tumor biology and host interaction, our cluster will identify signaling pathways driving tumor growth as well as host factors affecting patient outcomes. Innovative early phase clinical trials will be designed and conducted in our Translational Oncology Research International Network of community physicians, including those associated with the public county system. (Cluster Co-Leaders: J. Economou, J. Gasson, D. Slamon)

Addiction TRC

While social determinants of addiction sustain the behavior, escalation in drug use and relapse reflect impaired inhibitory control and its interaction with stress. This Cluster is focused on understanding inhibitory control and its interaction with stress. We will use a "think tank" approach to develop a clearer understanding of the neural basis of inhibitory control deficits in addiction and other neuropsychiatric disease. This will contribute to development of evidence-based treatments for addictions and will provide models that can be implemented locally to improve the health of those affected by addiction and its consequences. To advance substantially beyond prior work that was generally restricted to one or more domains, we will assemble an interdisciplinary team working at multiple levels of investigation (e.g., genetic, neuroendocrine, neuroimaging, behavioral and clinical). Team science will cut across individual research areas, basic and clinical science, institutions and communities to probe 1) the underlying mechanisms of self-control, 2) the role of stress in modulating inhibitory control and its neural substrates, 3) the design of potential treatments and 4) the evaluation of their acceptability and utility in community settings. (Cluster Co-Leaders: C. Evans, E. London)

HIV TRC

This Cluster seeks to reduce the burden and spread of HIV in Los Angeles. Each CTSI partner institution will target specific local populations for novel treatment/prevention interventions. The interventions may be medical, behavioral, educational or public health. Improved testing and referral strategies may include improved point-of-care HIV testing with immediate referral to treatment facilities and use of non-medical care integration (e.g., promotora programs and patient navigators). Medical prevention strategies may include pre-exposure and post-exposure prophylaxis and test-and-treat programs. Educational approaches may include sexual health and anti-stigma approaches. Public health strategies may include community mobilization and partner tracing. Outcomes will include: decreases in the incidence of HIV infection, improved retention in treatment, reduced time to getting into care, decline in morbidity/mortality due to HIV, improvement in quality of life and reduction in cost of care for individuals with HIV. Outcome measurements include: improvement in rates of HIV testing, better linkages to care, reduction in new HIV infections, reduction in community HIV viral load, reduction in total cost of HIV care, and reduction in AIDS-related mortality. Targeted populations can be defined by HIV status, gender, age, HIV risk groups, race/ethnicities, or a combination of these. (Cluster Co-Leaders: I. Chen, R. Mitsuyasu)

Based on discussions during the retreat and feedback from our post retreat survey, we are planning for the following innovations during the coming year. We will encourage applications from clusters that explicitly bridge existing boundaries across disease-focused strategies. This will focus on formation of transdisciplinary team science in a broader context. Several groups at UCLA are currently involved in research that can lead the way in this approach and assist others in framing investigations in a systems context. For example, Robert Bilder, PhD and colleagues established the Consortium for Neuropsychiatric Phenomics (CNP) as part of the NIH Roadmap Initiative's Interdisciplinary Research Consortium program (UL1DE019580 and 7 other linked awards including two center core projects). The CNP conducts research across different syndromes and species with a team of ~50 scientists, integrating contributions of disciplines including genomics, molecular and systems biology, basic and clinical neurosciences, psychometrics, and information sciences with the ultimate aim of providing frameworks for multi-scale mechanistic modeling of the myriad paths connecting genomic variation to complex syndromal phenotypes via intermediate biology. This approach will be adapted in the CTSI to advance understanding of the mechanistic bases of high risk behaviors, such as addiction, suicide, murder and reckless driving (motor vehicle accidents), that currently comprise such a prominent cause of morbidity and mortality among residents of Los Angeles County regardless of their ethnic and socioeconomic background. Dr. Bilder's group will be presenting work from the CNP at our next Translational Cluster Retreat.

6.1.1.2. Technology Transfer and Prototype Grants. In many instances, technology transfer responsibility and opportunity rest with the academic investigator's team and institution. Therefore, translating academic research into a potential clinical intervention usually requires creating a commercial entity that will generate funding for important steps in development such as animal toxicology and Phase I human clinical studies. Most academic investigators lack training in technology transfer and commercial interests required for this transition. As a result, many promising discoveries are not translated from bench to best clinical practices. To address a portion of this gap via the UCLA CTSI we are developing the following funding mechanisms.

The Technology Transfer Grants will serve as a mechanism to fund preclinical studies and Phase I trials. This grant program will provide one award per year in the amount of up to \$800,000 disbursed over three years. Most of these monies will be supported by research investment organizations and industry partners. Such grants can be applied in conjunction with the NIH-RAID Pilot (Rapid Access to Interventional Development) to make available, on a competitive basis, critical resources needed for the development of new small molecule therapeutic agents. Technology Transfer Grants can also be used in tandem with Small Business Innovation Research and Small business Technology Transfer Research grants to facilitate development from scientific investigations into final products for commercialization and application. Appropriate UCLA CTSI Office of Investigator Services components (e.g., Office of Industry Alliance; see **section 6.3.1 and Regulatory Knowledge and Support, Industry Relations and Research Ethics [Regulatory] Program**) will assist the PI with the application process.

Prototype Grants will be instituted initially on a small scale and later expanded depending on demand and results. Prototype Grants will supply up to \$50,000 to seed the development of a new clinical agent or device. Initially, two Prototype Grants will be funded per year. As with Technology Transfer Grants, we will be assisted

in the evaluation and funding for the grants by research investment organizations. UCLA has a history of successfully developing medical devices that hold promise for major advances. Notable examples include: 1) the nicotine patch, invented by UCLA addiction researchers Drs. Murray E. Jarvik and Jed Rose; 2) the Guillaume coil to treat aneurysms; 3) the MERCI Retriever clot removal device; 4) the Swan-Ganz catheter were all products of UCLA research.

6.1.1.3. Catalyst Grants. The UCLA CTSI is home to a diverse and vibrant faculty in life and physical sciences. In 2010 using local funding we initiated Catalyst Grants to create interaction opportunities between basic and clinical faculty to promote productive interdisciplinary collaborations. These catalyst grants led to our six disease cluster proposals described above in **section 6.1.1.1**. We envision that Catalyst Grants will stimulate new trans- and multi-disciplinary interactions. A number of different approaches will be considered for support under this program, ranging from lunch-time seminars to large, day-long symposia, all of which will include both UCLA CTSI investigators as well as outside faculty and community representatives. Beyond the traditional seminars and symposia platforms, CTSI will offer Catalyst Grants to encourage faculty to propose new programs to catalyze interdisciplinary interactions. For example, in 2010 we utilized catalyst funding to organize a Comparative Effectiveness Research Think Tank meeting, attended by 20 faculty. The result was assignment of a Research Facilitator (see **Regulatory Program**) and research project coordinator time and effort (see **Overview and Governance**) to promote collaborations and help in submission of grant applications based on those collaborations.

Examples of future Catalyst Grants projects include development of new translational courses, student-organized poster sessions, and joint industry-faculty meetings. Through a partnership with the UCLA Anderson School of Management, Catalyst Grants are also available to foster collaborations between MBA students and investigators who wish to develop a business plan for a start-up company (see **Regulatory Program**). These nascent partnerships can then apply for seed funding to procure preliminary data for full research applications. Specific invitations will be extended to community representatives and community practitioners to participate, identify community needs for research, and provide feedback to the academic community. The highest priority for this funding will be to facilitate transdisciplinary research across our partner institutions as well as collaborations with our CTSI colleagues at USC and UCI.

6.2. Specific Aim 2: Develop novel clinical and translational methodologies.

Emerging molecular insights and technologies promise to revolutionize the practice of clinical medicine. However, the existing barriers entrenched in the traditional academic system between clinical and basic researchers represent challenges to linking basic science to community-based research. Our Novel Translational Technologies and Methodologies (NTTM) Grants target this barrier with a strategy to foster the development of new technologies and methodologies, defined as any new research tool, technique or resource that has the potential of bridging critical gaps in the conduct of translational biomedical science. Examples of new clinical or translational methodologies include methods for producing more objective and quantifiable biomarkers for phenotyping; determining cost- or comparative effectiveness; research into clinical trial designs; clinical informatics for longitudinal studies; home-based research devices and methods; predictive toxicology in human populations and population-specific ethics research. This grant program will support the development of up to three promising new technologies and methodologies annually in the amount of up to \$100,000 each, renewable once on a competitive basis.

6.2.1. Infusing transdisciplinary team science into novel methods development. UCLA researchers have developed many clinical or translational methods that transformed biomedical science. Our breakthroughs include ■ development of limb-salvage techniques for cancer patients (Eilber) ■ invention of the PET scanner (Phelps) ■ co-discovery of the process behind ATP synthesis (Boyer) ■ discoveries about the roles of nitric oxide (Ignarro) and the ERBB2 oncogene (Slamon). Many of our outstanding achievements can be credited to the drive and determination of a handful of eminent individuals. However, as noted above (see section 4), the complexities of modern science require transdisciplinary teams and a culture of collaboration to support them. The CTSI provides a new opportunity to transform our approach and reach across institutions, schools, departments and disciplines to bring new thinking to emerging scientific challenges. In awarding our NTTM grants, we will give preference to transdisciplinary, community-focused teams with proposals that span the translational spectrum -- from design, through feasibility and pilot testing, to validation.

6.2.2. Our Wireless Health Institute (WHI) is a novel resource for development of clinical and translational technologies. We established our Wireless Health Institute in 2008 with support from Abraxis Bioscience, which is also committed to supporting our NTTM grant program (see below). The WHI unites innovators from computer science, engineering, business management, medicine, nursing, theatre, film and television to develop cutting-edge devices for health improvement and disease prevention. WHI Co-director Dr. Denise Aberle is an investigator in the CTSI **BIP** and WHI board member Dr. Arthur Toga is **BIP** Leader. Our CTSI will facilitate the formation of teams connecting the WHI and the community to ensure our inventions and discoveries are relevant to community needs. Novel projects in development at the WHI include: ■ remote blood pressure, glucose and weight monitoring systems ■ smart insoles for diabetics that sense when blood flow to the feet is compromised ■ smart glove tactile-recognition device for the blind, ■ wireless sensors for tracking mobility and exercise in stroke and cardiac patients ■ “video games for health” that combat obesity by requiring players dance, kick or run-in-place.

6.2.3. Our novel clinical and translational methods and technologies are focused on community application. With local funds in the pre-award period, we have been successful in facilitating research into new tools and approaches for clinical and translational work. We provide some examples below.

- Application of modern industrial engineering techniques to radiation therapy departments to provide a tested framework for reducing serious radiation therapy errors nationwide. (D. Low, P. Kupelian, M. Steinberg).
- Development of lens-free digital microscopy on a cell phone and demonstration of its use to image red blood cells, white blood cells, platelets and a waterborne parasite, *Giardia lamblia*. This device will provide cost-effective tools for telemedicine applications (A. Ozcan).
- Development of a new thin film Nitinol neurovascular stents to provide a superior, definitive treatment for neurovascular aneurysms and arteriovenous fistula in children. This device could dramatically reduce strokes in children with these conditions (D. Levi).
- Demonstration project guiding implementation of evidence-based behavioral treatments for HIV-negative methamphetamine-dependent gay/bisexual men to deliver HIV prevention in Los Angeles County in partnership with public health officials (S. Shoptaw).
- Work on development of networked, low-cost, remote physiological monitoring of first responders, including validation of fitness specifications for endurance, strength, cardiovascular and respiratory characteristics. The project recently received new support from the Department of Homeland Security, could dramatically improve incident command capabilities at all levels of a disaster response (C. Cooper).
- In collaboration with Healthy African-American Families, one of our UCLA CTSI community partners, developed a randomization method for community partnership research. The method provides community involvement in the creation of randomization tables and thus addresses concerns about bias often found in underrepresented communities (T. Belin).
- We completed preliminary work on adaptive clinical trial designs to improve the evaluation of drugs and medical devices and to use mixed methods to characterize and understand the beliefs, opinions, and concerns of key stakeholders during and after the development process. This collaborative research with the University of Michigan recently received new NIH support to design four innovative, adaptive clinical trials for the evaluation of drugs and devices for patients with acute neurological illness or injury. (R. Lewis).

This research is but a sampling of the diverse body of potential new research tools and methods we expect to develop within our CTSI and then share with the larger research community through the Greater Los Angeles CTSA Coalition and the National CTSA Consortium.

6.3. Specific Aim 3: Attract and enable the next generation of faculty to establish careers in team-based clinical-translational research through the UCLA Society of the CTSI.

6.3.1. UCLA Society of the CTSI: The UCLA Society of the CTSI will bring together promising young investigators with teams of interdisciplinary mentors focused on innovative clinical-translational research that will embrace paths linking the laboratory, clinic and community. It complements our Specialty Training and

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Advanced Research (STAR) Program and our other highly competitive research fellowships (see **CTSI-ED**). Members of the Society of the CTSI will be selected by our CTSI peer review committee. All earlier-phase faculty and post-doctoral fellows from our entire spectrum of Schools and partner institutions are eligible. CTSI Scholars will be awarded 1–3 year grants to develop and initiate translational projects. We have received institutional commitments to utilize the Stein-Oppenheimer Clinical-Translational Seed Grant Initiative to co-fund this program.

To ensure success, we will: a) establish formal mentoring relationships between teams of senior CTSI advisors and the Society's junior faculty members and postdoctoral fellows; b) evaluate the progress and outcomes of each CTSI advisor-fellow mentored relationship on a semi-annual basis; c) develop a new system of "think tank" groups of 8-12 investigators across four or more disciplines and research methods to develop multidimensional approaches health problems.

First time grant writers and others in need of coaching will take advantage of the Office of Investigator Services staff who will assist applicants through proposal development, expert referrals, collaboration advice and resources, regulatory approvals, education, and good practice; OIS Research Facilitators are chaperones who guide investigators through the pre-award stage to refine, with the help of specific key function Domain Experts (see **Regulatory Program**), such things as their proposal's design (e.g., Biostatistics Domain Expert) and general resource requirements (e.g., Technology Officers, CCRR staff). The OIS is maintained by the Regulatory Program. In addition the OIS will inform UCLA Society of CTSI Scholars of funding opportunities. They will also guide Scholars to the information available through the OIS and the Virtual Home regarding all CTSI-sponsored research training, continuing education and translational research programs, including community-based opportunities.

Through these OIS mechanisms, a basic scientist working in nanotechnology and interested in developing nanoparticles for cancer drug delivery might be brought into the program to facilitate the work of translational investigators in pre-clinical studies in animal models to test feasibility and evaluate effectiveness in tumor models. Or, a public health scientist could work with a community partner to study the implementation of evidence based practices for care of chronic conditions in clinic based settings.

6.3.2. Our Institutional Support and Matching Program. We will leverage each dollar of CTSI investment with a dollar or more from non-NIH sources including institutional, industry and donor funds, to fund our transformative Translational Research Grant Program, our NTTM Grants and our CTSI Scholar program.

As noted above (see **section 5**), we have been successful in directing institutional funds to support clinical and translational science. Based on this success, we plan to continue to utilize Stein Oppenheimer funds to leverage CTSA funds. In addition, institutional funds have been pledged from the UCLA Chancellor's Office and our partnering programs at UCLA-Westwood, Cedars-Sinai, Harbor-LA BioMed, and Charles Drew University (CDU).

We plan to leverage existing disease-specific seed grant programs including those administered by the Jonsson Comprehensive Cancer Center (JCCC), the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research, the UCLA AIDS Institute, and institutional programs at LABioMed and Cedars-Sinai. We will also leverage funding from two entities focused on translational research: the UCLA Institute for Molecular Medicine (IMED) and the Joint Center for Translational Medicine (JCTM), a collaboration between UCLA and Caltech. To ensure a smooth transition we have added the directors of each of these programs to the leadership team of the UCLA CTSI Pilot Program: Drs. Gasson (JCCC), Witte (Broad Center, JCTM), Chen (AIDS Institute), Wu (IMED), Meyer (LA BioMed) and Fine (Cedars-Sinai). Each of these program directors has agreed to participate in our peer review parent committee and will help select ad-hoc reviewers for the CTSI funding mechanisms.

We have been successful in our fundraising from private donors as well as from industry (see below). For the Technology Transfer and Prototype Grants, 50% of the required funds will be raised from our venture capital partners, 40% from donors and institutional sources, and 10% from the CTSI grant.

6.3.3. Our CTSI has established a broad-based partnership with a major local biotechnology company and CEO. Abraxis BioScience, Inc. is a fully integrated biotechnology company with headquarters minutes from the Westwood campus. The major stockholder and CEO of Abraxis, Dr. Patrick Soon-Shiong, is a former UCLA School of Medicine faculty member in Surgery with a keen interest in forging industry collaborations with

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UCLA. Soon-Shiong has initiated a \$12 million, 10-year partnership with the UCLA California NanoSystems Institute (CNSI) to fund basic research. The CNSI is a campus-wide interdisciplinary collaboration among the Schools of Engineering and Medicine and the College. Soon-Shiong has built a 4,000-square-foot laboratory within the CNSI and for the past two years they have been funding collaborative projects that are carried out jointly by scientists at UCLA and Abraxis, which has recently been acquired by Celgene. All of the intellectual property will belong to UCLA.

Soon-Shiong has recently committed an additional \$2.5 million over the next 5 years to expand his research program in the CNSI to target clinical-translational research projects. His interest with UCLA involves an even larger program of collaborative translational research focused on wireless health, electronic health record technologies, and their applications for clinical innovation. Last year Soon-Shiong pledged over \$200 million for a broadly based translational science initiative that included support for the UCLA Wireless Health Institute (WHI). The institute leads in the development of cutting-edge wireless solutions, including personal communication and monitoring devices, wireless wearable sensors, and a variety of other innovative technologies, for a wide array of health care-related applications. Soon-Shiong's strong involvement and pledge is one of the key elements of the institutional commitment devoted to Technology Transfer, Catalyst, and NTTM Grants.

In addition, our CTSI has received letters of interest from other UCLA corporate collaborators, including medical technology innovators Siemens, General Electric and Intel. Biotechnology companies expressing interest in furthering their collaborations with us through the UCLA CTSI include NovaDigm Therapeutics, a North Dakota-based biotechnology company developing vaccines based on UCLA discoveries; Momentum Biosciences of Los Angeles, a provider of support and laboratory space to UCLA biomedical spinout companies; Kite Therapeutics, a Los Angeles-based developer of cancer immunotherapies; Calimmune of Tucson, Ariz., a developer of stem cell therapies for AIDS; and Azusa, California-based MEDomics, a medical diagnostics company (see **Institutional Letters**).

6.3.4. Application, Review, and Selection Metrics. Information and applications for each of our CTSI grant opportunities can be found on the CTSI Virtual Home. Applications may be submitted online. The UCLA CTSI Grants Review Committee is composed of the Pilot Program Leader and Co-leaders, the CTSI Director, or a representative, a Technology Assessment Officer from **CTT** and a representative from each of the CTSI partner institutions.

One of the principal goals of our CTSI is the development of a unique national resource for clinical and translational research producing high-quality, cost-effective outcomes with an emphasis on community involvement and impact. We will have community representatives on the Grants Review Committee for Translational Research Cluster Grants and the other non-technology-driven programs.

The Grants Review Committee will have the authority to identify either internal or external ad hoc reviewers when specialized subject matter expertise is needed or if there is a potential conflict of interest in the review process. These individuals will be mid-career or senior investigators with expertise across the translational spectrum. We have assembled a diverse pool of 60 faculty volunteers with experience as grant reviewers to serve as ad hoc reviewers. By utilizing an interdisciplinary committee, the review process itself will broaden our translational perspective and may lead to additional collaborations. The CTSI Grants Review Committee will function as an Integrated Review Group (Study Section) in the NIH. Criteria for grant review will include the following: a) track record of investigators and the potential for future success in research; b) the spectrum of transdisciplinary members on the team; c) soundness of the approach, methodology, regulatory compliance, and plans for data analysis; d) time line for results and potential of delivery into a clinical application (therapy, device, prevention application, intervention); e) potential to impact patient care and responsiveness to the needs of the community; f) potential of the proposed research to positively impact health.

The review of Technology Transfer and Prototype Grants will be made by a subgroup of the Grants Review Committee. This subgroup, the Technology Transfer Review Group, will be composed of faculty from within and outside the committee with experience in technology transfer and industry interactions and with expertise in T1 to T2 research. It will be chaired by Dr. Kathryn Atchison, the UCLA Vice-Provost of Intellectual Property and Industry Relations and CTSI **Regulatory Program** Co-Leader and will interface with our venture capital partners to identify technologies with the greatest likelihood of adoption in clinical practice. Finally, the review and selection of the NTTM Awards will be coordinated by the Grants Review Committee and the ad hoc

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reviewers required to consider funding of concepts for novel technologies and methods. This group will evaluate the scientific underpinnings of each candidate technology or methodology, including potential limitations and alternatives. From a more pragmatic angle, this group will weigh the candidate technology's potential impact on the translational research.

The membership of the CTSI Grants Review Committee will make funding recommendations to the Pilot Program Steering Committee, which after review of the recommendations will forward these to the UCLA CTSI Executive Oversight Committee (EOC). The UCLA CTSI EOC will have the final authority in issuing grant awards. In coordination with CTSI administrative staff, the UCLA CTSI Pilot Program Co-Leaders will issue grant announcements, monitor receipt of grant applications at the CTSI Virtual Home, assign applications to the Grants Review Committee, collate priority scores from the review committee, and make funding recommendations. The Office of the Institute (see **Overview and Governance**) will have direct oversight over the grants application, selection, funding, and evaluation processes.

Progress Reports. At the end of the first grant year, PIs will be required to submit a progress report (3-page) in NIH progress report and abstract format, reprints of any publications, and manuscripts of research supported in whole or in part by the CTSI. Final scientific reports are submitted within 60 days of the grant termination date and report of expenditures within 90 days, together with a refund of any unexpended balance. Seed grant PIs will be required to attend and present a poster or an oral presentation at the CTSI Annual Research Retreat (see **Overview and Governance**). The reports will be reviewed by the Pilot Program Leader and Co-Leaders.

6.4. Specific Aim 4: Using a multidimensional recruitment strategy, recruit 30 new CTSI translational research faculty over the next five years to ensure that the UCLA CTSI fulfills its academic research and teaching mission.

6.4.1. New faculty recruitment to UCLA CTSI. The **Pilot Program** goal is to support the development of emerging leaders who will carry out interdisciplinary collaborations and develop emerging studies in translational and clinical research. An important strategy of the program is to direct and support the recruitment of additional promising translational scientists who will serve as catalysts for transdisciplinary collaborations within the UCLA CTSI. Here, we describe an aggressive interdisciplinary, inter-institutional initiative to recruit 30 additional full time faculty positions (FTEs) at UCLA over the next 5 years.

These 30 new positions will be for the recruitment of the most promising clinical translational faculty, and will be supported by institutional FTEs, release time, and resources that address traditional barriers to career success. These positions will be recruited in a multidimensional fashion, in collaboration between the UCLA CTSI Pilot Program Steering Committee and individual Organized Research Units (ORUs) co-sponsoring the position (see below). The faculty will be responsible, in a matrix fashion, to the Director of the UCLA CTSI (S. Dubinett) and the leadership of the co-sponsoring ORU.

A number of faculty positions have already been identified for this Aim. These include two unfilled FTEs co-sponsored by the newly established Institute for Molecular Medicine (IMED), under the co-direction of the CTSI PI (S. Dubinett) and Dr. Michael Phelps; two unfilled FTEs co-sponsored by the recently established Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research; four unfilled FTEs co-sponsored by the California NanoSystems Institute (CNSI), coordinated by Dr. Paul Weiss, CNSI Director; and one FTE committed by the UCLA Jonsson Comprehensive Cancer Center.

Vice Chancellor of Health Sciences and Dean of DGSOM, A. Eugene Washington, with the complete support of UCLA Chancellor Gene Block, has authorized \$12 million for new faculty over the next five years. These new UCLA CTSI faculty will be integrated into the interdisciplinary career development mechanisms. To ensure the success of this strategic recruitment initiative, we will: a) develop a CTSI recruitment-advisory committee to include one representative from each participating CTSI institution, an equal number of representatives from health and non-health UCLA Schools, and the DGSOM Associate Dean for Academic Diversity Dr. Lynn K. Gordon; b) establish multi-discipline recruitment search committees in collaboration with department-based recruitment of faculty for CTSI-supported FTEs. Examples of outstanding faculty recently recruited to UCLA include Dr. Donald Kohn, Director of the UCLA Human Gene Medicine Program and an expert in pediatric hematopoietic stem cell transplantation; Dr. James Byrne, Assistant Professor in the Department of Molecular and Medical Pharmacology and a specialist in the mechanisms of cell reprogramming; Dr. Jay M. Lee, Surgical

Director of the Thoracic Oncology Program, and Dr. Heather Christofk, Assistant Professor in the Institute of Molecular Medicine and specialist in cancer metabolism.

6.4.2. The UCLA/CDU Faculty Innovation Program. The UCLA CTSI is committed to enhancing its collaborative relationship with its partner CDU and to assisting in creating the requisite environment to enhance faculty recruitments, faculty scientific career development, and creating a culture of the highest level of scholarship within a framework of dedication to cultural diversity. The County of Los Angeles has recently committed over \$350 million to re-open the Martin Luther King Jr. Hospital with support from the University of California Regents. The need for collaborative academic support from UCLA and CDU will be critical to transforming the health of South Los Angeles. The UCLA/CDU Faculty Innovation Program will serve to increase the CTSI interdisciplinary translational research capacity at CDU in anticipation of the new MLK medical campus. The program identifies mentors from existing UCLA faculty for joint appointments at CDU. We have established a streamlined mechanism for a dual appointment at CDU (accepting the existing UCLA appointments package with a one page statement as to why one wants to be a CDU faculty) and an inter-institutional compensation agreement allowing UCLA faculty to retain existing benefits.

To further support this goal the UCLA CTSI proposes to help fund the recruitment of new CDU faculty who will be focused on translational sciences by providing three \$100,000 UCLA/CDU Faculty Innovation awards each year. These funds will be supplemented by additional institutional recruitment funding.

6.4.3. Recruitment and Retention of Faculty from Disadvantaged Backgrounds: An indispensable element of UCLA academic excellence is achieving and sustaining faculty diversity as evidenced by the recent appointment of a new Associate Dean, Dr. Lynn Gordon, to direct the Academic Diversity Program. In conjunction with efforts outlined in the both CTSI-ED and CCRR, the UCLA CTSI is working closely with Dr. Gordon to model recruitment efforts that have been successful in other programs. For example, Drs. Michael Rodriguez and William Cunningham have implemented multi-modality mentoring programs for junior faculty from underrepresented groups in the CDU/UCLA/RAND Project EXPORT in conjunction with UCLA's NIA-funded Resource Centers for Minority Aging Research (RCMAR) project.

Other examples demonstrate attention to faculty diversity in a broader and long term framework. The National Library of Medicine (NLM) has partnered with the Charles R. Drew University of Medicine and Science to develop a program of topics of interest to high school students considering careers in the health sciences. Presentations are made to students at the King Drew Medical Magnet High School, an affiliate of the university devoted to preparing minority high school students for health careers. Some presentations are local, while others are by videoconference from NLM. Selected presentations are archived, along with the material presented. Several of our CTSI faculty are participating in these presentations including Dr. Richard Baker whose presentation was entitled, "Careers in Medicine." Similarly, the UCLA CTSI is forming a collaboration with the Health Services Academy (HSA) High School located in one of the most under-resourced areas of Los Angeles (letter enclosed from Principal Erik Elward). This high school employs the theme of health care to provide students with rigorous college-preparatory instruction and application-based curriculums to help ensure that they are better prepared to excel in high school and to enter and succeed in college. Student demographics reflect the South Los Angeles community: 56% Latino and 44% African-American. UCLA CTSI faculty will be making presentations to HSA High School students and summer internships are being planned at all partner institutions. Expanding and maintaining diversity in clinical and translational research faculty is a critical aspect of addressing the continuing problem of health disparities in the US.

7. INVESTIGATORS

The **Pilot Program** is led by a team of senior investigators with extensive experience in the development of interdisciplinary translational research programs.

Leonard Rome, PhD, (Program Leader) is Senior Associate Dean of Research, David Geffen School of Medicine (DGSOM) and Associate Director, UCLA CNSI. Dr. Rome's research and scientific leadership centers on interdisciplinary biology of nanoparticles.

Richard Baker, MD, (Program Co-Leader) is Dean of the College of Medicine at CDU, and former Associate Vice President for Research, and Executive Director and co-founder of the CDU Urban Telemedicine Center of Excellence. Dr. Baker is also Associate Professor at the Jules Stein Eye Institute at the DGSOM.

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Timothy Deming, PhD, (Program Co-Leader) is Professor and Chair of the Bioengineering Department, School of Engineering, and Professor of Chemistry and Biochemistry at UCLA

Irvin Chen, PhD, (Program Co-Leader) is Professor of Microbiology, Immunology, and Molecular Genetics and the founding director of the UCLA AIDS Institute since its inception in 1991. He also served as the head of the multi-million dollar UCLA Center for AIDS Research (CFAR), National Institutes of Health infrastructure program for 16 years

Leon Fine, MD, (Program Co-Leader) is Professor of Medicine, Professor and Chair of the Department of Biomedical Sciences, and Director of Graduate Research Education at Cedars-Sinai.

Judith Gasson, PhD, (Program Co-Leader) is Professor of Medicine and Director of the Jonsson Comprehensive Cancer Center (JCCC) at DGSOM. As JCCC Director for the past 11 years, she has overseen the investment of over \$64 million in philanthropic funds for faculty recruitment, retention, discovery research, and shared resources.

Michael Irwin, MD, (Program Co-Leader) is a Professor of Psychiatry and Biobehavioral Sciences at the UCLA David Geffen School of Medicine and director of both the UCLA Cousins Center in Psychoneuroimmunology and the Inflammatory Biology Core of the Older Adults for Independence Center.

David I. Meyer, PhD, (Program Co-Leader) is president and chief executive officer of LA BioMed and former Senior Associate Dean at the David Geffen School of Medicine at UCLA.

Paul S. Weiss, PhD, (Program Co-Leader) is Professor of Chemistry and Biochemistry in the UCLA College of Letters and Science and Director of the California NanoSystems Institute at UCLA.

Dorothy Wiley, PhD, RN, (Program Co-Leader) is Associate Professor in the UCLA School of Nursing with a focus on Public Health Nursing and Community Health Nursing, essential to the success of the UCLA CTSI.

Owen Witte, MD, (Program Co-Leader) a member of the National Academy of Sciences, is Professor of Microbiology, Immunology, and Molecular Genetics and Founding Director of the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research.

Hong Wu, MD, PhD, (Program Co-Leader) is a UCLA Professor of Molecular and Medical Pharmacology and Associate Director of the Institute of Molecular Medicine.

These individuals comprise the UCLA CTSI Pilot Program Steering Committee. This Committee will meet monthly, and minutes will be maintained, and reviewed and approved at the subsequent meeting. They also comprise the Parent Grant Review Committee. They are responsible for reviewing grant proposals, appointing appropriate ad hoc reviewers from our pool of 60 well-qualified faculty volunteers, and recruiting new clinical and translational faculty for participation in collaborative projects. The Pilot Program Steering Committee will report to the UCLA CTSI EOC, the key oversight committee of the CTSI.

8. INTEGRATION OF UCLA CTSI KEY FUNCTIONS

The activities of Pilot Program are tightly integrated with other core programs of the UCLA CTSI. **CERP** participates in reviews of non-technical grants; **CCRR** provides shared oversight of grants involving clinical studies; **CTT** participates in grant reviews and nurtures development of new technologies; **Regulatory Program** oversees the OIS and OIA and participates in selection of Technology Transfer and Prototype Grants; **CTSI-ED** mentors UCLA Society of the CTSI Scholars; **BIP** maintains the Virtual Home and enables online grant applications.

9. EXTRA-UCLA COLLABORATIONS

Our CTSI is a member of the West Coast CTSA Consortium and the Greater Los Angeles CTSA Coalition. We have close relationships Greater Los Angeles CTSA Coalition partners, USC and UCI. For example, John Brekke, co-director of our Mental Health Translational Research Cluster, is also Associate Dean of Research at the USC School of Social Work and co-directs the Office of Community Engagement of the USC CTSI. Many of our awardees have CTSA collaborations. For example, Dr. Ong (see **section 5**) collaborates with investigators at four CTSA institutions: UCI, UC Davis, UC San Diego and UC San Francisco.

10. IMPLEMENTATION PLAN

Evaluation of success will be measured by publication rates, extramural funding for each project's specific aims, and impact on clinical practices, building on evaluation processes of DGSOM and JCCC. Annual progress reports, required from all funded projects, will be based on the NIH e-SNAP format.

Table 2. CTSI Pilot Studies Program Implementation Plan

Year(s)	Milestones and Key Activities	Evaluation/Tracking (E/T)
Aim 1. Advance transformative collaborative translational research through broad-ranging funding mechanisms		
1	<ul style="list-style-type: none"> Establish CTSI Grants Review Committee with community representatives participating in the review process 	<ul style="list-style-type: none"> Membership/Committee charge established
1-2	<ul style="list-style-type: none"> Develop on-line E-Grant application system 	<ul style="list-style-type: none"> Completion of on-line application system design
1-5	<ul style="list-style-type: none"> Create rigorous review and reporting processes/metrics Develop and implement new Grants Programs Translational Research Cluster Grants Catalyst Grants New Technology Transfer and Prototype Grants Develop new funding streams 	<ul style="list-style-type: none"> Design/refine criteria and metrics and integrate into on-line system Formative evaluation to improve programs Annual funding reports Annual progress report on each funded project Number and \$ amt of new funding sources
Aim 2. Develop novel clinical and translational technologies and methodologies		
1-5	<ul style="list-style-type: none"> Establish and conduct the Novel Translational Technologies and Methodologies Grants 	<ul style="list-style-type: none"> Annual funding reports; Annual progress reports
Aim 3. Attract and enable the next generation of faculty to establish careers in team-based clinical-translational research through the Society of the CTSI		
1	<ul style="list-style-type: none"> Establish CTSI Peer Review Committee Establish CTSI Society bylaws and procedures Form a network of senior CTSI faculty advisors 	<ul style="list-style-type: none"> Membership/Charge Semi-annual assessment of mentor/advisor relations (CTSI-ED web)
1-5	<ul style="list-style-type: none"> Establish formal mentoring relationships Conduct annual CTSI scientific meeting Initiate and activate think-tank program Implement peer mentoring via electronic networking Evaluate progress and outcomes of advisor-fellow mentored relationship on a semi-annual basis (See ET, elsewhere in this application) 	<ul style="list-style-type: none"> Think tank research agendas Number of pilot, RO1 grants funded Number of peer-reviewed publications Number of peer-reviewed publications
Aim 4. Using a multidimensional recruitment strategy, recruit at least 30 new CTSI translational research faculty over the next five years to ensure that the UCLA CTSI fulfills its academic research and teaching mission		
1-5	<ul style="list-style-type: none"> Recruit approximately 6 new faculty members per year based on strategic plan to build translational science capability 	<ul style="list-style-type: none"> Number and type of new faculty Number of minority faculty recruited
1	<ul style="list-style-type: none"> Develop faculty recruitment advisory committee with representation from each CTSI partner institution and equal numbers of health/non-health schools 	<ul style="list-style-type: none"> Annual search yield
1-5	<ul style="list-style-type: none"> Establish transdisciplinary search committees to recruit new faculty 	

ILSGP: CDU Integrated Life Sciences Graduate Program; TITG: Transformation & Innovation Think Group; CTSI-ED Web: web-based database and program management system is described in Education, Training, and Career Development Program, elsewhere in this application.

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Biomedical Informatics Program (BIP)



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Abbreviations: ADT – Admission, discharge and transfer, BIP – UCLA CTSI Biomedical Informatics Program, BTRIS – Biomedical Translational Research Information System, CENS – UCLA Center for Embedded Networked Sensing, CRF – Case report form, CTMS – Clinical Trials Management System, CTS – Common Terminology Service, CTS – Common Terminology Service, DGSOM – David Geffen School of Medicine, EAB – UCLA CTSI External Advisory Board, EOC – UCLA CTSI Executive Oversight Committee, FDB – Faculty Database, FISMA – Federal Information Security Management Security Act, i² – Institute for Informatics, IT – information technology, NLM – National Library of Medicine, PHI – Private health information, RAP – Research Action Planner, RDR – Research Data Repository, SPIRiT – sharing Partnership for Innovative Research in Translation, SSO – Single Sign-On

1. OVERVIEW

The UCLA CTSI Biomedical Informatics Program (BIP) seeks to integrate informatics throughout the translational research lifecycle. BIP prepares current and future CTSI investigators to optimize novel informatics tools to transform their studies. The BIP is managed and implemented through the new Institute for Informatics (i²), which UCLA created in recognition of the critical role for bioinformatics and Information Technology (IT) in advancing translational science. Significant investments in personnel, space, and equipment have been made for the institute.

In this proposal we have preserved the significant strengths of BIP recognized in the prior review, and we have addressed each of the concerns raised. Related to the Virtual Home, the reviewers noted it was *“unclear whether [we] have evaluated tools that have been developed at other CTSA.”* We are actively adopting several CTSA shared tools including i2b2 (Harvard University), REDCap (Vanderbilt University), RDS (University of Pittsburgh), and TIES (University of Pittsburgh). We plan to continue adding other CTSA-derived tools to our program (refer to **sections 5.** and **6.2.4.**). Another weakness was that *“description of the hardware, software, and networking measures to ensure data security is missing.”* The current proposal now describes how the Virtual Home and the Research Data Repository (RDR)-related systems will adhere to strict data security measures, at levels prescribed by the Federal Information Management Security Act (FISMA), including hardware and software policies, access controls, training, and documentation.

Related to the RDR, the panel noted the *“description of the federated Research Data Repository lacks detail... it is uncertain if the repository will contain identified or de-identified data... harmonization of models and data elements is not described.”* The RDR is presented in greater operational and logistic detail including how de-identification and private health information (PHI) issues will be managed (refer to **section 6.2.**).

Another weakness cited by the reviewers was *“clinical data collection and trials software are not described in detail, and it is unclear what systems are currently in place in each institution or how investigators will effectively access these resources.”* This concern has been addressed through our description of the Velos eResearch system, which now serves as our Clinical Research Management System. In addition, we are currently planning the linkage of clinical trial drug administration from the Investigational Pharmacy to data entry and validation in Velos (**sections 5.** and **6.2.3.**).

A criteria-specific concern was that *“There is no mention of how this CTSI will interact with other CTSA.”* To address inter-CTSA collaboration and communication, we have joined the **Sharing Partnership for Innovative Research in Translation (SPIRiT)**, the CTSA program’s first virtual consortium focused on data sharing (see **Institutional Letters**). In addition, we are also partners in the CTSA West Coast Consortium and Greater Los Angeles CTSA Coalition for regional activities. We have consulted with leading experts in the other CTSA informatics groups. Finally, related to Investigators, a concern was that *“details about steering committee and working group meetings are not provided.”* **Section 6** has been expanded to clarify governance of the BIP and the operation of its workgroups.

Please note that this section has been completely rewritten from its previous iteration. Hence, we are not marking changes in the document.

2. SPECIFIC AIMS

To fulfill our mission, BIP will pursue three specific aims, incorporating what has been learned from other CTSA programs.¹ We leverage biomedical informatics and information technology (IT) that are CTSI-wide in scope:

Specific Aim 1: Virtual Home. Expand and amplify our established internet portal that facilitates communication across the entire CTSI community and directs members of all CTSI user groups to the resources and expertise they need.

Specific Aim 2: Research Data Repository. Establish an RDR that provides secure access to de-identified clinical data from all CTSI partners for appropriate secondary uses;² a Common Terminology Service (CTS) to support data harmonization and interoperability, a Clinical Trials Management System (CTMS) to amplify the conduct of community-based clinical trials, and other research data services, including a biospecimen repository.

Specific Aim 3: Education and Training. Along with the **Research Education, Training and Career**

Development Program and Office of Investigator Services (OIS; **Regulatory Program**) train clinical and translational researchers and new biomedical informaticians from diverse basic science and clinical perspectives to effectively use informatics tools and methodologies to enhance innovation throughout the translational research lifecycle.

3. PROGRESS TO DATE

We have been staffed and supported by institutional funds over the past four years. The program's evolution has been guided by feedback from CTSI investigators, community partners, external experts, and national leaders in biomedical informatics and translational medicine. Specifically, we sought out consultants who direct programs associated with their respective institutions' CTSA: Michael J. Becich, MD, PhD (University of Pittsburgh); Clay Johnston, MD, PhD (University of California, San Francisco); Daniel Masys, MD (Vanderbilt University); and William Yasnoff, MD, PhD (National Health Information Infrastructure Advisors).

Here we summarize several significant accomplishments in informatics and IT as well as governance:

- **Enhancing Collaboration (Research Networking)**: We established central components of the CTSI Virtual Home and its toolkit of research IT resources and services.
- **Research Data Repository**: We are continuing development of an i2b2 prototype implementation to meet UCLA CTSI needs in discovery research functionalities and study subject identification.
- **Clinical Research Management Systems**: We conducted visioning sessions to review clinical trial data workflow and to prioritize functionality roll-out for our clinical trials management system, Velos eResearch, that was initially installed 2 years ago as a pilot at the UCLA Jonsson Comprehensive Cancer Center (JCCC). Patient tracking, regulatory management, and financial management were implemented in 2009. We are now assessing the linkage of clinical trial drug administration from the Investigational Pharmacy to data entry and validation in Velos. The Velos system currently has 175 users and supports 1,444 clinical trial protocols. As part of our RDR effort, the Velos System will be expanded across numerous departments and community partner institutions with integration efforts with REDCap, our electronic medical records (EMR) system, and our Tissue and Serum Banking Systems.
- **Tissue and Serum Banking Systems**: We are evaluating the Daedalus Biomaterial Tracking and Management system (caBIG compliant), purchased by UCLA in 2008. We have migrated four existing tissue banks into the system, with another three scheduled for transfer this year (2010). This UCLA-led work collaborating with University of Washington and Baylor College of Medicine was presented at the 2010 caBIG Annual Meeting.⁵ Daedalus has 15 core and 200 general-access users and manages over 30,000 specimens from 8,000 patients. Twenty-five tissue and serum collection protocols are already managed by this system.
- **Electronic Medical Record**: We had substantial participation in the just-launched installation-and-deployment process for Epic, the new integrated electronic medical record system selected by UCLA Health Care to serve as the core clinical information system across the Health Sciences. In close collaboration with CTSI health services researchers and experts in compilation and integration of large data sets, we are working closely with Epic system technicians and medical center IT staff to shape the research-relevant design and functionalities of Epic to meet the technical requirements of the Research Data Repository and related tools.
- **Regulatory Knowledge and Support**: In January 2010, UCLA launched webIRB (see **Regulatory Program**), its new online IRB application system. The system is an implementation of Click Commerce, a popular research management system. According to the vendor, UCLA has gone farther than any institution in creating structured fields and interactive guidance for investigators. As of Oct. 1, 2010, the use of webIRB is required for all new IRB applications and continuing reviews. Thus, by June 2011 and the beginning of year-01 of funding, all of the more than 4,000 active studies overseen by UCLA's IRB will be live on the system. UCLA is also participating with the University of California (UC) Office of the President in setting up a system, slated to go live in early 2011, that will streamline IRB review for studies involving more than one of the five UC medical centers.
- **CTSA Collaboration in Informatics**: We have established a partnership with the University of Pittsburgh-led SPIRiT "virtual consortium," which is focused on research networking, resource discovery, biospecimens,

and data sharing (see Letter of Support from Dr. Becich), which are all significant strengths of the UCLA CTSI partners. Dr. Becich has visited with us at UCLA to review our program and Dr. Toga has recently visited the Pittsburgh CTSA. Through this partnership, we will be well-positioned to serve as a major contributor to CTSA Strategic Goal 3: Enhancing Consortium-Wide Collaborations.⁶

- **CTSI Governance of Informatics and IT:** We have reduced the organizational and (inter-)institutional barriers related to governance of our data and other research support systems by convening the research IT leaders and stakeholders across the CTSI partner institutions (foremost, Chief Information Officers and heads of IRBs) to reach consensus on and mutual commitment to research data sharing policies and technical procedures for the RDR and IRB reciprocity and regulatory affairs alignment across the four partner institutions (see **Letters of Support**). Meetings are ongoing to achieve these goals.

To keep current with emerging trends in biomedical informatics and innovations in research IT tools, and to benchmark our own progress, we actively monitor the activities of the Biomedical Translational Research Information System (BTRIS) and the National CTSA Consortium in the arena of biomedical and clinical research informatics, particularly the CTSA Informatics Key Function Committee and its work on best practices for interoperability while ensuring privacy and confidentiality protections for human participants. We are positioning UCLA to make major contributions to the CTSA Strategic Goals. As detailed in this revised application, we have evaluated new software developed within the CTSA Consortium (i2b2, REDCap, RDS, and TIES) and have incorporated select components within the BIP toolkit of our Virtual Home (**section 6.1.**). Our progress in the last four years supports our potential to make significant contributions to the CTSA program.

4. SIGNIFICANCE

Informatics is key to the NIH Roadmap.^{3,4} Through informatics, the CTSI will achieve advances in the understanding of disease and its translation to improvements in health. Nationally, health care reform includes a massive investment in electronic medical records, which the CTSA Consortium is tasked to involve in clinical research. Online social networking and research resource inventories have likewise become important tools in connecting clinical and translational researchers with people and resources essential to their work. With this national agenda in mind, the UCLA BIP focuses on deploying an interoperable research data repository (RDR) and use the UCLA CTSI Virtual Home to promote the sharing of data, expertise, and resources across the UCLA network of sites, the Greater Los Angeles CTSA Coalition and the National CTSA consortium.

5. INNOVATION AND ENVIRONMENT

An important development to accelerate our transformational goals is the creation of the new **UCLA Institute for Informatics (i²)**. As BIP's home, i² demonstrates UCLA's commitment to informatics and translational science and the campus-wide leadership role of BIP and the CTSI. As Associate Vice Provost for Informatics at UCLA and the founding Director of i², BIP Chair Arthur Toga is overseeing the planning for new and renovated existing space on campus for this new core facility. Such support for a "concrete" i² versus the prevailing trend toward "virtual" informatics centers represents a bold step forward by UCLA. i² is strategically located adjacent to the Medical Campus (which includes the Ronald Reagan UCLA Medical Center) and the Court of Sciences, amidst the disciplines that comprise key contributors to the development and application of informatics methodologies to translational research: Medicine, Public Health, Mathematics, Biostatistics, Computer and Information Sciences, and Life and Physical Sciences. Scheduled for occupancy in late 2011, the carefully engineered environment of 2,961 square feet will encourage collaborative interactions, with a robust information infrastructure for biomedical informatics, collaborative workspace and offices, and open access to advanced computational resources, software and videoconferencing tools to facilitate inter-institutional partnerships such as the CTSI. Informatics research and research training at i² will include advanced computation, mathematical and statistical analysis, algorithmic development, and data mining. The first and highest priority of i² is the development and maintenance of resources required for the UCLA CTSI.

Applied Informatics to Create, Transform, and Deliver New Biomedical Knowledge: i² will provide CTSI scientists access to the computational infrastructure needed to transform vast quantities of biomedical and clinical data into testable hypotheses, resulting in new knowledge from data mining and secondary analyses. Examples include the role of cultural and environmental factors in predicting responses to Alzheimer's disease therapies as confirmed by positron emission tomography (PET) image data, the mapping of patient data and

geosocial data on local government services, or the mapping of patient data to environmental data collected from wide-area sensor networks. Conducting such complex analyses on a large scale with data drawn from distributed archives requires extensive computational and storage resources. The necessary, dedicated, networked computational infrastructure for these types of studies already exists at the new i^2 and will be expanded to meet the growing computational needs of CTSI scientists.

Promotion of Informatics in Biomedicine as a Discovery Science: i^2 will be a leader in generating new informatics resources for and approaches to biomedical and basic science research. Informatics techniques for mining data and creating and applying novel computational algorithms, information theory, and visualization approaches will enable CTSI researchers to better understand their data, including its full translational implications and potential.

Curation, Storage, and Preservation through Innovative Research IT for Decades-long Access to Primary Data: Storage of de-identified digital biomedical information, as raw and processed data, in secure databases is critical to data tracking, applying evolving algorithms to archival data, and examining historical trends in biomedical research. Often, especially in pathology studies, an archived image set is the only existing record of an individual's anatomy. i^2 has been designed to accommodate decades-long curation, availability, and storage of primary research data and to support redundant offsite storage and rapid disaster recovery.

6. APPROACH

The BIP infrastructure for developing, disseminating, and deploying innovative informatics and IT tools will enhance all phases of the research lifecycle. The partners of the UCLA CTSI each have information systems at different stages of maturity, and each system is a product of distinct organizational priorities. Our major challenge will be to leverage these existing systems and add value and cohesion such that CTSI researchers can interact with them as if they constituted one seamless system. We will also fill gaps in information systems across the CTSI either by creating new CTSI-wide systems or by collaborating with each partner to establish reliable bridges across institutional systems. To meet this challenge of system unification and interoperability, we will provide software tools to the CTSI, accessible through a single website called the CTSI Virtual Home.

To illustrate how each part of the BIP is being developed to work synergistically to support the needs of researchers, we provide the following step-by-step scenario:

- Data mining tools running in the RDR discover that African American women with diabetes progress at a high rate from benign breast biopsies to malignant cancer. The possibility that tumor biology may vary by race and diabetes status invokes the interest of investigators in the Breast Cancer Translational Research Cluster (see **Pilot and Collaborative Research Program**). Through the CTSI Virtual Home, they identify potential collaborative investigators within the Diabetes and Obesity Cluster.
- A multisite collaborative pilot proposal is generated to look at molecular markers and host factors in older African American breast cancer patients with diabetes. A preliminary (de-identified) cohort is selected via a query of the RDR. This demonstrates the need for a larger sample size to test the questions at hand, so an expanded cohort identification query is undertaken in collaboration with other CTSA sites. Further discussions with these new collaborators identifies an ongoing study called the Athena Breast Network (a cross-UC study) having substantial overlap with the cohort of interest and a registry of blood and saliva available for analysis. An application is submitted to the Athena Breast Network and the UCLA IRB for access to de-identified data with linked serum and saliva samples.
- The pilot study identifies molecular targets and host factors worthy of clinical investigation. Translational researchers design a clinical trial examining a novel therapeutic agent that may have a strong signal in this population (see **Clinical and Community Research Resources [CCRR]**). In addition, the community health services researchers define a lifestyle intervention for this population. The RDRs at the CTSI and other CTSA institutes are utilized for cohort identification while the Virtual Home is used to find collaborators for these clinical trials. The clinical trials are managed through the CTMS, patient surveys and clinical research form data are collected via Redcap, and tissue and blood samples managed via the biomaterial management system. The data and results from these studies reference a standardized ontology, enabling their sharing across CTSA sites and via the caGrid.
- These studies could identify new approaches that over the course of several years become available as

part of routine breast care. A health services research team (**Community Engagement Research Program [CERP]**) can select to utilize the information in our and affiliate RDRs to perform a comparative effectiveness analysis to determine the benefits and costs of these new approaches to set public policy and clinical guidelines.

6.1. Specific Aim 1: CTSI Virtual Home. To successfully support CTSI programs across diverse institutions and community partners throughout the LA County and to establish and maintain our national presence in the CTSA Consortium, we will continue implementation of our **CTSI Virtual Home** (refer to **Figure 1** in **section 6.1.** below and **Table 1** at the end of the document). The CTSI Virtual Home is an online working environment that supports communication, collaboration, and sharing of resources and information. The Virtual Home integrates modular applications (e.g., content and asset management system, calendar, knowledge base, group collaboration space, and news digest) accessible through a single point of access. All these tools are already in use, enabling relatively rapid expansion of the Virtual Home’s functional utility as our needs grow. In addition, the Virtual Home provides a portal for controlled access to the de-identified patient data in the RDR.

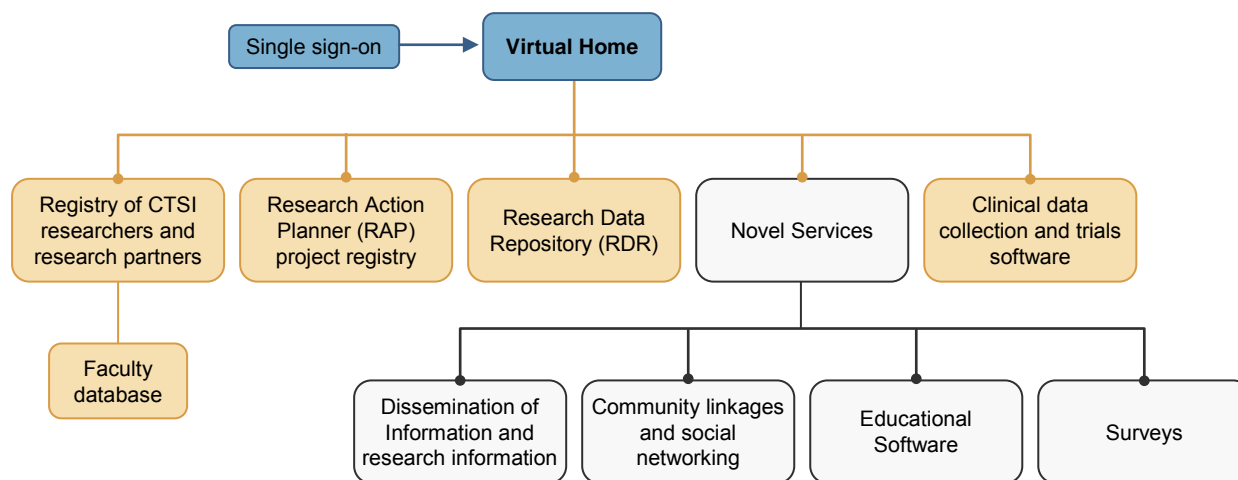


Figure 1. Shown is a schematic of CTSI Virtual Home applications.

6.1.1. Security and Access Control. The Virtual Home will organize and provide access to sensitive information from a number of sources, including trials and grants and de-identified clinical data from the CTSI partners. To ensure this information can only be accessed by appropriately authorized CTSI personnel, we will implement a secure Single Sign-On (SSO) authentication component using Bruin OnLine (our university system). The SSO will enable us to provide secure, role-defined access to specific components of the Virtual Home. This new service is compliant with the Dorian-based open-source Common Security Module that is also used in the NCI’s caBIG project. Information security will, in addition, adhere to policies prescribed in FISMA, including policies for risk assessment, physical protection, software standards, encryption policies for network transmissions, staff training procedures, and continuous monitoring.

6.1.2. Registry of CTSI Researchers and Research Partners. One core element of Virtual Home will be a database containing up-to-date information on all active researchers at CTSI partner institutions and leaders and other key personnel at community partner organizations, such as the Venice Family Clinic and Healthy African American Families (see **CCRR**). i² will build the **Researcher Registry** by extending UCLA’s Faculty Database (FDB) information to include investigators at the other CTSI partner institutions, including community partners. We will also use this expanded database to identify faculty who are involved in CTSI research collaborations for internal and external reporting. The FDB at UCLA includes a mechanism for populating the publication bibliography of each faculty member through PubMed, and we will extend the existing FDB system by adding an interface to the NIH RePORTer system to populate publicly available information on federally funded research projects. The FDB is already used by over 25 Web sites for various UCLA departments, hospitals, and clinical/research centers; and the data structure can easily accommodate all members of the CTSI. Essentially, this registry is the UCLA version of VIVO,⁷ a program currently under development at the University of Florida, Gainesville, a CTSA site. We are committed to ensuring our system is interoperable with this national research networking effort and consulting on development of VIVO.

To ensure that the Researcher Registry contains updated records on all CTSI-affiliated participants, we will

work with IT personnel at each institution and community organization, either creating automated interfaces with their academic personnel systems or reengineering the administrative work processes to keep the database maintained as a by-product of updated lists of publications and sponsored research for funding and regulatory agencies. We will investigate the possibility of including within this registry the documentation of potential conflict-of-interest relationships that require regulatory oversight. The system will also be extended to generate NIH and NSF biosketches and curriculum vitae in HTML or PDF format.

6.1.3. Research Action Planner (RAP) and Project Registry. Another core element of the Virtual Home will be a **Research Action Planner**, which provides support for creating initial plans for research projects, explores potential CTSI collaborators, and identifies CTSI resources (see **Center for Translational Technologies Program [CTT]**). At appropriate times of project maturation, RAP facilitates submitting requests for assistance to relevant CTSI services or resources, links investigators with IRB and other oversight committees, and facilitates entry of studies into appropriate clinical trials registries. RAP also tracks the completion of required training certification by personnel on projects with human or animal subjects. Use of this system will populate a central registry of research projects within the CTSI and, coupled with maintenance of the researcher database, will enable the CTSI to track and report the contribution of core resources in translational research.

Our basis for developing the RAP software resource came from our completed National Library of Medicine (NLM)-sponsored Integrated Advanced Information Management Systems InfoShare project at UCLA (G08LM007851, PI Alan Robinson). Modeled after a similar approach implemented at the Vanderbilt University Medical Center/CTSA (Paul Harris), we developed a Web-based research action plan system called **InfoWRAP**. This system begins with a dynamically branching questionnaire that efficiently collects essential basic information regarding a researcher's project. These data are then translated into (1) a set of ordered "to do" items that provide the necessary contact information to the appropriate regulatory office; (2) a set of links to relevant shared resources; (3) a list of publications from querying the NLM PubMed database for articles published in the last 10 years by CTSI affiliates related to the stated area of research; and (4) a list of CTSI faculty who might be collaborators or mentors in the described research project, which will be obtained from an automated search of the FDB and PubMed publications.

6.1.4. CTSI Research Education, Training and Career Development Program (CTSI-ED) Curriculum Tree. BIP is collaborating with **CTSI-ED** and the UCLA Electrical Engineering Department to complete the **CTSI-ED Curriculum Tree**, a dynamic and sophisticated interface that provides (a) uniform access by trainees and faculty to course material, online instructional resources, calendars, educational forums, and archive space to store samples of work and tests from prior years; (b) tracking of student and course performance; and (c) evaluation of curriculum and achievement of course goals. Developed by Ali H. Sayed, PhD, Professor and Chair of Electrical Engineering, this software has already been implemented by the Executive MPH program in the UCLA School of Public Health and is currently being expanded as the primary course management and evaluation system for all CTSI training programs.

6.1.5. Social Networking/Collaboration Spaces Services. All stages of research translation can be enhanced through the adoption of improvement science principles and practices, which encourage the introduction and testing of small-scale changes in rapid cycles. These rapid cycles accelerate learning about the effectiveness of each small change and making modifications in a timelier manner. Social networking tools support this rapidly iterative process and can be adopted among patients, clinicians, and researchers to foster evolving expectations, introduce opportunities for observational learning, and provide social and motivational support for new behavioral patterns and norms.

In support of the community engagement mission of the CTSI **Community Engagement Research Program (CERP)**, with the help of the CTT Program and the CTSI at large, our social networking efforts are focused on developing and maintaining collaborative innovation networks, which are virtual teams of self-motivated individuals with a collective vision, enabled by online collaborative tools to achieve a common goal by sharing ideas, information, and work. The key design principle is reducing the transactional costs of collaboration. We provide social networking tools for three core functions: (1) gathering people using Facebook groups for wider public involvement and internal Virtual Home groups for private interactions; (2) communicating information using 1-way (blogs), 2-way (discussion groups, email lists), pull (on-demand, hyperlink lists), and push (real-time) modalities; and (3) supporting dissemination through Twitter and knowledge wikis. The disease clusters established by the CTSA are organized to make optimal use of these new capabilities.

Our social networking plans are informed by novel collaborative technology developed by two NCRR-funded translational research networks, both emanating from within the CTSA Consortium. The first is the Cincinnati Children's Hospital Medical Center NIH Roadmap Transformative Research project "Open Source Science: Transforming Chronic Illness Care" (R01 DK085719; PI Peter Margolis), which is creating the Collaborative Chronic Care Network (C3N). UCLA investigator Neil Halfon contributed to design elements. C3N uses integrated, open-source social networking tools to join patients, physicians, and researchers together to prototype and evaluate a system for improving chronic illness care that disseminates knowledge and learning opportunities across multiple organizations and geographical locations. Specifically, we will draw upon (1) the C3N framework and design principles for constructing the collaborative system; (2) specifications for the C3N system as a whole, including measures for program evaluation; (3) an understanding of the conditions necessary for such networks to grow in membership size and participation; and (4) options for reducing transactional costs related to medical-legal issues of intellectual property and patient privacy, and lessons for enhancing trust and shared commitment. The second novel technology project is the Networking Research Resources across America (U24 RR029825, PI Lee Nadler), into which we are linked through the CDU Research Centers in Minority Institutions Translational Research Network (U54 RR022762, PI Keith Norris). This Network provides capacity to leverage **CCRR**- and **CERP**-affiliated projects with this unique test bed of IT tools within a national informatics network that, when fully implemented, will enable investigators across the US to locate research resources that were either unknown or inaccessible to them. Although the Networking Research Resources consortium will eventually make its toolkit and databases available as open-source deliverables, the Network linkage now enables the UCLA CTSI, through the Virtual Home, to be an early adopter of new tools for connecting people and technologies to accelerate the transformation of biomedical and biobehavioral science and the dissemination of new knowledge.

6.1.6. Additional Novel Services. We anticipate that the CTSI Virtual Home will provide a strong platform for achieving the BIP aims. We will also provide novel services for gathering, storing, and presenting information: (1) periodic surveys of community partner organizations to identify research interests and needs; (2) social networks to foster research collaboration, such as topic-specific Wikis, discussion groups, and researcher blogs; (3) tracking research questions that arise in these areas; (4) tracking funding opportunity announcements; and (5) the coordination of wireless communications and embedded sensing technologies being integrated by **CERP** and the UCLA Center for Embedded Networked Sensing (CENS). In addition, the Virtual Home will serve as pass-through portal to translational research tools developed by other CTSA sites that are accessible directly through their respective sites or via CTSA Web, such as ResearchMatch.org.

6.2. Specific Aim 2: Research Data Repository and Associated Services. The CTSI leadership and investigators are aware that the success of their translational science efforts depends on establishing clinical data repositories that can be used for exploratory research, hypothesis generation and testing, study planning and design, retrospective data analysis, and prospective data collection. BIP research data services will enable storage, retrieval, and analysis of data for varied research and educational purposes. The RDR will be a centerpiece of these services as it will centralize de-identified clinical data from CTSI partners. Information security for all these systems will adhere to the appropriate policies prescribed in FISMA (see **section 6.1.1.**)

Additional research data services will initially include (1) biospecimen data repositories (caTissue Suite); (2) array data repositories ; (3) image repositories (National Biomedical Imaging Archive); (4) clinical-patient care data (inpatient and outpatient); (5) queries across these data services; and (6) data warehousing tools, which will support projects that collate and combine data from various repositories for complex analysis.

6.2.1. Research Data Repository. A major role of the BIP is creation and maintenance of a data repository to be used exclusively for research that spans all CTSI partners. The RDR will contain information extracted from and loaded by each partner site to a central system and used to generate hypotheses and inform study planning activities (e.g., study cohort identification in preparation for subject recruitment). Authorized users will be able to enter queries combining health information criteria (e.g., ICD-9 diagnosis codes, laboratory values, etc.), and the RDR will return de-identified summary information (e.g., location, age categories, sex, and race-ethnicity) about patients who meet these search criteria in a format designed for use in grant funding and regulatory approval applications.

The data in the RDR will include, at minimum, encounter diagnoses, some demographic information, and laboratory values, all of which are commonly used for cohort identification. Patient data in the RDR will be de-

identified using the “safe-harbor” method specified in the HIPAA Privacy Rule, which includes the removal of the 18 identifier fields and changes to service dates and zip codes. Under current IRB policy (see **Regulatory Program**), the BIP will not need to obtain separate IRB approval for the storage of information from individual searches in a data repository intended for research purposes, as the de-identification makes the RDR exempt from IRB review under Category 4 of the Common Rule exemptions [45 CFR part 46.101(b)]. Our partnering institutions have agreed to this data sharing framework for de-identified data as part of our consortium “trust fabric” (see **Institutional Letters**). Each investigator will have access to queries that return only de-identified data, subject to certain limitations that restrict the narrowing of queries to identify individuals. The RDR will also include an RDR-specific identifier, which is the unique patient ID within the RDR. The clinical operations group at each partner institution will retain a link from the RDR identifier to the actual patient identity, as described in the Honest Broker discussion below. When researchers identify a cohort of interest through the RDR they proceed to recruitment of these patients via clinicians at each partner site, after obtaining the requisite IRB approvals. The investigator provides the list of RDR Patient IDs to the appropriate staff within each partner site’s clinical enterprise and these staff use the link file to initiate the IRB-approved outreach, generally via the patients’ clinicians, who could validate each patient’s eligibility prior to their being contacted.

Because each CTSI clinical partner is a separate “covered entity” with respect to the HIPAA Privacy Rule, each partner will need to conduct its own extraction and de-identification of patient data. However, BIP staff will work closely with each partner to implement a common algorithm to be run within each institution’s clinical data repository. UCLA-Westwood and Cedars-Sinai medical centers are now engaged in implementing the Epic electronic medical record system across their clinical enterprises. The Epic Clarity clinical data repository will be a primary data source for these institutions, along with repositories containing legacy data that will not populate into the Clarity architecture. Harbor-UCLA Medical Center and the Multi-Specialty Ambulatory Care Center (located adjacent to Charles Drew University [CDU]) are part of the LA County Department of Health Services and both feed all their clinical and admission discharge and transfer (ADT) data to the County’s QuadraMed enterprise clinical repository, which will serve as the primary RDR data source for these partners. CDU’s clinical data repository will initially provide data from its new Urgent Care Clinic, which uses Touch Medix’s EDIS, and will expand to include data from other sources as CDU opens more clinics.

To create this RDR with data from multiple sites, and to allow the researcher to transition from identifying de-identified cohorts within the RDR to recruiting actual subjects at individual institutions, a means to map from the RDR-specific patient ID to each institution’s patient ID is required. To solve this challenge, BIP staff will work with each partner to implement the **Honest Broker System** of the University of Pittsburgh (obtained through our SPIRiT collaboration). The University of Pittsburgh Biomedical Informatics team will conduct an on-site workshop at UCLA with the CTSI leadership of the BIP, CCRR, and Regulatory Knowledge/Support Cores in late 2010 to help us implement this important new tool. An Honest Broker at each site will generate RDR patient identifiers and map local-to-RDR identifiers in a link table (described above). Data with these RDR identifiers will then be merged into the central RDR, along with a site identifier to ensure unique identification of each patient between sites. This approach has been used successfully to federate the research data repository at Pittsburgh and will be implemented as a central goal of this aim.

Due to the geographic overlap in the areas served by each partner institution, we expect to find similar overlap in patients treated at and appearing in partner clinical data repositories. This presents a unique challenge for the construction of a merged, de-identified RDR because we should include only unique patients within the RDR. Without the ability to identify which patients are duplicated across partner sites, researchers would need to adjust for the possible overestimation of the size of available eligible cohorts. To address this challenge, we will seek IRB approval to study the extent of patient overlap across institutions, comparing a variety of commercial tools typically used in Health Information Exchanges to perform patient identity resolution. This study would require the use of patient-identifying information for a sample of patients from each site, under the protection of a data-use agreement and strict audits of data access in addition to the privacy and security controls needed for handling personally identified health information. Depending on the results of this study, and each institution’s experiences with the Honest Broker process, we will consider implementing a single Research Master Patient Index (RMPI), with centralization of the Honest Broker to create a single RDR-specific patient ID across all sites. Because this system would require the use of some potentially identifying data from each of the partner sites, it would have highly controlled and audited access and would require IRB approval and Data Use Agreements between BIP and each CTSI partner site.

The RDR will be built upon i2b2, an NIH-funded open-source data repository framework that has a growing suite of associated tools and a large user base, including several other CTSA-funded sites. These sites include the CTSA programs at UCSF and UC Davis, and we anticipate using i2b2 to enable UC-wide collaborations that amplify clinical research across California. One particular advantage of i2b2 is its “star schema” architecture, which can accommodate a wide variety of clinical data without requiring changes in the database schema. We expect the RDR will initially store limited demographic data (e.g., ages under 90, gender, race/ethnicity, 3-digit zip code of residence), billing diagnoses, and laboratory data and will incorporate other data (e.g., problem and medication list entries) as those data become available through EMR implementations and as BIP staff work with CTSI researchers to specify critical high priority research needs. We do not initially plan to include binary data, such as radiological images, which could be difficult to fully de-identify, or free-text-based data at this time.

Shared governance of the RDR will be critical. To this end, written policies governing access to and use of the RDR will be developed by BIP Policy and RDR Workgroups for review and approval by the BIP Steering Committee. The initial policy governing RDR queries will include limiting access to registered investigators and their designated analysts, requiring each user to sign a data-use agreement, and requiring the proposal or hypothesis being pursued to be registered (using RAP) for each query of the RDR. An audit trail of queries will also be maintained and will be open to inspection by the RDR Workgroup. Finally, we will work with the **CTSI Biostatistics, Study Design, and Clinical Data Management** and **CCRR** programs to ensure that the biostatisticians and clinical investigators’ needs are addressed in structuring clinical research data from the RDR for efficient analysis and transmission to investigative teams.

To aid with quality control, users will be asked to report possible anomalies, such as statistical outliers or improbable values. These values will be tracked as questionable and reviewed monthly by the Operations and the RDR Workgroups per their oversight duties in data use. If a review identifies a possible data error, this information will be fed back to the participating clinical institution for diagnosis and correction, especially in cases in which recurrent or systematic errors are suspected.

6.2.2. Common Terminology Service (CTS). We will implement a CTS consistent with the Health Level 7 standard to create the enterprise interlingua that will be used to store and translate research data. This service will be based on the core terminologies of NLM’s Unified Medical Language System, with an emphasis on LOINC, SNOMED CT, and ICD9-CM. The CTS will be maintained centrally, with local extensions. Concepts and codes provided by the service will be used to tag records for storage (e.g., a code for a clinical laboratory test or its result) and to code attributes that form the structure of a record (e.g., “unit” or “reference range”) and that are themselves valued. We will leverage work already underway to construct an enterprise terminology at Cedars-Sinai using commercial tools (e.g., Health Language, Inc.).

6.2.3. Clinical Trials Management System (CTMS). The Velos eResearch system is an online (caBIG compliant) comprehensive clinical research information system that addresses the areas of Account Management, Protocol Management, Patient Management/Patient Tracking, Data Management, Reporting, Budgeting, and creating and meeting Milestones. The UCLA Jonsson Comprehensive Cancer Center (JCCC) has now completed its Velos implementation and will begin Phase II of the project, which involves creation of electronic case report forms (CRFs) for investigator initiated trials, in the first quarter of 2011. The School of Medicine is beginning a Velos implementation for non-cancer clinical trials in fall 2010, facilitated by a new 3-million-dollar commitment from the David Geffen School of Medicine (DGSOM) for personnel. We expect the use of the CTMS will improve the efficiency, quality, and timeliness of data capture and reporting. BIP will focus on developing standard operating procedures for the development and design of CRFs to ensure a standardized format and use of standard data elements from a CSTI-supported data dictionary, which will promote data integrity and data sharing.

6.2.4. Registry of Research Databases. It may not always be possible to connect an existing or new data repository to the RDR. The repository may reside within the information system architecture of one of the CTSI partner organizations. To facilitate use of these data throughout the CTSI, we will construct a Registry of Research Databases that will allow the owner of the database to register its existence, descriptive metadata, and level of access centrally, including the levels of access that are available to those who wish to access it. Access will be mediated via our Virtual Home and implemented via secure Web services.

6.2.5. caBIG Theory to Practice. We have been an active partner with the NCI in leveraging the tools and

underlying infrastructure provided by the caBIG Initiative. UCLA has been actively involved in the Integrative Cancer Research workspace and has provided feedback on clinical trials management and data sharing and security tools. Our initial efforts and goals have focused on establishing biorepositories using the caTissue Suite in conjunction with our JCCC SPORE Programs in prostate and lung cancers and providing interoperability between our selected vendor tissue bank software (Daedalus) and caTissue. We are testing and evaluating caArray and caB2B as a means to augment existing tools at each institution and to provide a layer of interoperability and new capabilities for each institution's internal clinical and research systems.

An important test bed for integrating caBIG tools with other RDR approaches will be the ATHENA Breast Health Network, a large-scale project involving all five UC health centers (and their CTSA's). ATHENA is designed to revolutionize breast cancer care by more efficiently merging research, technology, financing, and health care delivery in a way that reduces the time needed to translate research findings into patient care practices. ATHENA will initially recruit 150,000 women throughout California to be screened for breast cancer. Core data from patient surveys, breast imaging, pathology tissue, oncology EMR data, and survivorship follow-up will be used to drive technical and medical innovation and research. As part of this ongoing effort, BIP will investigate the use of the National Biomedical Imaging Archive to house image data versus the use of caIntegrator2. This project will also serve as a model for data-sharing and security approaches that will inform the CTSI RDR and as a pilot for combining detailed pathology and clinical data in a research data warehouse.

The UCLA CTSI is also committed to data sharing via caGRID, and UCLA will work with UCSF, UCSD, and other non-UC institutions (e.g., University of Pennsylvania and Harvard University) to unite caGRID and i2b2. Although i2b2 is a relatively easy platform to import source data into regardless of its encoding, and it allows for mapping to standard coding, it has limitations in data sharing capability. caGRID has a more mature data sharing capacity and is platform agnostic but has some limitations in terms of data translation and encoding. It is our goal to work with other institutions to leverage the Ontology Mapper Cell of i2b2 and the caGRID Cell. We will also test this integration as part of the ATHENA Project.

6.3. Specific Aim 3: Education and Training. The education and training mission of BIP can be divided into two major efforts: (1) formal curriculum-based education and mentored research instruction in biomedical informatics, and (2) ongoing training of all CTSI participants in the use of the BIP developments.

6.3.1. Curriculum-Based Education. We will coordinate formal education of and provide opportunities for mentored research training to graduate students, postdoctoral fellows, and junior faculty. These efforts will be closely coordinated with the **CTSI-ED Program** so that interdisciplinary approaches and adequate exposure to regulatory and research ethics issues are addressed. For those wishing to either pursue a primary or secondary focus on biomedical informatics as an academic discipline, we will also introduce research practices on various topics, providing opportunities for trainees at various levels (undergraduate, graduate, medical school, residency, staff researchers, etc.) to work on projects in biomedical informatics under the supervision of senior faculty and staff mentors. These practical training experiences will also be open to community co-investigators, if sufficient interest arises. These projects will provide hands-on training on the use of BIP tools and data management infrastructure. We will compile and maintain a directory of appropriate mentors and ongoing projects as a clearinghouse to help match trainees with appropriate labs and mentors. To augment this mentored hands-on training and career development with formal coursework, we will develop and introduce into the curriculum of the UCLA K30 Program a new Track II Certificate module on biomedical informatics. Each K30 Track II module includes 4–8 two-hour lecture and discussion sessions taught by senior faculty from 5:30 to 7:30 PM once a week. Upon completion of the module and a certification test, a certificate is issued to the "graduate," verifying comprehension in the module content area(s). The bioinformatics K30 module will be a precursor to a broader but more refined curriculum and training plan in interdisciplinary research informatics to be developed as part of the T32 or K12 program in preparation for the scheduled board certification for physicians in Biomedical Informatics in 2012–2013.

Live training events will occur at each of the CTSI partner sites, coordinated with representatives of each institution (e.g., Dr. Ogunyemi at CDU, Dr. Fu at LA-BioMed). Additionally, we will evaluate the efficacy of the training process and make iterative improvements as appropriate.

As part of this effort, we will unify multiple biomedical informatics training efforts across UCLA-Westwood, Cedars-Sinai, Harbor-LA BioMed, and CDU. We have surveyed CTSI partner institutions to identify current educational resources for informatics training, of which the following are representative:

- **UCLA NLM Training Program in Biomedical Informatics (T15 LM007356, Alex Bui, PI):** This training program is 1 of only 18 programs nationwide funded by the NLM for graduate (MS, PhD) and postdoctoral training in informatics. Offered through the School of Engineering and the Medical and Imaging Informatics group, the program consists of a one-year core curriculum (10 classes) covering concepts central to biomedical informatics, after which students specialize in their interests with additional coursework and thesis/dissertation research.
- **UCLA Interdepartmental Programs:** Two newly organized T32-funded training programs, computational biology and bioinformatics, provide focused training in informatics. The computational biology program specifically addresses the multidisciplinary knowledge needed for neuroimaging research. The bioinformatics program focuses on areas of genomics, proteomics, and population-based genetic analyses, with faculty in computer science, pathology, molecular biology, and human genetics.
- **UCLA School of Public Health:** Additional classes covering informatics include a three-course sequence offered through the School of Public Health. In particular, Health Services 401 (Public Health Informatics) provides an overview of various topics (clinical, translational, imaging, biological).
- **UCLA School of Medicine:** A medical informatics clinical elective is available for medical students and residents, with a “rotation” of 3–6 weeks that combines didactic materials and an intensive project.
- **Charles Drew University:** Increasing informatics awareness has been achieved at CDU through a dedicated lecture series, workshops, and partnerships with other institutions, such as UCLA. Medical students in the CDU/UCLA program are encouraged to utilize informatics methods in developing their required medical school research theses. CDU has engaged instructors from the National Center for Biotechnology Information to teach bioinformatics mini-courses.

6.3.2. BIP Toolkit Training. BIP will provide training for all CTSI participants (students, research trainees, investigators, research support staff, community partners) on the effective use of informatics tools in clinical and translational research. Briefly, such training will be provided through:

1. **Super-user workshops.** Using a train-the-trainers approach, we will conduct workshops for each of the BIP-developed or BIP-supported tools, to create expert “super-users” at each participating institution. At least one workshop annually will be in-person, with the remainder taking place via internet to save travel time. After instructional materials have been developed and pilot tested, the CTSI Office of Investigator Services domain experts and research facilitators will become the primary instructional group for these workshops. CTSI staff will further develop the workshop materials in collaboration with BIP, and these materials will be made available on the Virtual Home.
2. **Walk-in training.** BIP will support certified super-users at each institution in implementing BIP-supported tools in their research settings and in handling day-to-day questions from users, making use of the workshop materials. As we gain experience with this process, more of these materials will be converted into self-instructional tutorials and training videos.

Our implementation matrix (**Table 2**) provides a blueprint on the objectives and milestones for each of the BIP aims. The UCLA CTSI **Evaluation and Tracking Program** will monitor BIP progress and identify ongoing needs for resource reallocation as they arise. The BIP evaluation activities involve the following:

- Monitoring the goals and implementation milestones of **Table 2**.
- Assessing the utilization (volume) and usability (quality) of the BIP virtual infrastructure (portal, databases, hardware, software) by CTSI investigators, trainees, patients, and the community.
- Ensuring input (qualitative and quantitative) from proposed new interactive BIP processes, user meetings, and chat room discussions are taken into account when making modifications and improvements to CTSI virtual infrastructure.
- Education and training activities evaluation.

The Evaluation and Tracking report will be sent to the CTSI Operation, Implementation, and Management Group (CTSA **Overview and Governance** narrative) and the BIP Steering Committee. The BIP agenda is ambitious, requiring substantial effort to develop each component and to integrate activities and systems across participating sites. Internally, we will conduct iterative, internal *process evaluations* to understand the barriers and facilitators to collaboration among the institutional and community partners. To meet this goal, we

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will conduct an annual survey to assess ease of communication among the partners, adequacy of education and training processes, and coordination of collaborative activities, specifically the CTSI Virtual Home, the framework for subject recruitment and scheduling, and the RDR. This information will be used to correct any problems flagged and ensure that the collaboration develops successfully.

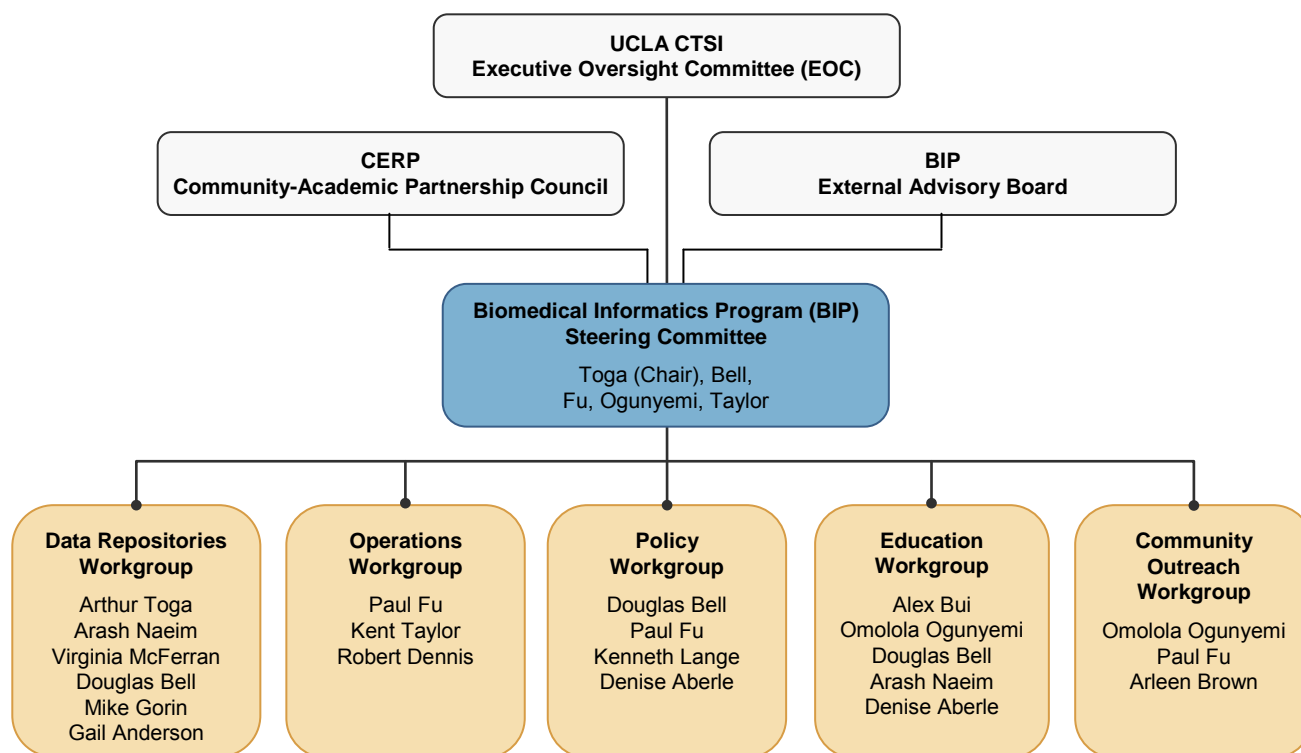


Figure 2. BIP Organizational Structure

7. INVESTIGATORS

7.1. BIP Leadership. The day-to-day operations of BIP will be overseen by the Program Leader, the Co-Leader for Clinical Informatics and three site Co-Leaders (**Figure 2**) who represent different areas of expertise from CTSI member institutions.

Arthur Toga, PhD, Leader is Associate Vice Provost for Informatics at UCLA and Professor of Neurology, Director of the i^2 , Associate Dean for Informatics, and Director of the Laboratory of NeuroImaging at DGSOM. As Associate Dean, Dr. Toga represents DGSOM on the campus Information Technology Planning Board and serves on the Medical Sciences IT Steering Committee. Through the administrative and scientific capacity and authority of these multiple roles, Dr. Toga is ideally positioned to advance the synergistic agendas of the CTSI and i^2 . Dr. Toga is internationally renowned for his contributions to computational neuroscience, biomedical data management, and numerous informatics initiatives, and he has extensive experience in managing large interdisciplinary projects, including P20, P41, T32, and U54 grants. He directs the Informatics Cores for the Alzheimer's Disease Neuroimaging Initiative, Huntington's Disease Neuroimaging Initiative, Parkinson's Progression Markers Initiative, and International Consortium for Brain Mapping, and he is one of four executive directors of the Biomedical Informatics Research Network. Dr. Toga is a member of the American Medical Informatics Association, an elected fellow of the American College of Medical Informatics, and has served on numerous national committees on data sharing and informatics. During his tenure as a member of the NCRR Council, he championed several informatics initiatives.

Douglas Bell, MD, PhD, Co-Leader is Associate Professor of Medicine at DGSOM and a Research Scientist at RAND whose research focuses on the design and evaluation of health information technology.^{21, 23} He is currently leading a 4-million-dollar, 18-month initiative funded by the U.S. Department of Health and Human Services to rapidly advance clinical decision support technology and to prepare the way for its adoption through physician payment incentive programs beginning in 2013. He is also leading a 2-million-dollar, 2-year

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project to exploring how electronic prescribing is taken up and used among community practices in the US, and he recently completed other influential projects evaluating advanced data standards for e-prescribing and a system for online management of specialty referrals. He has also led other pioneering informatics research projects, including studies of physicians' learning and retention from online educational exercises,^{22, 24-25} visualization of quantitative evidence as an adjunct to education,²⁴⁻²⁵ and assessments of the workflow effects of clinical information systems.^{21, 23}

Paul Fu, Jr., MD, MPH, Co-Leader is Associate Clinical Professor in the Department of Pediatrics at DGSOM, Associate Professor of Health Services at the UCLA School of Public Health, and faculty in the Division of General and Emergency Pediatrics at Harbor-LA BioMed. Dr. Fu is also the Medical Information Officer at Harbor-UCLA Medical Center. As Director of the Center for Biomedical and Public Health Informatics at LA BioMed, he leads research programs focusing on the use of aggregated clinical data sets for real-time quality assessment and reporting and evaluating the impact of health information technology on clinical efficiency and effectiveness.^{11, 12} Previously, he led the development of the LA County Department of Health Services enterprise clinical data repository. Dr. Fu will Chair the Community Outreach Workgroup focused on leveraging clinical data for health services and disparities research and oversee Harbor's participation in the RDR.

Omolola Ogunyemi, PhD, Co-Leader is Director of the Center for Biomedical Informatics and an Associate Professor in the Medical Sciences Institute at Charles Drew University (CDU). Her research interests include machine learning, 3D graphics and visualization, and medical decision support systems, with an emphasis on underserved communities.¹³⁻¹⁷ Dr. Ogunyemi will Co-Chair the Community Outreach Workgroup focused on leveraging clinical data for health services and disparities research and oversee CDU participation in the RDR.

Kent Taylor, PhD, Co-Leader is Laboratory Operations Director of the Phenotyping/Genotyping Laboratory at Cedars-Sinai. Dr. Taylor is also a member of the Genetics of Common Diseases Group at Cedars-Sinai's Medical Genetics Institute, and he is Associate Professor of Pediatrics at DGSOM. Dr. Taylor provides genotyping data and bioinformatics expertise¹⁸⁻²⁰ and support to the Genetics of Common Diseases Group and to various clinical investigators at Cedars-Sinai Medical Center. Dr. Taylor will Chair the Operations Workgroup and oversee participation from Cedars-Sinai in the RDR.

Arash Naeim, MD, PhD, Data Repositories Workgroup Co-Leader is Associate Professor of Hematology/Oncology at DGSOM and Director of Informatics at the JCCC. He has experience in implementing cancer-specific EMR and CTMS applications in support of researchers for the JCCC. With a PhD in public policy, he specializes in cost-effectiveness and decision making in the treatment of older cancer patients,²⁶⁻²⁸ and he is also involved in developing and deploying informatics applications in hematology/oncology, with a focus on how electronic databases and medical records can be used to support clinical trials and health care interventions.²⁹⁻³⁰ He is leading the JCCC's participation in the ATHENA Breast Health Network.

Alex Bui, PhD, Education Workgroup Leader and Investigator in the BIP is Associate Professor of Radiology at DGSOM and Director of the UCLA NLM training program in medical imaging informatics. He is involved in several national informatics committees, including the American College of Radiology Imaging Network (ACRIN) and AMIA. Dr. Bui's research interests include distributed information architectures for biomedical research and clinical environments; probabilistic modeling techniques, and medical data visualization.

Denise Aberle, MD, Investigator is Professor of Radiology and Bioengineering, Vice Chair for Research in Radiological Sciences, Co-director of the UCLA Wireless Health Institute, and Deputy Co-Chair of the NCI-sponsored American College of Radiology Imaging Network (ACRIN). She has expertise in the development and oversight of large clinical trials and biomedical informatics. With certifications in medicine and radiology, her studies focus on the applications of medical imaging and informatics technologies to inform best practices. She is a core faculty member of the UCLA Medical and Imaging Informatics (MII) program and Biomedical Physics (BMP), both NIH-sponsored post-graduate training programs. She is the national principal investigator of the ACRIN-National Lung Screening Trial (NLST), a 125-million-dollar supplement to ACRIN, which is a randomized controlled trial evaluating the effects of low-dose helical CT on lung cancer mortality reduction and its cost-effectiveness. The study involves 23 institutions and 19,000 participants.

7.2. BIP Organizational Structure. The BIP Steering Committee, comprising the BIP Leader, Co-Leader for Clinical Informatics and three site Co-Leaders, is responsible for BIP governance and operations oversight

(Figure 2). The Steering Committee will assess needs and make recommendations for resource allocation to the UCLA CTSI Executive Oversight Committee (EOC) for approval. The Steering Committee will adjudicate problem resolution; approve, prioritize, coordinate, and manage CTSI collaborative interactions involving informatics resources and services; and collaborate with the other CTSI core programs. The BIP Steering Committee will report to the UCLA CTSI EOC; the BIP Chair (Arthur Toga) is a voting member of the EOC. In addition, guidance and direction will be provided by a BIP External Advisory Board (EAB) and the CERP Community-Academic Partnership Council to ensure that all services and tools promote fulfillment of BIP aims and efficiently meet the needs of CTSI stakeholders, both academic and community-based. The BIP EAB will comprise approximately 6 informatics experts who are participating in other leading CTSA programs; the group will meet initially in-person and then semiannually by webinar to review progress and provide guidance.

Supporting the BIP Steering Committee are 5 workgroups. Each workgroup is meeting biweekly during its start-up phase and then will adjust their schedules as needed to meet their tasked responsibilities. The BIP Steering Committee conducts a monthly all-hands meeting at which representatives from each workgroup report on their progress. Current foci are on the design of the Virtual Home and on planning the RDR architecture based on initial pilot testing and on comparing the experiences of other CTSA institutions. At each CTSI partner site, the BIP faculty lead will be supported by a project manager and an interface programmer to facilitate the creation, ontology mapping, and data transfer to an RDR. Additional leadership and participation in each workgroup is as follows:

Data Repositories Workgroup: This Group is overseeing planning and development for the CTSI RDR, CTMS, and Velos, which constitute the centerpiece of BIP **Specific Aim 2**. In addition, this workgroup, in collaboration with the Policy Workgroup, will advise the CTSI on key informatics and IT-related policies to ensure HIPAA-compliant sharing and secondary use of health care data.² This group is co-led by Arthur Toga and Arash Naeim and includes Ms. Virginia McFerran (CIO for UCLA Health System), Drs. Bell and Gorin, as well as Dr. Gail Anderson, Chief Medical Officer for Los Angeles County Metrocare and Darren Dworkin, Vice President of Enterprise Information Systems and CIO for Cedars-Sinai.

Operations Workgroup: This workgroup is composed of individuals at each institution who are responsible for the implementation of CTSI tools, including selection of architecture and terminology systems, as well as changes to each institution's existing informatics systems, if necessary. This group also performs scoping, planning, and execution of BIP development efforts, and coordination of plans between BIP and the member institutions. This group is co-led by Drs. Paul Fu, Jr., and Kent Taylor and includes Robert Dennis, PhD, who is the managing director of the UCLA Computing Technologies Research Lab, which supports the biomedical research community at UCLA and developed the Faculty Database, Weekly Message Digest and Calendar system, and **InfoWRAP (Section 5.1.3)**. Dr. Dennis is also active in the national caBIG initiative and is leading efforts by the JCCC to test and implement selected caBIG technologies.

Policy Workgroup: This workgroup focuses on policies and procedures related to data sharing, patient privacy, security, compliance, intellectual property, and IRB adherence at each member institution. Letters of Commitment from CIOs, indicating commitment to shared data resources, are included in the Appendix. The Policy Workgroup is co-led by Drs. Bell and Fu. Other participants include Dr. Kenneth Lange, Professor of Computational Genetics and Chair of the Department of Human Genetics at UCLA, and Dr. Aberle.

Education Workgroup: This Group, under the leadership of Dr. Alex Bui, is providing strategic planning for the development of tools and services needed for BIP to achieve its educational mission to trainees and all members of the CTSI (see **Specific Aim 3**). The Group will oversee the CTSI's efforts toward this aim, including the coordination of curriculum development for biomedical informatics trainees, and the process of training in use of the Virtual Home and other BIP tools. Other Education Workgroup participants include Drs. Ogunyemi, Bell, Naeim, Aberle, and Dr. Anne Gilliland, Professor and Director of the Center for Information as Evidence, UCLA Department of Information Studies.

Community Outreach Workgroup: This workgroup focuses on developing the Virtual Home application (see **Specific Aim 1**) as well as other informatics tools and platforms that can be used with community partners and affiliates. In addition, this group will focus on supporting informatics to augment health services and disparities research. This group will be co-led by Drs. Ogunyemi and Fu, with other members including CTSI Program Leaders, particularly Dr. Arleen Brown (**CERP** Program Leader).

8. INTEGRATION OF UCLA KEY FUNCTIONS

Supported by local funding, we recently organized two symposia on enterprise-level informatics in translational research, both of which informed the development of i^2 and the transformational aims of this proposal. The first was a CTSI-wide symposium on clinical and research data repositories, held at UCLA-Westwood, which attracted more than 250 participants from all four UCLA CTSI institutions as well as numerous community partners. Several audience members and 5 of the 6 presenters were from national CTSA Consortium institutions. A second symposium, focused on the topic of developing centralized biorepositories, was held at Cedars-Sinai. These two symposia proved to be dynamic interactive forums for health science investigators, clinicians, and health IT administrators to share insights and identify potential barriers and to apply these insights in meeting our own needs, challenges, and opportunities. We also developed two needs surveys for investigators and their support staffs, the results of which directly shaped our specific aims.

9. EXTRA-UCLA COLLABORATIONS

Included among the ongoing inter-CTSA collaborative efforts are the following **Pilot Projects**:

1. Community-Based Clinical Trials - The Velos eResearch CTMS has been deployed into 25 community based oncology practices across the US that form the Translational Oncology Research International (TORI) network. This deployment required Data-Sharing, IT security, Compliance, and Business Associate agreements to be reviewed and approved. This deployment has been a national prototype for bringing cutting edge translational research with novel therapeutic agents into community settings.
2. EMR-CTMS data mapping - In conjunction with the UCSD CTSA, UCLA has begun the process of mapping clinical data elements, such as adverse event reporting and test results, between the Epic EMR and Velos. This important interface will be integrated into the workflow mapping and note documentation implementation. The goal is to use a combination of tagged field and natural language processing to ensure critical data for translational and clinic trials is integrated between the EMR and CTMS systems.
3. REDCap - CTMS integration - The CTSI is pilot testing the use of REDCap, a secure, internet application developed by the Vanderbilt CTSA for building and managing online forms and databases. The primary use will be for (a) online patient questionnaires, and (b) electronic CRFs. A successful pilot may provide an alternative option of linking electronic patient self-report and CRF data to other elements in the CTMS system.

Table 1. Depicted are the UCLA CTSI Virtual Home menu and primary user groups. The **CTSI Virtual Home** (Internet Portal) with BIP-supported functions for specific user groups. CTSI core programs and other users transmit content wish lists for development of the CTSI Virtual Home to BIP, which then assesses these requests for incorporation as novel online tools and integrated databases are developed by BIP.

BIP-Supported Functions	CTSI Private (Intranet)			CTSI Public
	Central Administrators	Investigators (Academia/Community)	Research Support Cores	Community at Large
Catalog of Research Resources: Core and Specialized Labs; Technology Cores (including the Directory of the Translational Technologies and Resources Program); sample requirements and preparation, costs, placing and tracking current orders, data retrieval	X	X	X	
Catalog of Research Data Resources: Biostatistics software manuals and guides; consulting services; data management programs (REDCap, Velos)	X	X	X	
Catalog of Research Resources: CCRR inpatient, outpatient, mobile nursing, and bionutrition services; community research centers, contact information	X	X	X	
Policies and Procedures: Research protocols (submission procedures for IRB), animal use (IACUC) and CTSI utilization, DSM plans and monitoring; grants/contracts forms; conflict of interest declaration, tracking and reporting tools, certificate logs	X	X	X	
Directories: Investigators, community researchers, mentors, and trainees; faculty lists linked to institutional partners' databases; listing of research staff and contacts	X	X	X	
Budget: Budget estimates, projections, cost recovery	X	X		
Forums: Research and technology affinity groups (disease-, technology- or method-focused)		X	X	
Enrollment: Volunteer registry/repository (HIPAA compliant), studies open for enrollment	X	X	X	X
Community Research Registry: Community-based organizations, physicians, clinics, health plans; listing and results summary of studies in which community organizations and individuals participated with CTSI researchers	X	X	X	X
Social Networking and Community Forum: Online community to elicit ideas and partners, and disseminate useful information and tools (e.g., wikis, Facebook, blogs)		X	X	X
Clinical: Clinical laboratory database and results, nursing and bionutrition procedures and database, participant scheduling tools		X	X	
Calendar: Seminars, workshops, lectures, webcasts	X	X	X	X
CREST Curriculum Tree: K12, K23, K30, T32, PhD programs: training opportunities, courses, videoconferences, and evaluation materials	X	X	X	
Archives: Webcasts, educational and informational materials, lay descriptions of research discoveries		X		X
Links: Research databases, terminology, data-sharing sites		X	X	
Documents: Publications, press releases, expert directory, research study directory and contact information	X	X	X	X

Table 2. BIP Synergistic Collaborations with Other CTSA Programs

Program	Collaboration
Community Engagement and Research	<ul style="list-style-type: none"> • Real-time Web- and podcasting and videoconferencing as well as archiving of community research symposia and workshops and community education lectures on translational medicine • Online interactive tutorials and distance-learning modules on community engagement and community participatory research, and on study design and methods • Community Research Registry • Online knowledge exchange regarding research opportunities and eligibility requirements, including feasibility vetting of community sites for particular protocols • Centralized Web-based process to provide HIPAA and IRB training and certification and a Web-based registry of certified community-academic partners. (joint collaboration with Regulatory Program) • Communications and social networking channels between community participants and CTSI investigators, including Community Engagement interest groups across CTSI partner institutions and community-based organizations, e.g., wikis, Facebook, SharePoint, online newsletters • IT infrastructure for electronic data collection and analysis for and about community-based studies, including database of specific protocols • 2-way, interactive, wireless or site-independent telemedicine technologies in clinical applications (access to specialty care through remote teleconsultation) as well as use in social networking infrastructure to maintain dialogue between academic researchers and their community partners • Community partner requirements for linking their current IT resources with the CTSI's collaborative computing environments • BIP toolkit training modules and walk-in training to facilitate use of CTSI IT resources by community partners.
Clinical and Community Research Resources (CCRR)	<ul style="list-style-type: none"> • Integration of CCRR sites through CTSI Virtual Home (VH), including means to contact OIS Facilitators and Experts • Online inventory and utilization tracking of clinical research resources, laboratory tests, new technologies, equipment availability, providing access via the VH to information about CCRR services and procedures at all CTSI partners • Online protocol submission for review by CCRR Scientific Advisory Committee (SAC) and appropriate IRBs, using the VH RAP and with IRB harmonization aimed at reciprocity (in collaboration with Regulatory Program) • Online cross-training resources for CCRR provider personnel, including Real-time Web- and podcasting and videoconferencing and of CCRR educational seminars, workshops, and lectures • Online dissemination of information regarding past (results reporting), current, and planned translational studies, to all academic institution and community partners • Support for project- group- and disease-specific research participant registries • Communication technologies for real-time reporting of recruitment statistics, data, and comments and feedback from study participants and community health centers to the investigators.
Biostatistics, Study Design, and Clinical Data Management	<ul style="list-style-type: none"> • Clinical Trials Database designed to support end-users of high-dimensional data generated by imaging, microarray, and proteomics analyses • Support for secure clinical data management systems, accessible across CTSI institutions and study sites • Real-time Web- and podcasting and videoconferencing and archiving of lectures, seminars, and workshops on biostatistics and study design, geared to both academic and community researchers as well as public at large • 2-way, interactive, wireless or site independent telemedicine technologies for biostatistical and study design teleconsultations across study sites.
Regulatory Knowledge and Support/Clinical Research Ethics	<ul style="list-style-type: none"> • Online menu of services for the Facilitator Program, including set-up of Velos system for protocol development and management • RAP portal for Facilitator Program to assist investigators in identifying and accessing technologies and specialized core resources, including imaging, genomics, proteomics, molecular screening, nanotechnology, and immune monitoring • Study registry and support systems, including RAP, for tracking protocols, regulatory activities (e.g., data and safety monitoring), adverse events, and interaction of these systems with IRBs and/or hospital information systems • Web Portal for training and continuing education for academic and community researchers, with online menus of the Office of Investigator Services, Research Ethics Consortium, and Office of Industry Alliances • Interactive interface of data de-identification mechanics with the Ethics and Regulatory Experts database.
Pilot, Collaborative Clinical and Translational Studies	<ul style="list-style-type: none"> • Online application process for all CTSI pilot grant-making programs • Online dissemination of information on the granting programs and Society of the CTSI. • Support for data harmonization projects (initially, the Mental Health Cluster's project with LA County)

Program	Collaboration
Translational Technologies and Methodologies	<ul style="list-style-type: none"> • Novel studies in clinical neurosciences, including brain imaging • Center for Translational Technologies and Methodologies (CTTM) Concierge Center, including Web-based directory, searchable database (catalog), and consultation service for ongoing technologies, methodologies, and incubators • Integration of the CTTM activities registry into the UCLA CTSI Community Engagement Program's Community Research Registry, including use of RAP research planning system to enable the CTTM Registry for outreach and in-reach between the CTSI institutions and local community organizations • Real-time Web- and podcasting and videoconferencing and archiving of Technology Affinity Group seminars and Continuing Education workshops, including uploading of digital video recordings and PDFs of syllabi • Protocols on specimen handling, advanced technology use and data pre-processing • Management of the Technology Affinity Group reference laboratory service for sample pre-processing and distributed biomarker testing.
Research Education, Training, and Career Development	<ul style="list-style-type: none"> • CTSI Education Office Website (Internet and intranet) and online databases (e.g., curricular and training programs, enrollee and trainee information, and post-graduation tracking of incubated translational scientists) • Real-time web- and podcasting and videoconferencing and archiving of training program and curriculum-based seminars, workshops, and lectures • IT infrastructure and support for greater multi-institutional faculty involvement in the K30 Program, enabling collaborative expansion of this program to scientists in training at all CTSI partner institutions • BIP-led training in biomedical informatics research and integration with other training curricula, regulatory issues, and responsible conduct of research

10. IMPLEMENTATION PLAN AND MILESTONES

Table 3. BIP Implementation

Year(s)	Measurable Objectives	Milestones
Transition to CTSA		
Pre-Award	<ul style="list-style-type: none"> • Planning meetings of BIP key investigators to design implementation methods • Design and initial implementation of the CTSI Virtual Home web portal • Survey biomedical informatics needs of all CTSI personnel • Extend the Velos CTMS to School of Medicine 	<ul style="list-style-type: none"> • Two brainstorming meetings of key BIP personnel • Implementation plan of translational databases/data archives • Inventory of bioinformatics needs to support CTSI mission
Aim 1: Virtual Home. Establish a Web portal that facilitates communication across the entire CTSI community and directs members of all CTSI user groups to the resources and expertise they need		
1 2 3-5	<ul style="list-style-type: none"> • Implementation of SSO and remaining CTSI Virtual Home modules, including full integration of the RAP • Registry of CTSI Researchers and Research Partners completed • Initial list of biomedical informatics mentors and projects and Project Registry, Center for Translational Technologies Resources Directory, and Protocol Templates • Develop and implement the CRESST Curriculum Tree and social networking services • Make available clinical trials protocols and contact information to potential research subjects through public systems 	<ul style="list-style-type: none"> • Number of queries, number enrolled in SSO system • Numbers and outcome of collaborations facilitated and grant applications submitted that used BIP resources • Web statistics and survey reported volume of use and satisfaction with tools • Number of protocols available to potential subjects through system • Number of users and usage levels for Curriculum Tree and social networking services • Number of patients recruited through clinical trial protocol sites
Aim 2: Research Data Repository. Establish a Research Data Repository (RDR) that integrates secure access to de-identified clinical data from all CTSI partners for appropriate secondary uses		
1 2 3-5	<ul style="list-style-type: none"> • Prototype for RDR (including Honest Broker implementation at each partner site), Common Terminology Service (CTS) • Implement CTSI-wide biospecimen repository (caTISSUE, Daedelus) • Initial Registry of Research Databases for Westwood campus • Registry of Research Databases expanded to all partner sites • Full implementation of RDR (including cohort identification via VH) CTS, and Clinical Research Applications 	<ul style="list-style-type: none"> • Observed vs. expected volume of patient data entering RDR from each CTSI site • Volume of use statistics and user surveys • Number of databases in registry • Number of database uses facilitated by registry

Year(s)	Measurable Objectives	Milestones
Aim 3: Education and Training. Train clinical and translational researchers and new biomedical informaticians from diverse basic science and clinical perspectives in the effective use of informatics tools and methodologies		
1	<ul style="list-style-type: none"> • Informatics training seminars outside degree programs 	<ul style="list-style-type: none"> • 2 seminars/year, 5 trainees/seminar
2	<ul style="list-style-type: none"> • Super-user Workshops on CTSI infrastructure tools • Initiate walk-in training on CTSI tools 	<ul style="list-style-type: none"> • 40 investigators and 40 staff trained as Super-users across CTSI sites trained
3-5	<ul style="list-style-type: none"> • Develop new biomedical informatics course on domain ontologies, controlled vocabularies, data models, data curation, and clinical/biological data/text mining that draws in part on data repository experience 	<ul style="list-style-type: none"> • First set of graduate students take new courses

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Biostatistics, Study Design and Clinical Data Management Program



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Abbreviations: BCSVD -- Bayesian Classification with Singular Value Decomposition, BSD-CDM -- Biostatistics, Study Design, and Clinical Data Management, BVS -- Bayesian Variable Selection, CDM -- Clinical Data Management, CPPR -- Community-partnered participatory approach, DGSOM -- David Geffen School of Medicine, EMR -- Electronic Medical Records, EOC -- Executive Oversight Committee, GCRC -- General Clinical Research Center, GWAS -- Genome-wide association studies, HSR -- Health Services Research, IBVS -- Iterative Bayesian Variable Selection, ICC -- Intraclass correlation, IPPCR -- Introduction to the Principles and Practice of Clinical Research, JSM -- Joint Statistical Meetings, MS -- Mass Spectrometry, MS -- Mass Spectrometry, MSCR -- Master's of Science in Clinical Research, NINDS -- National Institute of Neurological Disorders and Stroke, OIS -- Office of Investigator Services, RCA -- Research Center at Alhambra, ROC -- Research Operations Core, SNP -- single nucleotide polymorphisms, SPH -- School of Public Health, WGCNA -- Weighted Gene Co-expression Network Analysis

1. **OVERVIEW**

The Biostatistics, Study Design and Clinical Data Management Program (BSD-CDM) provides UCLA CTSI investigators with the integrated services and biostatistical support needed to conduct team science in our diverse community setting. BSD-CDM covers Research Design, Epidemiology and Biostatistics key functions. Research Ethics can be found in our Regulatory Program. Along with the University of Southern California and the University of California, Irvine, we are members of the Greater Los Angeles CTSA Coalition. We have collaborations with national CTSA members, including Boston University, Stanford University, the University of California, San Francisco, the University of Texas, Southwestern and Vanderbilt University

In our prior review, BSD-CDM was reviewed with the **Community Engagement and Research Program (CERP)** and received an aggregate score of 2. Reviewers praised our plans for integrating and coordinating our resources and services, the experience and quality of our leadership and our clear focus on research and innovation. In response to the reviewers' comments, we revised this section by 1) doubling the BSD-CDM budget and increasing both master's level statisticians and senior faculty; and 2) providing greater detail about our communication and cross-cultural training, our feedback mechanisms and metrics for assessing service quality, our financial mechanisms and our plans for community-based statistical research. To increase our capabilities in community-based research, we have added three outstanding members to our team with extensive biostatistical experience in community settings: Drs. Belin, Crespi and Sugar. Substantive revisions since our last submission are indicated in the left margin.

2. **SPECIFIC AIMS**

The University of California, Los Angeles Clinical and Translational Sciences Institute (UCLA CTSI) provides operations and governance necessary to facilitate successful transdisciplinary clinical and translational research. The overarching **mission** of the UCLA CTSI is to *transform our academic-clinical-community partnership into a borderless institute that brings our combined innovations and resources to bear on the most pressing health needs in our diverse community*. The UCLA CTSI partners: UCLA, the Burns and Allen Research Institute at Cedars-Sinai Medical Center (Cedars-Sinai), Charles Drew University (CDU) and Los Angeles Biomedical Institute at Harbor UCLA Medical Center (Harbor-LA BioMed) have considerable strengths in ■ clinical trial design ■ statistical genetics and proteomics ■ community studies methodologies ■ survey methods in urban populations ■ pharmacological statistics ■ epidemiological and nonrandomized studies ■ psychometrics, including quality-of-life studies ■ survival analysis and adaptive trials. The BSD-CDM will build on these strengths to deliver integrated services and support necessary to conduct biomedical research in our diverse community setting.

The mission of the BSD-CDM is to provide comprehensive design, biostatistical and data management services to UCLA CTSI investigators and their clinical and community collaborators. We will enhance development of novel clinical trial designs, develop innovative biostatistical methodology for clinical research, and create a secure user-friendly Clinical Data Management (CDM) system. In addition, BSD-CDM will offer expanded translational science courses in clinical trials methodology and new methods in biostatistics and modeling. To achieve our mission, we will pursue three Specific Aims.

Specific Aim 1: Provide coordinated, one-stop access to biostatistics consulting and CDM services.

Robert Elashoff, PhD and Steven Piantadosi, MD, PhD, Andre Rogatko, PhD and David Elashoff, PhD will implement the CTSI-wide network of biostatistics consulting services.

Specific Aim 2: Develop novel statistical applications and methodologies to address the complexities of biological data and the unique requirements of community-based research.

Aim 2.1 – Clinical Research: Robert Elashoff, Steven Piantadosi, MD, PhD, Andre Rogatko, PhD, Roger Lewis, MD, PhD, and Gang Li, PhD will oversee the development of adaptive clinical trials (e.g., phase IIB to phase III) and statistical revisions due to trial amendments and changes of primary endpoints.

Aim 2.2 – High-Throughput Biological Data Analysis Research: Steven Horvath, PhD, Xiuqing Guo, PhD, and David Elashoff, PhD will develop joint research in genomics, proteomics (including novel biomarkers and their evaluations), bioinformatics, and clinical correlates.

Aim 2.3 – Community Studies Methodology: Catherine Crespi, PhD, Thomas Belin, PhD, Teresa Seeman, PhD and Catherine Sugar, PhD will oversee development of specific methodologies relevant to community-based research.

Specific Aim 3: Provide biostatistical education and training.

In collaboration with the Research Education, Training, and Career Development Program (**CTSI-ED**), Robert Elashoff, PhD, Martin Lee, PhD, Peter Christenson, PhD and Andre Rogatko, PhD will coordinate short courses in select topical areas at study sites. The courses will be accessible online in real time via webcasting or point-to-point videoconferencing, and archived on the CTSI Virtual Home. In addition, BSD-CDM will conduct inter-institutional Biostatistics Grand Rounds and provide mentoring and service on PhD committees.

3. PROGRESS TO DATE

BSD-CDM has made substantial progress in the pre-award period with local funds. Receipt of a CTSA will enable us to accelerate this progress.

- We are collaborating with members of the Boston University CTSA on the UCLA-BU EDNR Biomarker Discovery Laboratory Grant from the National Cancer Institute. This collaboration aims to identify and validate early detection lung cancer biomarkers. (D. Elashoff).
- Working with CTSI biostatisticians and at UT Southwestern and health policy experts at UCSF, one of our CTSI investigators completed a cluster-randomized trial showing the effectiveness, and cost-effectiveness, of a barber-based intervention for hypertension control among African-American men (Victor et al., Arch Intern Med, 2010 in press).
- We developed a comprehensive model for clinical trials in which there are repeated visits for clinical endpoints and biomarker measurements. Our model includes both these types of endpoints; their correlation; missing data that is nonignorable and ignorable; handling of outliers and leads to a robust joint model with nonmonotonic, nonignorable data. Our recent paper, "Robust Inference for longitudinal data with nonignorable, nonmonotonic missing values," will be part of a special issue of the Journal of Statistics and Inference. This new work is illustrated by the Scleroderma Lung Disease Trial (National Heart, Blood and Lung Institute [NHLBI] – Tashkin, R. Elashoff) published in the New England Journal of Medicine. Based on this work, the European Rheumatological Association approved and recommended the scleroderma intervention. Four students also wrote their PhD theses on these problems.
- We extended the Weighted Gene Co-expression Network Analysis (WGCNA) methodology to include phenotypic and genotypic information and applied the technique to a study identifying candidate genes for familial combined hyperlipidemia in the Mexican population.¹
- Working with Healthy African American Families, one of our UCLA CTSI community partners, we developed a randomization method for community partnership research. The method, which provides community involvement in the creation of randomization tables and thus addresses concerns about bias often found in underrepresented communities, was presented at Joint Statistical Meetings (JSM) in 2010. (T. Belin)
- We opened the UCLA Master of Science in Clinical Research (MSCR) program to physicians at all four CTSI institutions via distance learning. External and internal Graduate Division reviewers assessed the MSCR degree program as a "gem." The external support for this program was included the K-30 grant which was recently funded again by NIH.
- We completed preliminary work on adaptive clinical trial designs to improve the evaluation of drugs and medical devices and to use mixed methods to characterize and understand the beliefs, opinions, and concerns of key stakeholders during and after the development process. This collaborative research with the University of Michigan recently received new NIH support to design four innovative, adaptive clinical trials for the evaluation of drugs and devices for patients with acute neurological illness or injury. (R. Lewis).
- Working with CTSI biostatisticians and at UT Southwestern and health policy experts at UCSF, one of our CTSI investigators completed a cluster-randomized trial showing the effectiveness, and cost-effectiveness,

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of a barber-based intervention for hypertension control among African American men (Victor, et al., Arch Intern Med, 2010 in press).

4. SIGNIFICANCE: THE BSD-CDM'S STRENGTHS AND OPPORTUNITIES

The CTSI has excellent resources in biostatistics, study design, and CDM. These include well-developed cores in biomathematics, biostatistics, and bioinformatics in the David Geffen School of Medicine (DGSOM) and the School of Public Health (SPH) at UCLA-Westwood, and at the General Clinical Research Centers (GCRCs) at Harbor-LA BioMed and Cedars-Sinai. The demand for novel statistics from our clinical and translational researchers outstrips current supply and requires a more streamlined system of accessing these resources.

The CTSI leadership surveyed CTSI investigators in 2010 to identify priorities for improving research support. Twenty-six percent cited biostatistical and data analysis and 6% cited research design. Asked what kinds of help they would most like to receive from the CTSI, 61% of faculty said biostatistical and data analysis and 27% said research design. The structure and organization of the CTSI affords us a unique opportunity to unite the resources of our partners to provide comprehensive services to all four UCLA CTSI institutions and community partners. The BSD-CDM design responds to the priorities highlighted in our survey.

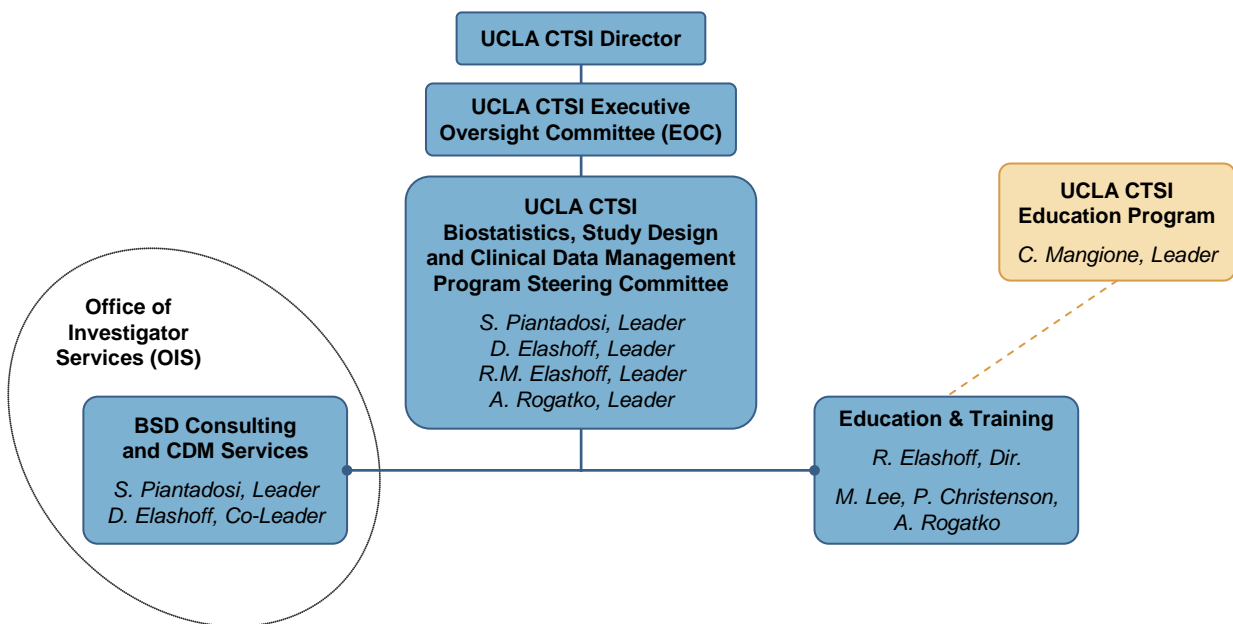


Figure 1. CTSI BSD-CDM Program. The dotted line refers to an ordinary role.

The BSD-CDM will provide CTSI investigators and their community and clinical collaborators with comprehensive and integrated services, instruction, and research methodologies. Through partnership with the Office of Investigator Services (OIS) (see Regulatory Program) we will provide one-stop, online access to consulting services. Basic services include: 1) contemporary data analysis methodology consultation, implementation, and epidemiology expertise, 2) the best available CDM software, 3) study design and grant preparation assistance 4) bioinformatic data analysis.

The Biostatistics core will provide unique, advanced consulting services and research collaboration to CTSI investigators with respect to recent advances in clinical trial design. We will also provide statistical genetics, genomics and proteomics to synthesize data; relate genomic and proteomic variables to physiologic and clinical endpoints; and elucidate the contribution of genomic and proteomic factors to effects of treatment in clinical trials. The BSD-CDM will also expand to meet the need for community studies and new methodologies in observational study design. The BSD-CDM will expand the range of studies supported by the CTSI to include clinical and genomic epidemiology.

The BSD-CDM will enable CTSI investigators to improve their research quality and have the necessary methodological tools to explore new directions in clinical and translational science. Thus, basic science investigators with little clinical research experience will be able to take their research interests and findings into the realm of clinical trials that are well developed and have strong potential for extramural funding. Clinical

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researchers will have the opportunity to directly interact with research design and statistics experts, access advanced techniques for clinical research, and design improved clinical trials using developments that incorporate biomarkers and clinical endpoints, and their interrelationships.

5. INNOVATION AND ENVIRONMENT

A wealth of existing collaborative assets in biostatistics and clinical data management are centralized within or strongly linked to the CTSI BSD-CDM.

Our BSD-CDM team includes more than 70 faculty statisticians and clinical data management professionals housed on the UCLA Westwood campus and outstanding colleagues at Harbor-LA BioMed, Cedars-Sinai, and CDU. Our resources include well-developed cores in biomathematics, biostatistics, and bioinformatics across our partners. BSD-CDM will draw on the strengths of the following institutions, schools, divisions and departments:

- Clinical departments in the DGSOM.
- Mega-research programs and centers, such as Jonsson Comprehensive Cancer Center (JCCC).
- Department of Biomathematics and Department of Human Genetics in the DGSOM.
- Divisions of Biological, Social, and Physical Sciences within the College of Letters and Science, including the Department of Statistics.
- SPH, including the Departments of Biostatistics and Epidemiology.
- Schools of Engineering, Management, Nursing, and Dentistry.
- GCRCs at Harbor-LA BioMed and Cedars-Sinai.
- Cedars-Sinai's Samuel Oschin Cancer Institute biostatistics and bioinformatics resource.

Table 1. **Biostatistics, Study Design and Clinical Data Management Program Opportunities and Transformations**

Opportunities	Transformation Processes
Enhance access to biostatistical design, analysis and clinical data management collaboration	Develop organizational structure to make statistical support more available to the community and provide resources to allow young investigators access to professional statistical services
Increase access to required statistical expertise	The Program Steering Committee will match investigators with the appropriate statistical collaborators among CTSI BSD-CDM faculty
Widen the scope of clinical-translational research designs and analysis methods	Through the Pilot and Collaborative Research Program, provide resources to develop new statistical methodology required for novel translational research
Improve access to CDM resources by all investigators	Through the CTSI BSD-CDM and collaborations with the CTSI Biomedical Informatics Program, provide a gateway to available CDM services across all sites and provide expertise to clinical and translational research community biostatisticians
Expand and improve existing biostatistics training	Provide support for an MS degree in Clinical Research and increase educational outreach through mentoring and short courses
Los Angeles-area logistic difficulties	Development of video- and teleconferencing and webcasting of courses, with archiving of recorded sessions and their supporting or handout materials (distance learning)
Separate sites: services	Support two or more statisticians (at least one PhD level and one MS level) at each site to interact with investigators and have weekly video- or teleconferences with participating statistical/biomedical investigators
Increase access to bioinformatic analytic services	Support for three faculty level statisticians specializing in genomics, proteomics and genetics to provide access to cutting edge bioinformatics methodologies and tools
Separate sites: research	We have formed three teams of statisticians, epidemiologists and physicians to develop new adaptive clinical trial designs; develop a genomics, proteomic group of statisticians, physicians, and basic scientists; and develop community research methodologies
Separate sites: biostatistics education and training	Cedars-Sinai and Westwood have faculty who teach courses at the other site, an approach that will be strengthened to include all CTSI activities

We have identified several opportunities to transform our biostatistical and CDM services (see **Table 1**). Challenges include: 1) logistical difficulties, 2) institutional structure; 3) decentralized CDM, as the CTSI has data management systems of various complexity and capability and new systems coming online; 4) a technological need to overcome these problems; 5) the need for regular organizational and administrative venues to facilitate collaboration and interactions, and 6) the need for a means for translational researchers to access specialized statistical expertise relevant to their particular needs. As outlined in **Table 1** and detailed below, we have developed a comprehensive program to address these challenges and develop an integrated biostatistical and CDM resource. For the first time, CTSI institutions will have a broad-based, centralized resource site to meet all of their clinical-translational investigators' needs in study design and data management and analysis.

6. APPROACH

6.1. Specific Aim 1: Provide coordinated, one-stop access to biostatistics consulting and CDM services.

The CTSI BSD-CDM will provide a full-service facility for the biostatistical, design, and data management requirements of clinical research. BSD-CDM will transform the currently isolated and fragmented biostatistics and data management services at UCLA and its partner institutions into an integrated organization that offers comprehensive services and eliminates unnecessary overlap and existing gaps in resources.

6.1.1. Investigator Access to the CTSI BSD-CDM. Investigators throughout the CTSI can access information about the BSD-CDM and tap into its network of resources and services through the efforts of the CTSI OIS and its Research Facilitators (see **Regulatory Program**). Through a partnership with the CTSI **Biomedical Informatics Program (BIP)** OIS maintains the CTSI Virtual Home, a website that provides information on biostatistical collaborators, the availability of data management tools, and educational opportunities in biostatistics. BSD-CDM service biostatisticians serve as Domain Experts in the OIS.

An investigator in need of biostatistical or data management consulting services first contacts OIS through the Virtual Home or by speaking with a Research Facilitator. Dr. Wang, a master's trained statistician with a medical degree, receives and triages referrals from the OIS under the direction of Dr. R. Elashoff or the lead service statistician. The lead service statistician will conduct the initial consultation and determine whether or not additional assistance from other BSD-CDM statisticians (faculty or staff level) is needed. There will be a lead statistician and a master's level statistician at each of the UCLA CTSI partner institutions. These new masters level statisticians leverage the time and expertise of core faculty, providing greater capacity of the CTSI to support statistical needs of investigators.

When the lead service statistician identifies projects that require additional expertise, he or she will consult with Dr. R. Elashoff to determine the optimal BSD-CDM faculty statistician collaborator. For example, a statistical analysis protocol for a research project may be defined and carried out by the site statistician. A joint site-network statistician team may be formed to proceed with the study analysis. Joint investigator-statistician team videoconferencing may take place, or the site statistician may find that he or she has the information to proceed without network backup. Lead statisticians will provide consultations in person or, when the lead statistician and investigator are at different sites, by videoconference. A graduate student may be involved during the videoconference. Thereafter, the graduate student will follow through on subsequent consultations.

Short write-ups of program-related activities are required when the BSD-CDM network is involved; this will feed periodic reports to the CTSI Director on network activities. These reports will be reviewed weekly by the BSD-CDM Program Leaders, and monthly or quarterly by the CTSI BSD-CDM Steering Committee (**Figure 1**).

Subsequent to identification and assignment of the appropriate faculty statistician/MS level statistician team to CTSI investigators, this team will provide all needed assistance (e.g., grant preparation, study design, data analysis) to the investigators. Completed collaborations will be logged and reports will be sent to the Steering Committee.

Besides providing services at academic and clinical sites, BSD-CDM will assist in community-based research. Our current collaboration with Research Center at Alhambra (RCA) is a model for this kind of work. We provide statistical support to the RCA for its research on the prevalence and progression of such common chronic diseases as diabetes in African-Americans, Latinos, and Asian Americans who reside in the San Gabriel

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Valley, the suburban Los Angeles County area where RCA is located. Data management support is provided by the UCLA Claude Pepper Older Americans Independence Center Research Operations Core (ROC). Since the RCA will be supported by the CTSI **Clinical and Community Research Resources Program (CCRR)**, we anticipate our collaborations with RCA will expand under a CTSA.

Community-based research conducted in close collaboration with the **CERP** is described in (see **CERP**).

Financing considerations regarding biostatistical support are described in **Section 6.1.5**.

6.1.2. Publicizing the BSD-CDM. We are publicizing the BSD-CDM in a several ways. Through the Virtual Home, we will disseminate information about the BSD-CDM and its statistical consultation services. A group of network statisticians, including on-site statisticians, will make presentations about the BSD-CDM and available services. We will publicize these presentations on the Virtual Home. In addition, we will work with the leadership of the **CCRR** (Participant and Clinical Interactions Resources key function) to ensure that clinical staff throughout the UCLA CTSI is familiar with these services. The OIS Research Facilitators will refer investigators to BSD-CDM.

We will also publicize the BSD-CDM through biostatistics classes taught by our faculty, such as a physician-oriented clinical trials course, "Controversies in Clinical Research" (see **section 4.3**). This course, part of the K30 program (UCLA Graduate Program in Translational Investigation), entails discussion of the CTSI BSD-CDM and will be a mode of publicizing the CTSI and the BSD-CDM network. This course will be available through videoconference and will be archived on the Virtual Home so clinicians can view recorded lectures at their convenience. Other courses (e.g., MSCR courses (described in **Aim 3**), Biostatistics Department consulting seminars) also will be accessible as audio or video online at each site.

6.1.3. Plan for Services. Our program will emphasize and use technology to implement several service activities, some of which include design and analysis for biomedical studies (including co-writing of grant applications); review of protocols for the CTSI CCRR Program; matchmaking for new interdisciplinary teams, including the CTSI BSD-CDM support staff; data analysis and oversight (e.g., clinical trials); bioinformatics consulting; and training of study staff and new investigators in CDM systems use.

6.1.4. Implementing Biostatistical Services. For the BSD-CDM to develop an integrated facility for resources and services (and its own research agenda), we must overcome logistical difficulties of personnel and investigators, and break down impediments. Physically, BSD-CDM faculty and staff are dispersed throughout our CTSI network and do not operate from a central site. Videoconferencing and webcasting will help us in these efforts, as will interactive, wireless or site-independent telemedicine technologies. The CTSI Virtual Home will provide resources for investigators and statisticians to share data and analyses through secure FTP-based transfer options that will ensure adequate protections for confidential data and allow for large files to be easily exchanged.

The UCLA Telemedicine Initiative (led by Alan Robinson, MD, Vice Provost of Medical Sciences and Executive Associate Dean of the DGSOM) will be central to this effort. This initiative is supported by a State of California Proposition (1D), which provides equipment for telemedicine for the DGSOM. With this funding UCLA is purchasing equipment and setting up network connections with the DGSOM, the Ronald Reagan UCLA Medical Center, Santa Monica-UCLA Medicine Center, Venice Family Clinic, the VA Greater LA Healthcare System, Olive View-UCLA Medical Center, Harbor-LA BioMed, CDU and Cedars-Sinai. We will also be developing telemedicine access to community sites yet to be identified. While the purpose of these funds is to provide teleconferencing for clinical activity, the clinical sites' overlap almost completely covers the academic, research, and clinical research sites that will be supported by the UCLA CTSI. UCLA has received confirmation that when these sites are not being used for direct clinical care, they can be used for teleconferencing capability for clinical research. This teleconferencing capability will allow more in-depth consultation service. As clinical research is initiated, information sharing among sites will be markedly enhanced by this teleconferencing network, an example of our reorganized approach to an integrated BSD-CDM services system.

We have planned for the development of a true integrated network for biostatistics, study design, and clinical data management services that unites all sites. The success of our program in the network institutions will enhance our opportunity for further growth. The weekly teleconference reviews will be an effective operations monitoring tool, as will the monthly meetings of the BSD-CDM Steering Committee.

6.1.5. Resources for Investigators. The BSD-CDM effort was designed to meet several requirements: (1) provide statistical service to investigators at their home sites, (2) provide statistical service to CTSI investigators (4) assist doctoral students and other trainees to increase their skill in collaborative studies.

We have developed criteria for establishing an effective responsive biostatistical network. We consider essential capacities to include expertise in: (1) clinical trials (including longitudinal trials); (2) survey research and practice; (3) pharmacological statistics; (4) genomic studies; (5) epidemiological and nonrandomized studies; (6) psychometrics, including quality of life studies; and (7) survival analysis and adaptive trials. Our backup for more specialized but less frequently encountered needs is the faculty of all four UCLA departments (i.e. Biostatistics, Statistics, Biomathematics, and Human Genetics) that are heavily involved in statistical methodology.

The subsidy-of-services for BSD-CDM includes greater statistical capacity as well as financial subsidies support for the biostatistical needs of CTSI investigators, with an emphasis on financial support to new investigators undertaking CTSI-approved protocols. Consultation for biostatistics, study design and clinical data management follow the same financial model. The faculty and staff of the CTSI BSD-CDM will provide partial support for lead service statisticians at their home sites. This support will supplement current site support and is expected to expand with future external funding generated by the successful collaborations with CTSI investigators. BSD-CDM will also provide support for CTSI statisticians at one site to participate in projects at other CTSI sites, depending on need and expertise. The BSD-CDM recognizes that the partial funding of effort for statisticians likely will not be sufficient to satisfy these service and teaching needs. Thus, investigators will have to meet statistical support for their studies using non-CTSI funds. We are aware that some investigators will require more extensive statistical consultation than is available using CTSI support. In these cases, Drs. Rogatko and R. Elashoff will facilitate the pairing of these investigators with CTSI or other statisticians at CTSI locations. These collaborations will use non-CTSI funds.

Some investigators will require assistance that can appropriately be carried out by graduate students. Drs. Rogatko and R. Elashoff will facilitate such interactions and provide oversight. Investigators use their own funding to partially cover the cost of graduate student consultations. For time consuming studies, the site and BSD-CDM network team receives funding support from investigators.

CTSI-approved protocols from new investigators at early stages in their research careers will receive biostatistical support for grant applications and preliminary data studies at no charge; the site and BSD-CDM network may require some institutional support for more extensive analyses. We have assigned two CTSI MS-level statisticians (each at 50% time) to each institution

6.1.6. Evaluation of Biostatistics Consulting Services. Our CTSI Evaluation and Tracking (E/T) Program will conduct CTSI Periodic Surveys. These Web-based surveys will be administered periodically to assess needs, availability and utilization of resources, and to track satisfaction with CTSI programs and services. The survey results will be discussed at the program leadership meetings and provided individually to the BSD-CDM leaders. These surveys will assess usage of the biostatistics program and determine whether any barriers to utilization exist. Additionally, they will measure access to and timeliness in receiving a consultation, perceived competency of the biostatistician in providing the service, and expected outcomes of the consultation. BSD-CDM will work with the E/T faculty to develop program improvement plans to improve satisfaction.

6.1.7. Implementing CDM Computer Systems. The sites in the consortia currently make use of multiple CDM computer systems. At present, the BSD-CDM recognizes that one system does not fit all needs of investigators across the CTSI. A function of the BSD-CDM will be to periodically review the various CDM services available at each site to provide matchmaking of investigators with CDM services that are most appropriate for their research projects. The researcher registry in the BIP Virtual Home will facilitate this review, enabling us to provide feedback on CDM services throughout the CTSI to improve their utility. Many CDM systems contain sensitive data that requires special protection, whether it was originally collected for purposes of research or patient care. The OIS and BIP will partner with the BSD-CDM to provide IT support and expertise to ensure high standards of data security while also facilitating appropriate data sharing among investigators. In some collaborations this may involve secure, automated synchronization of research databases across sites.

6.1.7.1. Sample CDM System. One such complete CDM system has been developed by the UCLA Semel Institute Biostatistics Core (SIStat). This system is used extensively to develop active secure database

websites that enable users to enter data directly into a centralized database on a host server, and to view and edit the data stored. Data entry on a centralized Internet-based system makes the project database instantly available to all authorized researchers in the system, and permits access from any computer. Such centralized databases enable ready online reporting to all projects, project management and quality assurance information dissemination, and distribution of composite data to relevant investigators on demand. Data or summary reports are automatically updated as the database changes. (A demonstration website displaying some of the available features is available online.) We will provide advice on which database systems will be most appropriate for the specific needs of a trial. The SISat system is a complete CDM system comprising Web access to multiple clinical sites, case report forms and their editing, linkage with radiographic and pharmacy cores, and specialized databases.

The JCCC members' system is Velos. Its use is required for members doing clinical research. Cancer studies developed within CTSI will be able to make use of this specialized system if desired. Members of the BSD-CDM will use specific systems based on the preference of investigators after full disclosure of each system is addressed.

6.1.8. Biostatistics and Design Grand Rounds. The Biostatistics Grand Rounds are described here although they are relevant to specific Aims 1 and 3. The BSD-CDM will host four Grand Rounds per year, rotating quarterly among institutions and with on-site participation from all members. A formal presentation of a consulting problem and its partial solution will be presented by a junior BSD-CDM member or by a consultee. The presenter will come from an institution other than the hosting site. One or two senior discussants (at least one from outside the host institution) will discuss the problem. Audience participation will be encouraged. Announcements to the research and clinical faculty will precede each Biostatistics Grand Rounds, and each session will last 1 hour.

6.2. Specific Aim 2: Develop novel statistical applications and methodologies to address the complexities of biological data and the challenges of community-based research, including design and analysis of clinical trials and observational studies (including epidemiological studies) and community and health services research.

The BSD-CDM will enable creation of multi-institution methodological collaborations between faculty statisticians and physicians. By partially funding protected research time and by providing a structure for direct interaction of geographically separated researchers, methodological collaborations will be created that otherwise would not exist. The results of the investigations will be more rapidly disseminated within the institutions since there will be collaborators from multiple institutions.

6.2.1. Clinical Research. In 2004, the FDA posed challenges to the biomedical community for paradigm changes to bring new drugs and intervention procedures to patients much faster. The enthusiasm in this FDA report for new approaches in clinical trials research has greatly stimulated clinical trial biostatistical research. To fulfill the Specific Aim of developing new designs and analysis methodologies for clinical trials and other types of clinical research, the BSD-CDM will focus on several important emerging problems and issues in design and data analysis, such as adaptive clinical trials and methodologies to deal with the challenges of genomic and proteomic data in translational and clinical research. In a series of papers² in the *Journal of Pharmaceutical Statistics* and *Statistics in Medicine*, problems and issues with adaptive clinical trial designs have been articulated and studied with increasing vigor. Hung et al.³ usefully summarized some of the major issues: 1) re-estimating sample size, 2) dropping treatment arms, 3) changing primary endpoint(s), 4) Bayesian monitoring methods, 5) development of composite endpoints, 6) approaches to missing data, 7) statistical treatment of measures using genetic prediction factors, and 8) clinical trial design with biomarker and clinical endpoints. Adaptive trials also include issues with nonperforming clinical sites. This delineation by Hung was in collaboration with Dr. O' Neill.

As the FDA emphasizes, efficient transition from phase II to phase III trials is an important need for clinical trial research. Members of the BSD-CDM team have already published 6 papers on joint models with longitudinal biomarker endpoints in multisite trials, based on a mixed-model, repeated-measures design combined with a competing risk time-to-event model⁴⁻⁶ and has submitted an additional three manuscripts generalizing the results in these papers using Bayesian models and monitoring procedures.⁷⁻⁹ The missing data model is for non-ignorable missing data. Leading this research for BSD-CDM are Dr. Gang Li and Dr. Robert Elashoff. Four of students mentored by Drs. Li and R. Elashoff wrote their doctoral theses on this research.

Dr. Roger Lewis will take the lead on developing adaptive trials in which amendments change eligibility. Drs. Roger Lewis and Robert Elashoff are considering biostatistical inference in adaptive trials with protocol amendments dealing with eligibility and related problems. A current example of this is a phase II clinical trial headed by Dr. Steve Dubinett. In this trial, biomarker inclusion criteria have been added to appropriate inferential modifications to the primary endpoint analysis.

Dr. Gang Li has formed a UCLA, Stanford University, and Cedars-Sinai collaboration, initially emphasizing a seamless transition from phase II to a phase III trials that involves sample size re-estimation based on an estimated treatment effect from the phase II trial, which will be truncated in the phase III. This approach has been discussed collaboratively with the FDA Biometrics division. Also, Dr. Robert Elashoff will be encountering this problem and will have a need for methodology in a multiple sclerosis phase II ongoing trial funded by The National Institute of Neurological Disorders and Stroke (NINDS) and the Multiple Sclerosis Society. Drs. Gang Li, Ying Liu (Stanford University) and Piantadosi will also be developing this methodology. Dr. Rogatko has been developing designs and analyses for phase 1 trials that enable the translation of basic science into initial single-arm studies. Our area of research interest is in designs for efficiency increases in early trials, such as phase I and phase IIA trials.

6.2.2. High-Throughput Biological Data Analysis Research. The rise in use of high-throughput (genetics, genomics, and proteomics) technologies in translational research requires development of novel statistical methods. We are forming a research group, which includes Drs. Steve Horvath, Xiuqing Guo, and David Elashoff, to develop new methods arising from these studies. There are clinical studies that obtain proteomic, gene expression, SNP, and other bioinformatics data. To be useful in most clinical research studies, such data must be appropriately analyzed. Three examples of our recent research in this area are gene co-expression network analysis, the statistical analysis of proteomics data, and genome-wide association studies. Because these research areas generate extremely large data sets that pose an expanding challenge to current database systems, this group will work with members of the BSD-CDM to develop database tools to address this need and support analytical efforts. We detail these areas below.

6.2.2.1. Weighted Gene Co-Expression Network Analysis. While the main emphasis of the BSD-CDM is to provide statistical and data management support to CTSI translational projects, we will carry out various statistical methodological efforts to provide state-of-the-art data analysis methods. An example is our novel method of weighted gene co-expression network analysis.¹⁰ Besides the standard gene expression analysis flow, we will also apply weighted gene co-expression network analysis. This kind of analysis is related to standard approaches, so it provides a systems approach to analyzing microarray data based on graph theoretic concepts. Gene co-expression networks are increasingly used to explore the system-level functionality of genes and to find gene modules.

The network construction is conceptually straightforward: nodes represent genes and two nodes are connected if the corresponding genes are significantly co-expressed across appropriately chosen tissue samples. In reality, it is not trivial to define the connections among the nodes in such networks. A major advantage of the network framework approach is the availability of gene connectivity measures (intramodular connectivity). Besides the standard gene screening methods mentioned above, we will use intramodular connectivity in conjunction with differential gene expression measures (e.g., t test, p values, fold change) to screen for biologically and statistically significant genes (network-based screening). There is empirical evidence that this network-based gene screening method may lead to improved validation success when dealing with microarray data.¹⁰

6.2.2.2. Statistical Analysis of Proteomics Data. One ongoing research project is the appropriate handling of proteomics data arising from mass-spectrometry (MS) technologies. The statistical handling of this data involves a two-step process: data pre-processing and analysis. Data pre-processing for MS consists of a series of steps: baseline subtraction, normalization, spectrum alignment, binning, transformation, peak detection, and peak clustering. These steps ensure comparability of spectra between different samples. However, the methodology for performing these steps is heuristic at best. Our research will investigate individual steps in this process, normalization, for example, and will aim to address questions such as “*Do we need to normalize, and if we do normalize what is the best method to use?*” We use various measures of success for specific data preprocessing methodology such as minimizing within-subject variability and maximizing within-subject correlation and between-subjects effect sizes. We have found, for example, that appropriate normalization

substantially reduces within-subject variability and increases statistical power for detecting differentially expressed proteins. Beyond the evaluation of each individual step in the process, we will investigate the effects of various combinations of pre-processing steps and different choices for each step to obtain a semi-optimal methodology.

6.2.2.3. Improving Power in Genome-wide Association Studies. Genome-wide association studies (GWAS) evaluate genetic variants spanning the entire genome, with the goal of identifying susceptibility genes for the disease of interest. These studies typically use a large number of single nucleotide polymorphisms (SNPs), with relatively small sample sizes, which leads to a serious multiple testing problem. One way to reduce the number of tests is to evaluate multiple SNPs simultaneously. To analyze multiple SNPs simultaneously when the sample size (n) is much smaller than the number of SNPs, we have developed two new methods: Iterative Bayesian Variable Selection (IBVS) and Bayesian Classification with Singular Value Decomposition (BCSVD). The IBVS method repeatedly uses the Bayesian Variable Selection (BVS) until a proper number of SNPs are selected.¹² To improve the running speed, Kwon and Guo further developed the BCSVD method.¹³ The BCSVD method is a variable search method that reduces the dimension of the model p parameters (markers) to that with n parameters derived from the SVD of the design matrix. Test procedures developed by Kwon and Guo¹⁴ and based on permutation and generalized likelihood ratio, can be incorporated to select significant genes.

6.2.3. Community Studies Methodology. A primary purpose of BSD-CDM is making vital contributions in study design and analysis to advance community-partnered research. Support includes consultations on study design, sampling strategies between and within communities, analytic methodologies and recruitment strategies, data collection strategies and statistical advice on how to present and publish data. Biostatisticians partner with investigators within community-partnered research to support the specific demands of design in translational biomedical and clinical interventions. BDS-CDM contributes novel alternative methodologies that meet the design challenges. One example is estimating causation in non-RCTs.

CTSI BSD-CDM faculty (Drs. Crespi and Sugar) are heavily involved in community studies in collaboration with the JCCC program in cancer control and prevention (headed by Patricia Ganz, MD and Roshan Bastani, PhD). Dr. Crespi focuses on intervention trials involving cancer screening and prevention, health disparities, effects of cancer as a chronic condition, and cancer survivorship. Dr. Crespi has extensive experience with the design, conduct and analysis of research studies in community settings with an emphasis on cluster-randomized trials and measurement of quality of life impacts. Dr. Crespi also conducts research in Bayesian data analysis and hidden Markov models for longitudinal data. A current study is developing new methods for the design of studies with clustered binary data by improving ICC prediction using exchangeable binary distributions. In contrast to the more commonly used random effects approach to modeling the ICC, which regards intracluster correlation as arising from between-cluster differences, the exchangeable binary distribution approach regards intracluster correlation as arising due to within-cluster mechanisms. Thus this approach opens new avenues for predicting the ICC by modeling within-cluster dynamics. The random effects approach also restricts the ICC to be positive, which is problematic for studies with small clusters, which can exhibit negative ICCs. Thus there are many potential advantages to using exchangeable binary distributions. Further work is needed to incorporate this new approach into sample size and power analyses.

Dr. Sugar's contributions to community studies include clustering, classification, and functional data analysis with an emphasis on finding patterns in high-dimensional or longitudinal data. She has been involved in numerous applied projects in the mental health arena, particularly in schizophrenia and depression. This work has focused on identifying patterns of symptoms or functioning in patient populations and exploring how those patterns evolve over time in response to treatments or other stimuli. Dr. Sugar's methodological expertise aligns with community-partnered research underway in the 70-Block Project demonstration project in **CERP** (see **CERP**).

Dr. Belin's primary contributions to community studies include developing mixture-modeling methods for performing linkage of multivariate records and contributing to mental health studies. Dr. Belin developed a novel randomization method to produce seeds for the random number generator in the randomization program.

Examples of current and future contributions include: (1) The Cancer Prevention Community Programs led by Dr. Bastani, an investigator with CERP; (2) The barber-based community-level intervention program for hypertension and cardiovascular risk factor management located at Cedars-Sinai (Dr. Rogatko, a CTSI faculty

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member is the lead statistician)¹⁵; and (3) Community Partners in Care (statistical collaborator Dr. Belin and Andrea Jones of Healthy African American Families), which uses a community-partnered participatory research (CPPR) framework to compare two strategies for implementing evidence-based depression treatments. Core principles of the CPPR framework, including respect for diversity, openness, equality, empowerment, and an asset-based approach give rise to a need for careful attention to statistical considerations as basic as implementing a randomization protocol.

6.3. Specific Aim 3: Provide biostatistical education and training. In collaboration with the CTSI-ED, the BSD-CDM will enhance its training programs across the CTSI. It will continue to direct the MS degree training program in clinical research and provide short-term instruction to fellows and clinical researchers. The BSD-CDM education and training will be lead by Drs. Robert Elashoff, Martin Lee, Peter Christenson, and Andre Rogatko.

6.3.1. Biostatistical Training. The UCLA Biostatistics and Biomathematics Departments together have over 22 faculty members. There are 75 graduate students between the two Departments and approximately 15 MS degrees and 5 PhD degrees are awarded annually. During the past 2.5 years, Drs. R. Elashoff and G. Li regularly co-chair doctoral theses.

New directions in departmental emphasis and research are reflected in its new and continuing appointments. Several of our new faculty appointments have been in Statistical Genetics. The Biostatistics Core of the Center for AIDS Research now resides in the Biostatistics Department and provides statistical support for much of the AIDS research on campus. An additional benefit of this Core is that it provides key support for new statistical faculty engaged in AIDS research, and has made it possible to recruit new in-residence faculty to the Department. Grant support in cancer research provides another avenue for faculty recruitment. The Department is part of a new interdepartmental program in Bioinformatics that grants a certificate to students in MS and Doctoral degree programs.

The BSD-CDM is developing a consulting short course and hands-on mentoring for biostatistics students and junior statistical investigators on issues of communication. The consulting short course will be led by an experienced faculty statisticians (Elashoff, Gjertson, Horvath) and involve CTSI investigators from **CTSI-ED** and **CERP** to teach effective statistical communication. Direct mentoring will pair students, staff and junior faculty statisticians with experienced faculty statisticians well-versed and active in clinical and translational community-partnered research including T. Belin, C. Sugar and C. Crespi. Mentoring sessions will include consulting meetings with CTSI collaborators at all stages of the process ranging from initial problem definition to explanation of statistical results. These new initiatives will add to the existing course offerings from the Biostatistics Department including Biostat 402 master's consulting seminar taught by Gjertson and Horvath and Biostat 409 doctoral consulting seminar. This course is being expanded to allow full access to the CTSI.

6.3.2. Master of Science in Clinical Research (MSCR). Dr. Robert Elashoff and Dr. Joy Frank in the DGSOM Department of Medicine (and a CTSI -ED investigator) have developed a highly successful MSCR program. This degree program is now a track of the UCLA K30 Graduate Training Program in Translational Investigation. A distinctive characteristic of this program is the direct, close mentoring students receive from faculty. All trainee physicians in the MSCR program from all campuses of the CTSI must complete a thesis for publication in collaboration with a quantitative mentor in biostatistics. The students (usually 10 per year) are a mix of fellows and faculty from a wide variety of clinical departments. As a result of our in-depth mentoring students achieve our program goal of having their thesis manuscripts published in peer-reviewed journals. For those in the program who additionally opt to write K23 grant applications, we will review and provide assistance and constructive criticism on the applications. Recent successful K23 awardees include Dr. S. Weigt for "The Role of Aspergillus in the Pathogenesis of Bronchiolitis Obliterans Syndrome." A paper based on his research, "Aspergillus Colonization of Lung Allograft is a Risk Factor for Bronchiolitis Obliterans Syndrome," was recently published in the American Journal of Transplantation.

In collaboration with CERP and CTSI-ED, we will contribute to an expansion of the MS Program in Clinical Research core curriculum to include theory and practice of community-partnered interventions. We will also develop community-responsive and -driven instructional elements in design, methods, and conduct of community-based clinical trials and observational studies. Drs. Crespi, Belin and Sugar contribute to this goal.

This program is partially supported by renewal funding in the K-30 grant, The K-30 is the principal support of the certificate program (below). The PI (Isidro Salusky, MD) collaborates with R.Elashoff. Dr. Salusky is Leader of the UCLA CCR and has a major stimulus grant to provide training for community translational research.

6.3.2.1. MSCR Program Logistics. We are using videoconferencing and webcasting to make the courses easily accessible across the CTSI. Lecture materials will be posted on the Virtual Home. Monitoring with UCLA-Westwood mentors will be carried out by videoconferencing, teleconferencing, and face-to-face meetings. We recognize the need to teach instructors how to make effective use of the system. The key to statistical training for clinical investigators is interactivity with the statistical faculty, which will be provided by the teleconferencing system.

6.3.2.2. Clinical Trials Coursework in the MSCR Program. Students receive lecture notes with readings, computer assignments, and literature critiques of major clinical trial errors. Topics include:

- Early phase trials
- Critique of early phase designs
- Examples of development of funded early phase trails
- Aspects of a complete protocol for early phase trials
- Approaches to randomization
- When to stratify and over-stratify and measurement error in stratification and covariance
- Sample size and its sensitivity analyses
- IRB and federal regulations and the importance of confidentiality
- Choice of endpoints (number, type) and justification
- Data analysis issues and practice in analyzing clinical trials
- Adaptive trials, repeated-measures trials
- Justification of the detailed data analyses
- Should we analyze data blind?
- Multiple testing
- Multiple analysis
- Equivalence vs. efficacy
- The ubiquitous world of missing data: statistical monitoring of adverse events and safety studies by morbidity and mortality committees
- Data management in all its forms
- How do we administer clinical trials?
- Role of different clinical specialties, changing endpoints
- Dropping treatment, re-estimation of sample size: What are we trying to do?
- Monitoring of trials for safety and efficacy

Besides coursework materials, Phase I/II material is presented to students, followed by in-depth studies of phase III trials. Class periods are usually reserved for review and discussion of these materials. The discussion is multipartite and interactive and expert visitors are invited as appropriate. All participants have intellectual gain outside their specialties.

6.3.2.3. Curriculum for the MSCR Program. Candidates complete 56 credit units. Required courses include:

- Introduction to Computer-Based Biostatistics (Fall)
- Regression Analysis for Clinical Investigators (Winter)
- Advanced Biostatistics (Spring)
- Clinical Pharmacology (Fall)
- Data Analysis 1 (Winter)
- Data Analysis 2 (Spring)
- Controversies in Clinical Trials (Winter)
- Methodology in Clinical Research: Observational Studies (Fall)
- Methodology in Clinical Research: Introduction to Clinical Trial Design (Spring)
- Methodology in Clinical Research: Advanced Clinical Trial Design (Fall)
- Ethics in Patient-Oriented Research (Fall)
- Three elective graduate courses.

6.3.2.4. Mentored Research. We offer two kinds of mentored research. For research theses with approved mentors, the thesis is presented in the form of a submitted manuscript(s) and in an oral presentation. For quantitative mentorship, trainees are assigned both a research mentor and a quantitative mentor to help with the statistical design of thesis research.

6.3.2.5. Faculty. These courses are presented as follows: Dr. Piantadosi teaches the course “Clinical Trial Design.” Dr. Roger Lewis gives lectures on monitoring for adverse events and efficacy in the advanced clinical trials course. Dr. Robert Elashoff teaches courses in controversies in clinical trials and advanced clinical trial design.

6.3.3. Certificate Program. This program is less intense than the academic MS degree program. The curriculum requires coursework in safety and regulatory, clinical trials, controversies in clinical trials, and introductory statistics. All courses in the MSCR program are open to Certificate students. In addition, all Track II Fellows are required to attend the K30 monthly meeting and participate in three required presentations and the following two courses:

1. CCRR summer 2-Week course: *The Essentials of Clinical Investigation: Developing a Research Proposal*
2. NIH Introduction to the Principles and Practice of Clinical Research (NIH IPPCR) Module 5 (Safety and Regulatory Issues in Patient-Oriented Research) from the K30 menu is recommended for fellows in the MSCR program, although not yet required. Currently this certificate program is underutilized. With the new K-30 funding this program will be expanded across the CTSI and subsequently made available more generally to other CTSI programs.

6.3.4. Biostatistical Collaboration on Dissertation Committees. Outside the MSCR program, CTSI BSD-CDM faculty will serve on dissertation committees of students across the health sciences programs. This service typically entails aid with design of experiments or observational studies, advice on putting together an appropriate statistical analysis plan, and assistance with interpretation of results of analyses.

6.3.5. Short Courses. During the initial CTSI program period, we will develop a set of lectures to be employed as short courses (6–8 lectures) for residents, fellows, and junior faculty of clinical departments. Topics for these courses will be study design, sample size determination, basic hypothesis testing, and interpretation of findings in medical research journals. Beyond courses in standard statistical methodology we will develop a series of courses for biomarker development and bioinformatics (analysis of microarray, proteomic and genomic data). These courses will revolve over each year, allowing clinicians multiple opportunities to take each course and enabling us to reduce class size to facilitate class discussion. Such short courses are already routinely provided at Harbor-LA BioMed and can serve as a model for the entire CTSI.

7. INVESTIGATORS

Our BSD-CDM has assembled an outstanding team of experienced leaders and investigators with wide-ranging expertise.

Robert M. Elashoff, PhD, **Leader** is a Professor of Biomathematics and Biostatistics at UCLA. His expertise is in clinical and translational trials and joint modeling.

Steven Piantadosi, MD, PhD, Leader is Director of the Samuel Oschin Comprehensive Cancer Institute at Cedars-Sinai and Professor of Biomathematics and Medicine at UCLA. His expertise is in clinical trials

David Elashoff, PhD, Leader is an Associate Professor of Medicine and Biostatistics with expertise in proteomics, SNPs, gene expression and clinical trials..

Andre Rogatko, PhD, Leader is Director of Biostatistics and Biomathematics at Cedars-Sinai and a CTSI service statistician with expertise in clinical trials.

Thomas Belin, PhD, is at the UCLA School of Public Health. He specializes in statistical methods for handling incomplete data, propensity-score methods in observational studies, survey design and analysis, and handling noncompliance in experiments.

Peter Christenson, PhD, is a GCRC and CTSI service statistician with expertise in laboratory and clinical research studies.

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Catherine Crespi, PhD, is an Assistant Professor of Biostatistics who focuses on statistical methods for the design and analysis of intervention trials and studies of cancer survivorship, with an emphasis on cluster-randomized trials and measurement of quality of life impacts. She collaborates widely on research involving cancer screening, health disparities, obesity, tobacco use, and effects of cancer as a chronic condition. Crespi also conducts research in Bayesian data analysis and hidden Markov models for longitudinal data.

David Gjertson, PhD, is Professor of biostatistics. He provides experience in study design, management and data analysis and teaches courses on statistical consultation and communication.

Xiuqing Guo, PhD, is Assistant Director, Mathematical Genetics at Cedars-Sinai Medical Genetics Institute and an Associate Professor of Pediatrics with expertise in genomic studies and genetic epidemiology.

Steve Hovarth, PhD, ScD, is Professor of Human Genetics and Biostatistics at UCLA with expertise in gene expression, gene networks, gene clinical correlations, and evaluation of biomarkers.

Martin Lee, PhD, is Professor of Biostatistics and CTSI service statistician with expertise in pharmacological statistics and clinical trials.

Roger Lewis, MD, PhD, is Professor of Medicine and Director of Research in Emergency Medicine at DGSOM. He specializes in pediatric preparedness in emergency group seer trials, adaptive trials and health services research.

Gang Li, PhD, is Professor of Biostatistics at the School of Public Health with expertise in adaptive trials, Bayesian inference, joint models group sequential designs.

Teresa Seeman, PhD, is Professor of Medicine and Epidemiology in DGSOM and School of Public Health with expertise in clinical studies in aging, epidemiology and observational studies.

Magda Shaheen, MD, PhD, is an Assistant Professor of Medicine, Charles Drew University. Her expertise is in survey research methods, urban area rapid survey and epidemiological methods.

Catherine Sugar, PhD, is an Assistant Professor in the Department of Biostatistics and the Director of the Semel Institute Statistics Core. Her methodological expertise is in clustering, classification, and functional data analysis with an emphasis on finding patterns in high-dimensional or longitudinal data. Her work in mental health has focused on identifying patterns of symptoms or functioning in patient populations and exploring how those patterns evolve over time in response to treatments or other stimuli.

He-Jing Wang, MD, MS, is a supervisory statistician in the Department of Biomathematics with expertise in clinical trial software and coordinating CDM trials.

7.1. Organization of the CTSI BSD-CDM. The BSD-CDM has four experienced leaders, reflecting the importance and expanded scope of this key function, Drs. R. Elashoff, S. Piantadosi, D., Elashoff and A. Rogatko have leadership experience in the complementary areas of biostatistics and bioinformatics and are well-qualified to lead BSD-CDM. Dr. R. Elashoff is PI of an NHLBI multi-clinic trial in Scleroderma Lung Disease and leads the statistics cores for ongoing trials in multiple sclerosis, neurorehabilitation and NCI-funded melanoma trials. His funded projects have resulted in development of a comprehensive model for clinical trials in which there are repeated visits for clinical trial endpoint and biomarker measurement. Dr. Piantadosi has expertise in clinical trial design and analysis, particularly in cancer, and has published research and guidance for translating basic science to the clinic. Dr. D. Elashoff has collaborated in basic and clinical research and contributes expertise in developing statistical methods for analysis of high throughput genomic and proteomic data. Dr. Rogatko has expertise the design and analysis of community studies, and designs enabling the translation of basic science into single-arm trials.

All four leaders oversee operations and have responsibility for periodic assessment of activities. They will communicate weekly in person whenever possible. When in-person meetings are not possible they will communicate either by phone or e-mail. These regular meetings will entail discussion of BSD-CDM collaborations, consultations, research and all administrative responsibilities. They are alert to problems investigators encounter in receiving timely and appropriate collaborative assistance with their projects. If conflicts arise they will consult with the BSD-CDM Steering Committee. The Steering Committee includes the leadership and Drs. Belin, Crespi and Sugar. Matters not resolved by the Steering Committee are referred to

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the Executive Oversight Committee (EOC). BSD-CDM Leaders issue regular reports to the EOC (see **Overview and Governance**). All communication will be bidirectional.

Dr. Wang and other MS-level statisticians will support biomedical collaborations across the CTSI and will be responsible for implementation of biostatistical analyses under the direction of faculty statisticians. This group will also assist investigators with statistical software and CDM implementation. We intend to grow the program faculty throughout the CTSI and affiliated sites such as the UCLA Research Center at Alhambra.

Graduate students and fellows receive support for and have full opportunities to receive hands-on training in BSD-CDM consultation in collaborative research. We will not limit the graduate students receiving support to those in the Departments of Biostatistics (SPH) and Biomathematics (DGSOM). Our plan is to support pre- and postdoctoral trainees who collaborate with CTSI investigators, with priority given to junior investigators. For example, community studies can be assisted by BSD-CDM faculty and graduate students in sociology, psychology, education, or similar fields. If they have good quantitative skills, they will be eligible for support, since they combine substantive research knowledge and quantitative skills.

8. INTEGRATION OF UCLA CTSI KEY FUNCTIONS

As noted throughout, BSD-CDM is highly collaborative and draws on expertise across UCLA institutions, schools and departments. The BSD-CDM has integrated activities with **CTSI-ED** in teaching, **CERP** in community-partnered translational research, **Regulatory** in the role of Research Facilitators and **Pilot Program** involving the Translational Cluster Research Program. Drs. R. Elashoff and Piantadosi have a collaboration that spans three decades. UCLA-Westwood and Cedars-Sinai faculty teach courses at one another's sites, as indicated in **Table 1**.

BSD-CDM is especially well integrated with the CERP. Dr. Sugar, a member of the BSD-CDM Steering Committee, is focused on access to healthcare among low-income, ethnic minority, and other underserved groups. As noted, three researchers with extensive experience and an intense interest in community-based research have joined our team: Drs. Belin, Crespi and Sugar. A BSD-CDM team member will sit on the CERP Steering Committee to facilitate collaboration between community and academia. We will work closely with CERP to ensure that biostatistics and design consultations requested by or recommended to communities as pertinent will be coordinated through that program. Using this approach, BSD-CDM and CERP can mutually provide the community with consultations that progress seamlessly from development of study questions meaningful to the community through clinical study design, implementation and analysis to evaluation.

9. EXTRA-UCLA COLLABORATIONS

As noted above Dr. Gang Li has formed a UCLA, Stanford University and Cedars-Sinai collaboration, initially emphasizing a seamless transition from phase II to a phase III trials that involves sample size re-estimation based on an estimated treatment effect from the phase II trial, which will be truncated in the phase III. This approach has been discussed collaboratively with the FDA Biometrics division. Also as noted (**section 1**) we are collaborating with Boston University, UT Southwestern, UCSF and Vanderbilt, all national CTSA members.

BSD-CDM provides study design, data analysis and CDM services for CCRR investigators. Our Domain Experts collaborate with the Regulatory Program's OIS. We also work with Regulatory Program to ensure our study designs meet the highest patient safety and ethical standards. We provide statistical study design and review for all studies funded through Pilot/Collaborative Program. Biomedical Informatics Program provides webcasting and archiving services for faculty lectures, seminars, and workshops; connects us to TSI investigators through the Virtual Home; and works with us to develop the Clinical Trials Database, ensuring it meets the needs of end users and ensures the privacy of study subjects. We conduct a range of educational activities with CTSI-ED, including an expansion of our MS in Clinical Research Program.

10. IMPLEMENTATION PLAN AND MILESTONES

The BSD-CDM will be evaluated by the CTSI BSD-CDM Steering Committee and the Evaluation and Tracking Program of the CTSI. Results will be communicated to the CTSI EOC, with feedback and recommendations to the CTSI BSD-CDM. Evaluation parameters and program milestones are shown in **Table 2** below.

Table 2: Implementation and Milestones

Year(s)	Milestones and Timeline	Evaluation and Tracking
Aim 1: Provide coordinated, one-stop access to biostatistics consulting and CDM services		
1	<ul style="list-style-type: none"> Investigator Access to the CTSI BSD-CDM Publicize Network through Virtual Home Implement biostatistician consulting services Form and implement biostatistician teams to provide assistance to investigators (prepare grant applications, study design and data analysis) Review protocols of the CTSI CCRP 	<ul style="list-style-type: none"> Set up videoconferencing, webcasting, virtual home and telemedicine technology Integration and formation of the CTSI BSD-CDM Number of CTSI investigators assisted Number of hours used in service activities Number of grant applications
1-5	<ul style="list-style-type: none"> Conduct matchmaking for new interdisciplinary teams Data analysis and oversight Train study staff and new investigators in the use of CDM systems Conduct grand rounds quarterly to discuss controversies in biostatistics 	<ul style="list-style-type: none"> Number of publications Number and type of grand rounds Satisfaction with services as assessed by Evaluation and Tracking program
Aim 2: Develop novel statistical applications and methodologies to address the complexities of biological data and the challenges of community-based research		
1-5	<ul style="list-style-type: none"> Conduct Statistical and Design Research in Clinical Trials Conduct Statistical Research for Methodological Development in High-Throughput Biological Data Analysis Conduct Weighted Gene Co-Expression Network Analysis Conduct Statistical Analysis of Proteomics Data Improve Power in Genome-wide Association Studies Conduct studies in community methodologies 	<ul style="list-style-type: none"> Publish specialization areas in biostatistics, study design and clinical data management Provide contact information on the CTSI Web Portal Number of methodological contributions published
Aim 3: Provide biostatistical education and training		
1-5	<ul style="list-style-type: none"> Continue Biostatistical Training 	<ul style="list-style-type: none"> Bring PhD students into CTSI
1-3	<ul style="list-style-type: none"> Expand Master of Science in Clinical Research (MSCR) 	
1-2	<ul style="list-style-type: none"> Expand Certificate Program and Short Courses 	
1-5	<ul style="list-style-type: none"> Continue Biostatistical Collaboration on Dissertation Committees 	

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Regulatory Knowledge and Support, Industry Relations, and Research Ethics



Program Team

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*Other Significant Contributor – Biosketch included

Abbreviations: AAHRPP – Association for the Accreditation of Human Research Protection Programs, AE – Adverse Event; BIP – Biomedical Informatics Program; C&G – Contracts and Grants; CDU – Charles Drew University; CERP – Community Engagement & Research Program; CITI – Collaborative Institutional Training Initiative; COI – Conflict of Interest; DGSOM – David Geffen School of Medicine; DSM – Data and safety monitoring; DSMB – data and safety monitoring board; DSMP – data and safety monitoring plan, EOC – Executive Oversight Committee, FTP – file transfer protocol, GCP – Good Clinical Practice; GCRC – General Clinical Research Center; IND – Investigational New Drug; IP/TT – Intellectual Property and Technology Transfer; IRB – Institutional Review Board; IT – Information Technology, MOU – Memorandum of Understanding; MTA – Material Transfer Agreements; NICHD – National Institute of Child Health and Human Development, OHRP – Office for Human Research Protection; OIA – Office of Industry Alliances; OIS – Office of Investigator Services; PARO – Post-Approval Research Oversight; QA – Quality Assurance; RAPID – Research Administration Process Improvement and Deployment; RSA – Research Subject Advocate; SAC – Scientific Advisory Committee, SAE – Serious Adverse Event

1. OVERVIEW

The Regulatory Knowledge and Support, Industry Relations, and Research Ethics Program (Regulatory Program) is the gateway to support services throughout the UCLA CTSI. It fulfills the Regulatory Knowledge and Support and Clinical Research Ethics key functions. Along with the University of Southern California and the University of California, Irvine, we are members of the Greater Los Angeles CTSA Coalition. The Regulatory Program was previously reviewed with Participant and Clinical Research Interactions key function and received an aggregate score of 2. Reviewers praised our leadership and our efforts to harmonize human subjects review activities. No weaknesses were noted. In this application, we report continued progress improving investigator access to CTSI resources. Substantive changes to this application since our last submission are indicated in the left margin.

2. SPECIFIC AIMS

The UCLA CTSI provides the operations and governance necessary to facilitate successful transdisciplinary clinical and translational research. The overarching *mission* of the UCLA CTSI is to *transform our academic-clinical-community partnership into a borderless institute that brings our combined innovations and resources to bear on the most pressing health needs in our diverse community*. Our Regulatory Program supports the mission of our CTSI in two ways. We guide investigators through the necessary but often complex regulatory, operational, and ethical requirements mandated for human research protocols. We also facilitate investigator access to the full range of CTSI resources. The following Specific Aims put us on the path to achieve our objectives.

Specific Aim 1: Harmonize regulatory mechanisms throughout the UCLA CTSI to promote easy access to translational research opportunities for scientists, staff, community members and study subjects.

Specific Aim 2: Develop pre- and post-approval regulatory support services through deployment of an Office of Investigator Services (OIS) and creation of a UCLA system-wide “one-stop-shop” for approval of CTSI-supported science.

Specific Aim 3: Create Office of Industry Alliances (OIA) to promote and sustain the linkage of the CTSI, its members and industry partners.

Specific Aim 4: Develop a Research Ethics Consortium and continuing education system for CTSI investigators and participants to enhance ethical sensitivity, understanding of regulations (e.g., FDA, ICH, etc.) and good clinical practices (GCP), mentoring and learning.

3. PROGRESS TO DATE

We have made substantial strides at UCLA to streamline and broaden access of scientists to translational science resources. These advances include:

- Creating a common, CTSI-wide protocol application form encompassing the required information for IRB, scientific, statistical and data and safety monitoring (DSM) approval. Establishing accelerated approvals and reciprocity of approvals for multi-institutional research proposals.
- Aligning off-site adverse event (AE) and serious adverse event (SAE) reporting requirements to annual listings.
- Addressing quality assurance (QA) issues studies in a course for public health and translational researchers entitled *Introduction to the Science of Implementing Evidence-Based Practice*.
- Accepting *post hoc* applications for institutional review board (IRB) approval of QA studies that become publishable.
- Adopting initiatives to create and streamline regulatory processes for inter-institutional research, including improvements in administration (IRB and Contracts & Grants [C&G] functions), education/training (Ethics, GCP) and industry alliances.

4. SIGNIFICANCE

The CTSI is streamlining regulatory processes to accelerate team science and collaboration among partner institutions while maintaining an appropriate regulatory environment for biomedical science. We have a threefold approach to transform the protocol approval process across the four CTSI institutions: UCLA-Westwood, Charles Drew University (CDU), Burns and Allen Research Institute at Cedars-Sinai Medical Center (Cedars-Sinai) and Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center (Harbor-LA BioMed). First, we are creating a CTSI-specific Scientific Advisory Committee (SAC) that will vet the scientific merit of projects, provide statistical and data and safety monitoring (DSM) review and follow-up for protocols, and allocate CTSI resources. Second, we are establishing common IRB, SAC and DSM application forms and templates that will allow investigators to submit for approval at all CTSI partner institutions simultaneously. In this regard, the CTSI IRB Harmonization Committee (see **section 6.1.1.**) has initiated efforts using a “reliance model.” The concept is to have the lead investigator of a CTSI-specific SAC-approved protocol obtain approval from his/her own institutional IRB with the IRBs of other collaborators’ institutions relying on the *Reviewing IRB’s* review and approval. Third, we are launching a program of reciprocal IRB approval among the partner institutions.

5. INNOVATION AND ENVIRONMENT

The UCLA CTSI partner institutions are spread over the largest county in the United States. The UCLA CTSI seeks ethical strategies to engage diverse communities in scientific study and ensure that scientists respond to the health and health care needs of communities using appropriate protections.

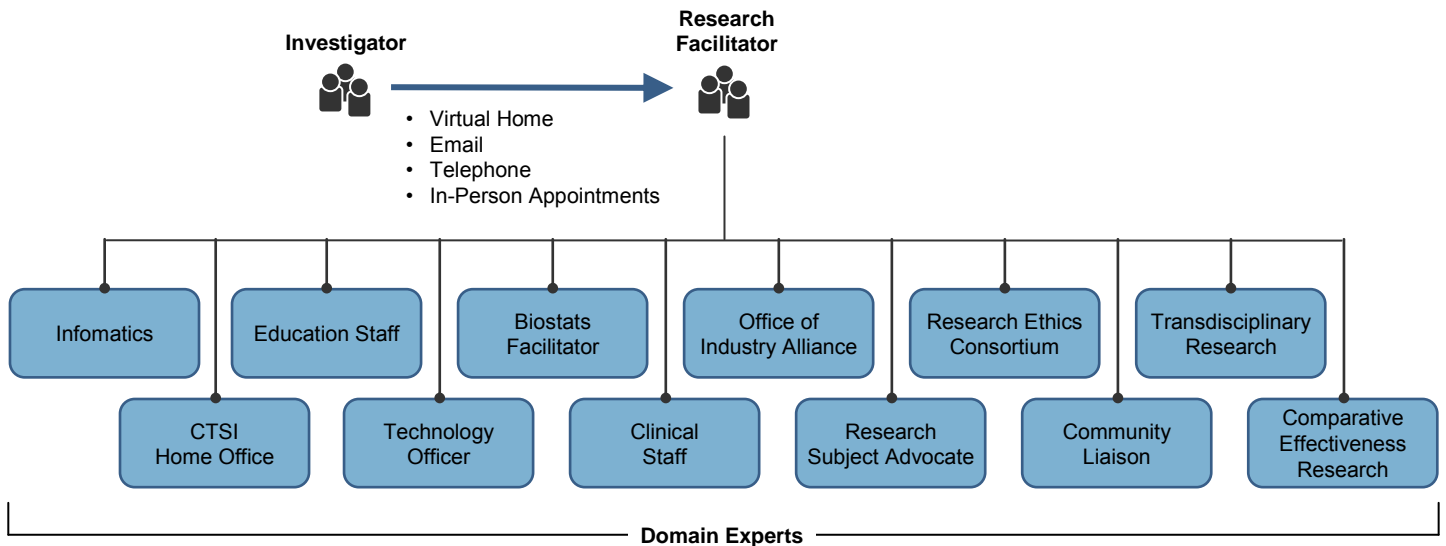


Figure 1. Shown are the means by which Research Facilitators chaperone investigators to various destinations and Domain Experts (blue boxes) within the CTSI Office of Investigator Services (OIS).

The UCLA CTSI has developed an innovative approach to help investigators initiate protocols that involve recruitment and community interaction. A new program, the CTSI Office of Investigator Services (OIS) (**Figure 1**), has been created to facilitate research from idea to application to successful adaptation. CTSI Research Facilitators, a tightly connected set of research project coordinators with superior interpersonal skills, will help investigators ■ navigate the complex regulatory requirements needed to enter the UCLA, regional or national CTSI environment ■ assisting them in identifying and accessing the appropriate regulatory offices for such tasks as completing the IRB process ■ creating an industrial alliance ■ counseling with a research subject advocate or dealing with a thorny protocol-related ethical issue. Investigators may contact our Research Facilitators in person or through our **Virtual Home**, a portal that provides online access to all CTSI services. If investigators need help with a non-Regulatory Program matter, our **Research Facilitators** provide referrals to **Domain Experts** in such areas as biomedical informatics, biostatistics and technology cores.

In addition to the OIS, the Regulatory Program is implementing other innovative initiatives (see below). Our Office of Industry Alliances (OIA) provides a business friendly bridge between CTSI investigators and industry.

To provide uniform guidance in research ethics to CTSI investigators, we have formed the CTSI Research Ethics Consultation team.

6. APPROACH

The Regulatory Program supports ongoing efforts and new initiatives. For example, a variety of Harmonization Committees have been established and tasked with developing mechanisms for addressing the issues outlined in **Table 1**.

6.1. Specific Aim 1: Harmonize regulatory mechanisms throughout the UCLA CTSI to promote easy access to translational research opportunities for, scientists, staff, community members and study subjects.

6.1.1. IRB Harmonization Committee. The IRB Harmonization Committee comprises Eifaang Li, Leader; Robert Dennis, Information Technology; Sharon Friend; Stewart Laidlaw; and Junko Nishitani. The Committee has piloted facilitated IRB review and approval under with a trans-institutional MOU. The process for facilitated review in place and has been tested for multi-institutional protocol review and approval for the past year. The Regulatory Program Steering Committee (see **Figure 2**) will monitor protocols requiring multi-institutional sites and advise Investigators on the facilitated approval process.

Table 1. Shown are the domain experts/leaders and the functions they oversee in each area of the innovative initiatives in the Regulatory key function of the UCLA CTSI. Abbreviations: PARO, Post-Approval Research Oversight; IP/TT, intellectual property and technology transfer; CE, continuing education; DSM, data and safety monitoring.

Innovative Initiatives						
	Harmonization Initiatives	Research Facilitator Service	Post-Approval Research Oversight (PARO)	Intellectual Property/Technology Transfer (IP/TT)	Research Regulation & Ethics Continuing Ed	Research Ethics Consortium
Leaders	E. Li; M. Smith; K. Atchison; R. Lewis	L. Shaker-Irwin	R. Lewis	K. Atchison	S. Laidlaw	S. Finder
Functions	IRB regulation	Provide research facilitators	Subject advocacy	Facilitate technology transfer	Continuing education	Ethics consultation
	Contracts and grants	Train facilitators	Quality assurance	Entrepreneurship	Research training requirements	Research in research ethics
	IP/TT	Coordinate facilitators	DSM assurance	Marketing commercial	Research training requirements	
	PARO	FDA interactions	Research compliance			

Since our last review, the Association for the Accreditation of Human Research Protection Programs (AAHRPP) and the Office for Human Research Protection shifted their opinions and no longer favor facilitated review mechanisms. As a consequence and as noted above, we propose moving to a reliance model for the CTSI. The Committee is now evaluating “total reliance” and “partial reliance” models for reviewing CTSI projects. The total-reliance model involves designation of a reviewing IRB, which assumes responsibility for the conduct of CTSI studies at all sites, similar to the way commercial IRBs function. With partial reliance, the primary award institution relies on the IRB of a participating institution to review the specific research activities at the participating institution. A decision tree identifying the reviewing and relying institutions was developed recently by the IRB Harmonization Committee to guide the CTSI.

We are now working on prerequisites to allow full implementation of a reliance model of IRB approval across the partner institutions. In particular, before reliance can occur, AAHRPP accreditation of all CTSI institutional IRBs is necessary. Presently, UCLA-Westwood and Cedars-Sinai are accredited. As an interim measure, a creative short-term solution acceptable to AAHRPP was arrived at for CDU, by allowing its IRB to participate in reciprocal review by using the webIRB system employed at UCLA-Westwood. With the commitment of the leadership of LA-Biomed to provide the institutional resources for the AAHRPP approval process at Harbor-UCLA, we anticipate being able to implement reliance across all partners by the end of the first year of our CTSA funding period. As an interim measure, the process of facilitated IRB review will continue to be utilized.

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In conjunction with this, the Committee will continue to refine the IRB component of the CTSI **Virtual Home**. This website provides a single gateway for investigators and staff to apply for regulatory approval of studies to be implemented across the CTSI. The investigator completes the common, combined CTSI-specific SAC-CTSI IRB application and identifies all sites where research activity will occur. The IRBs at all sites will have access to the decision and scientific review of the CTSI-specific SAC submitted through the Virtual Home, along with the IRB review from the primary institution's IRB to use in their facilitated review, thus avoiding the need for time- and energy-consuming sequential reviews.

Activation of the joint electronic IRB system, using a Click Commerce® product, now makes it possible to plan for a single application on the CTSI Virtual Home for all research. The IRB Harmonization Committee will work with compliance personnel throughout the CTSI, software vendors, the Office of Investigator Services (OIS) and the Biomedical Informatics Program (**BIP**) to develop a common front-end application that will deposit data into the respective programs. An analysis is under way and will be accelerated in years-01 to -03 of the grant, anticipating 2 to 3 years to complete integration. The CTSI will continue to support its CTSI-specific IRB personnel (see below), regardless of where they are stationed among the partner institutions. This will allow them to interact with CTSA **Regulatory Program** personnel and with the CTSA Regulatory Support Steering Committee.

The IRB Harmonization Committee has facilitated agreements among all institutions to utilize the same NIH template for informed consent documents. With this breakthrough, investigators need only a single form for multi-institutional research. The Committee is also developing a matrix of study requirements to be harmonized throughout the CTSI. Among these is use of human tissues obtained during research. Once finalized in year-01 of the grant, CTSI investigators will be able to create, maintain and use biorepositories throughout the CTSI. In parallel with this initiative and consistent with OHRP regulations, the Committee is developing uniform consent processes to maximize use of preserved tissues through clear protocols for acceptable use, storage requirements, anonymization and materials distribution. We anticipate matrix study completion by the end of year-02.

6.1.2. The Contracts and Grants Harmonization Committee. The C&G Harmonization Committee, led by Marcia Smith, includes Richard Katzman, Vice President for Academic Affairs at Cedars-Sinai, Maria Dias Romero, Rosemary Madnick and Stanley Korenman, Program Leader. The C&G Committee determined that CTSI institutions are File Transfer Protocol (FTP)-compliant institutions with similar standardized sub-award processes. In an analysis we found that delays within institutions are generally related to investigator or departmental delays or inaction. To identify and eliminate unwarranted delays, the committee has coded CTSI proposals at initiation and followed them through processing. Each institution has a designated C&G officer responsible for processing and tracking CTSI-specific proposals. Tracking reports will be reviewed semiannually by the C&G Committee to identify delays and improve performance. Research Facilitators (see OIS in **section 6.2.**) will also monitor progress of proposals they support and report to the C&G Committee.

The CTSI recognizes the need for sensitivity to special needs of community organizations in sub-awards and contracting and for integrating academics with the community in research. The C&G Committee is committed to maintaining open discussions and continuing education with the CTSI Community Engagement & Research Program (**CERP**) and its support of educational initiatives for community-based providers, organizations and investigators. These include practical training on ethical, legal, and financial issues of community involvement in research. In fact, one of our main community initiatives, the 70-Block Project, already was processed by the CTSI through CDU.

6.2. Specific Aim 2: Develop pre- and post-approval regulatory support services through deployment of an Office of Investigator Services (OIS) and creation of a UCLA system-wide “one-stop-shop” for approval of CTSI-supported science in the CTSI-specific Scientific Advisory Committee (SAC).

6.2.1. Use of the OIS to provide Research Facilitators and Domain Experts to investigators and to aid development of online resources for the investigator community. The OIS (see **Figure 1**) was created to ensure successful research from idea to application with emphasis on supporting research by new investigators, ensuring timely progression of ideas through the pipeline to completion. The OIS has matured conceptually to represent a means of proactive assistance for investigators all along the experience spectrum. The OIS will be physically located in the Office of the Institute and distributed virtually throughout the CTSI via the Virtual Home.

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It is led by Dr. Stanley Korenman with the support of a high-level administrator with a background in science and management, a dedicated Technology Officer and staff to support an array of Research Facilitators, Domain Experts, research subject advocates (RSAs) and quality assurance personnel.

6.2.1.1. Research Facilitators. Chief Research Facilitator, Laurie Shaker-Irwin, PhD, will design Research Facilitator training and supervise staff logistics. Over grant years-01 and -02, we will recruit and train up to six additional Research Facilitators into a tightly connected personnel set with experience in research project coordination. They will provide expert personal assistance to potential CTSI users through proposal development, referrals, advice on collaborations and resources, regulatory approvals, education and support for good practice (see **Figure 1**). Research Facilitators will enhance their knowledge of the evolving regulatory environment through continued education and training. The Research Facilitator service will build on CTSI resources to assist investigators and promote CTSI-wide interaction. The OIS and Research Facilitators will interact with Domain Experts (see **Figure 1** and **section 6.2.1.2.**) to ensure that investigators understand and have access to needed resources. Specifically, Research Facilitators will:

- Provide pre- and post-approval proposal assistance, including guidance with IRB submissions, meeting post-approval compliance requirements such as the appropriate use of RSA support, AE reporting and development of DSM processes and options.
- Be available with Domain Experts to assist investigators, RSAs, Research Ethics Consortium faculty, OIA staff, and Regulatory Program faculty as needed.
- Interact with research administrators and regulatory personnel at each CTSI partner and community-based institution, including C&G and IP offices at those sites.
- Specialize in identifying CTSI resources and services to optimize research and make appropriate contacts, supplemented by the CTSI Virtual Home (e.g., infoWRAP, protocol development and management software in Velos, etc.).
- Help maintain the CTSI resources database, which includes investigators, facilities, laboratories, community research locations, services, consultants (biostatistics, ethics, other), regulatory documents, tips and suggestions addressable by potential grantees, and templates of successful applications, in coordination with the Technology Officers in **CTT** and the **BIP**.
- Collaborate with the **Pilot Program** to help promising investigators prepare the best possible proposals for pilot funding and keep them apprised of other possible grant funding, especially with regard to “team science” or cluster and comparative effectiveness research grant opportunities.
- Advise investigators of all CTSI research training programs, hold regular seminars for new investigators to encourage using CTSI resources and participate in continuing education programs.
- Be an important nexus for identifying and responding to dynamic landscape clinical research needs in the community and promoting cost-effective growth opportunities for community-based research activities.
- Meet weekly to discuss changing regulatory requirements, develop facilitation practices, and ask about quality enhancement studies.
- Hone their areas of expertise, with Domain Experts (e.g., FDA regulation, compliance and monitoring, etc.), to cross-train and coordinate across research institutions.

6.2.1.2. Domain Experts. Investigators will have access to many Domain Experts, specialists with further knowledge and skills who are connected to CTSI Programs (see **Figure 1**). They are accessible to investigators via the Virtual Home or personally through Research Facilitators. In contrast to the Research Facilitators, Domain Experts will be managed with a matrix format in which each Expert responds to the appropriate Program Leader in the Regulatory key function. Some Domain Experts are staff recruited for this purpose (e.g., Technology Officers, Community Liaisons) and others are CTSI Program faculty or staff (e.g., Biostatisticians, Research Ethics Consortium members). Coordination of Domain Expert services will be primarily through Research Facilitators. The OIS Leader, Dr. Korenman, is responsible for Domain Expert oversight and quality control. Like Research Facilitators, Domain Experts will have administrative working areas in the Office of the

Institute and will rotate through the institutions to maintain familiarity with Institute-wide resources and to cross-train with their colleagues.

6.2.2. Facilitating protocol review and execution. Currently the four UCLA GCRC operations, one at each of the major partner institutions, have their own Scientific Advisory Committees (SACs) to vet protocols scientifically and statistically, assign institutional resources and provide comprehensive, RSA-coordinated DSM. As well, there are several IRBs at each institution that are required to approve those protocols for implementation at that institution only. A system of separate approvals by project and investigator does not encourage collaborative team science that emphasizes accelerated translation of discovery. The CTSI harmonization plan streamlines the inter-institutional processes for protocol handling.

6.2.2.1. Creation of a single online application for protocol review and IRB approval. The first step in simplifying the process of protocol submission and approval at multiple UCLA CTSI sites was the creation of a uniformly accepted protocol application form. The IRB Harmonization Committee recently produced a single online application form for all UCLA investigators and IRBs through the CTSI Virtual Home. This form contains: 1) information needed for scientific review and approval by the CTSI SAC including i) a scientific rationale and description of the protocol, ii) biostatistical and data and safety monitoring (DSM) plans and reports and iii) utilization requests and justifications; and 2) information that is standard for IRB processes such as informed consent documents, coordination of research compliance, DSM and AE reporting (see **section 6.2.2.2.** below). In year-01 of the grant, this application form will be rolled out via Click Commerce®. This will permit UCLA CTSI-sponsored research faculty to receive accreditation for research at other UCLA campuses, allowing them to conduct research and secure access to research participants in the most appropriate setting(s). With a single e-application in hand, we will launch initiatives to create a single CTSI-specific SAC and four site-specific IRBs.

6.2.2.2. Creation of a single CTSI-specific SAC at UCLA. The current system of four separate, institution-specific SACs vetting and allocating resources to protocols is on the “fast track” for remodeling. Regulatory key function participants have instituted a four-phase plan to develop a single UCLA-wide CTSI-Specific SAC: 1) inventory; 2) alignment; 3) harmonization; and 4) reciprocity. In the current inventory phase, we are assessing post-award activities throughout the CTSI to identify similar and disparate processes and understand institution-specific motivations for each activity. In year-1 of the grant we will undertake the alignment phase. The Regulatory Program Steering Committee (see **section 7.**) will work with CTSI personnel to reduce or eliminate differences in workflow, oversight requirements (e.g., data and safety monitoring plans [DSMPs] requirements) and protocol institution processes across UCLA CTSI sites. When alignment is completed, written standards for the review and approval of DSMPs, DSM reports and SAE reports will be identical. The harmonization phase will begin and end in year-02. During harmonization, detailed processes will be integrated. For example, DSMPs, periodic reports and AE reports from all sites will be submitted through a single portal, the CTSI Virtual Home. The final reciprocity phase will be in year-03. Processes for CTSI-sponsored protocols i) scientific and statistical review, ii) DSM and iii) allocation of CTSI resources will be interchangeable throughout the CTSI partner institutions.

By year-04 our aim is to develop a single UCLA CTSI-wide SAC to provide a “one-stop-shop” for approval of protocols before IRB submission. Analogous to an NIH study section, the UCLA CTSI-wide SAC will serve as the peer-review panel for investigators seeking protocol support from the CTSI. The CTSI-wide SAC will be constituted by voting and non-voting members from all UCLA partner institutions. Voting members will be appointed by the EOC and include: 1) a rotating panel of 20 CTSA-sponsored scientists serving staggered 3-year terms; 2) a panel of 4 CTSI nurse specialists or research project managers; 3) a panel of 4 research subject advocates (RSAs, see **section 6.2.3.1.** below); 4) a panel of 4 biostatisticians; 5) a bionutritionist; and 6) a panel of 4 community members. Non-voting, ad hoc members will include i) an administrative representative, ii) a Research Facilitator and iii) a Domain Expert from each of the partner institutions. In years-04 -05 of the grant, the CTSI-wide SAC will be chaired by Dr. John Adams, an associate director of the UCLA CTSI. He will report directly to the Executive Oversight Committee (EOC) of the CTSI with regard to SAC activities and actions, and be ultimately responsible to the Principal Investigator. Dr. Adams will serve as a non-voting member of the SAC unless he is called upon to break a tie in voting. Dr. Adams will be a “standing item” on the agenda of each EOC meeting to present for EOC approval the protocol and support decisions/actions recommended by the SAC.

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The SAC will meet at least monthly by videoconference and 50% of its meetings will be held at the partner institutions. Its review process will have three components to reflect the three functions. The scientific/statistical component will focus on issues relevant to protocol design. The DSM component will ensure at least annual oversight of the progress of protocols for adequate patient safety, power and data integrity. The third review component will focus on operational issues and assign a priority for use of CTSI resources based on scientific merit and need. Individual SAC scientific members (usually 4; 2 scientists, an RSA and a biostatistician) will be assigned to each protocol for review and presentation during videoconferences. Unless in conflict, each SAC member will vote a “number-letter” score (see **Table 2**). This combined score will define the overall enthusiasm for the protocol and its priority for CTSI support.

Table 2. The **left panel** embodies the IRB and DSM decisions that constitute the “number” score, while the **right panel** describes the scientific merit and need for CTSI resources “letter” score.

Score	Outcome	Score	Comment
1	Approval	A	Essential (highly meritorious, usually NIH-supported, could not be done without CTSI support)
2	Approval with comment (PI response not required)	B	Important (investigator initiated, CTSI resources would greatly facilitate study)
3	Approval pending PI response		
4	Approval deferred (requires submission)	C	Desirable (CTSI support would be a convenience but not a necessity for the PI)
5	Denial		

6.2.2.3. Establishing CTSI-specific IRBs. Once approved by the CTSI-wide SAC, the protocol, because its application already bears required information acceptable for IRB review at any partner institution, can be reviewed by an IRB at the investigator’s home institution; this is the IRB that retains responsibility for the welfare of the protocol’s participants. Because there are several standing IRBs at each CTSI partner, in year-1 of the grant each institution will create or morph an existing IRB into a CTSI-specific IRB, which, like the CTSI-specific SAC (see **section 6.2.3.2.**), will be populated by members especially attuned to reviewing protocols that use CTSA resources and personnel.

6.2.2.4. Investigator assistance with FDA approvals and compliance. Research Facilitators working with the Domain Experts and the Technology Officer in the OIS will provide guidance on the Code of Federal Regulations involving investigational and approved drugs and assist investigators with understanding FDA policies, procedures, and reporting requirements. This OIS team also will help investigators decide whether their studies require an Investigational New Drug (IND) application and guide them through that process. The CTSI has recruited its first specialized Research Facilitator, Kavitha Rajavel, PhD. She has experience with FDA submissions and is under the mentorship of Domain Expert Antoni Ribas, MD, PhD, a senior investigator experienced with the most complex FDA applications.

6.2.3. Develop a post-approval research oversight (PARO) system to enhance research quality and safety. The Post approval research oversight processes are overseen by Dr. Roger Lewis, Professor and Director of Research in the Department of Emergency Medicine at Harbor-LA-Biomed. Currently, he is also the DSM Advisor/RSA for the GCRC at Harbor-UCLA Medical Center. As such, Dr. Lewis has extensive experience as an RSA and in research monitoring. The system is composed of two functional units, the research subject advocacy system and the product of the PARO committee deliberations.

6.2.3.1. The RSA (Research Subject Advocate) system. RSAs, PhD-equivalent experts in human biomedical research, currently monitor human research protocols and DSM reports and are available to participants on site to address interpersonal problems, protocol violations, and adverse events. They enhance detection, correction and prevention of research problems. Since ambulatory clinical research activities predominate in the CTSI, RSA functions are currently focused on outpatient and community studies. We are seeking special contractual language for the entire CTSI to support involvement of RSAs in community research, i.e., research in which investigators are not staff or faculty anywhere in the CTSI. In collaboration with the CTSI Community Program, RSAs will receive cultural competence and community engagement training to ensure they are prepared to address salient issues among Los Angeles County’s diverse constituencies. RSAs will enhance regulatory and ethical competence of research staff and support proper conduct of community studies. As advocates, RSAs ensure the rights of children, pregnant women, cognitively impaired people and other vulnerable groups by i)

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analyzing protocols, ii) reviewing informed consents for content and readability and iii) ensuring study feasibility, safety and integrity. RSAs will meet regularly among themselves and related staff to facilitate awareness of developing ethical and compliance issues, discuss and systematically solve problems, and develop best practices. They will develop their own manual of procedures based on NCCR standards, regulatory requirements and actual practices. RSAs also will identify education/training “hot spots”, e.g., dynamic issues that are identified by their activities including some that are sure to surface in the wake of health care reform, to be developed into training programs.

6.2.3.2. PARO Committee (see **Table 1**). The PARO Committee will enhance research quality and safety by providing CTSI-wide clinical research compliance through QA, DSM, and advocacy for research participants, investigators, and responsible agencies. The oversight committee focuses on improving research quality and efficiency by harmonizing post-approval research processes across the CTSI. Research compliance officers, RSAs and QA staff are collaborating on standards for excellence in compliance, including conflict of interest and budgeting/billing, subject advocacy, DSM, QA, GCP adherence, and other assurances including HIPAA Part (a). As an example of our harmonization efforts to improve consistency of DSM reporting standards, we recently completed a protocol-exchange exercise among our partner institutions at UCLA in which personnel at one site reviewed a random sampling of protocols and DSMPs from the other. Insights from that assessment have led to reviews of DSMPs and DSM reports at one institution being accepted at the other. This reduces the reporting burden for investigators conducting multi-institutional studies.

6.2.4. Develop a Continuing Education System. The UCLA CTSI has developed a system to centralize, document, and enhance continuing education of research teams in Responsible Conduct of Research, Ethics, Mentoring, Federal Regulations and ICH Guidelines, Data and Safety issues, HIPAA compliance and GCP, by providing efficient comprehensive services. The effort is led by Dr. Stewart Laidlaw (see **Table 2**). The **CTSI-ED** program is responsible for formal training of translational investigators in responsible conduct of research, while the OIS will provide continuing education opportunities to all research team members, including staff and community researchers, who are not expected to undergo formal degree-level training. We emphasize core competencies in this effort.

The Regulatory Program Continuing Education Committee, led by Dr. Laidlaw, is an active committee in the CTSI that is developing curricular elements for more thorough training in the ethical and regulatory aspects of human subject research that are compatible with anticipated NIH guidelines requiring face-to-face and online educational programs. Some current activities sponsored by the CTSI Regulatory Program Continuing Education Committee include: ■ sponsoring numerous courses on responsible research conduct, some of which are recordings to be posted on the CTSI Virtual Home with selected National Resources and CTSA consortium materials ■ helping to grow the UCLA inter-institutional telemedicine capacity, extending it to community locations to accomplish face-to-face in-service education elements ■ keeping a database for cross-certification of investigators and research team members.

6.3. Specific Aim 3: The Office of Industry Alliances (OIA) to promote and sustain the linkage of the CTSI, its members and industry partners.

6.3.1. Leadership. The OIA will be led by a four-person team of senior-level co-directors from the technology transfer and industry alliances offices of the CTSI who are thought leaders on the appropriate balance of commercialization and conflicts of interest. Kathryn Atchison, DDS, MPH will lead the OIA. Jim Laur, Esq., Vice President for Legal Affairs and Cedars-Sinai's senior IP counsel since 1994 will guide development of new IP ventures. Keith Norris, MD, executive vice president for research and health affairs of CDU, is a recognized leader in health inequities and translational research. Arthur I. Zweben is the Director of New Business Ventures and Technology Management at LA BioMed. Dr. Norris and Mr. Zweben bring hands-on experience to negotiating research-related faculty, consulting agreements, university licenses, material transfer agreements and industry clinical trial agreements. Earl G. Weinstein, PhD, Associate Director of the UCLA Office of Intellectual Property and Industry-Sponsored Research will advise the OIA on industry relations. Dr. Weinstein has extensive experience starting and funding biomedical startups as a venture capitalist in Boston and has put together numerous technology transfer and industry alliance deals for UCLA's IP office. Meetings of the OIA team will be at least quarterly and ad hoc throughout the year. The OIA is housed and staffed by the UCLA Office of Intellectual Property and Industry Sponsored Research, an institution-wide, UCLA-supported resource (see **Figure 2**).

A key component of the OIA will be its Industry Advisory Committee, residing in the UCLA Office of Intellectual Property and Industry-Sponsored Research, comprising representatives of leading biomedical companies, startup companies, venture capital firms, and community representatives. This committee will be selected from local and national companies in critical industries to advise the CTSI on industry needs and best practice. As CTSI activities ramp up, a dedicated business development team will be formed to fully capitalize on the large range of industry collaborations that will likely arise.

6.3.2. Specific functions of the OIA. The OIA will be charged with the following:

6.3.2.1. Develop relationships and collaborations with select biomedical companies important to CTSI research initiatives. Southern California is a biotechnology and medical device hotbed and many global companies have a presence here. Utilizing the CTSI Virtual Home, the OIA will: 1) identify and list opportunities for industry collaborations; 2) work top-down identifying high-priority translational research; 3) work bottom-up identifying unique capabilities within the CTSI; and 4) pitch collaborations to industry around core areas of expertise. The Virtual Home will provide a business-friendly entrepreneurial bridge between the CTSI and the biomedical industry through a UCLA CTSI brand.

6.3.2.2. Facilitate industry interactions by identifying related IP across the CTSI in which bundling technologies creates a solid position for IP licensing. The OIA also will be a single contact point for medium and large companies by providing “one-stop-shopping” for industry in licensing CTSI-originated technologies. Industry partners will not have to piece together IP rights from CTSI institutions on their own. Among key activities will be business development to identify appropriate industry partners for commercializing CTSI-originated inventions. There will also be inter-institutional patent and license management agreements so that jointly owned IP for CTSI-originated inventions may be bundled into a single license for the industry partner by the OIA. Identification of synergistic pieces of technology that would not otherwise have been apparent to industry will be included. For example, efforts to link CTSI-specific basic discoveries made in the UCLA Nanotechnology Institute to a \$20 million California Institute of Regenerative Medicine cardio-myosphere stem cell project for heart attack victims at Cedars-Sinai.

6.3.2.3. Assist CTSI inventors and authors by providing a single contact point for technology transfer. The OIA will assist faculty and Technology Transfer offices at each step along the translational research value chain from discovery to industry commercialization to benefit society. Over the past 18 months UCLA has opened an on-campus incubator that has attracted the Los Angeles County investment and venture capital community, and been written about in the NY Times (*Collaborating for Profits in Nanotechnology* by James Flanagan, July 15, 2009). The California NanoSystems Incubator supports faculty entrepreneurs who need a year of support from the institution to develop milestones that will facilitate licensing. For faculty who wish to develop business plans, OIA will facilitate collaborations with MBA students at the UCLA Anderson School of Management. CTSI Catalyst Grants are available for such collaborations (see **Pilot and Collaborative Translational and Clinical Studies Program**).

6.3.2.4. “Push innovation” by bringing together CTSI investigators, especially junior faculty, to match clinician needs with technological solutions. One innovative idea that we devised and have pilot tested is a “push innovation” to link clinicians with clinical needs for technology to scientists in engineering and physical science. The two-fold purpose is to initiate collaborations among researchers at UCLA campuses in Los Angeles and develop collaborations between clinicians with medical problems and engineers with technological solutions. The plan is to offer one event per quarter in which a single clinician or panel of clinicians discusses a clinical problem (e.g., adherence to postoperative instructions) for which they need innovative technology. A separate panel would include engineers and scientists from specialty areas, electrical engineering, biomedical engineering, applied mathematical algorithms, etc. to discuss new technology approaches. The experiment is to facilitate dialogue and matchmaking of scientific teams. In our pilot test, the CRRR Leader, Dr. Wang, was embarking on an NIH-funded male contraceptive study for healthy volunteers that required daily intervention for 180 days without direct benefits to study participants. She was linked with the UCLA Wireless Health Institute engineers to devise a system to use text message SMS to remind subjects daily about their responsibility. The team met and developed an appropriate technology and submitted an addendum to the National Institute of Child Health and Human Development (NICHD), which was approved for pilot funding. The text message system is currently in use in the study. This model may be extended to other types of matchmaking.

6.3.2.5. Develop related educational programs in entrepreneurship and commercialization for CTSI investigators and the community. A critical step in building a robust pipeline of translational research partnered with industry is to build a culture of entrepreneurship within the CTSI and the community. One component will be educating faculty and the next generation of researchers and clinicians. This effort will include, among other topics, “forming industry collaborations”, “the nature of IP as it relates to translational research,” “technology transfer and commercialization” and “development of a uniform, complete, transparent, and verifiable system for documenting and judging industry partnership conflicts of interest.” In addition, we propose a unique leadership training (certificate) program on technology commercialization and entrepreneurship as part of the OIA to be offered in conjunction with the CTSI Committee on Continuing Education. To help establish a two-way relationship between academia and communities, the CTSI plans to prepare community health workers to develop ideas about how to apply new discoveries to the cultural and socioeconomic milieu in which they work. Under the direction of CTSI IAB member Al Osborne, Associate Dean of the Harold and Pauline Price Center for Entrepreneurial Studies, the UCLA Anderson School of Management will extend their intense Entrepreneurship Boot Camp to the CDU campus to provide community members with knowledge, skills and attitudes to take ideas from their experiences to help with T2 translation. If successful, the program will be expanded to other community settings.

6.4. Specific Aim 4: Develop a Research Ethics Consortium and continuing education system for CTSI users and community to enhance ethical sensitivity, understanding of regulations (e.g., FDA, ICH) and GCP, mentoring and learning. The central goals of this specific aim are to: 1) educate researchers about their ethical responsibilities; 2) promote inter-institutional cooperation on ethical issues and policies; and 3) advocate for robust and positive ethical relationships between research teams and the communities in which they work.

6.4.1. Research Ethics Consortium. The Research Ethics Consortium, led by Stuart Finder, PhD, overlaps with other aspects of the Regulatory Program because its members are critical to advising and teaching research teams. Its composition is in **Table 3**. Because rapid advancement of science continuously produces new research paradigms, it is crucial that researchers and institutions be prepared for new ethical concerns such as gene, siRNA and stem cell therapies or introduction of nanotechnology products or the ethical impact of biomarkers. To this end, the CTSI Research Ethics Consortium, whose members have specific expertise in clinical and research ethics, will provide timely consultations for CTSI researchers, research teams, and sites. The Research Ethics Consortium will continually update materials on ethical structure of human subject research and will work closely with UCLA’s Center for Society and genetics in discussions of ethical implications of genetics, stem cell research, and nucleic acid-based therapy discoveries.

Table 3. Shown are members of the UCLA CTSI Research Ethics Consortium, their position at UCLA and their area of specific interest and expertise.

Name	Position	Interest / Expertise
Stuart Finder, Leader	Director, Center for Health Care Ethics	Morality of decision-making in clinical and research practices
Roger S. Detels	School of Public Health Epidemiologist	Ethical issues in international research
Patricia Ganz	Director, Cancer Prevention and Research	Ethical issues in Public Health
Brian Kan	Research Subject Advocate	Prevention of chronic disease
Stanley G. Korenman	Associate Dean, Ethics, UCLA	Informed consent, conflicts of interest, research misconduct
Stewart Laidlaw	Research Compliance Officer	The law and IRB issues
Roger J. Lewis	Research Subject Advocate	Data and safety monitoring, consent, research design
Catherine Mao	Pediatric Endocrinology	Ethical issues in pediatrics research
Junko Nishitani	IRB Director	Genetic privacy, human subject regulations
Laurie Shaker-Irwin	Research Subject Advocate	GCP, ethical study design, recruitment issues
Neil Wenger	Director, UCLA Ethics Center	Informed consent, end of life and futile care

6.4.2. Working with the Community – The NIH Director’s Council of Public Representatives recent report Public Trust in Clinical Research. This document includes a very important recommendation for clinical researchers: build relationships with patients. It is accepted that “true partnerships with patients may not be

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possible, but bidirectional (two-way) relationships must be enhanced.” The Research Ethics Consortium will work to enhance those partnerships by working with the CTSI Community Engagement Program and its members that possess real expertise to help with practical and ethical issues in translation of science to the community to accomplish the goals set forth below. Issues such as the meaning of informed consent in genetic studies and the role of community in biobanks developed in the course of community research will be explored regularly.

6.4.3. Conducting empirical research on the responsible research conduct and research ethics. The empirical research field, merging scientific evidence into research ethics, is in its infancy. For example, Drs. Korenman, Wenger, Shaker-Irwin, and Raffel are investigating informed consent in the light of recent work in behavioral economics that has demonstrated that decision-making is not rational in the narrow sense and that humans are wired with unbalanced views of gain and loss. Other work shows that “framing” powerfully influences decisions and that there is no such thing as neutral presentation of information. The development of this research will be a priority of the Research Ethics Consortium. CTSI objectives to engage and retain our community partners in research include: ■ Invite community leaders to become Research Ethics Consortium members. ■ Establish and nurture clinical research interests of affinity groups in ethnic communities. ■ Organize educational programs. ■ Protect communities from exploitation. ■ Provide financial and personnel support for specific research programs.

7. INVESTIGATORS

The Regulatory Program organization is shown in **Figure 2**. The organization takes advantage of the multifaceted research and community environment of Los Angeles County and the UCLA faculty that represent various facets of this environment. The CTSI has assembled experienced leaders in regulatory affairs and ethics from throughout the broad spectrum and experience of UCLA faculty to form the Regulatory Program Steering Committee, including:

Stanley G. Korenman, MD, Program Leader. Dr. Korenman is Professor of Medicine, Associate Dean for Ethics at the David Geffen School of Medicine (DGSOM) at UCLA. He will coordinate the Regulatory Program and serve as co-chair of the CTSI-specific IRB. Dr. Korenman is himself an investigator with wide-ranging experience in clinical and translational research; Dr. Korenman developed the first commercially viable assay for estrogen receptors in breast cancer, characterized the changes in menstrual cycles throughout reproductive life and characterized hypogonadism in older men and its relation to erectile dysfunction. Dr. Korenman offers a 2-unit course entitled Ethics of Patient-Oriented Research in the K30 program, lectures widely on research ethics and wrote an e-book entitled *Teaching the Responsible Conduct of Research Involving Humans*. Dr. Korenman will be assisted by the following Program Co-leaders and investigators:

Kathryn Atchison, DDS, MPH, Program Co-leader and Office of Industry Alliances leader. Dr. Atchison is Vice Provost for Intellectual Property and Industry Relations at UCLA and manages UCLA’s Division of Industry Sponsored Research, Intellectual Property and Material Transfer Agreements (MTA); for which in the latter she prepared a new electronic MTA process using the same platform as the program. The new MTA form will be available for all CTSI organizations to accelerate CTSI-initiated MTAs. Dr. Atchison is a Professor in the UCLA Schools of Dentistry and Public Health and has a vast experience in research, teaching, administration and management of individual and institutional conflicts of interest related to industrial partnerships.

Roger Lewis MD, PhD, Program Co-leader and Post-approval Research Oversight Leader. Dr. Lewis is Professor and Director of Research in the Department of Emergency Medicine at Harbor-LA-Biomed, and is the current DSM Advisor/RSA for the GCRC at Harbor-UCLA Medical Center. A member of the National Academy’s Institute of Medicine, Dr. Lewis brings his internationally recognized interests and expertise in the interface among clinical research ethics, statistical design and analysis of clinical research studies to the UCLA CTSI community and its partners.

Eifaang Li, DVM, MPH, Program Co-leader and Leader of the IRB-CTSI Harmonization Committee. Dr. Li is Director of Research Compliance at Cedars-Sinai Medical Center where she implemented an online IRB submission system and led Cedars-Sinai to be awarded full AAHRPP accreditation, one of the first nine organizations nationwide to be accredited. She will serve as co-chair of the CTSI-specific IRB and be principally responsible for coordinating the IRB harmonization initiative set forth in Aim 2.

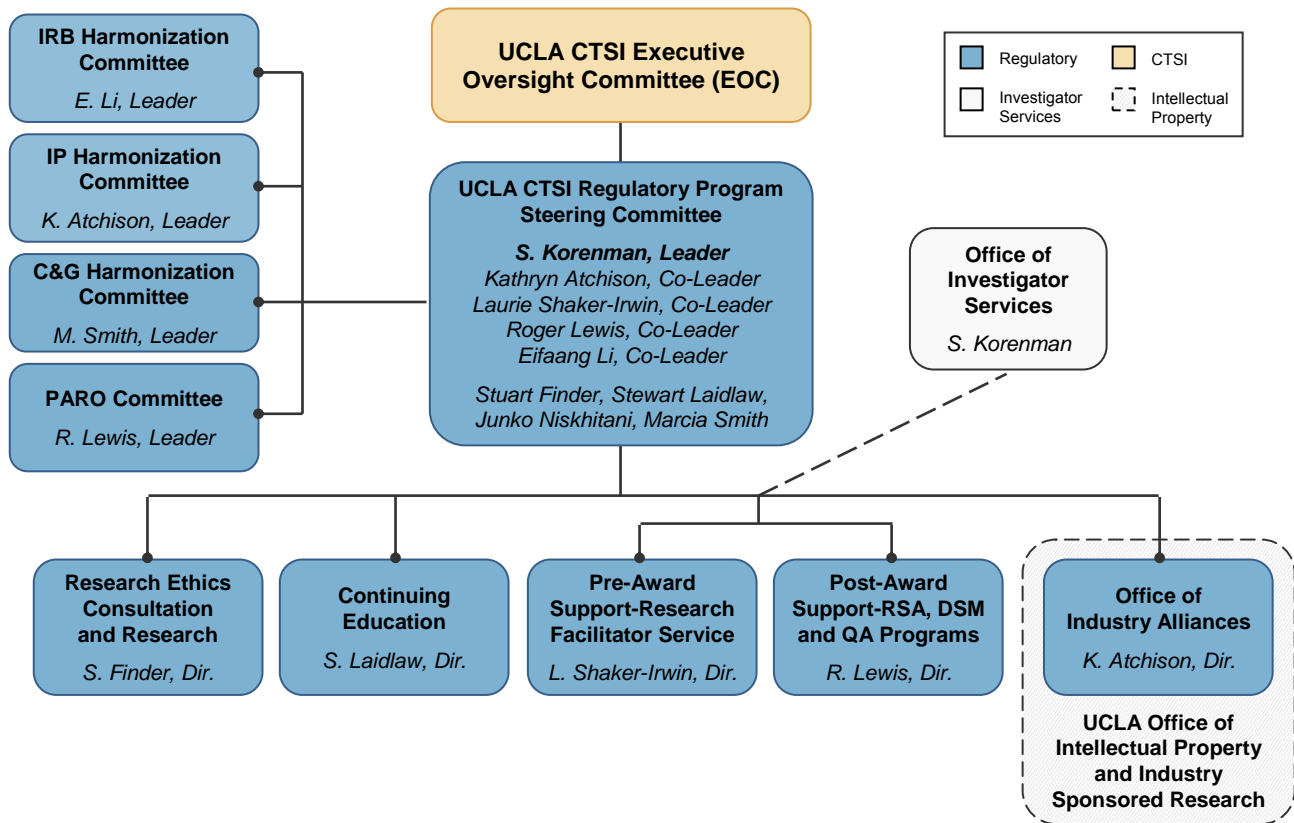


Figure 2. The organizational structure and key CTSI personnel of the operational and oversight functions in the Regulatory key function area (blue) as they interface with the CTSI Executive Oversight Committee (gold), the Office of Investigator Services (gray) and the UCLA-wide Office for Intellectual Property. Note that the letter resides in and is funded through the Chancellor’s office at UCLA (striped). The dotted line indicates an advisory function.

Laurie Shaker-Irwin, PhD, Program Co-leader and Chief Research Facilitator. Dr. Shaker-Irwin currently serves as the Research Subject Advocate (RSA) for the UCLA-Westwood General Clinical Research Center (GCRC) and manages the Office of Research Participant Advocacy. Dr. Shaker-Irwin is responsible for developing subject advocacy programs and policies, educating and assisting study teams, and addressing subject issues. She will participate in and coordinate the Facilitator Program in the OIS.

Stuart Finder, PhD, Program Investigator and Leader of the Research Ethics Consortium. Dr. Finder is the Director of the Center for Healthcare Ethics at Cedars-Sinai Medical Center. His office in the UCLA CTSI will be responsible for coordinating all ethics-related activities including clinical ethics consultation services. Previously, Dr. Finder was the Senior Associate Director of the Center for Biomedical Ethics and Society at Vanderbilt University Medical Center, where he and colleagues built a nationally recognized clinical ethics consultation service and developed a clinical ethics participation program in several clinical research studies.

Stewart Laidlaw, PhD, Program Investigator and Leader for Continuing Education in Research Regulation and Ethics. Dr. Laidlaw is Associate Vice President for Compliance, Director of Educational Outreach and Institutional Privacy Officer at Harbor-LA BioMed. Dr. Laidlaw conducts extensive ethics and regulatory training modules for investigative teams at his and other UCLA institutions. He will be responsible for CTSI-wide research team training programs in responsible conduct of research, human subject protection, and GCP. He successfully implemented Harbor-LA BioMed’s online IRB submission system.

Junko Nishitani, PhD, Program Investigator and member of the IRB Harmonization Committee. Dr. Nishitani is Director of the CDU IRB office and Assistant Professor of Otolaryngology at CDU. Dr. Nishitani teaches the science and ethics of conducting translational and clinical research involving human participants in the Masters of Science and Clinical Research Program at CDU. She is responsible for the CTSI-wide initiative to achieve alignment and reciprocity of IRB processes and approvals.

Principal Investigator/Program Director (Last, First Middle): Dubinett, Steven, MD

Sharon K. Friend, MS, Program Investigator and Member of the IRB Harmonization Committee: Ms. Friend is Director of the UCLA Office of Human Research Protection Program that includes IRB activities and educational outreach and on-site audits of clinical research studies. Ms. Friend successfully implemented an electronic web-based IRB submission and review system at UCLA and led UCLA and UCSF efforts to be awarded full AAHRPP accreditation. Ms. Friend is a member of this particular CTSI IRB Harmonization effort and the UC Medical Centers IRB Working Group that is also working towards harmonization of the five IRB clusters in the UC-associated CTSIs (the other four have all been awarded CTSA's).

Marcia Smith, Investigator and Leader of the Contracts and Grants Harmonization Committee. Marcia Smith is an Associate Vice Chancellor for Research Administration at UCLA and is responsible for the operations of research administration, contract and grant administration, extramural fund management, human and animal research compliance, and research administration systems. Ms. Smith leads the campus-wide Research Administration Process Improvement and Deployment (RAPID) project to implement improved procedures and systems to increase quality and efficiency of campus research administration operations.

8. INTEGRATION OF UCLA CTSI KEY FUNCTIONS

Figure 1 shows how the Regulatory Program is tied closely to the other CTSI key function areas via the OIS. As noted, the Research Facilitator service of the OIS will interact with the resource elements of the Center for Translational Technologies, the Biostatistics, Study Design and Clinical Data Management Program, the **CCRR**, the Biomedical Informatics Program and OIA to provide intellectual and physical resources. The Research Facilitators will work closely with the Pilot/Collaborative Program to encourage and assist promising and emerging investigators preparing to apply and receive pilot funding and with the Community Engagement program regarding initiation and monitoring of studies and research team education. The Regulatory Program team members will be important contributors to formal education programs, providing continuing education to researchers, staff and community members in cooperation with the **CTSI-ED** Program. Finally, all components of the Regulatory Program are dependent on the CTSI Virtual Home and will interact with the Evaluation and Tracking Program for instruction, direction and support.

As a multi-institutional resource, the OIS and the Regulatory key function at UCLA will be enabled by the CTSI Virtual Home. This is being created and serviced in the Biomedical Informatics key function area. The Virtual Home will service the needs of CTSI researchers by provision of tools needed to: ■ support collaborative initiatives ■ provide technology consultation services ■ make available tools for research process management and planning, regulatory oversight and financial management ■ act as a "store front" for workshops and training sessions for clinician-investigators, research support and administrative staff that are critical to clinical and translational studies.

9. INTEGRATION OF UCLA CTSI KEY FUNCTIONS

On behalf of the UCLA CTSI, OIS representatives will collaborate with the Greater Los Angeles CTSA Biomedical Informatics Program (CTSA's at USC and UC Irvine), the UC Biomedical Research Acceleration Initiative, Western Regional CTSI Biomedical Informatics Programs and the National CTSA Biomedical Informatics Consortium to accomplish the trans-institutional objectives of the CTSA's. For example, Dr. Roger Lewis, head of the PARO in the UCLA CTSI, working with CTSA-sponsored co-investigators at the University of Michigan, the University of South Carolina and Corporate America, the Berry Consultants, has just received one of four, 3-year \$2.5 million awards, entitled "Accelerating Drug and Device Evaluation through Innovative Clinical Trial Design," co-sponsored by the NIH and FDA to support research projects in regulatory science. The aim of these awards is to better inform scientists and regulatory reviewers alike about medical product safety, and improve the evaluation and availability of new medical products to the community. As another example, with the current application we have added two novel Domain Experts to the OIS (see **Figure 1**). One especially dedicated to the facilitation of transdisciplinary research of the type embodied in the Translational Research Cluster concept (see the Pilot/Collaborative Program and Overview and Governance) and another to comparative effectiveness research. Our research clusters, which focus on the most common disorders affecting the populace of Los Angeles County, include investigators from USC, Los Angeles County Health Department, as well as from UCLA and its academic and community partner organizations.

10. IMPLEMENTATION PLAN AND MILESTONES

Table 4. presents the UCLA CTSI Regulatory Program Implementation Plan, which describes the projected time line, measurable objectives, and milestones for implementing key tasks over a preparatory period and over Years-01 to -05 of the project period with respect to each of the program aims.

Table 4. CTSI Regulatory Program Implementation Plan

Aim 1. Harmonize regulatory mechanisms throughout the UCLA CTSI to promote easy access to translational research opportunities for clients, scientists, staff, community members and study subjects.

Year	Plan	Measures & Metrics
0	Complete multi-institutional MOU and Convene IRB Harmonization Committee of leadership from 4 CTSI partner institutions	<ul style="list-style-type: none"> Process measures to monitor e-IRB processing Number of e-IRB forms submitted and reviewed Completion time for cross-institutional IRB protocols Defined methods and testing for accelerated IRB approval Number of CTSI proposals Log of reciprocal C&G activities Record of delays and improvements accomplished through the C&G committee Number and type of educational programs for community partners
1	Join CTSA National Consortium Regulatory Key Functions Committee	
1	Each institute appoints a CTSI C&G officer	
1-5	Convene ongoing C&G Harmonizing Committee to identify problems, to reduce delays, and improve processes	
1-2	Continue harmonizing oversight and monitoring between IRB and PARO	
1-2	Continue harmonizing IRB single web submission procedure	
2-3	Implement AAHRPP approval at the remaining partner site	
3	Achieve full IRB reciprocity within CTSI	
3	Achieve full reciprocity throughout the UC Consortium	
3	Join CTSA-wide IRB reciprocity	
1-5	Develop educational initiatives for community partners to provide practical training in contracting and subcontracting to support community research	

Aim 1.2: Harmonize C&G procedures throughout the CTSI.

Year	Plan	Measures & Milestones
1	Each institute appoints a CTSI C&G officer	<ul style="list-style-type: none"> Number of CTSI proposals Log of reciprocal C&G activities Record of delays and improvements accomplished through the C&G committee Number and type of educational programs for community partners
1-5	Convene ongoing C&G committee to review any problems with processes	
1-5	Continue collaborating across institutions to reduce delays and improve processes	
1-5	Develop educational initiatives for community partner to provide practical training in contracting and subcontracting to support community research initiatives	

Aim 2.1. Collaborate with the OIS-BIP to Provide regulatory domain experts to investigators and Research Facilitators to aid development of online resources for the investigator community.

Year	Plan	Measures & Milestones
1-3	Recruit/train and identify existing facilitators to provide comprehensive array of services, market services and provide investigator support	<ul style="list-style-type: none"> Number Facilitators hired and trained Number and type of services utilized Outcome of invest efforts: number of proposals completed, submitted, funded Log of obstacles identified and overcome
1-5	Provide assistance with FDA approvals and compliance	
1-5	Collaborate with CTSI BIP to design the CTSI Virtual Home	
2-5	Develop operations and procedure manual	
2-5	Evaluate and continuously improve services	
3-5	Enhance databases	
4-5	Develop reporting system for obstacles	

Aim 2.2. Develop a Post-Approval Research Oversight (PARO) system to enhance research quality and safety.

Year	Plan	Measures & Milestones
1-5	Continue periodic multi-institutional PARO meetings	<ul style="list-style-type: none"> • Complete inventory of people and functions • Align and improve language and processes across sites • Harmonize agreements to integrate uniform language and processes • Use reciprocity in audits • Completion of RSA manual
1-5	Expand the training and role of RSAs to monitor research conducted in community settings	
1-2	Inventory similar and disparate research oversight processes and their rationales throughout CTSI	
2-5	Align processes across institutions to reduce or eliminate differences in workflow, oversight requirements, and processes	
2-5	Harmonize and integrate the PARO processes	
3	If found to be productive, implement reciprocity phase including partial reciprocity, full reciprocity, and just-in-time review	

Aim 2.3. Develop a Continuing Education System.

Year	Plan	Measures & Milestones
1	Inventory and map educational resources and curriculum	<ul style="list-style-type: none"> • Number of completed courses by research team • Increasing ratio of completed courses per investigators
1	Use the CITI system to certify clinical investigators and other members of the research team	
1-5	Make more advanced courses available through Virtual Home and using local/national resources	
2	Develop database on individual completion and achievements in CE	
2-5	Develop educational modules as needed	
2-5	Set up system to simulcast to CTSI, community partners, and affiliates	
3-4	Integrate CE systems	

Specific Aim 3. Create Office of Industry Alliances (OIA) to promote and sustain the linkage of the CTSI, its members and industry partners.

Year	Plan	Measures & Milestones
1-5	Convene meetings of the Industry Advisory Committee	<ul style="list-style-type: none"> • Number discoveries, patents, and licenses • Number startup companies • Number Industry-sponsored research agreements/clinical trials • Number technological innovations for clinicians • Number and type of educational sessions conducted
1-5	Develop collaborations around CTSI research initiatives	
1-5	Facilitate industry interactions by providing one-stop shopping for industry in licensing CTSI originated technologies and intellectual properties (IP)	
1-5	Assist faculty inventors and partners with technology transfer	
1-5	Push innovation by matching clinician needs with technological innovations	
2-5	Develop and conduct entrepreneur education program	

Specific Aim 4. Develop a Research Ethics Consortium (REC) and continuing education system for CTSI users and clients to enhance ethical sensitivity, understanding of regulations (e.g., FDA, ICH, etc.) and good clinical practices, mentoring and learning.

Year	Plan	Measures & Metrics
1	Identify and assemble REC. Join the CTSA Consortium Clinical Research Ethics Key Functions Committee	<ul style="list-style-type: none"> • Number and type of consultations • Number of research projects funded • Level of collaboration among partner sites and professional schools
2	Establish expertise for Research Ethics Consultation Service	
3	Participate in CTSA Consortium research studies. Begin development of research projects	
2-5	Carryout consultations	
1	Inventory and map educational resources and curriculum	<ul style="list-style-type: none"> • Number of completed courses by research team • Increasing ratio of completed courses per investigators
1	Use the CITI system to certify clinical investigators and other members of the research team	
1-5	Make more advanced courses available through Virtual Home and using local/national resources	
2	Develop database on individual completion and achievements in CE	
2-5	Develop educational modules as needed	
2-5	Set up system to simulcast to CTSI, community partners, and affiliates	

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1. Burman W, Daum R. Grinding to a Halt: The Effects of the Increasing Regulatory Burden on Research and Quality Improvement Efforts, Clinical Infectious Diseases. 2009 49:1 August, published online.
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Clinical and Community Research Resources (CCRR) (previously PCIR)



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Abbreviations: ACE -- angiotensin-converting enzyme, ACT – Adoptive Cell Transfer, BIP – Biomedical Informatics Program, CARE – Center for AIDS Research and Education, CDU – Charles Drew University, CERP – Community Engagement and Research Program, CRCD – Clinical Research Core for Dentistry, CTN – California Telehealth Network, CTSI-ED – Research Education, Training, and Career Development, CTT -- Center for Translational Technologies, DC – Dendritic Cell, DGSOM – David Geffen School of Medicine, DSM – Data & Safety Monitoring, DSMP -- Data & Safety Monitoring Plan, EMA – Ecological momentary assessment, EOC – Executive Oversight Committee, E/T – Evaluation and Tracking Unit, GCP – Good Clinical Practices, GLP – Good Laboratory Practices, GPS – Global positioning system, HIV – Human immunodeficiency virus, IND – Investigational New Drug, IRB – Institutional Review Board, IT – Information Technology, MSCR – Master of Science in Clinical Research, NICHD – National Institute for Childhood Health and Development, NICU – Neonatal Intensive Care Unit, OIA – Office of Industry Alliance, OIS – Office of Investigator Services, PICU – Pediatric Intensive Care Unit, QI – Quality Improvement, RCA – Research Center at Alhambra, RCMI – Research Centers in Minority Institutions, SAC – Scientific Advisory Committee, SOP – Standard Operating Procedure, STD – Sexually transmitted disease, TCR – T Cell Receptor, THE – To Help Everyone Clinic

1. OVERVIEW

The Clinical and Community Research Resources Program (CCRR) provides the integrated clinical infrastructure and flexible services our CTSI investigators need to conduct community-partnered research. It fulfills the national CTSA Participant and Clinical Interactions Resources (PCIR) key function. With the University Southern California and the University of California, Irvine CTSAs, we form the Greater Los Angeles PCIR Consortium. Top priorities for our local consortium are standardizing protocols across CTSAs and devising a plan for sharing mobile research resources. As detailed below, CCRR investigators have numerous productive collaborations with other CTSA-possessing institutions.

In our prior review, we were reviewed with Regulatory Knowledge and Support key function and received an aggregate score of 2. Reviewers praised our outstanding, experienced leadership; our high level of institutional commitment; our well-coordinated and comprehensive services; our high level of attention to ethical conduct and participant and clinical interactions. No weaknesses were noted. During the past year, we have further integrated our existing programs and broadened our outreach into our community. This integration and expansion in outreach activities has been made possible by the recent receipt of \$15,000,000 over the next 5-years (see appended letter) to transform the way we undertake participant research at UCLA. As such, we changed the name of this program to Clinical and Community Research Resources from PCIR Program. Changes in this revision application are indicated by a vertical line in the left margin.

2. SPECIFIC AIMS

The UCLA CTSI partner institutions serve Los Angeles County, the most populous and diverse county in the US. Over 10 million residents span the spectrum of socioeconomic status and ethnicity. Nearly 15% of families live below the poverty line. Only 59% of students in the Los Angeles Unified School District are proficient in English. Many students speak one of 90 different languages in their homes. Understanding and addressing this population's health care needs will be facilitated by the unifying influence of the CTSI. The UCLA CTSI provides operations and governance necessary to facilitate successful transdisciplinary clinical and translational research in our community. The overarching *mission* of the University of California, Los Angeles Clinical and Translational Research Sciences Institute (UCLA CTSI) is to *transform our academic-clinical-community partnership into a borderless institute that brings our combined innovations and resources to bear on the most pressing health needs in Los Angeles.*

The CCRR Program is key to the CTSI's goal of integrating translational research efforts. We are responsible for providing skilled research staff to assist investigators. Los Angeles County's size and diversity are strengths and obstacles; the CCRR must deliver research capabilities to the community and make it easier for residents to go to research centers when that is a safer environment. For our mission, we creatively overcome logistical barriers and capitalize on unique opportunities our multiple institutions provide to reach out more of Los Angeles County than would be feasible from any single location.

During the proposed grant cycle, the prime goal of the CCRR is to develop a flexible, cost-effective, multi-institutional clinical research infrastructure with capabilities to support the spectrum of translational T1→T4 research; T1 research seeks to move a basic discovery into a health application. T2 research assesses the value of an application for health practice leading to the development of evidence-based guidelines. T3 research attempts to move evidence-based guidelines into health practice, through delivery, dissemination, and diffusion research. T4 research seeks to evaluate the "real world" health outcomes of an application in practice.¹

To achieve this goal, we propose the following Specific Aims:

Specific Aim 1: To broaden the scope and efficiency of clinical, translational and community research by implementing the "CCRR without walls." This will be achieved by:

- Cross-training research staff so that they can support research in the inpatient, outpatient and community environments as needed.
- Initiating Mobile "Chaperone" Services to link the CTSI partners and communities.
- Assessing and modernizing CCRR staffing to provide an appropriate distribution of research nurses, phlebotomists, and community health workers based on the research needs of CTSI investigators.

- Creating a promotora program to i) engage local community members in research education and ii) encourage community participation in research projects.

Specific Aim 2: To promote collaborations across the CTSI partner institutions by:

- Increasing interaction among CTSI investigators through the CTSI Virtual Home and the Office of Investigator Services (OIS).
- Sharing common protocols, standard operating procedures (SOPs) including Good Clinical Practice (GCP), and teaching materials across all CCRR sites.
- Centralizing laboratories that follow Good Laboratory Practice (GLP) standards.
- Easing research approval barriers at partner institutions via creation of single, UCLA-wide scientific advisory committee and an institution-specific, CTSI-specific Institutional Review Board (IRB) for proposals seeking CTSA support and resources.
- Maximizing access of the UCLA CTSI community to a broader portion of Los Angeles County population.
- Enhancing academic-industry research partnerships.

Specific Aim 3: To recruit junior professionals into careers in translational clinical research by:

- Providing hands-on exposure to clinical research;
- Mentoring young investigators performing translational research;
- Leading CTSI efforts in training research staff to assure that research is performed by qualified and trained staff who are fully capable of completing research procedures accurately and with utmost safety for participants.

3. PROGRESS TO DATE

Over the past year we have enhanced our integration and broadened our mobility to meet the needs of clinical and translational investigation in many settings. The initial steps outlined below have focused on the critical logistics needed to make inter-institutional interactions possible. We have achieved the following:

- Established a CCRR Steering Committee including Drs. Wang, Martins, Raffel, Salusky, Atchison, Burnes-Bolton and Ms. Jones representing all UCLA CTSI partner institutions and community.
- We surveyed 200 NIH-funded UCLA scientists distributed across CTSI partner institutions regarding support for clinical and translational research facilities and services. Among 114 responders (57% response rate) most spent greater than 50% time and effort in research and had at least 16 years of research experience. Ninety percent used the outpatient setting and predicted increased patient recruitment for the next three years.
- Construction of a leading-edge ambulatory CCRR facility and “home” to the CTSA at UCLA (to open in January 2011), occupying 20,200 square feet and including outpatient areas, outpatient pharmacy, biosample processing, and biorepository cores, the Office of Investigator Services (i.e., resources service center), administrative offices, and conference rooms.
- Launch of the statewide California Telehealth Network (CTN) in collaboration with our University of California CTSI partner institutions. This creates a digital highway to expand health care and clinical research access throughout California.
- Initiation of monthly conference calls with the other UC CTSIs to plan mechanisms that will enable future CTSI West Coast Consortium joint clinical research.
- Successful development of the CTSI Virtual Home for investigators, a key feature for CCRR integration. Initially the Virtual Home was an online general information source without substantial interactivity. With recent improvements it allows investigators to: 1) access information about CCRR services and procedures at all CTSI institutions; 2) contact Research Facilitators from the OIS to gain individualized assistance in developing and implementing research throughout the CTSI; and 3) complete and submit IRB, Data and Safety Monitoring, and CCRR service application materials to initiate research throughout the CTSI.
- Creation of CTSI-wide: 1) common IRB and CCRR application forms (see below), 2) uniform DSMP and consent templates, 3) harmonized, facilitated IRB review and approval mechanisms, and 4)

transinstitutional agreements regarding intellectual property and technology transfer for multi-institutional, CTSI-based discoveries (see **Regulatory Program**).

- In collaboration with the Regulatory key function, an IRB Harmonization Committee was developed, and an inter-institutional agreement (memorandum of understanding [MOU]) was approved to develop a unified IRB application form. This included a uniform template for consent. The IRB application and informed consent form are now available for completion and submission through the Virtual Home.
- The CCRR leaders, collaborating with the **Regulatory Program**, have reached an understanding on establishing research privilege reciprocity across the CTSI, so that academic center- and community-based investigators can conduct research and secure access to research participants in the most appropriate setting(s). Meetings are underway to develop the process by which reciprocity will be granted.
- Regular meetings of the nursing and bionutrition staff are being held with the members of **Community Engagement and Research Program (CERP)** to discuss the coordination of CCRR services to support community-based participatory research.
- Community-partnered workshops are also being held to stimulate community research interest and understanding, such as “Establishing Community Partnerships to Prevent or Manage Diabetes and Other Chronic Conditions” with speakers from UCLA and Healthy African American Families, held at Harbor-LA BioMed on September 17, 2010.

4. SIGNIFICANCE: THE CCRR’S STRENGTHS AND OPPORTUNITIES

Los Angeles County’s size and diversity offer strengths and challenges. Racial and ethnic, socioeconomic, and age diversities provide unparalleled opportunities for translational studies in a range of care provision setting. Effective reach is essential to UCLA CTSI goals. The CCRR seeks to bring research capabilities into the community and facilitate bringing research participants from the community to the research center when it is a safer research environment.

The resources accessible by the UCLA CCRR include many hospitals; Ronald Reagan Medical Center in Westwood, Cedars-Sinai Medical Center in West Hollywood, Harbor-UCLA Medical Center in Torrance, the Greater Los Angeles VA Medical Center in West LA, and the County of Los Angeles Olive View Medical Center in the San Fernando Valley. The UCLA-affiliated hospitals have a capacity of more than 2500 licensed beds, by far more than any other academic entity in Southern California. This provides a broad range of settings in which to recruit participants for translational research. Our resources are even more extensive, as they also include the academic expertise of the faculty of the UCLA David Geffen School of Medicine (DGSOM), School of Nursing, School of Dentistry and School of Public Health; the Charles Drew University (CDU) School of Medicine, School of Nursing and College of Science and Health; the Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center (LA BioMed), and the Burns and Allen Research Institute at Cedars-Sinai. We are capitalizing on these multifaceted resources to develop our “CCRR without walls” initiative. In one recent example utilizing local funding we facilitated the research of Maie St. John, MD, PhD, a head and neck surgeon and K23 awardee. Research facilitators helped with her research that focuses on development of new biocompatible polymers for drug delivery to be implanted at the time of surgery in patients with advanced or recurrent oral and oropharyngeal squamous cell carcinoma. Dr. St. John is collaborating with the Schools of Engineering and Dentistry and the California NanoSystems Institute. She is developing clinical studies for Harbor-LA BioMed and UCLA Westwood, with CCRR support at both locations. Dr. St. John’s research has been facilitated by local CTSI pilot funding supplemented by the Jonsson Comprehensive Cancer Center and LA BioMed using mechanisms described in the **Pilot Program**. The CCRR key function will continue to expand opportunities for junior investigators by integrated activities with the **Pilot Program**, **CTSI-ED**, and the OIS. These research opportunities will continue to be facilitated across the partner institutions.

One important transforming asset has been development of the six disease-related “Translational Research Clusters” as part of the CTSI (see **Overview and Governance** and **Pilot Program**). This process and a new funding mechanism are already affecting change in the ease with which investigators across the CTSI can i) find out about others with overlapping research interests, ii) identify potential collaborators to become involved in existing translational research and iii) identify potential new colleagues for novel research endeavors.

5. INNOVATION AND ENVIRONMENT

Given the broad area served by the CCRR, key elements for effective integration include the capability to transport people and research materials physically among various locations and a comprehensive program of virtual interaction. The CTSI Virtual Home and telemedicine capabilities at each partner institution are important steps to integration. As part of its commitment to the CTSI, the UCLA DGSOM Dean's Office has donated three vans and three full-time drivers for physical transportation. Below are examples of innovative outreach programs and services already developed at UCLA. These will help leverage our transformation into a single CCRR network. These facilities include:

5.1. Ambulatory Clinical Research Facilities. Assistance with research in the ambulatory setting is the service CTSI investigators most often request. We are well equipped to assist such research, as all partner institutions have outpatient research units. ■ The new 20,200-square-foot UCLA Westwood ambulatory CCRR facility (to open in January 2011) includes outpatient areas, a service center with pharmacy and sample processing/triaging resources, and conference rooms. ■ The outpatient unit at Harbor-LA BioMed (4,300 square feet with 11 examination/consultation rooms) is in a research building adjacent to conference rooms and is the telemedicine hub at Harbor-LA BioMed. ■ The outpatient unit and research cores at Cedars-Sinai occupy 5,500 square feet, with 5 examination rooms, a bionutrition consultation room and onsite sample processing laboratory. ■ The CDU outpatient clinical research resource occupies an 8,000-square-foot clinical research suite in the new 62,000-square-foot Research and Nursing facility, with support for community-based participatory health disparities research.

5.2. Inpatient Clinical Research Facilities. The CTSI's two inpatient units, approximately 25 miles apart, allow investigators and research participants to select the closest site. The units include:

The new cutting-edge inpatient unit at the Ronald Reagan UCLA Medical Center (Westwood) contains 6 beds (3 institutionally supported). Additional beds can be accessed from the adjacent Telemetry Unit when research bed demands are high. The inpatient unit at Harbor-LA BioMed contains 6 research beds plus 6 beds supported by Los Angeles County. This is a flexible unit that transforms from a research unit to a medical surgical unit, dependent on research usage, providing an efficient, economical means to support research requiring intensive monitoring only available in an inpatient setting.

5.3. Mobile Units. A unique feature of the UCLA CCRR has been the deployment of mobile research staff who travel to research subjects, rather than subjects coming to the CCRR. Two of our mobile programs have been in existence for over 10 years and will serve as the model for additional mobile teams to be developed over the next 5 years (see **section 6, Approach** below). They are: ■ The Perinatal/Pediatric Clinical Research Unit is currently housed at Harbor-LA BioMed and serves the needs of scientists stationed at CDU and Cedars-Sinai. It is a flexibly organized mobile program that facilitates logistically demanding studies in mothers and babies. ■ Cedars-Sinai has a cost-effective mobile research unit that travels to the experimental subject. It is useful especially for the many large-scale family-based genetic projects active at UCLA.

This model has been adopted by PCIR sites nationwide. We plan to expand mobile programs to other UCLA CTSI activities. (see **Approach**).

5.4. Research Bionutrition Services. Full bionutritional services are available at UCLA-Westwood and Harbor-LA BioMed, and partial support (a research dietician but no metabolic kitchen) is available at Cedars-Sinai. Collaborating across institutions, the bionutrition service unit provides investigators with metabolic balance diets, diet modulation for in- or out-patient studies, nutritional assessment, food records and anthropometry assessment. Dual energy x-ray absorptiometry equipment for assessment of body composition and bone density is also available at Harbor-LA BioMed and Cedars-Sinai CCRR sites. For greater integration and cost-effectiveness we have extended these services to our community and hospital-based partners.

5.5. Unique Clinical Research Training Programs. Besides providing hands-on training and research support for K12, K23, K24, T12 and T32 trainees, the CCRR sites have developed unique programs for clinical research training outreach to undergraduates and high school students. For over 10 years Cedars-Sinai, collaborating with Harbor-LA BioMed, has sponsored a novel program to expose high school students to clinical research early in their educational development. Harbor-LA Biomed has developed NIGMS-funded minority outreach biomedical and translational research training programs for underrepresented students from

Cal State University Dominguez Hills. Working with the **CTSI Research Education, Training, and Career Development key function (CTSI-ED)** and **CERP** key function areas, CCRR engages young members of our constituent communities by providing them a unique opportunity to observe and participate in clinical translational and community-based research, under the tutelage of established CTSI investigators.

5.6. Research Centers in Minority Institutions (RCMI) Translational Research Network at CDU. In July 2007, NCRR awarded CDU (PI Keith Norris, MD) a \$17 million, 5-year grant to launch the RCMI Translational Research Network, designed to increase multi-site clinical and translational research among minority and other collaborating institutions throughout the US. The Network focuses on cancer, diabetes, renal disease, infant mortality, HIV/AIDS, and cardiovascular diseases, conditions that disproportionately impact minority populations. In the next 5 years of the CCRR, this resource will be leveraged heavily for the pursuit of comparative effectiveness research in many of the ethnically diverse regions of Los Angeles County.

6. APPROACH

During the proposed grant cycle, the fundamental goal of the CCRR is to continue to develop a flexible, cost-effective, multi-institutional clinical research infrastructure with the capabilities needed to support the entire spectrum of translational T1→T4 research. To achieve this goal, the CCRR must become highly integrated, coordinated, user-friendly, and community-accessible. With our existing infrastructure (see **Figure 1** below) and working with the CTSI investigators and communities UCLA serves, we will leverage our strengths and implement novel initiatives and strategies under three specific aims, as follows:

6.1. Specific Aim 1: To broaden the range of clinical, translational and community research by implementing the “CCRR without walls.”

6.1.1. Cross-training research staff so that they can support research in the inpatient, outpatient and community environments as needed.

The traditional model of clinical research, in which the subject comes to the research unit, is changing and the CCRR must be as flexible as possible in its approach to assisting research activities. In addition to supporting human research within the existing CCRR sites and units, CCRR must be capable of going off-site.

As noted earlier (see **section 5.2.**), the nurses and perinatal/pediatric nurses at multiple CCRR sites already conduct research in many locations, including neonatal units, delivery rooms, emergency departments, neurosurgical and medical intensive care units, and outpatient clinics. To build on this “scatter” or “mobile” nurse experience developed over the last 14 years, in the first 3 years of the grant we are beginning to expand, in a stepwise fashion, these services across our consortia generating a “CCRR without walls” to fulfill our mission of bringing research to participants spanning all ages throughout the CTSI partners and across Los Angeles County. For example, CCRR mobile nurses and registered phlebotomists will i) go to the bedside of research participants in all units of the medical center and ii) return with biological samples (i.e., blood, saliva, urine, serum, surgical samples, cells, etc.) and/or data, and iii) be deployed into the community to assist with research being performed in community health centers or even in subjects’ homes. To achieve this flexibility efficiently and cost-effectively, all CCRR research staff must be capable of functioning wherever they are needed. Thus, distinctions between inpatient and outpatient research staff, hospital-based staff and community-based staff are disappearing.

Our current videoconferencing capabilities will be extended for staff meetings across the CTSI, at which staff are familiarized with the needs of various research protocols approved by the CCRR-SAC and given in-service training on specialized clinical research procedures. Thus, although a particular research study may have a ‘home’ CCRR location where the bulk of research activity occurs, staff from other sites are able to accommodate research subjects who prefer to be seen at other locations, with assurance that the research is performed accurately by fully capable staff and with utmost safety.

As examples, based on the volume of research participants scheduled on a given day, a CCRR research staff member can be assigned to go i) to the UCLA Community Research Center at Alhambra (RCA) in East Los Angeles, where research on common chronic, multigenic diseases is performed, augmenting its well-trained, multiethnic staff, ii) to the Hubert Humphrey Community Health Center in South Los Angeles to assist with community partnered research being performed with members of the principally Hispanic and African-

American community there, or iii) to the Chicano Studies Research Center at Mission Community Hospital to assist the newly created Clinical Research Core for Dentistry (CRCD) at the Weintraub Center for Reconstructive Biotechnology in the UCLA School of Dentistry in their extensive research program focusing on the psychosocial and biological elements that determine the dental treatment options of preference in the Hispanic Community of Los Angeles.

6.1.2. Initiating mobile “Chaperone” services to link the CTSI partners and communities. To capitalize on Los Angeles County’s size and diversity in our research efforts, the CCRR must enhance integration of research across the CTSI partner institutions and effectively reach out to our community with the ability to bring research capabilities into the community and facilitate bringing research participants from the community to the research center when that is safer and more appropriate. As part of its institutional commitment to the CTSI, the UCLA DGSOM Dean’s Office has donated three vans, support for their maintenance and three full-time drivers to facilitate transportation. These mobile units are designed to transport investigators, trainees, CCRR staff, research subject advocates and research resources (such as meals prepared by the research dieticians) into the community to conduct research and collect feedback from community leaders and participants to direct our future research agendas (see also **CERP**). The vans are able to bring scientists, students, promotoras (see **section 6.3** below), and study participants back to the various PCIR sites to engage in training by teleconference or in person, in-house clinical and translational research projects, investigator team meetings, and for specialized research interventions that cannot be conducted in the field (e.g., body composition, radiological imaging *in vivo*). The vans are also used to convey biological samples (bar-code labeled to maximize subject confidentiality) from the field to the Service Core in the **Center for Translational Technologies (CTT)** (see **Pilot Program**) for distribution to CTSI cores and resources or to other CCRR sites. As interactions among the CTSA in Southern California expand (see letter RE: Greater Los Angeles CTSA Coalition), the vans will also be available to transport staff, community members, and specimens to other sites (e.g., USC, UCI, UCSD or Scripps); this type of interaction has been agreed to in principle by the PCIR/CCRR directors from UCLA, USC and UCI.

6.1.3. Assessing CCRR staffing to provide an appropriate distribution of research nurses, phlebotomists and community health workers based on the research needs of CTSI investigators. Careful ongoing assessment of the mix of research support being requested from the CCRR will be necessary to determine the number and type of CCRR staff needed by the CTSI research community. Based on usage trends over the past 5 years, it is clear that a substantial portion of clinical research has moved into ambulatory and community locations and the above-described plan for flexible assignment of research staff is designed to maximize the CCRR’s ability to satisfy these research needs. For example, in the last 4-5 years nearly 50% of the ambulatory services in the Departments of Medicine, Family Medicine, Pediatrics, Orthopedic Surgery and Neurosurgery from the UCLA Westwood have moved to the revamped UCLA-Orthopedic Hospital campus in Santa Monica, some ten miles and 30 minutes from the UCLA Westwood campus. As such, a substantial portion of the clinical and translational research performed in Westwood has moved to the Santa Monica campus. A full-time CCRR nurse and a research project coordinator are to be housed in Orthopaedic Hospital-dedicated outpatient space on the Santa Monica Campus to support these efforts. It is anticipated that mobile research team support from the Westwood campus (see **section 6.1.4.**) will be required to assist the onsite satellite team when protocol activity becomes especially brisk.

When an investigator requests CCRR protocol support, a domain expert (usually a nurse manager) will work with the investigator to define the number of hours of staff support required and type of staff needed (research nurse, phlebotomist, community health worker, dietician, recruitment specialist, etc.). This anticipated utilization information will be provided to the CTSI-specific SAC (**section 6.2.3.**) to use in its deliberations.

6.1.4. Additional mobile nurses. To meet community research needs and based on our documented success in GCRCs with nurses in this position, we propose to hire four additional CCRR “mobile” nurses (two in year-01, one each in years-02 and -03) to staff the mobile units, train community site personnel, train CCRR site personnel on community research, and participate in Community Research Symposia and Project Forums designed to understand community research needs. Utility of this model will be evaluated annually from year 1 onward. Moreover, as detailed in **CERP**, CCRR will collaborate on locating a CCRR nurse and/or research assistant at each of the 14 participating community clinic partners (see **Table 1** below). These staff will work half time in the clinic and half time on CCRR projects.

Table 1. Shown are the UCLA CTSI-affiliated regional community health centers in Los Angeles County and the ethnic makeup of the populations they serve.

Community Partners	Ethnicity				
	White	African American	Hispanic	Asian	Other
North and West Los Angeles <ul style="list-style-type: none"> • Alhambra Research Center • Northeast Valley Health Corp • Venice Family Clinic • Mission Community Hospital 	45%	9%	25%	11%	8%
North and Central Los Angeles <ul style="list-style-type: none"> • Saban (LA) Free Clinic • People Coordinated Services • Para Los Ninos • Healthy African American Families 	23%	18%	46%	10%	3%
South and Central Los Angeles <ul style="list-style-type: none"> • King Multi-Service Ambulatory Center • THE Clinic • Hubert Humphrey Comprehensive Health Center 	4%	35%	55%	5%	1%
South and West Los Angeles <ul style="list-style-type: none"> • Coastal Cluster Health Centers • Wilmington Health Center • Bellflower Health Center • Long Beach Comprehensive Health Center 	12%	20%	57%	7%	4%

6.1.5. CCRR-CERP joint research promotora program. A *promotora* is a community-based lay health worker. Because the CTSI has a vast repertoire of large-scale clinical and epidemiological research programs that focus on disease in specific ethnic or racial groups (see **CERP**) and because these groups are concentrated geographically around the Los Angeles Basin, we intend to engage local promotora staff. We propose beginning and maintaining 4 promotora FTEs in the grant period. Collaborating with the UCLA Chicano Studies Research Center among other partners and with the extensive use of teleconferencing, we will promote community education about and participation in research projects as well as community participation in the conduct of research (community-partnered participatory research). Promotoras will be recruited and trained as one component of the **CERP** agenda in community-partnered participatory research, in part by building outward from the existing successful Chicano Studies Research Center Promotora Program at Mission Community Hospital. Recruitment and training of these promotoras in collaboration with **CERP** and CCRR is underway. In the spirit of bidirectional knowledge transfer, the lay health workers are learning about research methods from CCRR and **CERP** staff and investigators, who in turn are learning new community engagement techniques and strategies for recruiting diverse populations from these lay health workers.

6.1.6. Inpatient research staffing. While outpatient and community research is the CCRR's major focus, inpatient clinical research is still important, especially in early phase clinical trials, when new agents are being administered to subjects for the first time and careful, prolonged monitoring is imperative. As an example, the UCLA CCRR inpatient unit serves as a key resource for a study combining chemotherapy and immunotherapy strategies in patients with metastatic melanoma. This clinical trial (NCT00910650, IND 13859, RAC 0802-901) employs adoptive cell transfer (ACT) of T cell receptor (TCR)-engineered lymphocytes to genetically engineer a human immune system capable of inducing robust antigen-specific antitumor responses in patients with cancer. The inpatient unit also provided safety monitoring for Nanofiltered C1INH (Cinryze), Pasteurized C1INH (Berinert), and Ecallantide (Kalbitor) as new therapies for hereditary angioedema, a rare but life-threatening condition which before these approvals had no effective treatment. Other examples include a NIDA-supported phase 1 study of a novel therapy for methamphetamine abusers that will commence in Fall 2010 and a first-in-man study of an NICHD-developed modified androgen for male contraception is scheduled to start in January 2011. Both studies will require multiple admissions and careful inpatient monitoring in the Harbor-LA BioMed inpatient CCRR.

Our experienced CCRR staff will continue to support these studies in the inpatient units, but with increasing financial support from our local partner institutions. The leadership at Ronald Reagan UCLA Medical Center and Harbor-LA Biomed has committed to supporting investigator access to inpatient research beds and has agreed to cost-sharing procedures that will make it financially realistic for the CCRR to continue to support research requiring inpatient stays (see **Institutional Commitment Letters**). Currently, three of the 6 beds in the newly opened unit at the Ronald Reagan UCLA Medical Center are institutionally supported and 6 of the 12

beds in the inpatient unit at Harbor-LA BioMed are supported by Los Angeles County. At present, inpatient research bed usage is 1485 bed days. Our current projections for future inpatient bed use are based on recent trends and prospectively collected survey data from users. These projections include an anticipated influx of complicated research studies of novel therapies through investigator-initiated Investigational New Drug (IND) and device applications by CTSI investigators, as well as through collaboration with industry, facilitated by interaction with the **Office of Industry Alliances** (see **section 6.2.12.** below). Using yearly projections and continuous assessment of need and expense, cost-sharing plans are expected to halve the number of inpatient beds among the CTSI partner institutions that will be NIH-supported in year-01, with subsequent cost-shifts to the institutions and users at a rate of 25% per year. We anticipate that a combination of institutional support and user cost-sharing will provide total financial support for these inpatient units by the end of year-05.

6.1.7. Expanding bionutrition research and service to all CCRR sites. Currently two CTSI partners have full bionutritional support. Integrated research bionutrition services using standardized procedures and protocols will be provided at all partner institutions and affiliated community sites, under the bionutrition team led by Rachelle Bross, RD, PhD, the current research dietician at Harbor-LA BioMed. Services available to investigators include: 1) nutritional consultation in protocol development and review; 2) standardization of research meal preparation across sites; 3) a body composition core facility offering standardized anthropometry, total body water with stable isotopes, body composition and bone densitometry assessment by DXA; and 4) continuing education and training of CCRR bionutrition staff and graduate and undergraduate nutrition students across the CTSI. The chaperone service vans will be used to transport dieticians to different locations, research participants to and from the body composition core facility and research meals to sites without metabolic research kitchens.

6.1.8. Implementing mobile health (mHealth) and teleconferencing technologies for community-based research and education. Rapidly occurring advances in telecommunications are providing researchers with dramatically improved means of recruiting subjects, collecting data and educating both research participants and staff (see **section 5. in Pilot Program**). CCRR will continue to work with UCLA Wireless Health Institute and with the **BIP** to make these capabilities available to CTSI investigators; the burgeoning CTSI “Push” initiative (see **Regulatory Program**) in one such experiment to facilitate dialogue and matchmaking of scientific teams. The broad availability and utilization of the internet and mobile phones hold strong potential to bring transformational change to clinical research and practice. Since retrospective methods of self-reporting are subject to recall error and bias and paper-based methods are easily delayed or ignored, we in the UCLA CTSI are now using a method known as Ecological Momentary Assessments (EMAs). EMAs are a survey method developed to capture real-time health status, behavior and experiences using electronic devices to prompt participants several times a day. We are using global positioning system (GPS)-enabled mobile phones to collect EMA data across a broad range of diseases and demographics. This approach provides a uniquely broad and affordable means of engaging patients in research and clinical care when they are outside the traditional clinical setting. Mobile phones equipped with GPS and accelerometers are in use by a number of UCLA investigators who are using mobile phone-based EMA methods for prompting users to self-report in real time about their behaviors and experiences. This is intended to help in understanding the impact of these behaviors and experiences on their lives. Examples include:

- **Diet, Stress and Exercise in new mothers at risk of cardiovascular disease.** In this application we have implemented three new self-monitoring functions on GPS- and accelerometer-equipped smartphones to monitor diet, exercise, and stress for young overweight mothers through the provision of continuous, time-stamped, location and activity information.
- **Scalable sleep studies using mobile phones: technical.** This pilot is focused on development of a scalable instrument for sleep studies across broad populations to understand the importance of sleep hygiene in obesity, diabetes, cognitive function, and mental health. The phones prompt, record and upload geo-tagged and time-stamped survey responses about selected behaviors and capture mobility data in the background based on recorded GPS and accelerometer readings. Participants’ data are automatically uploaded to a private website to provide a way to visualize these behavior patterns over time by providing a time-corrected plot of their data contributions.

The CCRR will also tap into the capability of the UCLA Telemedicine Initiative (supported through the Dean's Office with \$20 million in Proposition 1D funding from the State of California) and equivalent telemedicine/connectivity capabilities at the other CTSI partner institutions (supported by state Prop 1D funds and Federal American Recovery and Reinvestment Act of 2009 RCMI supplementary award to CDU). These state and federal funds are earmarked for patient care and education of the underserved. Each of the four CCRR academic partner sites has been equipped with "smart classrooms" with teleconferencing capability, and full and instant communication among all participants for any individual presentation. With this functionality, research team in-service education, discussion of specific protocols, and screening and interviewing potential research participants at distant sites by expert investigators can be done at all sites. In years -01 to -03 of the grant, three additional community-based telemedicine facilities at the Venice Family Clinic in West Los Angeles, the Wilmington Community Health Clinic in Southwest Los Angeles and the Hubert Humphrey Community Health Clinic in South-Central Los Angeles (see **Table 1**) will be brought online.

6.2. Specific Aim 2: To promote collaborations across the CTSI partner institutions.

6.2.1. The CTSI Virtual Home. The Virtual Home is key to an integrated "CCRR without walls". An interactive website, The Virtual Home allows investigators and community members to access information, apply for research support and communicate with experts remotely. The CCRR collaborated with the Office of Investigator Services (OIS) (see **Regulatory Program** and **section 6.2.2.**) and **BIP** to assure that investigators can readily access information about CCRR research support services, apply for CCRR-SAC and IRB approvals, and receive expert assistance (see **Figure 2**). Significant upgrades to the CTSI Virtual Home have been made. It now allows investigators to: 1) access information about CCRR services and procedures at all CTSI partners; 2) contact Research Facilitators and Domain Experts from the OIS for individualized assistance for research studies at any CTSI partner; and 3) submit IRB, DSM, and CCRR service applications to initiate research at any CTSI partner. Further developments will incorporate cutting-edge informatics tools and communications and social networking platforms to integrate human and material resources across CCRR sites. CCRR will partner with OIS and BIP to identify research IT needs and opportunities to improve effectiveness and efficiency. With the advent of the CTSI-wide disease-related Translational Research Clusters program, Virtual Home IT needs will increase. The CCRR will amplify the Virtual Home with tools like project-, group- and disease-specific participant registries and resources for participant tracking and managing.

6.2.2. Research Facilitators in OIS. The CTSI Virtual Home is the entry point to a novel Research Facilitator service for investigators. Collaborating with experts in the other key function areas, CCRR staff serve as Domain Experts within a concierge service, the OIS, within the CTSI Office of the Institute (see **Regulatory Program**). Trained Research Facilitators are key in helping investigators access Domain Experts, arrange for advanced biomedical technology and laboratory support for their human studies, and prepare applications and supporting materials for IRB approval and CCRR utilization permission. It is our expectation that this process substantially streamlines IRB and CCRR-SAC approval, by assuring that investigators have sought out expert consultations and refined their protocols prior to IRB and SAC submission.

Working with the Research Facilitators and Domain Experts, CCRR staff help investigators navigate protocol development, research collaboration, study design, biostatistics, budget development, regulatory processes (IRB and DSM), drug development processes, grants and contracts services, laboratory and technology services, and research support services. Situations in which Facilitator services are of particular importance include complicated trial designs requiring pre-IND FDA approval, questions related to complicated research ethical issues such as human tissue/sample banking, sample sharing and analyses, or concerns about availability of high-quality, rapid turnaround laboratory assays. For instance, the research protocol of one of our junior investigators, a K30 graduate, calls for acquisition of sera and peripheral blood mononuclear cells from individual subjects at an outlying clinic, before and after treatment of vitamin D deficiency. With a fully operational OIS, Dr. Liu will be able to contact a Research Facilitator, who will chaperone him to the correct CCRR Domain Expert. A nurse or bionutritionist-led mobile unit will be tasked to i) support the PI in recruitment of candidates on-site in an outpatient clinic, ii) arrange for enrolled subjects to have their biospecimens of interest collected for processing by the CCRR, iii) have the de-identified sample processed, stored or triaged to the appropriate CTSI Technology Core and iv) have the integrity of the resulting data and safety of the research subject monitored appropriately.

6.2.3. Unified CCRR-specific Scientific Advisory Committee (SAC) review and approval. The investigator who wishes to utilize CTSI CCRR resources will submit a combined SAC/IRB application to the central UCLA-wide CCRR-specific SAC, whose members will be interdisciplinary scientists, broadly spanning a range of clinical and translational research areas and representing all of the CTSI partners. The CCRR-specific SAC review will include assessment of scientific merit, appropriateness of biostatistical approaches, statistical power, and suitability of plans for DSM. The DSM and statistical reviews will ensure that there is at least annual assessment of oversight of to assure progress of the protocol in regard to patient safety, power and data integrity, and confirm that study progress is adequate. The final component of the review process will focus on operational issues and assign a priority for use of CTSI resources based on scientific merit and need for CTSI resources (see **Regulatory Program**).

Once CCRR-specific SAC has approved a study, the investigator will be granted a specified amount of support that can be applied to CCRR services. Any additional CCRR support above and beyond the resource allocation will need to be cost-shared by the investigator. The CCRR Steering Committee will track utilization on a monthly basis to determine whether utilization projections for different studies are being met. If under-utilization is recurrent, the investigator will be contacted to assess the causes and possible remedies. If over-utilization is impacting the CCRR's ability to assist other projects, then the investigator will be notified that the maximum number of study visits that can be scheduled is being reduced.

6.2.4. Standardized cost-sharing. Standard policies and procedures of cost-recovery and cost-sharing for nursing, bionutrition, and other service/core utilization will be developed by CCRR administrators and reviewed and approved by the CCRR Steering Committee. CTSI investigators will be required to provide cost-sharing for each procedure/test through a unified recharge mechanism. At the time of CCRR-SAC approval, studies will be allotted CCRR resources, which may cover all or part of requested support. In general, there will be three tiers of charges posted on the CTSI Virtual Home: (1) *low* for investigator-initiated NIH or other federal or state-supported peer-reviewed studies; (2) *intermediate* for investigator-initiated and foundation or industry-supported protocols; and (3) *high* for industry-initiated studies for which full recovery of costs will be sought from the investigator. CCRR utilization will be reported by the program area leaders to EOC.

6.2.5. Increasing interaction among CTSI investigators. CTSI partners draw investigators, patients and research participants from diverse populations. By offering to recruit and study research subjects at any CTSI partner and in community clinics, CCRR plans to promote interactions among investigators at different partner institutions who might never have met. Because the UCLA CTSI emphasizes Translational Research Clusters and offers collaborative funding for the program, OIS Research Facilitators, CCRR Domain Experts and CCRR-specific SAC will offer suggestions for potential collaborators in different specialty areas. SAC members will be multi-specialty and drawn from all partner institutions, so the SAC will be suited to suggest interactions. SAC will give priority to new investigator teams when reviewing studies for CCRR support.

6.2.6. Assuring that CCRR sites share protocols, SOPs and teaching materials. The first step in assuring quality is guaranteeing that GCP are applied rigorously throughout the CCRR. GCP compliance ensures protection of study subjects' rights, safety and well-being and accuracy and credibility of data. GCP training and certification of CCRR personnel is required (see **section 7.3.**). Periodic quality assurance audits by the OIS ensure compliance with GCP. With the **E/T** key function, we will implement a quality improvement (QI) program to increase efficiency, stimulate innovation and improve operational effectiveness of the CCRR. Pilot QI activities already underway will be expanded jointly by the CCRR and QI faculty in the **E/T** key function; initially, two CCRR-based QI pilot projects have been proposed: 1) a core laboratory protocol redesign and 2) workforce training program to expand CCRR services from medical centers to the community (see **E/T**).

CCRR leadership developed a catalogue of research support services available to all investigators through the CTSI Virtual Home. In the catalogue, protocols, SOPs, and teaching materials are collated, updated and standardized (e.g., oral glucose tolerance testing, frequently sampled IV glucose tolerance testing, ACTH stimulation testing) to be used at all CCRR locations and community partner sites. Investigators with protocols that differ from CCRR standards will need to provide detailed procedures and scientific justifications for the modifications. If a procedure is scheduled at a CCRR site where the staff lacks experience, experts from other sites will provide in-service training and ensure that the procedure is performed accurately and safely. If an investigator requests CCRR support for a procedure with which no CCRR staff has experience, the investigator

is asked to give in-service training on the specifics of the protocol design and, when appropriate, contact our colleagues in the West Coast CTSA consortium for assistance in identifying a neighboring PCIR that could assist in training our staff.

6.2.7. Facilitate access to centralized laboratories that follow GLP standards. Investigators in the UCLA system, particularly those in the community, require easy access to reliable biological testing. The CCRR will provide a single gateway to traditional laboratory tests and cross-cutting new technologies. All CCRR research samples will be tested in laboratories that follow GLP and meet relevant regulatory requirements and licensing (e.g., Clinical Laboratory Improvement Amendments, State of California Occupational Safety and Health Administration). “One-stop” service and consultation will be provided by CCRR Domain Experts, Research Facilitators and the Technology Officers of the **CTT**. Sample transport to laboratories will be by the mobile chaperone service (see **section 6.1.2.**). Samples will be bar-coded using a standardized system, aliquoted, catalogued, and triaged to different CTSI core laboratories. Residual samples will be stored at the site that receives the sample but with a centralized inventory in firewalled sectors of the CTSI Virtual Home. Measures will be implemented to ensure full confidentiality of all samples at all times after collection.

6.2.8. Eliminate redundancy to increase efficiency. All core services associated with the CCRR will be reviewed for cost-effectiveness and productivity at yearly intervals to avoid duplication of efforts. The CTSI-supported laboratory cores and technology resources will foster dialogue among core laboratories that provide common technologies so that workloads (especially for major projects) can be distributed for more efficient turnaround time and by sharing best practices, reducing costs, improving efficiency, and enhancing quality. Anticipating integration, the laboratory directors at all CCRR sites have agreed to adhere to the principle of broad availability of tests, increased efficiency, and reduced redundancy. Tracking utilization of laboratory services by CTSI-supported protocols will be done by “voucher accounting” annually to determine if a given service is of benefit to sufficient numbers of CTSI investigators to warrant ongoing financial support from the CTSI (see **CTT Program section 6.1.**).

6.2.9. Easing barriers to approvals to perform research at the partner institutions. As detailed in **section 3** above, harmonization of pre- and post-protocol IRB and DSM processes has been successfully implemented in the UCLA CTSI. This has made it much simpler for an investigator to perform research involving several CTSI partner institutions. Several strategies will be undertaken during the first 2 years of the grant period to build on recent progress. The IRB Harmonization Committee (see **Regulatory Program**) continues to work on implementation of a “reliance model” of IRB approval across all partner institutions, which will supersede the current facilitated review process. Full reliance will be possible when all partner institution IRBs achieve AAHRP accreditation. With the commitment of institutional support for this process at LA-Biomed and CDU, we anticipate this achievement within the next 2 years. Concurrent with IRB Harmonization, DSM harmonization and the CCRR service application process also have been initiated. Investigators can access the common DSMP template and the common CCRR OIS application through the Virtual Home. Unified DSM review and institution of a single CCRR-SAC to review and allot CCRR support services will occur within the first grant year. The other barrier to integrated performance of research across the CTSI is the ability of investigators from one partner institution to perform research activities at other partner locations. Reciprocity in research privileges across the CTSI has been agreed upon, allowing academic center- and community-based investigators throughout the CTSI to conduct research and secure access to research participants in the most appropriate setting(s). The logistics for implementing reciprocity are being defined and are expected to be in place by the time CTSA funding is initiated.

6.2.10. Maximize successful completion of research projects through access to a broader portion of Los Angeles County. A critical factor in successful translational research is the ability to recruit individuals who meet study criteria and are willing to participate. It has been estimated that fewer than 50% of clinical trials meet their targets; failure to achieve enrollment goals is costly, delays completion of research and may bias data by reducing statistical power.² Numerous studies have demonstrated that ethnic minorities and individuals of lower socioeconomic status are generally underrepresented in research studies.^{3,4} Given the diverse population of Los Angeles County, it is critical that the CCRR and **CERP** work together with investigators to establish collaborations between CTSI researchers and the community to overcome these barriers. CCRR will initiate a new research participant recruitment consultation service, supported by ResearchMatch.org, to work with investigators, their staffs, community researchers and community liaisons (e.g., promotoras; see **section**

6.1.5. above) to develop subject recruitment strategies and targeted enrollment timelines. A recent survey of 200 UCLA clinical and translational scientists (September 2010; 114 respondents) determined recruitment assistance to be their most pressing need (58% of respondents). Thus, we will provide two individuals with experience in clinical research, marketing and communication about research studies to diverse communities to serve as recruitment consultants. Two recruitment consultants with experience in clinical research will advise on marketing and communication strategies regarding research studies in diverse communities. Each consultant will be responsible for a geographic portion of Los Angeles County. Each recruitment expert will be assigned a portfolio of protocols and will meet regularly with investigator groups and community health leaders to identify and address barriers to research participation.

6.2.11. Encouraging pediatric/perinatal translational research. Human subject research in vulnerable populations, including children and pregnant women, requires highly specialized research procedures and expertise. The CCRR mobile Perinatal/Pediatric Research Units developed from collaborations between CDU, Cedars-Sinai and Harbor-LA BioMed provide support to pediatric and perinatal investigators. Investigators seeking these populations receive support from skilled research staff in these Units who have experience working with pregnant women, infants and children, in delivery rooms, nurseries, neonatal intensive care units and pediatric intensive care units. The CTSI is strengthening its capacity for successful recruitment through the CCRR mobile research nursing staff currently involved in recruiting 4,000 multiethnic women for the National Children's Study. This provided the CTSI with an opportunity to develop new recruitment methods to meet enrollment targets given the intensive requirements for women and children over a 25 year study period. The CTSI is developing novel strategies for outreach, recruitment, enrollment and retention through the community-partnered efforts underway in 55 communities throughout Los Angeles, which primarily include traditionally hard-to-reach populations. These evolving strategies include new social networking, cultural messaging and community mobilization efforts and testing the Hi/Lo Dynamic Enrollment Model among UCLA and 7 other CTSA's that may be particularly valuable for populations with high mobility. The CCRR leadership will consult with members of the Committee on Maternal, Child and Adolescent Health (MCAH) regarding strategic planning and research recruitment in these areas.

6.2.12. Enhancing academic-industry relationships in clinical and translational research. CCRR will use the expertise of the CTSI Office of Industry Alliances (OIA) to make industry representatives aware of our research capabilities, facilities, and infrastructure for developing joint projects with industry partners. The CCRR leadership, in collaboration with the **Pilot Program** (see **Pilot Program section 6.1.1.2.**) and the OIA, will help investigators engage industry to translate discoveries from CTSI laboratories. CCRR will provide necessary research support for these projects' early phase clinical trials. Examples of past academic-industry partnership successes include the discovery of HER2-overexpression in breast cancer, adoption of Trastuzumab as treatment for breast cancer,^{5,6} use of recombinant alpha-L-iduronidase in the treatment of Mucopolysaccharidosis⁷ and alpha galactosidase A to treat Fabry's Disease.^{8,9}

6.3. Specific Aim 3: To recruit junior professionals into careers in translational clinical research. The CCRR will expand its training and career development activities to encourage physicians, nurses and other health care professionals to consider careers in clinical investigation. Health care professionals learn about clinical research during their training and the many programs detailed in the CTSI-ED key function will offer excellent educational opportunities to students and young professionals within the UCLA community. However, attending classes and reading published research articles is not sufficient to provide inexperienced individuals with a clear understanding of what clinical research entails. Just as young bench scientists often have vivid memories of the first time they picked up a pipette, the CCRR offers the opportunity to engage young clinicians by providing their first hands-on exposure to clinical research. Working with our colleagues in the CTSI-ED key function, CCRR will complement the exposure provided in more formal educational activities by offering students and young investigators the chance to observe and participate in translational research.

6.3.1. Introducing students to clinical research before and during college. The GCRCs at Cedars-Sinai and Harbor-LA BioMed have collaborated with Long Beach Polytechnic High School to expose high school science students to clinical research. Students who express interest in careers in biomedical research can enroll in a semester-long, for-credit high school honors program in which they receive instruction on such topics as experimental design, patient safety, and ethics, while being paired with an investigator mentor actively engaged in clinical protocol work. The semester concludes with a poster session program at the

participating medical center and another at the high school for interested students and faculty. Based on survey data from the first 67 graduates of the program, all entered university and 92% reported that the high school experience had strong or moderate influence on their career choices. At the time of the survey, 50% reported that they were engaged in research as an undergraduate or graduate student. Half matriculated to schools in Southern California that have or are actively seeking CTSA's; three quarters of these matriculated to UCLA. The UCLA CTSI is committed to building a conduit for training the next generation T1-T4 scientists who will stay and work in Los Angeles County (see **CTSI-ED** and **Pilot Program**).

Based on the success of the Long Beach Polytechnic High School Clinical Scholars program, with the current CTSI application it is our plan to extend the high school curriculum to three additional minority high school sites within the LA Unified School District with the goal of initiating the program at one additional school per year from years -02 through -04. We will also explore options with UCLA faculty in the Schools of Engineering, Management, Law and College of Letters and Science for garnering NCCR-supported Science Education Partnership Awards and Howard Hughes grants involving K-12 students in CTSI-guided research activities within their local communities.

6.3.2. Mentoring junior investigators performing translational research. Encouragement and education of young investigators is and will remain an integral part of CRR activity. The Research Facilitator program (see **section 6.2.2.** above and **Regulatory Program**) is anticipated to be especially beneficial to young investigators as they formulate and attempt to implement research projects. The CRR-SAC also provides young investigators pre-review and constructive feedback on study design to enhance the scientific merit of their proposed research. When appropriate, the SAC recommends additional didactic training (e.g., K30 curriculum) or mentoring and assists in the development of formal junior-senior scientist mentee-mentor pairs by matching young investigators with appropriate senior mentors CTSI-wide. The CRR recruitment experts help young investigators develop strategies for subject recruitment and retention, which is a commonly identified need.

6.3.3. Education in community-partnered research. Junior investigators often have not been exposed to community-based research. In collaboration with **CERP** and drawing on the expertise of the CDU Community Research Program in the College of Science and Health, CRR is developing teleconferenced (see below) workshops and seminars to introduce junior investigators to community-based and -partnered research and is providing opportunities for junior investigators to interact with community members and organizations. CRR and **CERP** Domain Experts are available to assist young investigators in beginning community-partnered research.

6.3.4. Educational opportunities for research team members. As detailed above, the CRR is committed to the education of young faculty and students. It is equally important to ensure that research team members (study coordinators, phlebotomists, dieticians, nurses, respiratory therapists) are appropriately educated and trained in clinical and translational research methodologies and regulations. Staff who understand basic research concepts and methodologies, along with the applicable regulatory requirements, are better prepared to assure that the research activities they perform meet the highest possible standards. CRR will lead CTSI efforts in training research staff. Along with investigators, nursing personnel, support staff and other health professionals, investigators doing research within the CRR will be required to complete standard courses in principles of GCP, pass an online test and attend an annual course(s) on human subjects' protection and HIPAA (see **Regulatory Program**). Certificates of completion of GCP training will be issued and monitored by authorized CRR staff via a Virtual Home database. CRR staff will work with investigative teams to identify translational research topics of relevance and will organize seminars specifically designed for research staff.

7. INVESTIGATORS

The CRR Steering Committee, (see **Figure 1**) will oversee management of the CRR with input from the CRR Scientific Advisory Committee (SAC). The CRR Steering Committee will meet at least once a month, rotating to each CRR site, to facilitate interaction between the CRR leadership and investigators at each of the participating sites; a program co-leader is appointed at each site to represent that partner should the Steering Committee site leader be unable to attend. The CRR Steering Committee will review census, utilization, productivity, staffing, and cost-sharing to ensure that the most utilized resources are given the most support, and will coordinate interactions and

collaborative efforts with other CTSI programs, including **CERP**, **Biostatistics**, **BIP**, **Regulatory**, **CTT**, **CTSI-ED** and the OIS.

Christina Wang, MD (Leader, CCRR Southwest site), will lead the CCRR Steering Committee. A Professor of Medicine and Assistant Dean for Clinical and Translational Sciences, DGSOM, she is a renowned clinical and translational investigator, and mentor and advocate for junior faculty and trainees. Dr. Wang has conducted many translational studies and coordinated and monitored international studies for the World Health Organization. Before CCRR transformation, she administered the joint Harbor-LA BioMed and Cedars-Sinai GCRC for 15 years.

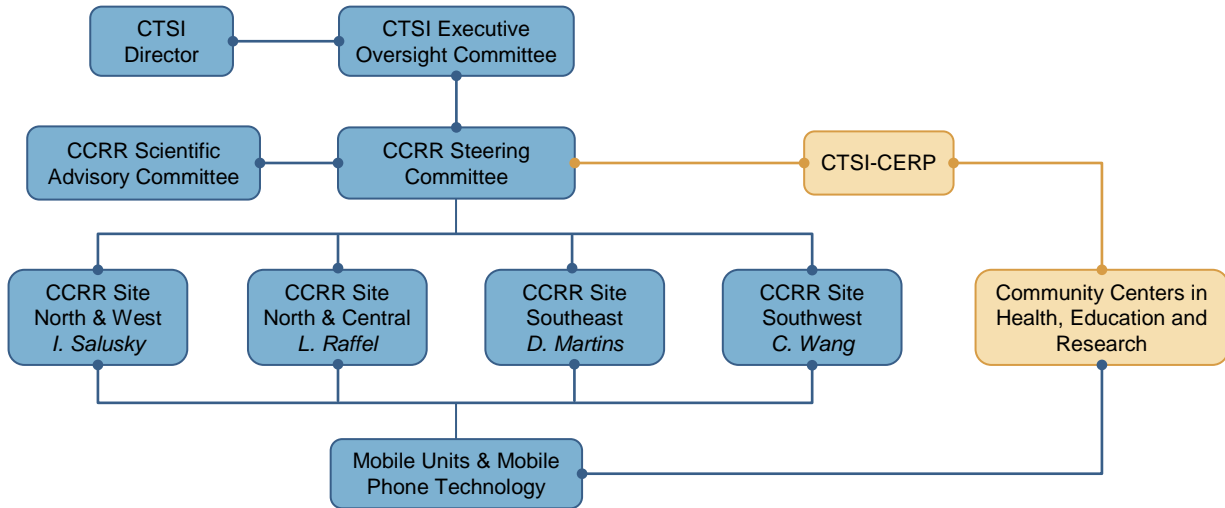


Figure 1. Shown is the organizational structure of the CCRR key function and interactions with the Community Engagement and Research Program (CERP) key function and Community Centers in Health Education and Research. SAC= Scientific Advisory Committee. Blue boxes are in the purview of the CCRR key function and gold boxes in the purview of the CERP.

Other members of the CCRR Steering Committee are:

David Martins, MD, MS (Leader, CCRR Southeast site): Dr. Martins is Assistant Dean for Research and Education, and Assistant Professor of Medicine at CDU. For 10 years the Medical Director of To Help Everyone (THE) Clinic, he remains active in the Southside Coalition of Community Clinics. He is a board-certified internist and holds the UCLA Master of Science in Clinical Research (MSCR) degree and the UCSF Center for Health Profession Healthcare Leadership fellowship.

Leslie J. Raffel, MD, MS (Leader, CCRR North and Central site): Dr. Raffel is Professor of Pediatrics and Assistant Dean for Clinical and Translational Sciences at DGSOM. Since 1995 She was Assistant Program Director for the GCRC at Cedars-Sinai before becoming Program Director in 2008. Dr. Raffel has research experience in genetics of common disease, multicenter research, provision of core services, and graduate and medical education. She will ensure that pediatric research and outreach are integrated into the CTSI.

Isidro B. Salusky, MD (Leader, CCRR North and West site): Dr. Salusky is Distinguished Professor of Pediatrics, Director of the UCLA Pediatric Dialysis Program, and Associate Dean for Clinical Research at DGSOM. He is a world-renowned clinical and translational scientist doing active research on abnormalities of bone and mineral metabolism in children with chronic kidney disease. He is also involved in investigator training and career development, as a K23 mentor and the PD/PI of the UCLA K30 Program, overseeing that program's successful renewal in 2009 and achieving a Recovery Act Administrative Supplement for Comparative Effectiveness Research Workforce Development. He also will ensure that pediatrics is incorporated into all aspects of the UCLA CTSI.

Kathryn Atchison, DDS, MPH (CCRR Investigator): Dr. Atchison is UCLA Vice Provost for Intellectual Property and Industry Relations. She manages UCLA's Industry-Sponsored Research and Intellectual Property and Material Transfer Agreements, and has experience in research, teaching, administration, and

management of individual and institutional conflicts of interest in relation to industrial partnerships. She will advise CCRR on industry and academic relations and liaise with industry to generate collaborative research.

Linda Burnes Bolton, MSN, MPH, DrPH (CCRR Investigator): Dr. Burnes Bolton is Vice President and Chief Nursing Officer and Director of Nursing Research and Development at Cedars-Sinai. An Associate Clinical Professor at the University of California, San Francisco, and Associate Clinical Professor and Graduate Faculty at UCLA, her research focuses on women's health, health policy, and organizational development. She will ensure maximum community engagement of CCRR nurses and facilitate CCRR community engagement.

Loretta Jones, MA (CCRR Investigator): Ms. Jones is the founder and executive director of Healthy African-American Families, a nonprofit, community organization to improve health outcomes, quality of care, and social progress of African American and Latino communities in Los Angeles County through education, training, and collaboration with community, academia, researchers, and government. She has shared her expertise in community engagement as a member of NIH advisory boards and workshops, and as a national mentor for community-partnered participatory research. As the initial rotating **community member** on the CCRR Steering Committee, Ms. Jones will work with Dr. Burnes Bolton to ensure community engagement and adequate attention to community-based research agendas.

8. INTEGRATION OF UCLA CTSI KEY FUNCTIONS

The CCRR collaborations with other CTSI Key Functions include: ■ With the **Regulatory Program**, further developing the OIS, a central clearinghouse to guide investigators to CTSI research resources ■ With the **Regulatory Program**, continuing to develop an institution-wide Scientific Advisory Committee for protocol approval across the CTSI ■ With **CERP**, operating a mobile chaperone service as a convenient way to move staff, clients, samples, meals, and community members across Los Angeles County ■ With **CERP**, expanding the promotora program in the community to promote outreach, bi-directional communication, and education ■ With **CTSI-ED** and the **Pilot Program**, expanding the Clinical Scholars Program to minority high schools associated with the CTSI to build on our successful pilot program to train the next generation of clinical and translational scientists in Los Angeles County.

9. CCRR PARTICIPATION IN REGIONAL AND NATIONAL CTSA CONSORTIA

The UCLA CTSI and USC and UC Irvine CTSA formed the Greater Los Angeles CTSA Coalition to discuss common issues and collaborations. So far we have agreed to:

- Participate in the UC-wide Biomedical Research Acceleration Initiative, a working group of the University of California (UC) CTSA's to address Bioinformatics, Contracting and IRB harmonization across the four UC CTSA's and UCLA. Dr. Dubinett has been on monthly conference calls and he and Dr. James Economou have been invited to the fall retreat at UCSF. The leaders of the CCRR will have future meetings on aspects of IRB harmonization and other new initiatives to be addressed by the working group.
- Expand the UCLA CTSI mental health translational research cluster, led by UCLA investigator Joel Braslow, who has collaborated with John Brekke, Co-Leader of the cluster at USC, to examine pathways by which genetic, clinical, and sociocultural factors interact in expression of severe mental illness (SMI) and metabolic disorders within SMI populations and how these factors moderate outcomes.
- Extend the concept of a "CCRR without walls" throughout Southern California, offering research participants flexibility at the most convenient PCIR location for research-related activities that do not rise to a level that meets the Office of Human Research Protection definition for research engagement.
- Work to standardize test protocols across regional CTSA's, which will assure data comparability in collaborative studies at multiple CTSA's.
- Incorporate the UCLA scientific community in finding gene-directed pathways that underpin common diseases that cause the most morbidity and mortality in Los Angeles County. With the Greater Los Angeles CTSA Coalition and National CTSA PCIR Consortium efforts to further research identification of susceptibility genes for complex human disease states (e.g., cardiovascular disease), CCRR-based genetics investigators at UCLA are at the forefront of many NIH-funded efforts in that direction.

10. IMPLEMENTATION PLAN

Table 2. presents the UCLA CTSI CCRR Program Implementation Plan, which describes the projected time line, measurable objectives, and milestones for implementing key tasks over a preparatory period and over Years-01 to -05 of the project period with respect to each of the program aims.

Table 2. CTSI CCRR Implementation Plan

Year(s)	Key Activities	Milestones and Measures
Current Activity: Prepare for transition to CTSI.		
Pre-Award	<ul style="list-style-type: none"> Construction of a new ambulatory CCRR facility and “home” to the CTSA at UCLA (to open in January 2011) Launch of the statewide California Telehealth Network (CTN) to create a digital highway statewide for healthcare and research Initiation of monthly conference calls with the other UC CTSIs to plan the CTSI West Coast Consortium joint clinical research. Successful development of the CTSI Virtual Home, an on-line portal Creation of CTSI-wide forms and agreement from Harmonization Initiative Regular meetings of the nursing and bionutrition staff with the members of Community Engagement and Research Program (CERP) to coordinate CCRR services Establish strong relationships between participating centers and their respective communities and community-based providers 	<ul style="list-style-type: none"> Common IRB and CCRR application form Uniform DSMP and consent templates Harmonized, facilitated IRB review and approval mechanisms Trans-institutional agreements # Community workshops convened # Community trials conducted, e.g., African Amer study of kidney disease and hypertension
Year(s)	Key Activities	Milestones and Measures
Aim 1: To broaden the range of clinical, translational and community research by implementing the “CCRR without walls.”		
1-5	<ul style="list-style-type: none"> Cross-training research staff so that they can support research in the inpatient, outpatient and community environments as needed. 	<ul style="list-style-type: none"> # Staff recruited and cross-trained for various settings and functions
2-3	<ul style="list-style-type: none"> Initiating Mobile “Chaperone” Services to link the CTSI partners and communities 	<ul style="list-style-type: none"> Mobile units initiated (year 2) and fully operational (year 3)
1-5	<ul style="list-style-type: none"> Assess and modernize CCRR staffing to provide an appropriate mix of research nurses, phlebotomists, and community health workers based on the research needs of CTSI investigators 	<ul style="list-style-type: none"> Staffing assessment and personnel plan completed (year 2)
1	<ul style="list-style-type: none"> Initiate a Promotora program to enhance recruitment and communication with participants 	<ul style="list-style-type: none"> Functioning promotora program in each of the community-based research centers (years 2-4)
1-5	<ul style="list-style-type: none"> Continue standardizing nursing and bio-nutrition operating procedures across all sites 	
Aim 2: To promote clinical collaborations across the CTSI by facilitating the ability of research to be performed at all CTSI partner institutions by:		
1-5	<ul style="list-style-type: none"> Increasing interaction among investigators through the CTSI virtual home and Office of Investigator Services (OIS) 	<ul style="list-style-type: none"> # Translational Research Clusters formed and research agenda established
1-2	<ul style="list-style-type: none"> Share common protocols, SOPs, and teaching materials across all CCRR sites 	<ul style="list-style-type: none"> Amplify virtual home with tools for project, group, and disease specific participant registries (years 2-3)
1-3	<ul style="list-style-type: none"> Centralizing laboratories that follow Good Laboratory Practice (GLP) standards 	<ul style="list-style-type: none"> Conduct projects to improve operational effectiveness (years 2-3)
1-3	<ul style="list-style-type: none"> Easing research approval barriers at partner institutions. 	<ul style="list-style-type: none"> Completion of IRB reliance model across the CTSI partner institutions (year 2)
3-5	<ul style="list-style-type: none"> Maximize access of Promotora Program to a broader portion of LA County 	<ul style="list-style-type: none"> # CTSI projects that obtain industry partners/ sponsors for early phase trials
1-3	<ul style="list-style-type: none"> Enhance academic-industry research partnerships through the Office of Industry Alliances 	
Aim 3: To recruit young professionals into careers in translational clinical research by:		
1-3	<ul style="list-style-type: none"> Expand training and career development activities to encourage physicians, nurses and other health care professionals to consider careers in clinical investigation 	<ul style="list-style-type: none"> # orientation sessions to expose high school and college students and investigators from other schools to clinical research
1-2	<ul style="list-style-type: none"> Provide hands-on exposure to clinical research 	<ul style="list-style-type: none"> # staff completing the on-line course in principles of good clinical practice, completing exams, annual course, and HIPPA
1-5	<ul style="list-style-type: none"> Leading CTSI efforts in training research staff to ensure research is performed by certified staff who are fully capable of completing research procedures accurately and with utmost safety for participants 	

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Community Engagement and Research Program (CERP)



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Abbreviations: AXIS—Accelerating Excellence in Translational Science, BIP—Biomedical Informatics Program, BSD-CDM—Biostatistics, Study Design, and Clinical Data Management Program, C3N—collaborative chronic care network, CAB—Community Advisory Board, CAP—Community-Academic Partnership Council, CC-HEATR—Community Centers in Health Education and Translational Research, CCALAC—Community Clinic Association of Los Angeles County, CCHMC—Cincinnati Children's Hospital Medical Center, CCRR—Clinical and Community Research Resources, CBPR—community-based participatory research, CPPR—community-partnered participatory research, CDU—Charles Drew, CENS—Center for Embedded Network Sensing, CERP—Community Engagement in Research Program, CPIC—Community Partners in Care, CSRC—Chicano Studies Research Center, CTSI—Clinical & Translational Sciences Institute, CTSI-ED—Research Education, Training and Career Development Program, CTT—Center for Translational Technologies, DGSOM—David Geffen School of Medicine, EOC—Executive Oversight Committee, GIS—Geographic Information Systems Technology, HAAF—Healthy African American Families, HCNI—Healthy Community Neighborhood Initiative, HSR—health services research, ICTS—Institute for Clinical and Translational Science, IT—informatics technologies, LAUL—Los Angeles Urban League, LCRN—Life Course Research Network, MS—Master of Science, NCEMA—National Coalition of Ethnic Minority Nurses Association, NCS—National Children's Study, NEVHC—Northeast Valley Health Corporation, OIS—Office of Investigator Services, PBRN—Practice Based Research Network, PRIME—Program in Medical Education, RCMI—Research Centers in Minority Institutions, THE—To Help Everyone Clinic, TR01—Roadmap Transformative Research Projects Program, VA—Greater Los Angeles Veterans Administration

1. OVERVIEW

The **Community Engagement and Research Program (CERP)** is the primary link between the University of California, Los Angeles Clinical and Translational Science Institute (UCLA CTSI) and our diverse local residents and practice communities. It fulfills the Community Engagement and Research key function. We create strong bidirectional partnerships to ensure that new scientific discovery is relevant to community needs and adaptable and scalable across health care practices and populations. We are members of the Greater Los Angeles CTSA Coalition with the University of Southern California and the University of California, Irvine. CERP collaborations include researchers at CTSA institutions.

In our prior review, CERP was reviewed with the Biostatistics, Epidemiology and Research Design key function and received an aggregate score of 2. Reviewers praised the depth and scope of our partnerships, our comprehensive strategies to address barriers to community engagement and bridging cultural barriers to T1 research, our commitment to sustainable engagement with communities, our creative use of social networking and technology, and our commitment to a leadership structure that ensures the integrity of our nationally renowned approach to community-based participatory research (CBPR).

CERP has strengthened several components in response to reviewer recommendations ■ we identified Healthy African American Families as a key partner and have given it more resources to reflect its value within the CTSI ■ we have established a formal conflict resolution plan for mitigating any conflict between academic and community partners. This includes use of external dispute resolution and/or local, internal mediation ■ we are applying innovative, feasible technologies in underserved communities ■ we are adopting strategies to realign financial incentives for sustained partner participation based on consultation with our partners ■ CERP now includes health services research (HSR) to co-develop research priorities with communities; advance a broader scope of translational research including comparative effectiveness, implementation, dissemination and diffusion research; and bring cutting-edge methods into community-partnered research. Substantive improvements to this application since our last submission are indicated in the left margin.

2. SPECIFIC AIMS

The UCLA CTSI provides the operations and governance necessary to facilitate successful transdisciplinary clinical and translational research. The overarching **mission** of the UCLA CTSI is to *transform our academic-clinical-community partnership into a borderless institute that brings our combined innovations and resources to bear on the most pressing health needs in our diverse Los Angeles community*. CERP's role in the CTSI is to strengthen relationships among partners, catalyze investigation into community health and health care priorities, and mobilize resources to produce an effective, reliable and innovative system of community-based translational research. CERP provides a sustainable platform for accelerating and translating scientific advances to improvements in health and health care across the life course. The overall goal of CERP is to improve health and health care in diverse communities through partnerships between researchers, clinicians, community-based organizations and residents that spur development of effective clinical interventions across the life course and accelerate translation of discovery into practice. CERP achieves its mission through five Specific Aims.

Specific Aim 1: Promote and sustain bidirectional knowledge sharing between community and academia.

- Stimulate networking and collaborations through research symposia and follow-up working groups
- Increase the research orientation and reach of lay health workers in underserved communities
- Build academic and community researcher skills in partnered research, regulatory compliance and ethics in research, and organizational and practice change
- Apply innovative networking and information dissemination technologies

Specific Aim 2: Strengthen community infrastructure for sustainable partnered research.

- Establish centers in communities that support community engagement and research
- Promote novel study designs

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- Strengthen incentives and motivation for research participation of community health care providers

Specific Aim 3: Drive innovation in community engagement that accelerates the volume and impact of partnered research in diverse communities.

- Foster strategic demonstration projects that enhance CERP's community reputation and capabilities
- Implement comprehensive community-partnered research initiatives

Specific Aim 4: Build Health Services Research (HSR) methods into partnerships to accelerate design, production and wide adoption of evidence-based practice and behavior.

- Strengthen HSR translation methods within community-partnered research

Specific Aim 5: Establish a governance and operations structure that strengthens existing partnerships and builds new bridges between community and academia for research.

- Formalize CERP governance including leadership, working groups and conflict resolution procedures
- Create a Community Research Liaison Office that builds trust, encourages community participation, supports investigator readiness, and links investigators with community partners

3. PROGRESS TO DATE

CERP accomplishments in the pre-award period include:

- Formalized and launched the CTSI Healthy Community Neighborhood Initiative (70-Block Project) with the Los Angeles Urban League (LAUL), using competitively awarded funding from The California Endowment.
- Harnessed new technology strategies for partnered research that fit communication patterns and capabilities in low-technology communities, including use of cell phones for patient-oriented text messaging to inform and monitor disease self-management.
- Developed strategies to reduce barriers to community partners participating in research.
- Conducted community research symposia and post-conference working groups to bolster the bidirectional partnerships between basic science (T1) researchers and clinical and nonclinical community partners.
- Formalized and achieved large-scale results in implementation science partnership with a professional pediatrics network reaching physicians in four counties, serving 100,000 children.

4. SIGNIFICANCE: RATIONALE FOR THE COMMUNITY ENGAGEMENT AND RESEARCH PROGRAM

Community engagement in research has been defined as “the intersection of the complementary efforts of members of the lay community, community non-profit organizations, health practitioners and medical and public health researchers to improve health.”¹ Effective and enduring community-academic partnerships are challenging to most academic medical centers. Challenges such as recruiting sufficient and representative community-based clinicians, community organizations and patients have limited the impact of scientific discovery on clinical practice.²⁻⁴ CERP investigators have been leaders within the national discourse about optimal community engagement goals and strategies for academic health centers and the communities they serve. We have made progress in Los Angeles in surmounting some of the typical barriers to community-partnered research. These barriers include: (1) traditional power differentials in which control and distribution of resources favor the academic partner; (2) differing values and priorities; (3) time demands of participation; (4) different languages and styles of expression; and (5) limited training and opportunities for academic researchers and community members to build partnering and methodological skills for translational research.⁵⁻⁸

CERP fosters community-academic partnerships by combining the unique richness of diverse Los Angeles communities with the world-class biomedical sciences of our academic environment. We promote a translational culture using principles of community-partnered participatory research (CPPR), a term derived from CBPR,⁹⁻¹⁰ to emphasize true partnering with shared input into project selection, design, implementation, assessment, and dissemination, as well as overall responsibility and authority.¹¹⁻¹³ CERP enriches the translational research processes by linking translational scientists with the populations whose health will

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ultimately test the effectiveness of the model. T1 research seeks to move a basic discovery into a health application. T2 research assesses the value of an application for health practice leading to the development of evidence-based guidelines. T3 research attempts to move evidence-based guidelines into health practice, through delivery, dissemination, and diffusion research. T4 research seeks to evaluate the “real world” health outcomes of an application in practice.¹⁴ Partnerships between community and academia guide the CERP research agenda and the recruitment and training of a cadre of academic and community leaders who collaborate to develop interventions, and evaluate and disseminate the evidence on individual and community health outcomes. CERP builds capacity within communities in the human capital, clinical resources and technological infrastructure needed to sustain improvements and develop new programs and interventions.

5. INNOVATION AND ENVIRONMENT

Los Angeles County is an ideal environment for developing effective translational strategies. It encompasses the full spectrum of best-to-worst in health care services, delivery capacity, and outcomes. It is the most populous U.S. county with 10 million residents dispersed over 4,000 square miles. There are large immigrant communities, and thirty-five percent of residents speak a language other than English at home. High rates of preventable disability and death¹⁵⁻¹⁶ bring communities and scientists into alignment around a mutual desire to understand causes and how to address them. About 23% of Los Angeles school-age children and 21% of adults are obese. Among the adult population, nearly 9% have been diagnosed with diabetes, 25% with hypertension, 8% with heart disease (e.g., coronary heart disease, angina or infarction), and 13% with depression.¹⁷⁻²¹ Los Angeles faces challenges common to the national CTSA network including sizable subpopulations who are underrepresented in all phases of translational research, and fragmented and often low-performing health care systems that require implementation, dissemination and diffusion research for scientific discovery to have a large social impact.

At the same time, Los Angeles has assets for increasing translational research. UCLA has national leaders in the concepts and practice of community-partnered research, cutting-edge biomedical and clinical researchers, strong community leaders who value translational research and are dedicated to the CTSA mission, and a virtually unlimited source of potential community partners and populations. CTSI investigators bring a wealth of innovative tools that can be applied to translational goals, such as social networking and ways of adapting existing technology in otherwise technology-poor communities to support research. **Table 1** describes how CERP transforms the research environment. Examples of innovations include:

- Residents of Boyle Heights, a largely Latino community in East Los Angeles, and Deborah Estrin (a CERP Investigator) and colleagues at the UCLA Center for Embedded Network Sensing (CENS) in the School of Engineering are using mobile phones and internet technology to generate “activity traces” (geocoded maps of daily activity using wireless/geocoded technology) to characterize environmental and social exposures in their neighborhoods, schools, workplaces, and homes that influence dietary and exercise patterns and other health behaviors. Community organizations lead the protocols for data collection with the support of Center for Embedded Network Sensing (CENS). CERP is adapting these protocols for community partnered projects, such as the 70-Block Project.
- UCLA and Cincinnati Children’s Hospital Medical Center (CCHMC) are the developers of a collaborative chronic care network (C3N) in which patients, physicians and researchers create a platform for scientific discovery and improvement in chronic illness care. These groups share perspectives and their own data to drive science, using open source internet applications. The C3N research effort is supported by the Roadmap Transformative Research Projects Program (TR01), which was created under the NIH Roadmap for Medical Research to support exceptionally innovative, high-risk research with the potential to create or overturn fundamental paradigms. This prototype provides design options for CERP networking goals.
- Dr. Robert Bilder directs “LA2K”, an integrated T1/T2 study within the Consortium for Neuropsychiatric Phenomics and NIH Roadmap Initiative investigating the interface of clinical psychiatric illness, genes, and environment/culture in a community-based sample of whites and Latinos and a cohort of patients with mental illnesses. CERP consults on strategies for recruiting and retaining a diverse sample of participants.

Table 1. Challenges to Community-Partnered Research and CERP/CTSI Transformation Process

Barriers / Opportunities	Transformation Process	CERP Select Activity
Promote true partnership between community and academia	Involve community representatives in all key decision-making bodies. The CERP leadership collaborates with the Community-Academic Partnership Council to guide program operations and set partnered research agendas	Shared decision making, including the governance structure and the Community-Academic Partnership Council
Enhance trust between community and academia	Involvement of community in decision making, selection of research questions, training, and implementation of research activities, and focusing research on improving the health of communities, will build value and trust	Social networking, education to demystify research, training of academic and community researchers, productive collaboration
Expand true academia-community collaborations fostering exchange of ideas, information, and accurate knowledge about one another	Develop social networking pathways, community-participatory symposia and workshops, training of academic and community researchers and collaborations that build relationships	Build a community-partnered participatory model so that informed partners pose and make key decisions across all phases of research
Streamline and increase research involving resident and practice communities	Develop an interdisciplinary program engaging community in a continuous and sustained manner, built on trust, voice, and mutually valued goals	Develop structures and process to support partnered approaches across all research activities
Increase perceived value of community engagement within communities and academia	Create stable community-academic partnerships that support clinical-translational research and produce measurable results in clinical care and population health	Training programs, discussion of clinical and research topics of interest to both, and an applied real-world program
Redesign of IT infrastructure to support multiple dimensions of community engagement	Incorporate IT functions for community engagement to elicit and collect input from a wide variety of participants, disseminate educational materials, mobile networking and standardized flexible IT	Include ongoing IT support to build community capacity. Build the CTSI Web Portal and the Community Research Registry, for bi-directional networking
Enhance integration of CTSI core resources-and-services programs with community	Build the Community Research Liaison Office to support collaborations among community stakeholders and academic researchers, and expand community and academic research facilitators	Shared decision making, resource allocation to build community research capacity, creation of centers for health education and translational research
Ensure adequate funding of pilot studies for community-partnered interventions	Develop CTSI-funded pilot projects for community engagement and research; encourage practical trials that consider feasibility and cost	Community-Academic-partnered CERP demonstration projects directly addresses this concern
Focus attention to the unique challenges of conducting research in community settings	Increase the visibility within academia of the importance and difficulty in conducting community partnered research	Challenges of conducting research in community settings are now key elements of the institution's health education curricula
Enhance support for community sites and networks	Establish infrastructure to leverage academic-community partnerships so as to improve clinical care while also introducing research opportunities	Develop model Community Centers of Excellence in Translational Research to house active learning laboratories
Increase attention to the health of the community	Partner with the Los Angeles Urban League to improve the health of an underserved 70-square-block community	Los Angeles Urban League-CTSI HCNI
Increase interventions and uptake for underserved populations	Partner with communities to test and implement interventions that work for local practice and culture	Develop and test interventions in diverse populations
Improve measures of impact for adapting interventions for community implementation	Introduce new measures of disease, therapy and economic outcomes	Develop and test measures in HCNI

- The Charles Drew University (CDU) Medical Geographic Information Systems Laboratory provides a "virtual center" for the storage, management, analysis, modeling, and mapping of spatially referenced health-related data using state of the art Geographic Information Systems Technology (Medical GIS). Two CERP collaborations with Dr. Paul Robinson include Neighborhood Structure and Cardiovascular Disease (R03 HL088622) and Environmental Determinants of Metabolic Syndrome Related Conditions (SC3 GM087224), which use geographic analysis to detect associations of social and physical environment with cardiovascular disease management at the individual level. Dr. Robinson regularly shares these tools with community groups and is developing with CERP investigators a CPPR agenda using GIS technology.

6. APPROACH

Our Specific Aims are designed to produce (1) improved validity, utility and social impact of health-related research through enhanced community input into research questions, design and implementation; (2) two-way knowledge exchange that builds social capital and research opportunity through community engagement strategies and innovative technologies; (3) creation of novel community-academic-partnered projects that use social determinants and systems frameworks to accelerate the translation of scientific advances to patients' doorsteps; (4) streamlined processes that enable communities, organizations, and health care systems to more rapidly and efficiently "scale up" successful individual and system interventions; and (5) improved health and wellness of Los Angeles County communities and their capacity to address health-related needs over the long term.

6.1. Specific Aim 1: Promote and sustain bidirectional knowledge sharing between community and academia.

6.1.1. Provide opportunities for networking and generating collaborative research ideas through community research symposia. CERP co-sponsors "Building Bridges to Optimum Health Conferences" as a series of opportunities for knowledge transfer among community and academic partners. These symposia increase community understanding of and involvement in research and provide researchers with insights into community challenges and priorities and how to build bridges for T1 projects. Symposium themes are selected by the **Community-Academic Partnership (CAP) Council**, a body with advisory and directive functions whose members include academics and community members (see **Specific Aim 5, section 6.5.1.**). They are held at various community venues. Examples of recent symposia include Violence; Diabetes throughout the Life Span; Women's Health Conference: Enhancing Communication between Patient and Physician; Witness 4 Wellness: Focus on Depression; Before, Between, and Beyond Pregnancy; State of Emergency: Access to Care in Los Angeles; World Kidney Day: A Community Dialogue to Increase Awareness of Kidney Disease and Promote Its Detection and Prevention; and It Takes a Village: Beating Depression in Our Community (Community Partners in Care).

Each conference leads to a series of community-academic-partnered working groups focused on enhancing care, research, and advocacy around conference-developed initiatives using a modified Delphi process.²²⁻²⁵ The post-conference working groups explore key community-driven questions on how research can impact the health of communities and how community priorities and input can impact research. These discussions are grounded with transparency in design, data, and methods to build community research capacity and social capital. For example, two Town Halls in 2010 led to resident participation in working groups to address community-level strategies to reduce obesity and diabetes, a plan for more participation of additional CTSI investigators in future events, and the design of site-based interventions to improve the health of the community. An average of 350 people have participated in these day-long symposia, generating 3 workgroups with 25 to 30 people each who continue to meet after the symposium. CERP plans to sponsor 2 or 3 events per year. In collaboration with the CTSI **Biomedical Informatics Program (BIP)** these events will be webcast live and then archived at the CTSI Virtual Home, a Web portal that provides access to CTSI information and resources.

6.1.2. Increase the research orientation and reach of lay health workers who outreach to underserved and underrepresented communities. The CERP supports local community lay health worker staff linked with each of our academic partners. These community health workers improve recruitment of underserved participants into research projects and increase community participation in the conduct of research. They also provide patients of all literacy levels with accessible information on CTSI research and help streamline uniform data collection for clinical studies. We are already recruiting and training lay health workers in collaboration with the **Clinical and Community Research Resources (CCRR)** Program. Some of our clinic partners have existing lay health worker or promotora programs; we are folding these into a coordinated system that increases access as well as training opportunities. The lay health workers learn about research methods from **CCRR** and CERP staff and investigators, who in turn are learning new community engagement techniques and strategies for recruiting diverse populations from these lay health workers.

CERP leverages other resources to expand the network of lay health workers who play one or more of these roles. For example, a new **CCRR-CERP** collaboration with the **UCLA Chicano Studies Research Center**

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trains *Promotoras de Salud* (lay health educators in Spanish-speaking communities) to promote outreach and community education about and participation in clinical and epidemiological research. **Project ALTO** is a California Endowment-funded project of Mission Community Hospital in the San Fernando Valley to identify, educate, and screen low-income, uninsured Latinos and refer them to appropriate care, and to provide culturally sensitive education that promotes diabetes self-management and more effective patient-provider communication. Several of the Project ALTO promotoras have participated in CERP's "train the trainer" programs, and their expertise can be leveraged to bring these programs to other clinics and communities.

6.1.3. Build community research skills of academic and community researchers through extracurricular training. CERP is establishing a series of training events to: encourage community members in the process of inquiry; (2) enhance understanding of study design and methods and bolster proficiency in research support skills among interested community members; (3) provide relevant regulatory knowledge and support and research ethics, study design, and methods for CBPR/PPR; and (4) teach scientists who are new to CBPR/PPR to learn alongside community members how to build community-engaged studies from the ground up.^{8,22-25} These training sessions build on previous work of several CERP members. Ms. Loretta Jones has authored a workbook for community and academic investigators on conducting community-engaged scholarship, and Drs. Wells and Brown, along with community partners, have developed an innovative curriculum that they teach to the Robert Wood Johnson Clinical Scholars and other health services research fellows annually. These training events will be led by academic and community instructors from the Robert Wood Johnson Foundation Clinical Scholars Program; the National Research Service Award Fellowship; the NIH-funded Project EXPORT, Resource Centers for Minority Aging Research (RCMAR), Vulnerable Populations centers at the CTSI institutions, and others who are also key members of CERP. Our goal is to develop a series of online interactive tutorials or distance learning modules, accessible through the CTSI Virtual Home, similar to Learning Management Systems, with automated administration, tracking, and reporting of training events. CERP has also developed an innovative "Academic Boot Camp" course to introduce community leaders to concepts such as research principles, the ethical conduct of research, and analysis strategies. CERP members, including Ms. Jones and Drs. Keith Norris, Roberto Vargas, and Nell Forge, all teach in the CDU Community Faculty Program, which to our knowledge is the first program in the nation to train community members to serve as community faculty.

The content of these educational offerings is aligned with the new didactic and mentoring programs developed by the CTSI Research Education, Training and Career Development Program (CTSI-ED) for community leaders and pre- and postdoctoral trainees in community-based research. In particular, CERP has helped to develop a new Executive Master of Science (MS) with a concentration in Community Translational Research to expand the already successful Executive MS Program in the School of Public Health. This new program will be available to community members and CTSI-affiliated scholars and faculty. Also, in collaboration with the Education Program, CERP has helped to develop the new T32 PhD Training Program in Clinical and Community-Partnered Translational Research for educating team-based T2 scientists.

6.1.4. Use innovative informatics technologies (IT) that are accessible and functional for communities. Optimal community outreach and engagement requires use of technology, which is challenging in communities and populations that historically have had minimal access. CERP faculty and community partners draw on knowledge of how communities already communicate electronically to assess the effectiveness of different tools already in use (e.g., text messaging, blogging) and what innovative strategies have the most promise for making technological solutions readily and easily accessible to all of our community partners. Whenever possible, CERP adapts the functionality of widely available technology, such as cell phones.

Adapting existing communications technology for research purposes. Dr. Deborah Estrin, a CERP co-investigator at the UCLA Center for Embedded Network Sensing (CENS), plays a pivotal role in identifying appropriate technology for innovative data collection (see Innovation above). CERP works closely with **BIP**, academic partners in the UCLA School of Engineering, and leaders of the California Telehealth Network, a statewide consortium that includes CERP leaders. This Network created a partnered working group to explore what technologies are the most acceptable, affordable and effective under what conditions and for which sub-communities.

Using Internet applications of the Virtual Home and the Community Research Registry. CERP optimizes community and academic partner access to **CTSI Virtual Home** (see **Regulatory Program**). The Virtual Home

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serves as a networking hub, a central repository for information crucial to CERP-supported research, and an access point to clinical research tools for data collection, management, and communication and IRB submissions. The Virtual Home provides an interface to the **Community Research Registry**, which contains up-to-date information about the people involved in CERP and CTSI-affiliated local provider organizations, health plans, and CBOs in research collaborations. The registry enables CTSI community partners and faculty to identify collaborators with common interests for potential projects and ongoing studies that are enrolling patients. The registry also serves the important function of presenting published research results (in the form of research summaries, lay-oriented fact sheets, and study data sets) of studies in which community organizations and individuals participated with CTSI researchers. The registry will include partner and community descriptions that UCLA is compiling for the National Children's Study (NCS) (see **section 6.1.5.**).

CERP ensures that Virtual Home on-line technologies offer more to communities than traditional research functions. CERP is spearheading an online community through the CTSI Virtual Home to promote the engagement and collaboration of individuals and organizations and encourage community networks and cross-institutional interest groups. These groups can build areas of common interest and share strategies. BIP ensures that adequate security precautions are implemented and care is taken to filter Internet information and referrals so they are free of commercial interests.

Making use of telemedicine technologies. CERP plans to use telemedicine resources already deployed by the DGSOM Program in Medical Education (PRIME)/Telemedicine and by the CDU Urban Telemedicine Center of Excellence at community sites throughout Los Angeles County. PRIME provides point-to-point telecommunications connections for health care delivery and training at the hospitals, emergency departments, and community clinics in the UCLA Health System, including remote teleconsultations with UCLA specialists for otherwise isolated and underserved rural and urban patients and health care providers throughout Southern California. The CDU Urban Telemedicine Center of Excellence, established in 1996 and directed by Richard Baker, MD, a **Pilot Program** Co-Leader, uses telemedicine technology to increase access to cost-effective, quality specialty care to three inner-city housing projects and a high-volume county clinic serving over 200,000 patients a year. CERP will coordinate utility and cost analyses with the **CTSI Evaluation & Tracking Unit** to determine which functions are most conducive to telemedicine technology intervention.

6.1.5. Increase communication about clinical research by leveraging effective dissemination channels. CERP takes advantage of effective dissemination channels to achieve goals and promote sustainability. CERP research opportunities and results will be integrated into the Chicano Studies Research Center (CSRC), research pipeline (funded by Hewlett Foundation). This includes CSRC's Latino Policy & Issues Briefs series which reaches thousands of key stakeholders (e.g., public officials, community organizers, academics) via electronic and printed formats; CSRC's multi-media mechanisms (Facebook, website, electronic newsletter); and production of Public Service Announcements (PSAs) to be distributed among key stakeholders. CSRC has a long tradition of partnerships with key community organizations locally, nationally, and internationally, which offers additional potential platforms for broader dissemination.

CERP also leverages UCLA's National Children Study (NCS) assets for communications about research. The NCS is a multisite, longitudinal, community-based population study to examine the effects of environmental and genetic influences on children's health and development. UCLA operates the largest national study center and will enroll 4,000 target children in 55 local communities in Los Angeles. NCS has implemented an extensive community engagement process to meet the demands of recruiting and maintaining a cohort over 25 years, which includes engaging over 80 Los Angeles birth hospitals. NCS Community Advisory Board (CAB) and Neighborhood Liaison Committees in each NCS community are co-developing community needs assessments, recruitment, retention and dissemination strategies, and developing strategic messaging using anthropology and other expertise to use storytelling and language effectively. NCS has connected with many forms of local media and holds regular community meetings to discuss child health and environmental issues (ultimately sharing findings and obtaining feedback) with residents. NCS maintains a website of study updates, news and findings that links with the Virtual Home. These relationships and resources can be used for communication about other CERP research and results.

6.2. Specific Aim 2: Strengthen community infrastructure for sustainable partnered research.

6.2.1. Develop a series of model Community Centers in Health Education and Translational Research (CC-HEATRs), as a vehicle for sustained and reliable engagement of communities. CC-HEATRs create a

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strong interface with community to replace the current intermittent, disparate, and often disconnected research efforts with stable, multi-function venues near community health care settings. The CC-HEATR provides a functional repository of studies of interest to communities, computers/kiosks to access local health resources and learn about ongoing clinical trials, and access to archived tutorials and community symposia. It gives a local “face” to the CTSI that links community members with academic resources. It provides physical space for on-site focus groups and satellite clinical trials. CC-HEATRs may also house community-based satellite research units to create an integrated community engagement environment (see **CCRR Program**)

CERP is collaborating with the 70-Block Project community partners to develop the initial CC-HEATR site in Southwest Los Angeles. The To Help Everyone (THE) Clinic is our clinical partner (see **CCRR**). THE Clinic is one of the few nonprofit health care clinics in Southwest Los Angeles, serving part of a dense urban area of over one million people, almost one-third of whom are uninsured. THE Clinic is a key agency providing clinical services for our major 70-Block Healthy Community demonstration project (see **Specific Aim 3**). CERP will continue to work with community and political partners to expand the number of venues in a phased rollout. (see **Table 2**). We envision establishing our second CC-HEATR with existing CERP partners in the San Fernando Valley, including the Northeast Valley Health Corporation, which is led by Dr. Campa, a CERP Co-leader.

As each CC-HEATR matures in its administrative and scientific operations, CERP will transition this entity into a hub with satellites designed to meet the needs of large-scale multisite translational studies. CERP is developing a model for this hub concept. The prospective network partner is the Community Clinic Association of Los Angeles County (CCALAC) with 43 community clinics and 114 sites throughout Los Angeles. CCALAC houses a data warehouse, and member clinics have served as study sites of CTSI investigators for many years. Dr. Campa is a recent past chair of the CCALAC Clinical Advisory Group. As CCALAC is a central component of the CERP development strategy, we will provide annual funding for a 0.5 FTE community liaison based at CCALAC. CERP is also pursuing extramural funds to “seed the way” for new sites into our community network, building this expansion on a project-by-project basis under a plan of controlled and community-vetted growth.

Table 2. Examples of Potential Community Centers of Health Education and Translational Research (CC-HEATRs)

Community Centers of Health Education and Translational Research	Potential Studies to Be Conducted in Venue
<p><u>THE Clinic</u>, within Healthy Community Neighborhood Initiative (HCNI)</p>	<p>Efficacy of Community-Partnered Participatory Research in improving chronic condition care and outcomes in a low-income, underserved community. Multiple studies of basic science (e.g., biomarker studies of cardiovascular disease, diabetes, and chronic kidney disease among adults and children), geomapping, health services, clinical and bioinformatics research.</p>
<p><u>Northeast Valley Health Corporation</u></p> <ul style="list-style-type: none"> • Promotoras for diabetes and chronic disease management • Navigators for breast, cervical and colorectal cancer screening 	<ul style="list-style-type: none"> • Promotora based care • Biomarker studies • Use of social networking technology • Bioinformatics technology
<p><u>Venice Family Clinic</u></p> <ul style="list-style-type: none"> • Health of the Homeless (VA) • Health of Homeless and Domiciled Low Income Clinic Patients • Use of Services by Homeless and Low-Income Domiciled Clinic Patients • Improving Health Habits: Self-Care Priorities • Community Health Improvement Collaborative • Patient Assessment Surveys I, II, III (LAC Dept. of Health Services) • Improving diabetes care with patient decision aids: A randomized controlled trial in community-based primary care (RWJF 63828) 	<p>Venice Family Clinic and CERP investigators have already initiated the project “Improving Health Habits: Self-Care Priorities” and are considering collaboration on other projects to improve rates of colorectal cancer screening and chronic disease self-management</p> <ul style="list-style-type: none"> • Low-cost technology, e.g., tele-dermatology
<p><u>QueensCare</u>⁴</p> <ul style="list-style-type: none"> • “Improving Health Habits in Impoverished Populations” (DK071065) • “Preventing Drug Use in Low Income Clinic Populations” (DA022445) • “Community Partners in Care” (MH078853) • “Partnered Research Center for Quality Care” (MH082760) 	<p>Partnered interventions to improve health promotion, disease prevention and adherence to prescribed chronic disease care</p>

Community Centers of Health Education and Translational Research	Potential Studies to Be Conducted in Venue
<p><u>Magnolia Place Project</u> Magnolia (Pico-Union) is a network of providers and resident groups in a 100 square block area that is home to 100,000 residents and 35,000 children, 92% of whom are Latino. Currently prototyping outcomes and quality measurement at a population level and introducing life course concepts to outcomes-linked CBPR undertaken by 12 promotoras from 4 community organizations</p>	<ul style="list-style-type: none"> • Implementation science in network of 70 medical and social service providers • Implementation and diffusion research • Low-cost technology for resident networking and communication using mobile phones • Geomapping and social network mapping
<p><u>JWCH Institute, Inc.</u> JWCH participates in numerous research studies in areas of the medical, social, and behavioral sciences, including NIDA- and CDC-funded studies of the status of persons who are homeless, at risk for HIV/AIDS and other comorbidities; teen pregnancy prevention; hepatitis C; and obesity</p> <ul style="list-style-type: none"> • “HBV Prevention for Homeless At-Risk for HBV/HCV/HIV” (DA016147) • “Community Partners in Care” • “Preventing Drug Use in Low Income Clinic Populations” (DA022445) • “Hepatitis B and C Among Homeless Adults. Rockville, MD: National Institute on Drug Abuse (DA14294) • “TB/HIV Risk Reduction With Homeless and Drug Addicted” (DA011145) • “HBV Prevention for Homeless at Risk for HBV/HCV/HIV” (DA016147) 	<p>Strategies for managing chronic conditions among homeless patients</p> <ul style="list-style-type: none"> • T1 research on infectious diseases • Bioinformatics/Low-cost technology

6.2.2. Reduce barriers to research participation for community health care providers. CERP responds to the national CTSA charge of studying how clinical protocols work in practice so that discovery translates to real-world settings. We know from experience that community health care providers who participate in research have difficulty sustaining research efforts that disrupt the flow of clinical care, consume substantial staff resources, or introduce a myriad of unplanned requirements that interfere with office operations and management. The competitive and productivity-driven environment in which community clinicians and clinics practice medicine today increases the burden of research participation. These issues are of particular concern in lower-income communities and clinical settings where providers and resources are scarce and academic-community partnerships are new. Nonfinancial benefits such as improved patient care, and mitigation of some disincentives (e.g., burdensome inclusion/exclusion criteria, inefficient data collection strategies) only partially offset provider costs. Heavily involved clinicians face transportation costs and time on committees. This is a barrier to extending research beyond academic medical centers and well-resourced clinical settings. CERP draws on expertise of our community and academic partners who have successfully and efficiently conducted research in community practices to develop strategies that offset these costs of partnership. CERP focuses on valuing community partners’ time (compensation, scheduling), offering quality improvement supports and cost reimbursement for clinical activities, and streamlining research activities to ease participation.

Over the past year, we have met with our community clinic partners to plan specific strategies. We propose direct compensation to each CC-HEATR for the cost of clinical activities related to research. There will be regularly scheduled in-person contacts between **CCRR** mobile units (composed of investigators, research nurses trained in community outreach, and lay health workers), CC-HEATR facilities and other community and private clinics interested in engaging in research. We will support the salary of a research assistant from the **CCRR**, who works 80% time in each CC-HEATR and 20% time for the CTSI, to facilitate information exchange between investigators and clinicians, reduce the workload on other clinic staff, and streamline research activities in community settings. Further, we will work with the community clinics to identify a **CCRR** nurse who will help to coordinate care and visits across 4-5 of the participating partner clinics for patients with prioritized conditions. CERP plans to support partners through quality improvement initiatives focused on health promotion, disease prevention, and chronic disease management for children and adults in the community.

CERP continues to explore innovative and sustainable ways of involving a wider range of community health providers in partnered research. For example, a possible mechanism is offering physicians in partnered translational research “Performance in Practice” credit toward new American Board of Pediatrics and American Board of Family Medicine requirements for maintaining board certification. Subspecialty boards are also introducing this requirement. Performance in Practice is a major time and cost burden for physicians who search individually for approved quality improvement projects. UCLA is one of relatively few national academic institutions with Board-approved projects for family medicine and pediatrics physicians. The CTSI has the good

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clinical practices (GCP) and quality improvement expertise to guide physicians in testing improvements in care and collecting modest data from patients. A collaboration between the CTSI and the local American Academy of Pediatrics (AAP) chapter in 2009-2010 that offered Performance in Practice attracted 40 practices that had not previously participated in implementation research.

We propose close consultation with **BIP** to develop innovative and practical solutions to technological barriers that may constrain participation in research and interfere with the provision of high-quality clinical care. CERP also responds to new opportunities as they emerge. For example, nearly all of our clinical partners have or will soon implement electronic medical record (EMR) systems, receiving support from the Health Information Technology for Economic and Clinical Health Act (HITECH Act), of the American Recovery and Reinvestment Act of 2009 in EHR vendor selection, workflow redesign, on-site technical assistance, education and training, and meaningful use benchmarks. **BIP** and **Regulatory** cores can aid clinical partners in patient registries and other means of streamlining participation in research projects. This will be a major contribution of the CTSI to community health and research in a broad range of communities in Los Angeles County.

6.2.3. Develop novel study designs for community research. Sustained interest from community members and clinicians in research is more likely if study designs reflect the realities of their lives and practices. Clinicians and others familiar with community settings are well positioned to assess the feasibility of study designs in particular practice settings. To bridge the gap between basic science and clinical applications, CERP, in collaboration with the **Biostatistics, Study Design, and Clinical Data Management (BSD-CDM) Program**, will sponsor forums to discuss and evaluate the adaptation of study designs to community practice settings. Biostatistics investigators Thomas Belin PhD, Catherine Crespi PhD, and Catherine Sugar PhD contribute to novel study designs in CERP. Examples include adaptations to randomization protocols to increase acceptability in communities, design of studies with clustered binary data, finding patterns in longitudinal data, and cluster-analytic methods for defining and analyzing health state models in conditions such as depression and schizophrenia.

6.3. Specific Aim 3: Drive innovation in community engagement that accelerates the volume and impact of partnered research in diverse communities.

6.3.1. Strengthen CERP reputation and capabilities through demonstration projects. Translational research that is truly developed by and for community creates knowledge that can be applied immediately to pressing health issues in communities. CERP has multiple active research partnerships with diverse communities in Los Angeles. **Table 3** shows examples of CERP community partners.

Table 3. Selected CERP Community Partners

Community Partner	Description	Target Community
American Academy of Pediatrics, Chapter 2	Professional organization for more than 3,000 pediatricians in 7 counties including Los Angeles	Community pediatricians
Behavioral Health Services	Public sector substance abuse treatment provider	Substance abusing populations
Community Clinic Association of LA	Association of 43 community clinics and health centers across 114 sites in LA	Safety net providers and their low-income patients
Community Practice Network (UCLA Health System)	Funded as an Agency for Healthcare Quality and Research (AHRQ) practice based research network for 200,000 patients at 20 outpatient and 3 inpatient sites	Diverse practice locations and populations
Esperanza Community Housing Corporation	Comprehensive community development organization	Low-income Latino communities in South Central Los Angeles
First 5 LA	Quasi-public organization that supports community-based interventions	Children and pregnant women countywide and in 14 large prioritized low-income communities
Healthy African American Families	Community-based organization for African American health promotion	African Americans and Latinos
John Wesley County Hospital (JWCH) Institute, Inc.	Private nonprofit health agency	Low-income and medically underserved persons in communities served in clinic network
Kaiser Permanente, Southern California	Southern California region serves 3 million members with 3,600 physicians	Practices and patients in staff model managed care organization

Community Partner	Description	Target Community
Koreatown Youth and Community Center	Nonprofit, community center serving Korean Americans	Korean and low-income immigrant families
Korean Resource Center	Community Center serving Korean Americans	Korean and low-income surrounding communities
L.A. Care Health Plan	Largest national Medicaid managed care health plan with 800,000 members	Medicaid beneficiaries and practice network
Los Angeles County Department of Health Services	Provides care for 1 million low-income and uninsured in Los Angeles	Low-income and uninsured patients
LA Free Clinic	Private nonprofit health agency and clinic network	Low-income and medically underserved persons
Los Angeles Unified School District	Second largest U.S. school district, with over 906,700 students in 947 schools	Diverse high-risk student population
Los Angeles Urban League	Local affiliate of the national civil rights service and advocacy organization	Socioeconomically disenfranchised and medically underserved populations
Magnolia Community Initiative	Community network of 70 organizations	100,000 low-income residents in Pico-Union
Mission Community Hospital (San Fernando Community Hospital)	Two-campus, private nonprofit community safety-net hospital, state-designated Disproportionate Share	Medically underserved and low-income communities in San Fernando Valley
Olive View Foundation	Private, nonprofit organization advocating on behalf of underserved populations	Low-income, uninsured, immigrant Latino families
Public Health Foundation Women Infants and Children (WIC)	Nutrition and education program serving 3% of all U.S. eligible clients	400,000 low-income pregnant women, mothers and children under age 5
QueensCare Family Clinics	6 federally qualified family community health centers	Underserved patients and faith-based settings
QueensCare Health and Faith Partnership	Health outreach to partnership of 50 multi-ethnic churches, schools, agencies	Low-income and faith-based communities
Skid Row Homeless Healthcare Initiative	Partnership of 25 agencies integrating services for homeless	Ethnically diverse homeless persons
Southside Coalition of Community Health Centers	Network of autonomous nonprofit community clinics in south Los Angeles	Low income, publicly insured and under- or uninsured persons
To Help Everyone (THE) Clinic	One of the few nonprofit healthcare clinics in southwest Los Angeles	Low income, publicly insured and under- or uninsured persons
UCLA Health System	65 community clinics with 140 primary care MDs	Diverse practice locations and populations
Greater LA VA Medical Center, U.S. Dept. of Veterans Affairs	Largest health care facility in the VA, with 1,056 beds	Veterans
Venice Family Clinic	Largest nonprofit free clinic in the United States	Low-income, immigrants

Over the initial 5-year CTSA program period, we also plan to conduct up to six intensive community-university partner demonstration projects. As with all of our community-partnered research, these projects will lead to patient-centered and community-feasible strategies for improving health. They will include all of the conceptual, experiential, and practical aspects of CPPR embraced by CERP and partners. As demonstrations, these specific research partnerships enable CERP to refine its processes of community engagement and both capabilities and reputation as a reliable and forthright partner. Concentrating effort in demonstration areas also helps CERP train a new generation of health professionals and researchers in all of the dimensions of effective community-partnered research. Our strategy is to focus initially on communities with active research and engagement and with whom CTSA investigators already have established at least fledgling partnerships, and then branch outward.

6.3.2 Implement the Healthy Community Neighborhood Initiative

We begin in Year -01 with the Healthy Community Neighborhood Initiative (HCNI), also called the 70-Block Project, in a 70-square-block area of South Los Angeles. The 70-Block Project was developed as part of a 5-year strategic plan to create healthy urban communities and reduce racial/ethnic inequities. Our collaborations

Principal Investigator/Program Director: (Last, First, Middle): Dubinett, Steven, MD with the 70-Block Project align with the Translational Cluster Research Program (see **Pilot Program**) because these clusters address identified community priorities in the Project area including obesity, diabetes, cardiovascular disease, and mental health and stress. Based on virtually every indicator, South Los Angeles residents experience among the worst health outcomes in the United States. This area ranks last in life expectancy (75.2 years) of the 102 communities in Los Angeles.¹⁶ Diabetes rates are 44% higher than elsewhere in the county, HIV/AIDS rates are 38% higher, and the infant mortality rate is 20% higher than the county as a whole.^{16,19,26} South Los Angeles is in great need of scientific discovery and effective translation. The goal of the 70-Block Project is to improve health promotion, disease prevention, health care, and clinical outcomes in chronic diseases that align with the CTSI priorities.

CERP partners with 70-Block Project to guide the development of multifaceted interventions to improve individual level and community health. The initial stage of the 70-Block Project program has leveraged competitively awarded philanthropic funding from The California Endowment to develop a health agenda, including a health education program; deploy community health workers (with CDU and UCLA students) for baseline clinical and environmental assessments; and establish multiple support mechanisms and strategies to ensure that clinical problems for 70-Block residents are prevented, identified, and addressed. The strategic plan is unfolding in phases. THE Clinic is ready to accept patients identified in the 70-Block Project and screen them within the research endeavor. This partnership plans to include screening and referral services focusing on women's health, cardiovascular disease risk reduction, diabetes, obesity, and improving the functional status of older adults, which includes referral for participation in partnered research. A related initiative, the Youth Health Academy at Cedars-Sinai, provides mentors to Crenshaw High students within the 70-Block Project from among the hospital's nurses, physicians, educators, research scientists, health educators, and management team. Crenshaw High is in the heart of the 70-Block Project. Preliminary findings are being used to develop a set of feasible and sustainable interventions to improve key health and social indicators in the community. For example, maps describing physical and social features of the neighborhood are being linked to Los Angeles County parcel maps and resident surveys to better understand how land use, neighborhood resources, transportation patterns, and other features of the environment may influence dietary and physical activity patterns and ultimately obesity. These co-developed strategies address immediate health needs while serving shared translational goals of our community-partnered research.

In addition to developing interventions in prevention, treatment and behavior, the 70-Block Project demonstration also includes innovative studies of social networking and information technology. An example of novel approaches includes data collection among community members such as those used by CERP investigator Dr. Estrin. CERP, CCRR nursing mobile units, and other CTSI cores are contributing to scientific inquiry in the 70-Block Project. BIP will work with the CERP to ensure that the websites that gather and use information and the databases that retain this information will conform to the UCLA Medical Center IT security protocols, which are intended to adhere to the HIPAA guidelines as well as constitute best practices in data management and security. Before any database or website goes live, it will undergo security software checks and review by IT specialists to ensure that the appropriate safeguards have been put into place. BIP will have the ability to monitor access to these databases by all authorized users to limit the potential for inappropriate use and/or disclosure.

D'Ann Morris, MPA, a CERP is an executive staff member of LAUL who has engaged CDU, HAAF, UCLA and the CERP management team in biweekly meetings over the past 2 years. Another CTSI partner institution, Cedars-Sinai, has provided key health outreach activities for 70-Block Project. Our collaborative plan is incremental; we started with a focus on chronic disease care, because the community expressed a sense of urgency in that area. As CERP infrastructure grows in the neighborhood, we will expand the CERP/CTSI agenda in the 70-Block Project, in Year -03, to health promotion and disease prevention.

6.4. Specific Aim 4: Build Health Services Research (HSR) methods into partnerships to accelerate design, production and wide adoption of evidence-based practice.

CERP integrates key concepts and methods of community engaged research with HSR methods to strengthen research across the translational phases from bench to patients to practice and community. HSR uses concepts and methods from a range of disciplines such as economics, management and psychology to understand health-related behavior and how people act in health care systems. Combining HSR methods with community research helps to (1) identify barriers translating discovery into optimal health, health behavior and

provider practice, (2) learn what works in which situations and under what conditions, (3) design interventions and compare alternatives using outcomes and comparative effectiveness methods, (4) identify strategies for broad reliable adoption of interventions, and (5) study outcomes in large systems and the impact of emerging health policies, including many implications of national health care reform for health care delivery.

6.4.1. Strengthen HSR translation methods within community-partnered research

CERP brings health services researchers together with investigators and community partners who work at each stage of translation, ranging from prioritization of biomedical topics to development of new therapies to widespread diffusion. HSR investigators participate in agenda-setting symposia and town halls about the science of risk and disease, behavioral patterns and health care responses to priority conditions for communities. This helps communities pose and answer questions about how health care systems can best achieve their goals. HSR supports academic-community partnerships to develop measures and comparisons that show which interventions are working, where they fall short of expectations and why. Implementation science researchers partner with communities to study ways of adopting the vast amount of knowledge that emerges from research.

Because HSR has virtually unlimited potential to advance community translational goals, CERP and HSR leaders prioritize how HSR resources are used and match community partners with HSR investigators, within the CERP governance structure described in **Specific Aim 5**. CERP also links community partners with HSR investigators in UCLA centers and with development opportunities in industry and other extramural sources. **Table 4** describes some of the rich HSR expertise available in CERP from UCLA-Westwood, CDU, Harbor-LA BioMed, Cedars-Sinai, and two UCLA-affiliated institutions, the Greater Los Angeles Veterans Administration (VA) and RAND. The CTSI's wealth of expertise includes national leaders in their fields who are housed in highly productive research centers (see **Table 5**). Specific HSR goals and roles in CERP include:

- Studies of disease, care patterns and disparities for diverse populations enable HSR to provide input and education to T1 and T2 scientists in areas in which new therapies and interventions addressing shortfalls in health outcomes are likely to have the greatest impact. Lead investigators include M. Wong, M. Shapiro and A. Brown.
- Studies suggest that at least 25% of patients do not adhere to treatment protocols.²⁷⁻²⁸ Compliance is affected by many factors, including depression and social support.²⁹⁻³¹ CERP brings together communities, behavioral and biomedical sciences to study and intervene with these problems. Lead investigators in patient uptake of appropriate care include R. Victor, N. Wenger, A. Ortega and C. Fox.
- Developing effective provider interventions requires translating discovery into guidelines and developing effective care management through protocols and prepared practice teams. Lead investigators include P. Shekelle, K. Wells, R. Bastani and B. Vickrey.
- Evaluating impact of alternative translational interventions requires measures of access and barriers, health outcomes, cost and quality of care for interventions, and patient beliefs, attitudes and behaviors. It also requires community dashboarding and surveys in quality of care and patient experiences. Lead investigators in measurement include R. Hays, N. Wenger, S. Ettner, G. Kominski and H. Rodriguez.
- Some scientific discovery spreads too quickly (driving up costs without improving health) while other innovations spread too slowly (widening health care and health disparities). Many health care resources are not used optimally because they are spent on low-quality or cost-ineffective care. Comparative effectiveness research (CER) identifies care that produces the most health for the maximum number of people. HSR analyzes cost and cost-effectiveness of potential translational interventions and economic outcome evaluations for CERP linked/sponsored research collaborations. Lead investigators include M. Shapiro, P. Shekelle, S. Ettner, G. Kominski, M. Ong, N. Wenger, R. Hays, R. Andersen, H. Rodriguez and P. Ganz.

Table 4. Health Services Research (HSR) Expertise in CERP

Community Partner	Description	Target Community
Measurement of health outcomes	Developed some of the best known and widely used quality-of-life instruments ³²⁻³⁸	Ganz, Hays, Kaplan, Litwin, Mangione, Vickrey, Weisman
Comparative and cost-effectiveness analysis of costs, and financing of care	Studies have offered new innovations in methodology and have evaluated cost-effectiveness in major trials ³⁹⁻⁵³	Escarce, Ettner, Joyce, Keeler, Kaplan, Kominski, Ong, Rice, Rodriguez
Access and barriers to care	Research has defined new approaches to the study of access ⁵⁴⁻⁷³ and of patterns in U.S. and global populations including immigrant and border populations	Andersen, ER Brown, Cunningham, Halfon, Hobel, Inkelas, Norris, Ortega, Shapiro, Wong
Quality of care	Researchers have been leaders in quality-of-care research and have conducted seminal studies on guideline development and physician execution of guidelines ⁷⁴⁻⁹³	Asch, Brook, Kahn, McGlynn, Needleman, Rubenstein, Shekelle, Weisman, Wenger, Zingmond
Health behaviors	Researchers are international leaders in studies of health consumer behavior and patient compliance ⁹⁴⁻⁹⁸	Bastani, Coates, Fox, Frosch, Kaplan, Miller, Ong, Ortega
Interventions in prevention and treatment	Researchers develop novel interventions in preventive care and treatment ⁹⁹⁻¹⁰⁴	Bastani, Casillas, Fox, Gelberg, Victor, Wells
Life course health development (including women, maternal, and child health)	Researchers are leaders in maternal-child health quality and outcome research, determining the preconception, perinatal, and childhood events that affect child health outcomes; mental health; and factors modulating the long term outcome of cardiovascular diseases in women ¹⁰⁵⁻¹²⁶	Bairey Merz, Gregory, Halfon, Hobel, Lu, Rotheram-Borus
Regional, state, and federal health policy	Researchers conduct analyses for local, state and national audiences on a broad range of issues, including specific health care topics, health insurance coverage, clinical practice standards and evidence-based medicine, health care for subgroups, and health care reform ¹²⁷⁻¹³⁵	ER Brown, Halfon, Inkelas, Kominski, Shekelle

Table 5. Examples of CERP/CTSI-Affiliated Research Centers Relevant to HSR

Centers	Director(s)	Mission
AHA UCLA Outcomes Research Center	Barbara Vickrey	One of three national centers focusing on outcomes research in heart disease and stroke. Special focus on stroke in underserved communities.
California Comparative Effectiveness and Outcomes Improvement (CEOI) Center	Carol Mangione	NHLBI-funded Center to develop sustainable statewide infrastructure for comparative effectiveness research on primary and secondary prevention of cardiovascular disease (CVD) among managed care populations. Collaboration among three UC campuses (UCB, UCLA, UCSD), RAND and the California Department of Managed Health Care.
Cedars-Sinai Women's Heart Center	Noel Bairey Merz	Funded in part by the NHLBI, the only regional center to focus on outcomes research in cardiovascular and heart disease affecting women.
CDU Medical Geographic Information System (MGIS) Laboratory and Geo-Spatial Data Archive	Paul Robinson	Provides extensive expertise and technical support to researchers interested in neighborhood and "built environment" influences on disease-related behaviors and clinical outcomes. Geo-Spatial Data Archive contains hundreds of health-related spatial databases, including boundary files and other public health data.
CDU Urban Telemedicine Center of Excellence	Richard Baker	Uses state-of-the-art telemedicine technology to increase access to specialty care, improve quality of care, and reduce cost of care for minority, underserved urban populations in three inner-city housing communities. In cooperation with LA County Community Development Commission and LA County Health Department.
CDU/UCLA EXPORT Center	Keith Norris Martin Shapiro	National Center on Minority Health and Health Disparities Center studies health disparities and community interventions to reduce disparities, including HIV, diabetes, depression, and new developing new scholars in disparity research.
Semel Global Center for Children and Families	Mary Jane Rotheram-Borus	Global behavioral science research on prevention, treatment and management of child health issues including HIV/AIDS, chronic illness and trauma.
UCLA Center for Health Policy Research	E. Richard Brown	Advances health policy through research, community partnership in data analysis and use, and dissemination. Conducts the California Health Interview Survey.

Centers	Director(s)	Mission
UCLA Center for Healthier Children, Families, and Communities	Neal Halfon Moira Inkelas Michael Lu	Conducts research, policy analysis, measurement, implementation science and quality improvement science emphasizing pediatric health care and community systems. Focuses on early childhood, chronic illness, maternal health and life course.
UCLA Center for Research, Education, Training, and Strategic Communication on Minority Health Disparities	Vickie Mays	Analyzes health, health care, access to care, and health behaviors of diverse populations in California to understand and address racial/ethnic health disparities.
UCLA Center for Translational Research on Addiction	Edythe London	National Center on Drug Abuse funded center to integrate preclinical studies to directly inform clinical research on drug addiction. Links basic scientists studying neurobiological components of addiction with clinical intervention investigators.
UCLA Center for Vulnerable Populations Research	Deborah Koniak-Griffin	National Institute of Nursing Research Center in the School of Nursing develops strategies to enhance capability of communities to eliminate health disparities.
UCLA Jonsson Comprehensive Cancer Center, Division of Cancer Prevention and Control Research (DCPCR)	Patricia Ganz Roshan Bastani	Division of Cancer Prevention and Control Research studies a continuum of primary prevention, screening, early detection, continuing care and rehabilitation interventions and outcomes research.
UCLA Kaiser Permanente Center for Health Equity	Antronette Yancey Roshan Bastani	Conducts community-based participatory intervention research in health promotion and disease prevention to mitigate disparities, links community and academic researchers, trains future leaders in health disparities research, provides technical assistance for evidence-based programs, hosts annual community symposia.
UCLA Center for Population Health and Health Disparities	Alexander Ortega	National Heart, Lung & Blood Institute funded center to study and reduce cardiovascular disease risk in East Los Angeles.
UCLA Resource Center for Minority Aging Research	Carol Mangione	Supports development of new minority investigators interested in a range of issues involving the health of minority elderly.
UCLA/RAND Center for Adolescent Health Promotion	Paul Chung	Centers for Disease Control and Prevention-designated Prevention Research Center with studies including interventions to improve child nutrition and exercise, and reduce obesity.
UCLA/RAND NIMH Center for Research on Quality in Managed Care	Kenneth Wells	Studies how to improve mental health care quality of care across the lifespan. Integrates perspectives of diverse stakeholders (employers, consumers, plans, policymakers, providers).
UCLA/VA Center for Outcomes Research and Education	Brennan Spiegel Eric Esrailian	Design and implementation of clinically relevant research to measure the structure, process, and outcomes of health care across a broad spectrum of topics.
VA/UCLA/RAND Center for the Study of Healthcare Provider Behavior	Lisa Rubenstein Elizabeth Yano	Develop intervention evidence syntheses in core areas including mental health, end of life care and cross-cutting applications including implementation science, organizations and business case research

- Lack of fidelity to clinical protocols and guidelines undermines impact of evidence-based interventions in community settings. Implementation research identifies factors and strategies that lead to optimal impact of evidence-based interventions in the right settings. Lead investigators include H. Rodriguez, C. Fox and M. Inkelas.
- Dissemination research examines how knowledge can be spread to target audiences (residents, health care providers, health care systems and policymakers) for widespread use of effective interventions. Lead investigators include ER Brown, N. Halfon and A. Yancey.
- The 2008 best practices summary “Researchers and Their Communities: The Challenge of Meaningful Community Engagement” identified diffusion as a key Community Engagement goal for the CTSA network.¹ Research leading to widespread use of effective interventions includes meta-analyses, structured reviews, and theoretical and observational studies analyzing the influence of policies, regulations and financial incentives on whether or not effective interventions translate into sustained practice change. Lead investigators include P. Shekelle, R. Andersen, M. Shapiro, ER Brown, M. Wong, D. Zingmond, N. Halfon.

6.5. Specific Aim 5: Establish a governance and operations structure that strengthens existing partnerships and builds new bridges between community and academia for research.

6.5.1. Formalize a governance and operations structure with community and academic stakeholders.

CERP integrates community into governance structures to demonstrate commitment to partnership and to ensure equity in decision making. The **Executive Management Team** includes two Leaders and two Co-leaders who will regularly receive the advice and directives of our **Community-Academic Partnership (CAP) Council**, a consortium of respected CERP academic and community investigators. The team implements program operations (**Figure 1**). To facilitate communication, the CAP Council elects from their group two members from Academia and two members from the Community (i.e., an Academic Chair and Vice-Chair, and a Community Chair and Vice-Chair) to represent them in regular communications with the CERP Executive Management Team. These CAP representatives rotate yearly. The Executive Management Team reports to the CTSI Executive Oversight Committee (EOC), which has the primary responsibility within CTSI governance of reviewing program implementation, requesting resources, serving in the process of conflict resolution, and ensuring maximum efficiency in the management of the CTSI programs and core resources (see **Overview and Governance**). With quarterly input from the CAP Council, the CERP Executive Management team works with the CTSI EOC to transform the research culture across the academic partners from fragmented activities occasionally or opportunistically extending toward community, into an interdisciplinary collaborative program that engages community in a substantive manner built on trust and mutually valued goals. The team also builds synergies with the other 8 CTSI core support programs.

CERP CAP Council. The CAP Council, composed of locally and nationally recognized community and academic experts in community engagement and interdisciplinary research, is advisory and directive to the CERP Executive Management Team. The CAP Council assists in identifying key community priority areas for community-engaged research, reviewing CERP progress, engaging in strategic planning for future directions, and strengthening community and academic relationships. CAP Council members serve as ambassadors within the larger scope of CTSI operations and as educators in CERP bidirectional knowledge transfer programs (symposia, workshops, and journal clubs) on CBPR/CPPR. Members of the CAP Council also serve as liaisons to their respective institutions and as mentors to student and junior faculty researchers on CPPR principles and practices. The CAP Council also advises the CERP and **BIP** leadership on issues of IT technologies and format selections/applications from the perspective of community needs (see **BIP**).

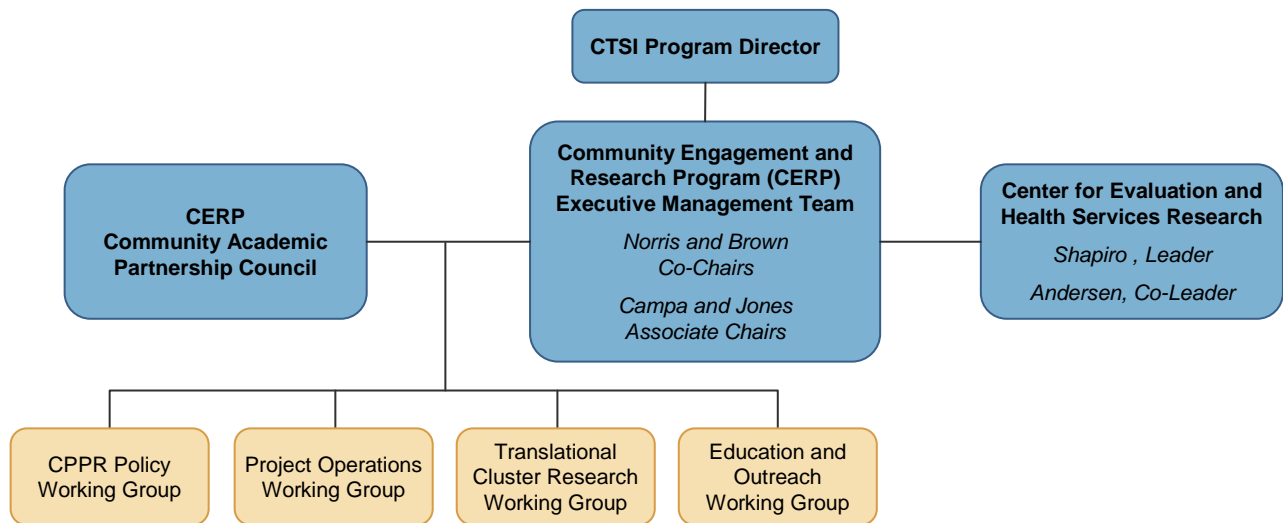


Figure 1. CERP Organizational Chart

The membership of the CAP Council is developing in two phases. In the first completed phase, the CERP Leaders and Co-leaders solicited participation for half of the Council membership from known local academic and community experts in translational science, community engagement, and social determinants of health. Current membership includes 16 leaders listed on the Face Page of the CERP section and Dr. Campa, Ms. Jones, and Ms. Wright (see **CAP Council letters**). In the second phase that is underway, the sitting half of the

Principal Investigator/Program Director: (Last, First, Middle): Dubinett, Steven, MD

Council is selecting the balance of the membership by identifying “who is missing from the table.” Once the selection process is complete, the Council membership will total approximately 30 individuals, representing a broad and inclusive cross-section ranging from translational scientists to members of advocacy groups and public and private agencies dedicated to building bridges between academia and community, stimulating community social capital, and supporting faculty and community development. In Year 1, the CAP Council will meet three times, foremost to select their executive leadership. The CAP community and academic Chairs and Vice-Chairs will meet in person for 90 minutes every 2 weeks during the first 6 months of the CTSA grant period, and monthly thereafter. Each CAP Council session will be a half-day long. CAP Council meetings will be supplemented by CERP Open Forums or Town Halls, twice per year, where community members can participate in open-microphone sessions with the CERP management team, the CAP Council, and T1 and T2 investigators to ask questions, voice concerns, and provide recommendations.

CERP Working Groups. The Executive Management Team identifies members of the CAP Council to serve with them on one or more of five interacting working groups (see **Figure 2**) for 2- to 3-year appointment periods, based on their individual expertise and experience in CPPR and the scope of work to be accomplished. CERP Working Groups are charged with bringing innovative ideas, approaches, and solutions to CERP and, in many instances, leading initiatives. These groups also strengthen relationships between CERP and the other CTSI cores that are bolstering their involvement in community translational research. Pairs of CERP Working Group members (one from community and one from academia) serve as liaisons to the other CTSI Programs, to ensure that programs are up to date on CERP activities and that the cross-program collaborations are dynamic and enduring.

- The **CPPR Policy Working Group** focuses on macro-level policy-making pertaining to bidirectionality of academic-community partnerships and the maintenance of a CPPR-conducive environment throughout the UCLA CTSI. For example, in collaboration with BIP, this working group is formulating policy on the eligibility criteria for tiered access rights of community participants to the non-public sectors of the CTSI Virtual Home, calibrated in a manner that is equitable and appropriate to the conduct of translational research in comparison to academic investigators. To keep this working group close to the pulse of Community, the membership includes a representative from each of the working groups that emerge annually from the Building Bridges to Optimum Health Conferences (see **section 6.1.1**). That individual serves on the CERP Policy Working Group until the particular conference-derived working group disbands upon work completion.
- The **Project Operations Working Group** focuses on “nuts-and-bolts” implementation issues of CPPR projects planned and underway and day-to-day programmatic operations and procedures, including allocation of resources and services. This group also provides regular updates on and input into key projects (**Aim 3**), such as the 70-Block Project. Like the Policy Working Group, the Operations Working Group includes representation from the Building Bridges symposia to encourage community input into the CERP CPPR research agenda.
- The **Translational Cluster Research Working Group** ensures that the community engagement research agenda is aligned with the CTSI Translational Research Clusters. CERP investigators participate in current research clusters in mental health and cognitive disorders, diabetes and obesity, cardiovascular disease and stroke, cancer, addiction, and HIV/AIDS. (see Pilot/Collaborative Program).
- The **Education and Outreach Working Group** works closely with the CTSI-ED and CCRR Programs to ensure that education and training opportunities for academic and community investigators and participants (see **section 6.1.3**) encourage effective CPPR and are responsive to stakeholder needs.
- The Executive Management group collaborates with the leaders and co-leaders of the **Center for Evaluation and Health Services Research (ET/HSR)** to facilitate integration of HSR into community partnered research. Leaders of CERP and Center build on their existing close working relationships. This collaboration also produces quarterly performance reports designed to increase efficiency, stimulate innovation, and enhance operational effectiveness in CERP resource allocation and programmatic implementation.

6.5.2. Establish a formal conflict resolution plan that offers a range of options for community and academic partners. To mitigate the potential power differentials between community residents/CBOs/CSAs and academic partners, we require that all members of the CERP Executive Management Team and the

Principal Investigator/Program Director: (Last, First, Middle): Dubinett, Steven, MD

CERP CAP Council participate in training sessions led by the Los Angeles County Dispute Resolution Center. We have also established a local "Mediation Team," led by CERP investigator Paul Koegel, PhD, at RAND and Ms. Aziza Wright of HAAF/RAND and staffed by representatives from the community and each of the academic partners, as a first option for addressing conflicts between or among community and academic partners within CERP. Dr. Koegel and Ms. Wright have led the conflict resolution process for Community Partners in Care (CPIC) project, a community-academic partnered study to improve identification and management of depression in community settings, which is directed by CERP investigator Kenneth Wells MD. The Los Angeles County Dispute Resolution Center's conflict resolution team will serve as a second option for disputes that cannot be resolved within CERP.

6.5.3. Create a Community Research Liaison Office that increases effectiveness and sustainability of translational research in communities. The Liaison Office will build productive two-way collaborations among community stakeholders and academic researchers across diverse community settings. As a collaborative effort of academic and community representatives, the Liaison Office supports communities in terms of their (1) readiness for research; (2) availability of services and staff necessary to engage in specified research projects; (3) training needs and resources to engage the community in research; (4) clinical service needs that can be served by the academic partnership; and (5) concerns about research ethics or applicability of the proposed research to the populations served.

The Liaison Office will be staffed by two full-time high-level personnel employed by our community partners and recognized within their respective communities as experts in community engagement. These individuals will oversee a cadre of **Community Liaisons**, who originate in either the community or academia, and will serve as coaches, navigators, or translators to ensure the successful undertaking and completion of CPPR. The Community Liaison Office staff and the Community Liaisons will work in collaboration with individual investigators and with the **Research Facilitators** in the **CTSI Office of Investigators Services (OIS)**. The OIS provides comprehensive services to the CTSI investigator community and their staff to ensure the successful and efficient development and application of innovative research ideas, and includes Research Facilitators and a variety of domain experts, such as the Community Liaisons (see Regulatory Program).

Community Liaisons will work with community research coordinators, lay health workers, and CCRR assets to deploy resources where they are needed, as directed and approved by the CERP Executive Management Team. They also ensure that all investigators and research support personnel who interface with the community are appropriately trained in community engagement techniques and protocols. Community Liaisons also facilitate presentations regarding community topics as a mechanism for providers and communities to gain exposure to potential topics for research. For example:

- Liaisons at the Venice Family Clinic and the To Help Everyone (THE) Clinic provide information in linguistically and culturally appropriate ways about research that is underway in the CTSI including eligibility and investigators involved. They also make academic researchers aware of each organization's priorities and strategic plans, resources, databases, and decision-making structures.
- Specialized nurses from the National Coalition of Ethnic Minority Nurses Association (NCEMA) can serve this role for projects on genetics/genomics. CERP is partnering with NCEMNA to link the nurses in that partnership with the National Human Genome Research Institute to ongoing T1 genetics and genomics research projects and community organizations and to pilot-test tools to improve collection of genetic and genomic information through use of family histories among a diverse group of patients in academic and community settings.
- LA2K investigators (Dr. Bilder) regularly consult with members of CERP on strategies for recruiting and retaining a diverse sample of participants, assessing beliefs in Latino communities, disseminating results of the study widely in ethnic communities, and obtaining community input on the implications of the research.

7. INVESTIGATORS

Keith Norris, MD, (CERP Leader), is Executive Vice President for Research and Health Affairs of CDU and CTSI Co-Director. He is PI of two NCCR-funded projects: Research Centers in Minority Institutions (RCMI) Translational Research Network (**U54 RR022762**), which supports multi-site clinical and translational research

Principal Investigator/Program Director: (Last, First, Middle): Dubinett, Steven, MD among minority and other collaborating institutions throughout the nation, and Accelerating Excellence in Translational Science (AXIS) Program (**U54 RR026138**), a catalyst grant to consolidate and integrate the Comprehensive Center for Health Disparities (CCHD) and Clinical Research Center (now a CTSI CCRR site) into the new home at CDU. His services to the CERP will be supported through his role as a CTSI Co-Director.

Arleen F. Brown, MD, PhD, (CERP Leader) is Associate Professor of Medicine at the UCLA David Geffen School of Medicine (DGSOM) Division of General Internal Medicine and Health Services Research. She has over 10 years' experience conducting community-based participatory research and community-partnered trials in Los Angeles. Her prior work also includes quantitative and qualitative research on quality of care, racial/ethnic and socioeconomic disparities, and the influence of neighborhood socioeconomic and nutrition environments on the health of adults with chronic conditions.

David Campa, MD, MPH, (Co-Leader) is Chief Medical Officer of Northeast Valley Health Corporation (NEVHC), a private, nonprofit, federally qualified health center based in Los Angeles County's San Fernando Valley. He has a federal appointment to the National Advisory Council on Migrant Health.

Loretta Jones, MA, (Co-Leader) is the founder and executive director of Healthy African American Families (HAAF), a nonprofit, community serving organization whose mission is to improve the health outcomes, quality of care, and social progress of the African American and Latino communities in Los Angeles County through education, training, and collaborative partnering with community, academia, researchers, and government. Her work is featured in a 2007 *JAMA* article, "Strategies for Academic and Clinician Engagement in Community-Participatory Partnered Research,"¹³ and a 2009 *JAMA* article, "'Research' in Community-Partnered Participatory Research." Ms. Jones will ensure adequate attention to shared decision making and resources in the CTSI.¹⁴¹ Her services to CERP are integrated with contributions as a CTSI Co-Director.

Martin Shapiro, MD (Leader of the Center for ET/HSR) is Professor of Medicine and Health Services and Chief of the Division of General Internal Medicine and Health Services Research in the Department of Medicine. Dr. Shapiro led the largest translational study to date of a chronic disease to evaluate diffusion of therapy and patterns of care (the \$25 million HIV Cost and Services Utilization Study) and maintains an active research program in access to care and strategies for influencing patient behaviors to reduce health disparities. Dr. Shapiro will lead the ET/HSR activities in the CTSI and the HSR activities within CERP, ensuring that HSR investigators integrate seamlessly into community-partnered research and address priorities of community partners.

Ron Andersen, PhD (Co-Leader of the Center for ET/HSR) is Professor Emeritus of Health Services. Dr. Andersen developed the behavioral model of health care that has framed much of the research on access to care and factors affecting utilization of services. Dr. Andersen will co-lead ET/HSR activities, analyze data to assess health and health care patterns in Los Angeles and identify CERP priorities for HSR activities.

8. INTEGRATION OF UCLA KEY FUNCTIONS

CERP fosters community research that builds on decades of collaborative efforts in communities that involve multiple academic departments, professional schools, partner hospitals, and research centers and institutes across the CTSI. CERP is positioned to strengthen connections between UCLA Schools of Law, Engineering, Nursing, Public Health, Public Affairs, Dentistry, and Medicine, the College of Letters and Harbor-LA BioMed, Cedars-Sinai, and CDU. The 70-Block Project and other community initiatives provide a more organized environment for these collaborations. The scientists and community experts who engage in research partnerships through CERP are aligned with specific CTSI resource programs (**Table 6**). CERP will link at least one community and one academic CERP CAP Council member as liaisons to each of the other CTSI core programs, as detailed in **Section 6.5.1**. This cross-fertilization brings community perspectives to other CTSI key functions.

Table 6. CERP Collaborations with Other CTSI Key Functions

CTSI Program	Resources in Support of CERP	CERP Contribution to Other Programs
Clinical and Community Research Resources (CCRR)	<ul style="list-style-type: none"> Expansion of research through new community collaborations to include a significant number of new PIs Sophisticated diagnostic, therapeutic, and IT research resources to community study sites through efforts such as the mobile nursing units. 	<ul style="list-style-type: none"> Ongoing counsel to CCRR on development and conduct of CCRR-without-Walls, which will allow for direct interaction between T1 / T2 investigators and community residents and organizations in these settings
Biostatistics, Study Design, and Clinical Data Management	<ul style="list-style-type: none"> Consultations on study design, including sampling strategies between and within communities, analytic methodologies and recruitment strategies Support of data collection, statistical advice on how to present and publish data 	<ul style="list-style-type: none"> Partnership to design and field-test ethical study designs and data analysis methods that facilitate and respect community research Sponsor community forums to discuss adaptation of study designs to community practice settings.
Regulatory Knowledge and Support, Industry Relations, and Research Ethics	<ul style="list-style-type: none"> Facilitator availability to guide the research team through IRB approval, ethical contractual, and other regulatory hurdles Consultations regarding ethical implications of proposed community-based studies Research subject advocates to oversee research and ensure good clinical practices, including following data and safety, assisting in recruitment Advice and counsel on intellectual property and technology transfer for community and academia Web-based process and community educational sessions to provide HIPAA and IRB training and certification 	<ul style="list-style-type: none"> Advice regarding establishing guidelines with community, and maintaining a facilitator office, to ensure ethical contractual relationships are put into place on every project to protect both community partner and academic researchers Enhancing community and academic partners' understanding of challenges and opportunities and effective strategies to succeed in community-based practice networks and participation research
Pilot and Collaborative Translational Clinical Studies	<ul style="list-style-type: none"> Access to competitive pilot funding for community-based research 	<ul style="list-style-type: none"> Collaboration with other CTSI Programs on pilot proposals and pilot studies to advance community focused translational science
Translational Technologies	<ul style="list-style-type: none"> File of available technologies and consultations about their usefulness Occasional studies for clinical diagnostic purposes Insights into novel study questions that could benefit communities 	<ul style="list-style-type: none"> Development of and collaboration on relevant proposals Facilitation of communication with community; dissemination and education around new technologies and their clinical implications Enhanced science relevance by adding community level input in study design and interpretation of results
Biomedical Informatics	<ul style="list-style-type: none"> Provision of (a) structure for data gathering and analysis for community-based studies; (b) communications channels between community participants and CTSI investigators; (c) education and training channels for the dispersed community participants; and (d) consultation 	<ul style="list-style-type: none"> Facilitation of 2-way communication (including via audio-visual telemedicine technologies) with CBOs, providers, and researchers regarding their needs for informatics to participate in community research, and ongoing activities
Research Education, Training, and Career Development	<ul style="list-style-type: none"> Access to offerings for trainees, continued education for physicians, nurses, and others on research teams to a whole palette of courses 	<ul style="list-style-type: none"> Development of community research training/mentoring programs for academic and community partner researchers by adapting and enhancing existing programs. Providing mentors for junior investigators conducting community research: physicians, nurses, dentists, public health students
Evaluation and Tracking	<ul style="list-style-type: none"> HSR resources associated with the Center for Evaluation and Health Services Research are integrated into community-partnered research 	<ul style="list-style-type: none"> Community investigators participate in Evaluation activities of the CTSI

9. EXTRA-CTSA COLLABORATIONS

CERP leaders have begun to meet quarterly with the Los Angeles Basin Clinical and Translational Science Institute's Office of Community Engagement at USC to create local synergies and work collaboratively with any shared community partners. Examples of CERP collaborations with regional and national CTSA's include:

- The National Children's Study (NCS) is a \$7 billion multisite, longitudinal, community-based population study to examine the effects of environmental and genetic influences on children's health and development. Investigators from the CTSI lead an innovation collaborative to design, test and scale novel community-partnered outreach, engagement, and enrollment methods for hard-to-reach populations. Study Centers

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 include CTSA from University of Colorado, Johns Hopkins University, University of Utah, Vanderbilt University, University of Pittsburgh, Northwestern University, and University of Illinois.

- Dr. Ong directs a \$10 million comparative effectiveness randomized controlled trial of alternative inpatient-outpatient transition interventions to reduce hospital readmissions among heart failure patients for the Agency for Healthcare Research and Quality (AHRQ) Clinical and Health Outcomes Initiative in Comparative Effectiveness (CHOICE) program. This CTSI collaboration includes 4 California CTSA. Dr. Ong received a seed grant from our CTSI that yielded preliminary data about variations in heart failure care at six California academic medical centers [see Pilot and Collaborative Translational and Clinical Studies (Pilot/Collaborative) Program] and led to AHRQ grant funding for this T2 project.
- UCLA is home to the Life Course Research Network (LCRN), which was funded by the Department of Health and Human Services Maternal and Child Health Bureau to advance research on the epidemiology, origins and impacts of factors that influence health and health disparities over the life course. The LCRN includes researchers from CTSA including University of California San Francisco, Stanford, Johns Hopkins, University of Cincinnati, University of North Carolina, Harvard University, University of Washington and Boston University.
- The CTSI leveraged a \$5 million foundation grant to support collaboration between a newly established practice network within CERP (a partnership with the local American Academy of Pediatrics chapter, which covers Los Angeles and 6 other counties) and the Practice Based Research Network (PBRN) of the Community Engagement Unit in the University of California Irvine Institute for Clinical and Translational Science (ICTS). This collaboration involved 25 practices from 5 Southern California counties.

10. IMPLEMENTATION PLANS AND MILESTONES

Table 7 presents the CERP Implementation Plan, which describes the projected time line, measurable objectives, and milestones for implementing key tasks over Years 1–5 of the project period.

Table 7. CERP Implementation Plan and Milestones

Year(s)	Specific Aims, Milestones and Key Activities	Evaluation/Tracking (E/T) Measures and Metrics
Aim 1: Promote and sustain bi-directional knowledge sharing between community and academia		
0-5	<ul style="list-style-type: none"> • Stimulate networking and collaborations through research symposia and follow-up working groups* 	<ul style="list-style-type: none"> • Number community-academic health symposia
1-3	<ul style="list-style-type: none"> • Prepare a community workforce for receiving and sharing knowledge with underserved communities 	<ul style="list-style-type: none"> • Number of trained lay health workers trained to work in underserved communities
1-5	<ul style="list-style-type: none"> • Build academic and community researcher skills in partnered research, regulatory compliance and ethics in research, and organizational and practice change 	<ul style="list-style-type: none"> • Needs assessment to identify the high priority research training needs in partnered research • Number of community research training sessions
2-5	<ul style="list-style-type: none"> • Exploit innovative networking and information dissemination technologies 	<ul style="list-style-type: none"> • Number, type, and perceived effectiveness of key information technologies and dissemination channels
Aim 2: Strengthen community infrastructure for sustainable partnered research		
1-5	<ul style="list-style-type: none"> • Establish centers in communities that support community engagement and research 	<ul style="list-style-type: none"> • Criteria for success to establish community research centers vetted through the EOC
2-5	<ul style="list-style-type: none"> • Promote novel study designs • Strengthen incentives and motivation for research participation of community healthcare providers 	<ul style="list-style-type: none"> • Number and type of community centers established • Number of novel study designs that are feasible and practical for reproduction in other communities • Needs assessment to determine incentives and disincentives to improve community healthcare providers participation
Aim 3: Drive innovation in community engagement that accelerates the volume and impact of partnered research in diverse communities		
1-5	<ul style="list-style-type: none"> • Foster strategic demonstration projects that enhance CERP's community reputation and capabilities • Implement comprehensive community-partnered research initiatives, such as the "70 Block Project" 	<ul style="list-style-type: none"> • Number of community partnered research projects • Number of existing/new community partnerships • Number of pilot/seed grants and larger awards to conduct community partnered research • Number of reports and peer-reviewed publications • Number and type of new health education, health care navigation, and evidence-based policies

Year(s)	Specific Aims, Milestones and Key Activities	Evaluation/Tracking (E/T) Measures and Metrics
Aim 4: Build health services research (HSR) methods into partnerships to accelerate design, production and wide adoption of evidence-based practice		
1-5	<ul style="list-style-type: none"> Form HSR teams and conduct 2-4 methods studies annually, e.g., compliance, CER, implementation, diffusion, dissemination research Collect and analyze HSR data for translational research initiatives of community-partnered research involving analysis of needs, development of new interventions and/or implementation research 	<ul style="list-style-type: none"> Number peer reviewed HSR methods/policy studies Number of pilot/seed grants awarded Number of demonstration projects funded Number of products disseminated for broad community use (e.g., lay research summaries)
3-5	<ul style="list-style-type: none"> Expand HSR to analyze high priority delivery system, population, programmatic, and cost concerns to inform policy 	<ul style="list-style-type: none"> Involvement of HSR investigators in Translational Research Clusters Program
Aim 5: Establish a governance and operations structure that strengthens existing partnerships and builds new bridges between community and academia for research		
1	<ul style="list-style-type: none"> Formalize CERP governance including leadership, working groups and conflict resolution procedures 	<ul style="list-style-type: none"> Extent of shared governance and shared priority setting
1-2	<ul style="list-style-type: none"> Create a Community Research Liaison Office that builds trust, encourages community participation, supports investigator readiness, and links investigators with community partners 	<ul style="list-style-type: none"> Structured mechanism for conflict resolution Number of contacts/collaborations through the Community Research Liaison Office

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Translational Technologies and Resources Program: The Center for Translational Technologies (CTT)



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Abbreviations: AAMC — American Association of Medical Colleges, ADC—Alzheimer’s Disease Center, BIP — Biomedical Informatics Program, BSCRC — Broad Center of Regenerative Medicine and Stem Cell Research, CDU — Charles Drew University, CNS — Central Nervous System, CNSI — California NanoSystems Institute, CTSI — Clinical & Translational Sciences Institute, CTSI – UCLA CTSI Research Education, Training and Career Development Program, CTTM — Center for Translational Technologies and Methodologies, CVR — Center for Vaccine Research, DGSOM — David Geffen School of Medicine, EOC — Executive Oversight Committee, E/T – UCLA CTSI Evaluation and Tracking Program, GRAND — Group on Research Advancement and Development, IBD — Inflammatory Bowel Disease, ICMIC — In vivo Cellular and Molecular Imaging Center, IMED — Institute of Molecular Medicine, IRAS — Insulin Resistance and Atherosclerosis Study, ISB — Institute for Systems Biology, IUPAC — International Union of Pure and Applied Chemistry, LONI — Laboratory of NeuroImaging, MESA — Multi-ethnic Study of Atherosclerosis, NIDDK — National Institute of Diabetes and Digestive and Kidney Diseases, NSF — National Science Foundation, OIS — Office of Investigator Services, ORU — Organized Research Unit, PET — Positron Emission Tomography, TAG — Technology Affinity Group, TTR – Translational Technology Resource

1. OVERVIEW

The UCLA Center for Translational Technologies (CTT) is charged with fulfilling the Translational Technologies and Resources key function. We provide the structure necessary for investigators to readily access UCLA's rich resource of more than 100 biomedical cores. In addition, CTT accelerates the transition of emerging technologies into functional Translational Technology Resources (TTRs). With the University of Southern California and the University of California, Irvine, we are members of the Greater Los Angeles CTSA Coalition. The Coalition has indentified cores as one area where it can create infrastructure to foster collaboration at little cost.

In our prior review, CTT was reviewed with the Pilot and Collaborative Translational and Clinical Studies Program key function (**Pilot Program**) and received an aggregate score of 2. Reviewers praised the extensive experience of our CTT leadership; the wide variety of core resources offered; our plan for evaluating investigator needs; the many seminars, lectures and workshops planned on novel technologies; and our pilot grant program for encouraging technology development. In this application, we discuss how we overcome geographical boundaries with a transport service and multisite cores. We have moved the Translational Methodologies portion of the Clinical and Translational Technologies and Methodologies key function to our **Pilot Program**, where it receives greater prominence. To align CTT with the revised overall goals of the UCLA CTSI, this section has been substantially rewritten. Changes in this revision application are indicated by a vertical line in the left margin.

2. SPECIFIC AIMS

The UCLA CTSI provides the operations and governance necessary to facilitate successful transdisciplinary clinical and translational research. The overarching *mission* of the UCLA-CTSI is *to transform our academic-clinical-community partnership into a borderless institute that brings our combined innovations and resources to bear on the most pressing health needs in our diverse community*. The CTT provides the technological engine to drive this process forward. Medical discovery has long been linked with the development and application of new technologies and methodologies. These resources have elucidated the biological and molecular basis of health and disease and facilitated the design of improved tools and targeted therapies.

UCLA's culture of innovation has produced a wealth of cutting-edge technologies that have enabled groundbreaking translational science in cancer, cardiovascular disease, HIV and other grave diseases. However, our cores exist primarily as independent entities that are spread across individual investigators, laboratories, programs, centers and institutes. This can make them inherently difficult to learn about and access. In this context, a primary function of the CTT is to provide organization and structure, as well as a conduit through which translational investigators and technology developers can better collaborate. In a survey distributed to 200 clinical and translational researchers at UCLA in September 2010, 21% of respondents told us they needed better access to TTRs in order to conduct translational science. Our basic researchers have told us they need insights from clinical scientists to better develop TTRs. To overcome these barriers, the CTT's central focus is to provide streamlined access to cores to accelerate scientific translation and to spur development of novel TTRs. To achieve this mission, we will pursue three Specific Aims.

Specific Aim 1: Implement a system for providing centralized access to and ongoing performance monitoring of Translational Technology Resources (TTRs).

- Continue to evolve an all-inclusive, online database to connect translational researchers with core services in partnership with the UCLA CTSI Biomedical Informatics Program.
- Provide streamlined core access to CTSI clients through a voucher system based on peer-reviewed rationale and justification for core use.
- Conduct ongoing needs assessments of new and existing TTRs.

Specific Aim 2: Create an efficient mechanism for developing promising new technologies into functional TTRs.

- Promote cross-disciplinary interaction that will catalyze development of new technologies.

- Create a structured process to evaluate, prioritize and test whether emerging technologies can be developed into new CTSI TTRs.

Specific Aim 3: Conduct personalized counseling and continuing education programs to facilitate collaboration and assist translational investigators in selection and optimal use of TTRs.

- Recruit and train Technology Officers to advise individual Investigators and facilitate networking and core utilization.
- Establish a continuing education program and young investigator training with the **UCLA CTSI Research Education, Training and Career Development Program (CTSI-ED)**.

3. PROGRESS TO DATE

CTT accomplishments in the pre-award period include:

- Co-developing an Office of Investigator Services (OIS) with the Regulatory Knowledge and Support, Industry Relations, and Research Ethics Program (**Regulatory Program**) and Biomedical Informatics Program (**BIP**) to provide translational investigators with online tools to identify and access TTRs.
- Extending a systematic process for assessing the ongoing needs and trends for TTRs.
- Establishing investigator-initiated targeted grants programs to support the collaborative use of existing TTRs and the development of new TTRs.
- Establishing CTSI-wide educational programs on the use of TTRs with **CTSI-ED**.
- Pilot-testing a “voucher” system for CTSI-supported expenditures in existing cores.

4. SIGNIFICANCE: THE CTT CORE MANAGEMENT RATIONALE

Technological advancement waits for no one. The field is in a constant state of flux as technologies are born, reach maturity and eventually are superseded by new technologies. By extension, a TTR will have the same inherent life span as the technology upon which it is based. Some will be more transient, others more long lasting but no TTR can be expected to be permanent.

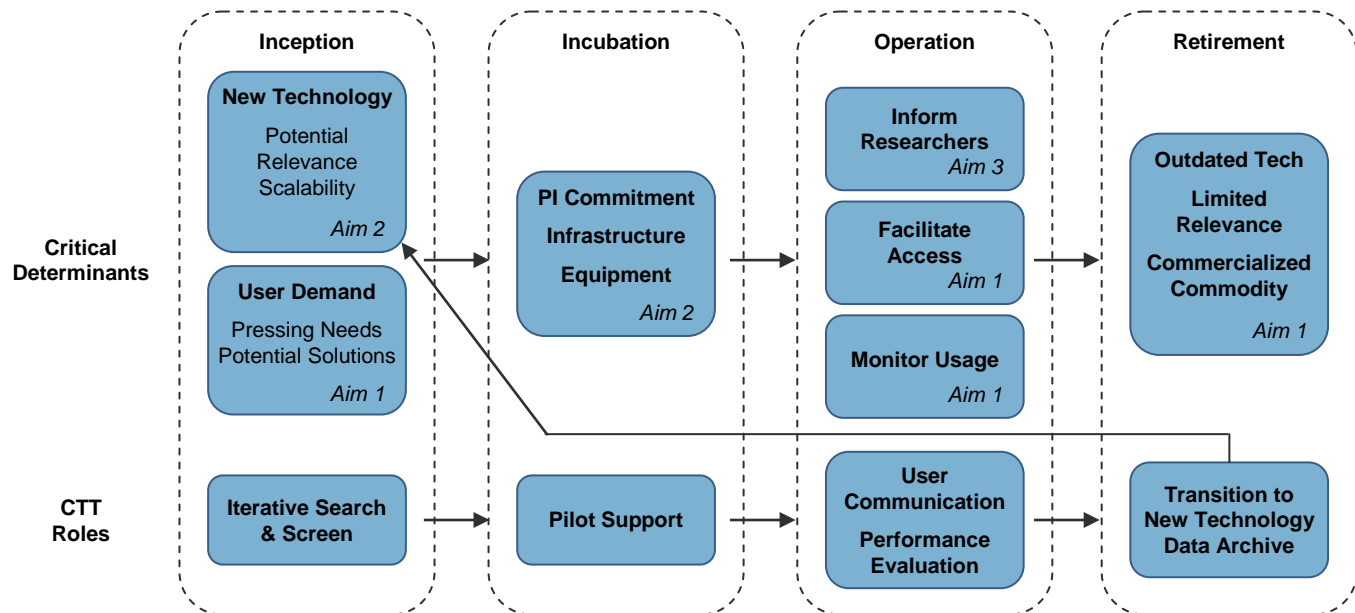


Figure 1. Workflow depicting major stages in the life cycle of a Translational Technology Resource. Stages are boxed. Arrows indicate directional development from inception to retirement. Critical determinants and CTT roles in the progression between stages are itemized. Diagonal arrow indicates transition path from old to new technology.

A primary role of the CTT is to foster the growth and progression of a TTR at every step of its expected life cycle (see **Figure 1**). At the earliest phases, the CTT seeks out promising new technologies that offer new

research venues or meet pressing needs of translational investigators. In the incubation phase, the process of expansion and standardization that is necessary for a technology to become a TTR is catalyzed. Critical questions include: ■ Is the technology sufficiently robust and scalable to meet investigator needs? ■ Are there pre-existing standards or do they need to be developed?

When the two above requirements are met, the nascent TTR enters its operational phase. The CTT informs/educates potential users, facilitates access and monitors the usage volume and quality of the output. Inevitably at some point, a TTR, either as a technology or a core service, ceases to be useful to translational investigators. When this happens, the CTT archives data to make sure that it remains available to investigators and expedites the transition to superseding technologies and TTRs.

Given its depth and juxtaposition of basic science and patient service facilities at all UCLA CTSI partner sites, the greater UCLA biomedical community provides an exceptionally rich and diverse array of technologies that could be developed into TTRs. However, it is anticipated that in the next five years of the CTSI, few if any technologies will run the gamut from inception through retirement. Many technologies have already made the transition to highly functional core services. Therefore, CTT will use “voucher” data to prioritize existing technologies, parse them into life cycle stages and establish a consistent and unified operational framework (see **Specific Aim 1**).

5. INNOVATION AND ENVIRONMENT

5.1. A fertile environment for inter- and multidisciplinary translational research exists within the UCLA CTSI. The cumulative strength of the UCLA CTSI Technology Program stems from the diversity and track record of its four partner institutions: the University of California, Los Angeles (UCLA Westwood Campus), Charles Drew University of Medicine and Science (CDU), Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center (Harbor-LA BioMed) and the Burns and Allen Research Institute at Cedars-Sinai Medical Center (Cedars-Sinai). UCLA is recognized leader in biomedical research and education. CDU is a leading minority academic medical institution. Harbor-LA BioMed and Cedars-Sinai represent premier academic county- and community-based medical institutions, respectively. The UCLA CTSI institutions have been at the forefront of: ■ building interdisciplinary research teams that create a fertile environment for synergistic discoveries ■ integrating powerful new technologies ■ facilitating the development of new investigators ■ developing novel strategies to facilitate the flow of information from the bench to the bedside to the community and back.

5.2. Bioscience Initiative and Technology Affinity Groups (TAGs) are the structures that organize UCLA biomedical core facilities. Coupled to an extensive and varied research community is an exceptionally strong technology base. Two independent campus-wide efforts have been made to create an organizational framework through which to access these technologies. In 2005, the Biosciences Initiative was instituted from the Chancellor's office as a mechanism to directly support biomedical core facilities. Core applications for these monies are peer-reviewed and prioritized annually. In the first half of 2010 alone \$874,500 was dispersed over 23 cores to catalyze biomedical research. In addition to giving direct financial support to cores, the Biosciences Initiative also imposed an organizational structure on core services. This resulted in creation of a searchable interactive website that currently lists almost 100 core services and which has been functional for the last three years. Each core listing contains: ■ a core description ■ contact information ■ links to core-specific Web pages ■ links to related services. This dynamic searchable Bioscience Initiative website will be made available to the CTSI Virtual Home and expanded to include the TTRs upon receipt of a CTSA (see **section 6.1.1.**).

The Biosciences Initiative demonstrates high-level commitment of the UCLA leadership for support of technology cores, it does not deal directly with challenges of performing translational research. To address this issue in 2006-2007 the UCLA CTSI convened a series of meetings to group cores into TAGs. TAGs were based on level of importance across the UCLA CTSI, and substantial translational and transdisciplinary activity. The result of this process was the identification of eight TAGs (see **Figure 2**) selected from a wide range of available technologies. These TAGs support clinical science and underpin the technological backbone to further the development of translational medicine within the UCLA CTSI. Using this framework, each of the available and developing TTRs falls under the purview of one of these eight parent TAGs.

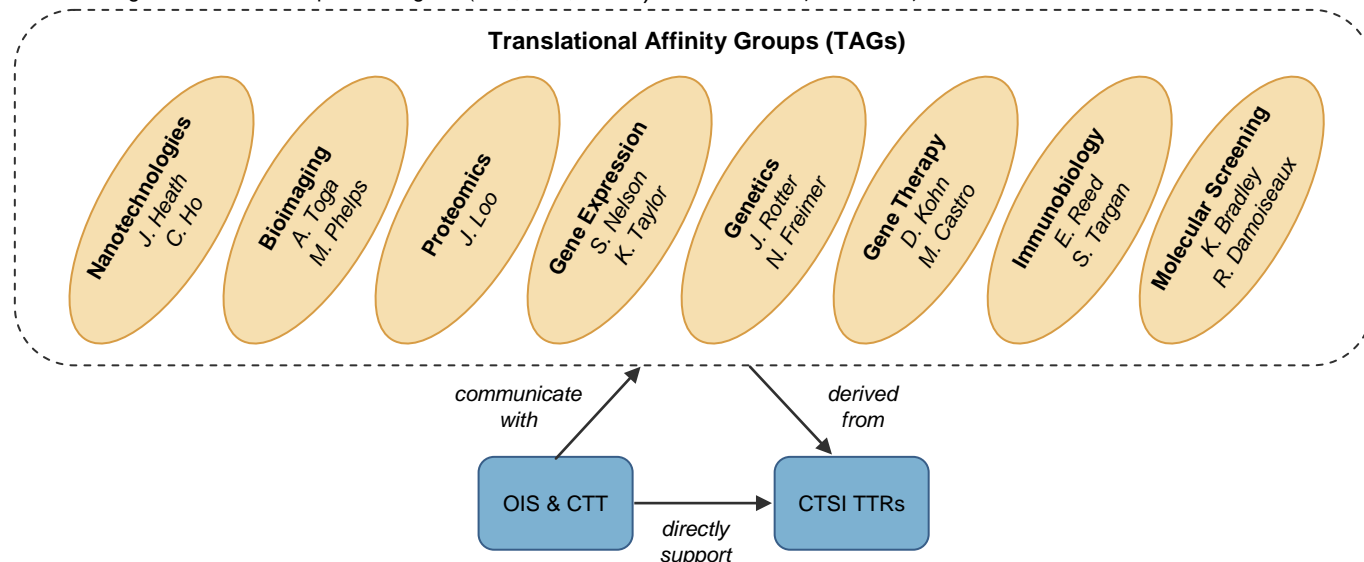


Figure 2. Technologies within the CTSTI scientific community have been organized into eight Technology Affinity Groups (TAGs); with associated TAG leaders indicated. These TAGs provide a framework from which selected technologies are developed into CTSTI-supported Translational Technology Resources. Interactions are described in italics. Legend: OIS – Office of Investigator Services; CTT – Center for Translational Technologies; TTR – Translational Technology Resource

5.3. Bioimaging demonstrates UCLA’s capability for developing translational technologies. Though space restriction precludes offering in depth descriptions of all eight TAGs, Bioimaging serves as illustrative example. By developing and applying a wide range of novel technologies, we have created core facilities for imaging research subjects running the gamut from small animals to humans. Small animal models have long played central roles in preclinical testing of new therapeutics. Recognizing that traditional preclinical testing methods were both slow, lacked precision and required large numbers of animal subjects, in 1996, UCLA researchers Harvey Herschman and Michael Phelps initiated a multi-disciplinary program to develop novel imaging technologies. This resulted in the creation of the first non-invasive positron emission tomography (PET) instruments suitable for imaging small animals. In 2000, this program was one of the first three In vivo Cellular and Molecular Imaging Centers (ICMICs) to be awarded by the NCI/NIH; it has just received its second consecutive five-year renewal. Over the last decade, PET evolved and now has multiple clinical applications, including the detection of Alzheimer’s disease and staging various cancers. The UCLA ICMIC has developed novel technologies that utilize state of the art imaging instruments (microPET scanners, microCT, optical imaging instruments, whole-body digital autoradiography) to non-invasively study disease progression, stratification of subject phenotypes and response to therapy. Of great importance, the ICMIC community has expanded from its original basic science disciplines (e.g., synthetic chemists, materials science engineers, molecular/cellular biologists) to now include clinical investigators directly involved in patient care.

Complementing these advanced small animal imaging facilities are equally robust efforts to develop tools that can be applied directly to human imaging studies. The Laboratory of NeuroImaging (LONI) headed by Dr. Arthur Toga, who is also directs **BIP**, has been a leader in creating bioinformatic methods for quantitatively measuring and comparing both structural and metabolic (dynamic) neuro-anatomic features across human populations. This capability has already led to uncovering key neural features associated with normal development and human disease.

5.4. Longstanding tradition of cross-departmental research programs. While the breadth and depth of the UCLA CTSTI community and technology base are strong assets, the key to catalyzing translational research has been the ability to create high functioning inter-departmental research entities. A recent example of this activity is the Institute of Molecular Medicine (IMED), a multidisciplinary community of basic and clinical scientists. IMED is organized along team concepts focused on elucidating fundamental biological processes that are common across a number of diseases with the intent of developing novel molecular diagnostics and therapeutics. IMED Program Areas now range from specific cancers, to inflammation and infectious disease, to degenerative neurological diseases. IMED was initiated in 2004 under the direction of Drs. Michael Phelps

(Chair of Molecular & Medical Pharmacology) and Jonathan Braun (Chair of Pathology & Laboratory Medicine) using 50,000 square feet of newly renovated space in the David Geffen School of Medicine (DGSOM). IMED has 24 founding faculty (~60% are MD/PhD or MD) of clinicians, biologists, bioinformaticians, systems biologists, chemists, mathematicians and physicists along with funded partnerships with 78 faculty at UCLA, Caltech & the Institute for Systems Biology (ISB) in Seattle. While IMED has members of the National Academy of Sciences and HHMI, it has a major constituency of young clinical and basic scientists. IMED also has a PhD program in Molecular Medicine that requires two mentors, one a basic and the other a clinical scientist, as well as a privately funded program in "Clinical Translational Scholars." It conducts a weekly seminar series on multidisciplinary topics. The NIH funding of IMED includes the Caltech/UCLA/ISB NCI Nanotechnology Center of Excellence grant (renewed in 2010 for five years) and an NCI Molecular Imaging Center grant (renewed in 2010 for five years). In summary, IMED represents on a small scale the kind of transdisciplinary team-based science we expect to catalyze across our four institutions and community partners through the UCLA CTSI.

5.5. Our cores are facilitating successful translational research. Access to advanced technologies and cores and a research faculty committed to excellence are key ingredients for creating an environment that promotes translational research. These examples show our capacity to cross institutional, geographic and disciplinary boundaries to achieve translation by using these cores. The CTT will further catalyze the translational process.

- Using microarray core technologies, investigators Paul Mischel and Stan Nelson were able to identify distinct and prognostically significant subsets of patients suffering from glioblastoma multiforme. Using similar technologies, Drs. Stephan R. Targan, Jerome Rotter and Jonathan Braun have delineated the interplay of host biology² and enteric microbial phenotypes, establishing powerful biomarkers for Inflammatory Bowel disease management in children and adults.³⁻⁵ This collaboration between researchers from Cedars-Sinai and UCLA-Westwood demonstrates our ability to cross physical boundaries.
- The CADUCEUS Trial, an NHLBI-funded cardiac stem cell clinical trial, was designed by Eduardo Marban and colleagues in nanotechnology. It is a novel, phase I randomized, dose escalation study testing the safety and efficacy of intracoronary delivery of cardiomyosphere-derived stem cells in patients with ischemic left ventricular dysfunction following a recent myocardial infarction research.
- UCLA chemists and cancer investigators utilized the small molecule screening facility to develop a novel anti-androgen compound (MDV3100) that is currently in clinical trials for resistant prostate cancer.
- Utilizing the Jonsson Comprehensive Cancer Center GMP facility, CTSI investigators prepared an innovative lung cancer vaccine based on UCLA discoveries. The phase I trial is ongoing. Using this same GMP core, Dr. Donald Kohn is studying the ability of recombinant replication deficient retroviruses to rescue pediatric patients with congenital immunodeficiencies.
- Drs. Irvin Chen and Jerome Zack used small animal core facilities to develop murine model systems to gauge effectiveness of hematopoietic stem cells transduced with shRNA or ribozyme constructs in treating HIV. Together with Dr. Ron Mitsuyasu and collaborators, these strategies have recently been advanced to phase I and II clinical trials.
- Using the nanopico and small animal imaging cores, Drs. Fuyu Tamanoi and Jeffery Zink have developed mesoporous silica nanoparticles that can target delivery of anti-cancer agents in preclinical tumor models.

6. APPROACH

6.1. Specific Aim 1: Implement a system for providing centralized access to and ongoing performance-monitoring of currently available TTRs. Currently more than 100 functioning, but often underadvertised and underutilized, cores offer a potential wide range of services to the UCLA biomedical community. The CTT's task is to provide the structure needed to promote optimal utilization of these cores. As noted above, solutions to some of these tasks have already been set in motion. CTT will extend and refine these ongoing efforts.

First, the CTT will further refine mechanisms for connecting translational researchers to cores through online tools (e.g., the CTSI Virtual Home) and personalized education and counseling. Second, CTT is in the process of implementing centralized practices to address the physical separation across four different campuses and

redundancy in particular services. Third, CTT will apply its recently piloted peer-reviewed financial (“voucher”) support plan to optimize performance for translational researchers. The Research Services Funding Opportunity provides vouchers of up to \$20,000 per year. In the first 17 months, we awarded a total of 26 vouchers totaling more than \$100,000.

6.1.1. CTT will streamline and facilitate access to UCLA cores. The plethora of core services that are currently in service can be both a boon and a bane to translational researchers. On the plus side, the depth of on-hand technologies is a tremendous asset to the biomedical community. Who would ever opt for less? On the downside, the sheer number of cores makes it easy to lose track of what is available even for experienced researchers. For new investigators, the numerous options can overwhelm and in effect render them inaccessible. Where do they start? To provide an approachable structure to address this problem, CTT will organize current core services across the four campuses of UCLA CTSI into three tiers, based on their relevance to translational research and support by the CTT:

- BioSci cores. These base-level cores will be included in the CTT core internet resource and in annual user surveys administered through the CTT; service from these cores can be gained with CTSI use “vouchers”.
- TTR level-1. Core at this level will also receive direct use monitoring and inclusion in educational outreach programs (see **section 6.1.3.**); service from these cores can be gained with CTSI use “vouchers”.
- TTR level-2. These cores have the highest translational impact and will receive direct financial support through the CTT (in addition to the voucher means of support given to lower tier cores).

Since the UCLA CTSI consists of four distinct campuses, location of cores will be taken into consideration for those services requiring physical user-core interactions. For example, one of the highest utilized UCLA cores is the flow cytometry lab run through the Jonsson Comprehensive Cancer Center. This core encourages investigators to use core equipment after sufficient user education. Similar flow cytometry cores exist at Cedars-Sinai and LA Biomed. In this context, support of a multi-location core service could be warranted. The CTT steering committee will review core assignments annually and assess core prioritization by user demand, core usage and core performance. In anticipation of this eventuality, we have established a transport service to provide access to single-site cores (see **section 6.1.2.1.** below).

We are in the process of updating our online tools to logistically tie cores together and enhance accessibility to translational researchers. Working with BIP, we will unite these two entities into a unified structure in the CTSI Virtual Home. Extending the internet platform already in service for the Biosciences Initiative, the CTT will create an all-inclusive, accessible and searchable resource that connects translational researchers to core services regardless of where they exist in the UCLA academic network of campuses and community resources. This database-backed website will be updated biannually and CTSI membership will receive electronic notification of changes in core services.

6.1.2. CTT will directly support TTR level-2 resources. In year-01 of the grant this decision of which TTR level-2 cores to support will be based on formal survey data collected from UCLA faculty at all CTSI academic and community sites in Los Angeles County. Thereafter, annual core utilization will determine the level and specificity of CTT support. Initially, we estimate that eight to 10 cores will merit TTR level-2 status. Considering that these cores are already high functioning, in year-01 of the grant the CTT will primarily support and supplement pre-existing facilities. From year-01 onward and using the peer-reviewed mechanism detailed below, we will individualize our support to TTR and investigator needs. For example, support may involve purchasing necessary equipment and/or recruiting skilled personnel to the core; such an option may add a degree of extensibility to core services in high demand. Alternatively, CTT may aid researchers by supporting data analysis assistance, a pressing need for TTRs generating large and complex datasets. Finally, in the future it may be that CTT discrimination between what is a level-2 and level-1 TTR is no longer possible, because CTSI-supported investigators are using such a broad range of core resources. If this is the case, then the CTT Steering Committee in conjunction with the EOSEO may decide to convert all expenditures on behalf of CTSI investigators to a voucher system for core use.

As described below in **section 6.1.2.3.**, the “feed-forward” side of the utilization equation a peer-review mechanism for prioritization of core use and a voucher system paying for core utilization by individual investigators will be established. On the “feed-back” side of the utilization equation TTRs will receive funding

proportional to the volume of service promised by the awarded vouchers. In this way, the CTT will stimulate both TTR growth and investigator usage in a coordinated fashion.

6.1.2.1. The CTT Service Core will provide a centralized framework of operation for TTRs. We will create a Service Core to oversee interactions with level-2 and to a lesser extent level-1 TTRs. When functional, this core will be unique in that its primary function is to coordinate the operations of other TTRs. Three Technology Officers will man the Service Core to guide user access to TTRs (see **section 6.3.**) and facilitate the functioning of level-2 TTRs. Using a comprehensive reference laboratory model, the Service Core will provide a mechanism for sample pre-processing and distributed biomarker testing. Specifically, the Service core will:

- Create efficient and homogeneous specimen encounter and pre-processing procedures;
- Establish daily schedules of transport between different CTSI campuses and TTR laboratories; and
- Implement a bar-code tracking system, linked to the specimen encounter system, to monitor status and location of specimens.

The CTT Service Core will use procedures already implemented for the NIH-funded UCLA Clinical Immunology Research Laboratory, which serves multiple UCLA CTSI academic and community sites and is currently under the direction of Dr. Anthony Butch (see Investigators below). In this way, the Service Core will facilitate the flow of samples to TTRs across the UCLA CTSI partner institutions.

6.1.2.2. Supervised access to level-2 TTRs will be established. The CTT Technology Officers will have responsibility for coordinating use of level-2 TTRs by CTSI investigators. Initial access will be through the CTSI Virtual Home, built upon the current Biosciences Initiative portal, that provides links to TTR specific sites. The CTT Technology Officers will also work with the BIP to enhance existing websites that provide information regarding methodologies, sample and access requirements to core laboratory technologies as well as approaches for data delivery to investigators. They will update the website as needed to reflect new technologies that are being introduced into pre-existing TTRs, and they will highlight new services to raise user awareness. Technology Officers will monitor sampling coordination and dispatch, turnaround time and data quality; identify problems; and implement corrective actions. To maximize efficiency, each Technology Officer will serve as the primary contact for several level-2 TTRs, although all officers undergo regular cross- and group-training. This unifying infrastructure will transform the selection, access and use of TTRs by translational investigators across the UCLA CTSI.

6.1.2.3. A streamlined system of project review and payment for level-2 TTR services will be utilized. Translational investigators will have a number of options for accessing core personnel support through the CTSI: 1) they may interact directly with TTRs; 2) they may request support in the context of a CTSI-sponsored "protocol" (see **Clinical and Community Research Resources [CCRR]** and **Regulatory Knowledge and Support, Industry Relations and Research Ethics [Regulatory]** Programs); or 3) they may request core services and support by using the CTT key function personnel as an intermediary. The latter mechanism will be used when i) the investigator seeks a price discount and/or priority service, ii) prolonged or high volume TTR service is needed as a part of a large project, iii) service is being supported through a young investigator or seed grant awarded through the Pilot Program. Under any of these circumstances, Technology Officers will parse core requests into three categories: 1) studies that have been peer-reviewed and funded by recognized extramural agencies; 2) studies that have not yet been approved for funding by a peer-review system, but that are not requesting additional CTSI support beyond the negotiated rate (see below); and 3) studies that have not yet been approved for funding by a peer-review system and that are requesting additional CTSI support beyond the negotiated rate.

For those studies in category #1 above, UCLA CTSI researchers requesting use of a CTSI-supported TTR, will complete a two-page request form briefly outlining the study. For studies not previously peer-reviewed and funded, we will require that the investigator provide an overview of the study's: 1) objective, hypothesis, and significance; 2) potential for translation; 3) study design and feasibility, and data analysis plans; 4) track record of the investigator; 5) collaborative nature of the study; 6) involvement of community; and 7) funding (actual or proposed) source. We will offer two avenues for possible approval:

- *Expedited (regular) review:* The Technology Officer will be empowered to approve studies for Core utilization after a review of the application, consultation with the Core Director and estimation of utilization

costs and the level of cost recovery from the investigator. Review and approval will be completed within 7 days. This expedited review will apply only to requests that do not exceed \$25,000 in total estimated core costs (before cost recovery).

- *Full review:* If the total estimated core costs of the study exceed \$25,000, the study is industry-initiated and supported, or the Technology Officer or Core Director are uncertain about the nature or extent of the request, they will forward the proposal with their comments to the CTT Steering Committee for review. The Committee will meet monthly, and will determine the priority of the utilization proposed and the level of recovery of cost from the investigators (see below). Minutes of its deliberations will be kept.

Allocation of service vouchers, in denominations of \$1,000, \$5,000 and \$10,000, will be made on the basis of scientific merit and need for the resources, using 5-point number scale for merit and a 3-point letter scale for need (see **Table 1**). Priority for and the amount of vouchers allocated will proceed from 1A, 2A, 1B, 3A, 2B, 3B, 1C, 2C, 3C; deferred or denied request will not be considered for support. Once the core request is approved and voucher amount determined, the investigator becomes responsible for contacting the core director to discuss details of implementation of the study, although Technology Officers may assist with this process.

Table 1. Shown is the 5-point number scale for merit and a 3-point letter scale for need used to score CTT services for resource allocation.

Score	Outcome	Score	Comment
1	Approval	A	Essential (highly meritorious, usually NIH-supported, could not be done without CTSI support)
2	Approval with comment (PI response not required)		
3	Approval pending PI response	B	Important (investigator initiated, CTSI resources would greatly facilitate study)
4	Approval deferred (requires submission)	C	Desirable (CTSI support would be a convenience but not a necessity for the PI)
5	Denial		

6.1.2.4. Core cost recovery and cost-sharing with investigators will be implemented. Ideally once established, TTRs can be run as self-contained small businesses with a fixed subsidy from the CTSI. To achieve this, the CTT Steering Committee will develop standard policies and procedures of cost recovery/sharing for resource and core utilization. Such policies and procedures will require approval of UCLA CTSI Executive Oversight Committee (EOC). Investigators may be required to help defray the cost for each procedure/test through a re-charge mechanism as determined by the CTT Steering Committee. In principle, there are three tiers of charges:

- *Low* for investigator-initiated NIH, federal, state-supported, peer-reviewed studies; investigators may be charged for recovery of costs of reagents, technical time or recurrent fixed costs;
- *Intermediate* for investigator-initiated and foundation- and industry-supported protocols; and
- *High* for industry-initiated or -sponsored studies; in such cases, CTT will seek full recovery of costs, including administrative costs and fees for protocol review and startup, from investigators.

This three-tiered cost schedule for procedures, tests, and services will be posted in the secure intranet of the UCLA CTSI Virtual Home. Depending upon cost and need, special reductions in cost sharing may be given to young investigators to allow them to generate data for extramural grant application.

6.1.2.5. Level-2 TTR performance and utilization will be tracked. The CTT Steering Committee will track utilization statistics and quality control performance metrics of each level-2 TTR on a biannual basis. The administrative office at the core site will provide utilization data to the CTT Steering Committee and to the UCLA CTSI **Evaluation and Tracking Program (E/T)**. The CTT Steering Committee will review over- and under-utilization and implement necessary constructive changes to ensure optimal utilization of each core. For example, a persistent drop off in a particular level-2 TTR's utilization, in spite of consistently strong core performance, may indicate that the TTR is nearing the end of its maximum usefulness and approaching retirement phase (see **Figure 1**). The CTT Steering Committee will decide whether to convert that level-2 TTR with direct CTT support to an indirect, "voucher-paid" (see **section 6.1.2.3.**), level-1 TTR (see **section 6.1.3.** below); this decision will be made with solicited feedback from the core director as well as input from translational researchers who have recently used the core.

6.1.3. Level-1 TTRs will use a TAG approach. Though not directly financially supported by the CTSI, level-1 TTRs still represent potentially important resources to translational investigators with granted vouchers to spend (see **section 6.1.2.3.**). The CTT will utilize its Technology Officers to guide UCLA CTSI investigators to the availability, use, limitations, and logistics of currently available level-1 TTRs. In addition our Technology Officers will develop agreements with these existing TTRs for discounted or standardized rates. To provide an organized approach to level-1 TTRs, the CTT will utilize the pre-existing TAG structure (see **Figure 2**). Each TAG will be represented by 1-2 individuals from one of the UCLA CTSI institutions. If a certain Level-1 TTR is being utilized by a number of CTSI-supported investigators and services being paid for with CTSA vouchers, the CTT Steering Committee will negotiate on behalf of UCLA CTSI investigators for beneficial cost recovery rates with a laboratory or resource within a TAG through the TAG leaders.

Primary responsibility for facilitating and monitoring use of TAGs belongs to the Technology Officers, working in collaboration with OIS Research Facilitators (see **section 6.3.1.**). The Technology Officers will actively engage the supervisors of TAGs so that they have a good sense of demand and can recommend when one or more labs should work collaboratively and/or expand their services. In this manner, the CTSM will provide information that may help labs find new collaborators and/or decide if there is sufficient demand to expand. Finally the TAG leaders participate in seminars to alert and educate CTSI investigators about level-1 TTRs (see **section 6.3.2.**).

6.1.4. Systematic ongoing needs and trends assessment for TTRs will be performed. In order to ensure that the technological needs of the UCLA CTSI community of translational investigators is continuously met, the CTT will undertake periodic and systematic needs assessments. This will include ongoing and periodic reviews of both UCLA and outside CTSI resources to provide a broad perspective on new knowledge and trends in TTRs. CTT will perform needs assessments at both individual and system-wide levels. We will generate informal assessments of the needs of the CTSI investigator community through queries fielded by the Counseling Service (see **section 6.3.**) and through personal contact between the Technology Officers and the TTRs and investigator community. In this regard, the Technology Officers will be expected to visit regularly with investigators across the performance sites of the CTSI. This will be accomplished by scheduled brown bag lunches in conjunction with TAG seminar series. In addition, the Technology Officers will regularly perform investigator interviews with individuals identified through regular discussions with the CTT leadership, the leaders of other UCLA CTSI Programs and the sources they identify for further follow-up; this is likely to also include Technology Officers at other CTSA in the region and across the country. This will assure ongoing communication between Technology Officers and CTSI investigators spanning the bench to bedside to community translational continuum. Finally on system-wide level, the CTT will proactively conduct an annual online needs survey of the CTSI investigator community.

In many ways, the needs of translational investigators can best be monitored through their research projects themselves. To maintain close contact with the CTSI community, Technology Officers, in a staggered fashion, will attend a significant proportion of scientific presentations within the CTSI as well as a selection of relevant national meetings. Technology Officers will conduct weekly debriefings with the entire team. They will report monthly on new trends in TTRs and identified needs within the CTSI to the CTT Steering Committee.

6.2. Specific Aim 2: Create an efficient mechanism for developing promising new technologies into functional TTRs. There is no consistent and definitive source of new ideas. According to legend, Sir Isaac Newton simply had to meet the right apple while sitting under a tree to divine primary laws of physics. In contrast, Kary Mullis required a late night road trip up the Pacific Coast Highway for the idea of the Polymerase Chain Reaction to take form in his head and revolutionize molecular biology. The UCLA CTSI is blessed with an exceptionally rich and creative biomedical research community that provides a steady flow of new ideas and technologies. A primary role of the CTT will be to cast a broad net and cull out those ideas that have the most promise in a translational research setting. At the same time, the CTT will take an active role in promoting cross-disciplinary interaction to catalyze development of new translational technologies. We have established a structured process to evaluate, prioritize and test whether these technologies can be developed into new CTSI TTRs.

6.2.1. Diverse sources will be reactively tapped and proactively stimulates to find new TTR technologies. Innovation often arises not from those immersed in a field but from those who are approaching the field from a completely different perspective. For this reason, it will be crucial to maintain a broad and

constant surveillance for promising new technologies from a wide variety of potential sources (see **Figure 6**). CTSI and CTT investigators, technology officers, TAG leaders and core directors will all be recruited to this effort. Potential finds will be electronically communicated directly to the CTT through short online forms circulated on the Virtual Home intranet that briefly describe the new technology, its potential benefits/impact and pertinent contact personnel. While such reactive strategies have proven fruitful in the past, the CTT will also take proactive measures to stimulate interactions and catalyze the active interchange of ideas across different disciplines. These events will be open to all scientific, clinical and community members of the CTSI interested in learning about translational technologies. By bringing together people with a diverse mix of interests and experiences, these events will not only foster ideas for new technologies but also lead to translational research collaborations. Events include:

- Monthly seminars to highlight new TTRs within and outside the CTSI, including those still in development;
- Once-yearly workshops on an emerging TTRs within the CTSI, and their potential applicability to ongoing CTSI-based research and core function;
- Monthly interdisciplinary lectures that focus on presenting speakers and topics which are not traditionally found within biomedical disciplines, such as philosophy, business, manufacturing, government, or engineering. The current weekly seminar series sponsored by IMED is a prime example of this sort of wide-ranging and cross-disciplinary effort that will be engaged to promote new translational research interactions.

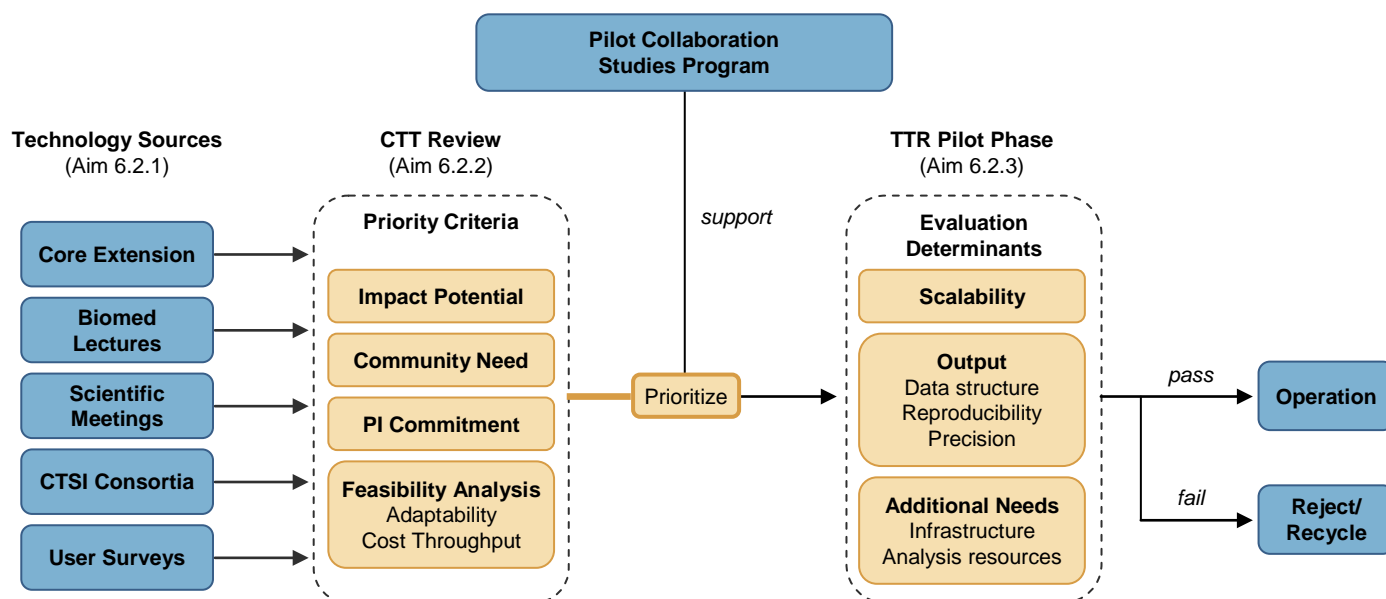


Figure 3. Workflow for creation of new TTRs. New technology sources, evaluation criteria and outcomes are boxed. Actions are indicated by arrows with italicized text. Outcomes appear in dash-line boxes.

As Initial descriptions of new technologies are submitted to the CTT, staff will directly contact labs harboring these technologies for further information, including the desire and willingness of the PI to offer the technology as a TTR. CTT leadership will assess this information at its monthly meetings. If the consensus is positive, the CTT will encourage and assist the PI in submitting an application for a Novel Translational Technologies and Methodologies Award. These awards will support the development of up to three promising new technologies and methodologies annually in the amount of up \$100,000 each, renewable once on an annual basis. They will be offered through the **UCLA CTSI Pilot Program**.

6.2.2. New TTRs will be closely monitored during their incubation phase. What may have looked good on paper rarely directly transmutes into fact. There are almost always unforeseen bumps in the road to developing a new core service. Furthermore, preliminary estimates of a candidate technology’s scalability, reproducibility and precision, can differ greatly from actual results. Expectation does not always match reality. Finally, it may become clear during the development process that additional support is needed either in the form of equipment and/or infrastructure. As such, the CTT will take an active role in nurturing and supporting new TTRs; since we have made the investment, we want to see them succeed. Each new TTR in development will be assigned a

CTT investigator or Technology Officer who will oversee the process on a weekly to monthly basis. The assigned CTT investigator will work with the technology PI or officer to create a feasible time line for new TTR development. Common goals include:

- Optimization of assay conditions and empiric determination of limitations in 6–9 months;
- Establishment of core workflows and performance of at least 3 trial runs in 9–12 months.

The CTT will make every effort to address any unanticipated needs that arise, on an ad hoc basis if necessary. The hope is that by the end of 12 months a new technology will be ready to enter operation and become available to the CTSI community as a new TTR. (see **Specific Aim 1**).

6.2.3. Support for new TTRs will be leveraged with pre-existing UCLA programs. An immediate goal for new TTRs developed through the CTT, is that once functioning, they will also be competitive for support through other UCLA programs such as the Chancellor's Biosciences Initiative. Taking a broader perspective, forming substantive links between the CTT and programs such as the Biosciences Initiative, will enhance both efforts. As a step in this direction Dr. Chris Evans head of the Biosciences Initiative, will serve as a CTT investigator and Dr. Chris Denny head of the CTT, will be on the Biosciences Initiative Selection Committee.

6.3. Specific Aim 3: Establish personalized counseling resources and continuing education programs to assist translational investigators in selection and optimal use of TTRs. The ultimate tragedy of any core service is death by non-use. The best technology coupled with the most efficient workflow strategy all comes to naught if investigators simply do not show up to use the facility. For this reason, a firm connection to its user base is a key prerequisite for any successful core. To accomplish this goal the CTT will reach out to translational investigators at both individual and programmatic levels.

6.3.1. Services will be extended to assist investigators in understanding, selecting, and utilizing the optimum TTR for their research. Translational investigators vary in their awareness and understanding of available TTRs and often need guidance on the availability and optimal choice of TTR needed. This barrier is to be addressed by the CTT Service Core, by recruiting and training of Technology Officers, who will liaise with and advise individual Investigators, and facilitate networking and maximize utilization.

Technology Officers will serve as domain specialists within the Office of Investigator Services (OIS), situated within the CTSI Regulatory Program. The OIS is the initial point of contact between investigators and the UCLA CTSI. It provides information and makes referrals to UCLA CTSI Programs, including the CTT. Following the experience and model of the UCLA Genomics Expression Core, we know that investigators lacking expertise in an advanced technology are typically impeded on how best to consider alternative technology platforms and how best to initiate collaboration vs. core service interactions for technology utilization. TAG faculty, Technology Officers and CTT TTR Directors are available to investigators for such consultations by e-mail, phone inquiry, and office visits. Inquiries by individual investigators, staff or OIS Research Facilitators are triaged by the Technology Officers, who will respond to most questions directly; more complex inquiries will go to appropriate core directors or TAG members. Core directors and TAGs will develop "on-call" or office-hour schedules to permit investigators timely and orderly access to the required consultations. In particular, the consultation service will be a critical starting point for recruitment of new investigators into the interdisciplinary research teams. A critical barrier for adoption of new technologies is frequently cost, particularly for new or emerging investigators. The **Pilot Program** seed grants provide support to investigators seeking to integrate new technologies and related collaborations into their studies. The Technology Officers provide expert guidance to investigators in seeking out such funding. The Technology Officers will work with the staff of the UCLA CTSI Biomedical Informatics Program (BIP) to refresh the CTT Resources Directory in the Virtual Home.

We intend to have two Technology Officers (.75 FTE each), who will cross-train and be familiar with all TTRs at all partner institutions. We expect Technology Officers to develop specific areas of TTR expertise (e.g., genomics and hormonal assays), In addition, we expect them to have a presence at all partner institutions on a rotating basis. This will ensure that they are familiar with the needs of investigators and the available and emerging TTRs at each UCLA CTSI institution. The Technology Officers will be coordinated and directed by Anthony Butch, PhD, head Technology Officer, coordinates and directs the Technology Officers with oversight from the CTT Steering committee. Dr. Butch is also responsible for reporting operational information on cores which will permit evaluation of their quality and productivity to the CTT Steering Committee.

6.3.2. Program of continuing education on the use of TTRs will be established. Through the CTT, we will amplify our current activities in this aim by a) teaching translational technologies and methodologies to medical and PhD students, and clinical and translational post-docs and fellows, as part of their overall training and b) establishing ongoing lecture series, of varying formats, coordinated by the staff and leadership of the CTT. Education and training will be provided by CTT Technology Officers, TAG leaders, CTT leadership and invited faculty/investigators. These activities will be coordinated through a Technology Training Committee, led by Dr. Scott Filler and in conjunction with the **CTSI-ED** Program.

6.3.2.1. Focusing on junior or emerging clinical and translational investigators. Each of the UCLA CTSI partner institutions offers “junior investigator” courses through the K30 program (see UCLA CTSI Education key function) designed to assist developing new investigators. Subjects include: obtaining research funding; designing experiments and clinical trials; analyzing and interpreting data. TAG leaders will develop a module for the K30 program dedicated to Translational Technology to complement the Genetics module currently in the curriculum. This Technology module is specifically devoted to the topic of utilizing innovative technology to address translational research questions. Young investigators will also be informed as to the structure and functions of the CTT and its activities. This strategy is intended to help remove barriers between established investigators and technology experts on one hand and in developing new clinical and translational investigators on the other.

6.3.2.2. Educating through TAGs. We plan to utilize the TAG structure to undertake a significant proportion of the educational effort in the selection, use and limitations of TTRs. The TAGs will institute a seminar series devoted to the general topic of how to use their specific types of technologies to address research questions. This seminar series will occur twice monthly and individual TAGs will rotate responsibility for organizing expert speakers for their technologic discipline. With the assistance of the OIS staff, these series will be webcast via live video feed and stored in a Web-accessible archive for future reference as we are doing currently for the K30 webcasts. Each TAG will also institute a biannual workshop for more intensive continuing education on each technology area. This will be facilitated by materials created for the seminar series and may be done more frequently depending on the level of interest in the UCLA CTSI community. Again, rotation of workshop sites among the CTSI partner institutions and Web/pod-casting will be used to disseminate content throughout the UCLA CTSI community.

7. INVESTIGATORS

An outstanding team of translational scientists with wide-ranging expertise in the development and application of novel technologies leads the CTT. The CTT Steering Committee is the core group responsible for CTT governance (see **Figure 4**). All investigators listed below form the CTT Steering Committee, which is chaired by Dr. Denny. This committee establishes the needs and priorities for resource allocation; adjudicates problem resolution; approves, prioritizes, coordinate and manages CTSI collaborative interactions involving informatics resources and services; and collaborates with the other CTSI core programs on informatics initiatives and planning. The CTT Steering Committee is also charged with developing long-term strategies for the growth, continued relevance and success of CTSI translational efforts and identifying translational opportunities within the CTSI that have the greatest potential impact on public health (in keeping with broad themes and emphases of the Institute). The CTT Steering Committee reports to the UCLA CTSI Executive Oversight Committee (EOC), the key oversight committee of the CTSI.

- **Christopher Denny, MD**, Professor of Pediatrics in the division of hematology/oncology, chairs the CTT. Dr. Denny has over 20 years of productive experience performing translational research investigating molecular mechanisms underlying pediatric sarcomas. Dr. Denny has immediate experience in two aspects that are crucial to the success of this program: 1) direct participation with running a busy technology core; and 2) direct involvement in developing internet tools to support core services. Together with Dr. Stan Nelson, Dr. Denny has been the co-director of the Gene Expression Core of the Jonsson Comprehensive Cancer Center. With Dr. Robert Dennis he also co-directs the Computer Technology Research Lab, a bioinformatics service focused on creating database-backed websites to support research and education in the UCLA School of Medicine.
- **Donald Kohn, MD**, Professor, Department of Pediatrics and Department of Microbiology, Immunology, and Molecular Genetics, and member of the Eli and Edythe Broad Center of Regenerative Medicine and Stem

Program Director/Principal Investigator (Last, First, Middle): Dubinett, Steven, MD

Cell Research Center will also serve on the CTT. For the last 20+ years, Dr Kohn has been a leader in developing and applying novel gene therapy strategies to treat pediatric immunodeficiency diseases through transplantation of genetically engineered hematopoietic stem cells.

- **Jerome Rotter, MD** is the Director of Research and Co-Director of the Medical Genetics Institute, Director of the Division of Medical Genetics (Department of Medicine) and Director of the Common Diseases Program at Cedars-Sinai, and Professor of Medicine, the David Geffen School of Medicine (DGSOM) at UCLA. Dr. Rotter's research focuses on identification of the genetic basis of common diseases by applying genomic technologies including genome-wide association (GWAS) and exome sequencing.
- **Scott G. Filler, MD** is a Professor of Medicine, Associate Professor of Infectious Diseases and the Co-Director of the Harbor-LA BioMed Research Institute Flow Cytometry Facility. His areas of research encompass fungal pathogenesis and endothelial cell physiology.
- **Anthony W. Butch, PhD** is an Associate Professor, Department of Pathology & Lab Medicine; Director of Chemistry, Toxicology, Immunochemistry, and Support Services, Clinical Laboratories; Director of the Clinical Immunology Research Labs; and Associate Member, Cousins Center for Psychoneuroimmunology, Semel Institute for Neuroscience and Human Behavior, UCLA-Westwood. Dr. Butch is an expert on functional immunology, proteomics, and metabolic analysis, and directs multicenter NIH-funded biomarker core laboratories.
- **Timothy Deming, PhD** is Professor and Chair of the Bioengineering Department, School of Engineering, and Professor of Chemistry and Biochemistry at UCLA. His current research interests include polypeptide synthesis, self-assembly of block copolypeptides, and biological activity of polypeptides, for which he has received young investigator awards from the National Science Foundation (NSF), US Office of Naval Research, Arnold and Mabel Beckman Foundation, Alfred P. Sloan Foundation, Camille and Henry Dreyfus Foundation, Materials Research Society, and IUPAC Macromolecular Division.
- **Pedro Lowenstein, PhD** is the Director of the Board of Governors Gene Therapeutics Research Institute at Cedars-Sinai and the Bram and Elaine Goldsmith Endowed Chair in Gene Therapeutics. An internationally recognized leader in gene therapeutics research, Dr. Lowenstein has pioneered cutting-edge breakthroughs in experimental gene therapeutics.
- **Leonard Rome, PhD** is the Senior Associate Dean of Research, DGSOM. Dr. Rome is the founding leader of the interdisciplinary biologic nanoparticle initiative at UCLA, and presently serves as Director of the CNSI. As Senior Associate Dean for Research, he has organized strategic planning for research in the School and spearheaded campus-wide efforts in genomics, proteomics, and computational biology. He is the past chair of the Association of American Medical Colleges (AAMC) Group on Research Advancement and Development (GRAND). He is director of the Pilot and Collaborative Translational and Clinical Studies Program.
- **Christopher Evans, PhD** is a Professor, Psychiatry and Biobehavioral Sciences, DGSOM. His research accomplishments include identification of a number of novel endogenous opioid peptides and the cloning of the first opioid receptor. Dr. Evans is currently Director of the UCLA Brain Research Institute. He also leads the Chancellor's Biosciences Initiative that provides funding and organizational structure to almost 100 biomedical cores at UCLA.
- **Jay Vadgama, PhD** is a Professor of Medicine, Endowed Chair in Cancer Research, Chief of the Division of Cancer Research and Training, Medical Sciences Institute, and Director of The Charles Drew Cancer Cluster and of the Molecular Oncology Program. The focus of his work is in cancer genomics and proteomics in minority populations.
- **Michael Phelps, PhD** is the Norton Simon Professor, Chair, Department of Molecular & Medical Pharmacology, Director of the Institute for Molecular Medicine (IMED) & Director of the Crump Institute for Molecular Imaging. He is the inventor of the PET scanner, a member of the National Academy of Sciences and a member of the Institute of Medicine. He directs the largest molecular imaging program in the world ranging from preclinical & clinical research to clinical service. The Nuclear Medicine & Clinical PET service are uniquely in the Department of Molecular & Medical Pharmacology to integrate molecular therapeutics and molecular imaging diagnostics, from the basics sciences to the care of patients.

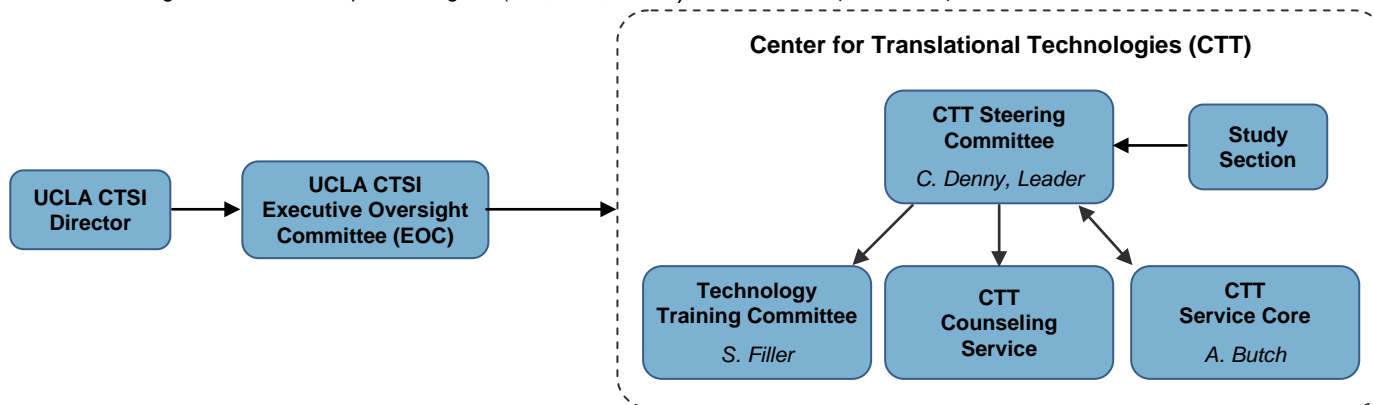


Figure 4. Organizational chart of the UCLA CTSI Technology Program and Center for Translational Technologies.

8. INTEGRATION OF UCLA CTSI KEY FUNCTIONS

The CTT will work closely with several programs within the CTSI. First, the CTT will work with the **Pilot Program**, to administer a voucher system as a primary mechanism to both stimulate TTR use and support translational investigation in a coordinated fashion. Second, the CTT will collaborate with the **BIP** to create an accessible internet utility that will allow CTSI researchers to find and productively interact with TTRs. Third, the CTT will work with the **CTSI-ED Program** to integrate TTR workshops and seminars into the curriculum tree for new translational investigators. Fourth, the CTT will work with the **CCRR Program** to assure that necessary technology resources to support clinical studies are in place. Finally, for those TTRs that generate large datasets, the CTT will coordinate with the **Biostatistics, Study Design and Clinical Data Management Program**, to assure that investigators have sufficient analytic support to both design well controlled studies and to rigorously interpret results.

9. EXTRA-UCLA COLLABORATIONS

Not only do CTT cores catalyze translational research within the UCLA Biomedical community but they also promote collaborative efforts with neighboring CTSA. Examples of such interactions include:

- The UCLA CTSI TTR program in collaboration with similar programs at the University of Southern California, and the University of California, Irvine has identified the concept of regional TTRs as one way to create cost-effective infrastructure.
- In conjunction with the small molecule screening core, UCLA investigator Jing Huang has collaborated with CTSA-supported researchers from the University of California, Irvine to develop molecular enhancers of rapamycin; rapamycin is an inhibitor of the mTOR pathway that is activated in several human malignancies.
- Making use of the transgenic mouse core, UCLA researchers Louis Parada and Hong Wu worked with investigators at CTSA awarded institutions, University of California, Irvine and University of Texas Southwestern, to develop a new model of astrocytoma based on defined mutations in PTEN, NF1 and p53 genes.
- Using the electron microscopy core, UCLA investigator Yi Tang collaborated with CTSA researchers from the University of Southern California, to develop novel proteolyzable nanoparticles that can be used as programmable therapeutic delivery vehicles.
- UCLA researchers Lily Wu and Michael Carey along with CTSA-sponsored collaborators from Stanford University, employed the small animal imaging core, to create a novel two-tiered gene expression system that can sensitively and specifically detect prostate cancer in preclinical models.
- Using the microarray core, UCLA investigator Philip Koeffler, in collaboration with researchers at University of Southern California, identified novel mutations in genes other than the BCR/ABL fusion, in patients with chronic myelogenous leukemia that had developed resistance to tyrosine kinase inhibitors.

10. IMPLEMENTATION PLAN AND MILESTONES

Table 2. Summarizes the Implementation Plan including specific aims, milestones and key activities, and evaluation and tracking measures and indicators.

Table 2. CTT Implementation Plan

Year(s)	Milestones and Key Activities	Measures and Indicators
Aim 1: Implement a system for providing centralized access to and ongoing performance monitoring of Translational Technology Resources (TTRs)		
1-2	<ul style="list-style-type: none"> Establish an all-inclusive, accessible and searchable on-line database to connect translational researchers with core services in partnership with the UCLA CTSI Biomedical Informatics Program 	<ul style="list-style-type: none"> Conduct Yr 1 CTSI investigator technology needs assessment
1	<ul style="list-style-type: none"> Provide streamlined core access to CTSI clients through a voucher system based on peer-reviewed rationale and justification for core use 	<ul style="list-style-type: none"> Track number and type of CTT service core performance and utilization
1-5	<ul style="list-style-type: none"> Conduct ongoing needs assessments and trends of new and existing TTRs 	<ul style="list-style-type: none"> Voucher system pilot tested and refined
1-2	<ul style="list-style-type: none"> Develop standard operating procedures for cost recovery and cost sharing 	
2-3	<ul style="list-style-type: none"> Organize non-CTSI supported TTRs using Technology Affinity Groups 	
Aim 2: Create an efficient mechanism for developing promising new technologies into functional TTRs		
1-5	<ul style="list-style-type: none"> Promote trans-disciplinary interaction that will catalyze development of new technologies. 	<ul style="list-style-type: none"> Number and type of new TTR educational sessions (lectures, seminars and workshops)
2-3	<ul style="list-style-type: none"> Create a structured process to evaluate, prioritize and test whether emerging technologies can be developed into new CTSI TTRs 	<ul style="list-style-type: none"> Quarterly reporting on emerging technology using structured evaluation process (see section 6.2.2)
Specific Aim 3: Conduct personalized counseling and continuing education programs to facilitate collaboration and assist translational investigators in selection and optimal use of TTRs		
1	<ul style="list-style-type: none"> Hire and train Technology Officers to advise individual Investigators and facilitate networking and core utilization 	<ul style="list-style-type: none"> Number, type, and \$ amount of grants/awards funded
1-5	<ul style="list-style-type: none"> With the UCLA-CTSI Pilot & Collaborative Clinical & Translational Studies Program, provide seed funding to investigators on a competitive basis to foster collaborations around new technologies 	<ul style="list-style-type: none"> Annual progress reports from grantees Number of pilot studies resulting in RO1s and \$ amt
3	<ul style="list-style-type: none"> TAGs develop training module for young investigators 	<ul style="list-style-type: none"> Number and type of new TTR educational activities (lectures, seminars and workshops)
4-5	<ul style="list-style-type: none"> Create didactic series (seminars, workshops, and interdisciplinary lectures) to foster innovation 	

11. REFERENCES

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Research Education, Training, and Career Development



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Abbreviations: BIP – Biomedical Informatics Program, BIRCWH – Building Interdisciplinary Research Careers in Women’s Health, BRI – Brain Research Institute, BSD-CDM – UCLA CTSI Biostatistics, Study Design and Clinical Data Management Program, CCRR – Clinical and Community Research Resources Program, CDU – Charles Drew University, CER – comparative effectiveness research, CERP – UCLA CTSI Community Engagement Research Program, CREST Clinical Research Education and Specialized Training, CRISP – Computer Retrieval of Information on Scientific Projects, CSP – Clinical Scholars Program, CTT – UCLA CTSI Center for Translational Technology, CTSI – Clinical and Translational Sciences Institute, CTSI-ED – UCLA CTSI Research Education and Training Program, DGSOM – David Geffen School of Medicine, DPM – Database and Program Management, EMPH – Executive Master of Public Health, HSR – Health Services Research, IMED – Institute for Molecular Medicine, IMSD – Initiative for Maximizing Student Diversity, MCSDPA – Geriatrics Mentored Clinical Scientist Development Program Award, Master of Science in Health Services, NCRR – National Center for Research Resources, NIGMS – National Institute of General Medical Sciences, OIS – Office of Investigator Services, PRIME – Pediatric Research, Innovation, and Mentoring Experience Program, PHSA – Public Health Student Association, RCMAR – Research Centers for Minority Aging Research, RCMI – Research Centers in Minority Institutions, RISE – Research Initiative for Scientific Enhancement, RTRN – RCMI Translational Research Network, RWJF CSP – Robert Wood Johnson Foundation Clinical Scholars Program, STAR – Subspecialty Training and Advanced Research, STTP – Short-term Training Program, TTRP – Translational Therapeutics and Technologies Research Program U-STAR – Undergraduate Student Training in Research.

1. OVERVIEW

The Research Education, Training and Career Development Program (CTSI-ED) is charged with conducting and coordinating clinical and translational science education for the UCLA CTSI. UCLA has an outstanding record of advanced training in translational and clinical sciences. Our numerous successful NIH-funded and institutionally supported programs annually train over 1,200 pre-and post-doctoral scholars. However, traditional training environments tend to isolate community researchers and clinical and basic scientists, impeding interdisciplinary team-based translational investigation.

CTSI-ED received a score of 1 in our prior review. Reviewers commended our cadre of outstanding mentors, our strong plans for research and development, and our many community-based training initiatives. This application retains our highly rated plans and programs. CTSI-ED also strengthened several components in response to reviewer comments; ■ we offer a staffed center and virtual resources that link applicants with programs, and retain K12 awardees by nesting projects in team science programs; ■ we require at least three of four votes from K12 Mentored Interdisciplinary Translational Therapeutics and Technologies Research (TTTR) Program leaders for decision-making; ■ We will spread peer mentoring to all CTSI trainees; ■ we clarified that four T32 students will be awarded degrees each year. To further strengthen and build interdisciplinary research teams, we introduce new CTSI K12 and T32 programs. Also, we have new curricula that will focus on leadership in science training and communication of science skills. Substantive changes to this application since the last submission are indicated in the left margin.

2. SPECIFIC AIMS

The UCLA CTSI provides the operations and governance necessary to facilitate successful transdisciplinary clinical and translational research. The overarching *mission* of the UCLA CTSI is to *transform our academic-clinical-community partnership into a borderless institute that brings our combined innovations and resources to bear on the most pressing health needs in our diverse Los Angeles community.*

We propose to transform education and training in translational medicine with the following Specific Aims:

Specific Aim 1: Establish the CTSI-ED Office to optimize cross-disciplinary training and integrate community input into training into research activities throughout the CTSI.

Specific Aim 2: Transform translational education through new curricular elements in highly successful existing programs and create new programs (K12, K30, T32 and others) incorporating community engagement and interdisciplinary methodologies and technologies.

Specific Aim 3: Provide mechanisms to integrate patient-oriented research training through a course menu, expansion of didactic programs (the CTSI-ED Curriculum Tree), and an integrated assessment program providing a sophisticated, computer-based learning-management system.

Fulfilling these Specific Aims is transformative in the following ways: For Aim 1, a new CTSI-ED office to support mentoring, training, and education within the CTSI-ED will be the program's new physical home. The CTSI-ED also will synergize with the CTSI **Biomedical Informatics Program (BIP)** and the Office of Investigator Services (OIS; see **Regulatory Knowledge and Support, Industry Relations, and Research Ethics [Regulatory] Program**) to create a Virtual Home of resources that extends the mission and goals of the CTSI-ED online.

The leaders of the CTSI-ED form the Clinical Research Education and Specialized Training (CREST) Committee, which conducts the mission of the CTSI-ED. The multidisciplinary CREST Committee will:

- Define and teach skills that trainees need to be effective at partnered research with communities.
- Develop a cadre of community mentors and identify the most appropriate mentor for each CTSI trainee.
- Ensure easy access among trainees to the operational and didactic resources provided by this core.

To ensure integration among CTSI programs, the CREST Committee will have:

- Representation from all four CTSI partners in basic, clinical, health services, and community-partnered research;
- Participation by Chairs from the **Community Engagement in Research Program (CERP)**, the **Biostatistics, Study Design and Clinical Data Management Program (BSD-CDM)**, the **Center for**

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Translational Technologies (CTT), CTSI-ED, and **Clinical and Community Research Resources Program (CCRR)** given the close collaboration required among these core programs to fully achieve the CTSI-ED goals;

- Two senior community representatives from the large multi-ethnic urban community in Los Angeles who are well versed in research partnerships between academic medical centers and communities (see Ms. Loretta Jones and Ms. Laura Trejo in **Institutional Letters**)

For Specific Aim 2, we will expand our highly successful, institutionally supported Subspecialty Training and Advanced Research (STAR) Program to include trainees from all four CTSI partners. For CTSI-ED trainees who are developing expertise in T3 or T4 research (for definition, see **section 3** below), we will expand the availability of our highly successful RWJF Clinical Scholars Program (CSP) curriculum. This group of trainees will be transformed by greater levels of community partnership to develop and implement research in diverse populations. The CTSI's formal linkage through **CERP** and Charles Drew University (CDU) to the Los Angeles Urban League's Healthy Community Initiative, a five-year demonstration project designed to enhance health and wellness by mobilizing residents in a high-risk 70-block urban setting to implement evidence-based health promotion and disease prevention strategies, will provide trainees with vibrant settings to design and implement collaborative, partnered community interventions.

Specific Aim 2 will also develop didactic and mentoring programs in concert with other CTSI Programs. These new programs will address community needs by adding community mentors to virtually all CTIS trainees' interdisciplinary teams and by creating innovative educational programs for pre- and postdoctoral trainees in clinical and translational, health services, and community-based research. Four new programs are proposed:

- The K12 Mentored Interdisciplinary Translational Therapeutics and Technologies Research Program (TTTRP)
- A T32 PhD Training Program in Clinical, Comparative Effectiveness, and Community-Partnered Translational Research
- A PhD Track of Molecular Medicine with an emphasis in Translational Systems Biology
- A new Executive Master's of Public Health (EMPH) in Community Research

For Specific Aim 3 we will expand and Integrate Didactic Course Structure including the K30 Program and the Curriculum Tree. To integrate and increase access to established and new courses, the CTSI-ED will modify an existing program developed in the UCLA School of Engineering to construct a Curriculum Tree (see **Table 9**), which will:

- Help establish a range of explicit training goals
- Closely align coursework with goals
- Evaluate faculty by ability to instruct toward goals
- Evaluate trainees' abilities to achieve goals.

The system will enhance knowledge and access by mapping all translational coursework at all four CTSI partners and enable effective evaluation and dissemination of CTSI-ED didactic innovations.

3. PROGRESS TO DATE

We have successfully pursued many activities to enhance translational research. CTSI-ED defines research translation as T1 to T4. T1 research seeks to move a basic discovery into a health application. T2 research assesses the value of an application for health practice leading to the development of evidence-based guidelines. T3 research attempts to move evidence-based guidelines into health practice, through delivery, dissemination, and diffusion research. T4 research seeks to evaluate the "real world" health outcomes of an application in practice.¹ Examples of our progress include:

- Recently awarded K30 supplement to develop a Comparative Effectiveness Curriculum for trainees who focus on T2 to T4 science.
- The successful pilot-test of the UCLA Society of CTSI scholars program. Four promising young faculty with translational projects were selected to receive \$25,000 a year for three years. In the coming year, we are expanding this program (see **section 6.2.2.1**).
- The launch of our multi-institutional seminar series for T1 to T4 research. Our inaugural seminar, "Antibody-Based Therapies," featured panelists Drs. Denis Slamon (breast cancer treatment), Dermot

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McGovern (inflammatory bowel disease treatments), Richard Baker (health care disparities and community participation in science), and Robert Kaplan (opportunity costs for personalized treatments in breast cancer care). The **BIP** set up real-time videoconferencing at CTSI partner institutions so that 120 scientists and community members across Los Angeles could participate in a vibrant question-and-answer period.

4. SIGNIFICANCE: CTSI-ED RATIONALE

Los Angeles is rich in ethnic and cultural diversity. This is mirrored by the diverse CTSI partners, which are located throughout the Greater Los Angeles area. They are UCLA-Westwood, CDU, Los Angeles Biomedical Institute at Harbor-UCLA (LA BioMed), and the Burns and Allen Research Institute at Cedars-Sinai Medical Center (Cedars-Sinai) (see **Overview and Governance**). The CTSI academic community has been at the forefront of clinical and translational investigations and discoveries that have led to major contributions to health care.²⁻²²

CTSI partners have trained some of the nation's foremost translational, clinical, health services, and community-based scientists. But we have accomplished this mainly by staying in disciplinary silos. We believe that addressing the complexities of modern translational research will require interdisciplinary teams that consist of T1 to T4 scientists who partner with communities to prioritize and implement research and disseminate best practices. The CTSI offers an unprecedented opportunity to create a new kind of scientist by unifying education and training in patient-oriented investigation and infusing the community perspective across the spectrum of research. We believe that training scientists in this way holds the greatest promise for improving the health of people in Los Angeles.

5. INNOVATION AND ENVIRONMENT

Programs that enable students to participate in biomedical research at UCLA begin in high school and extend through undergraduate, predoctoral, postdoctoral, and faculty-level education. Many mechanisms help trainees obtain mentored research experience and didactic training in clinical, health services, and community-partnered research and basic sciences.

The highly ranked Medical Scientist Training Program (MSTP) educates qualified individuals for careers as physician researchers. This program is supported in part by a T32 training grant but also relies on 2.7 million dollars in institutional support annually. Medical students not participating in the MSTP are encouraged to participate in a Short-Term Training Program (STTP), in which they conduct a clinical, basic, health services or community-oriented research project. Approximately 80 MD students per year participate in the institutionally supported STTP.

The Specialty Training and Advanced Research Program, provides physicians training in basic, clinical, health services, or community-oriented research in a program that is integrated with the clinical specialty fellowship or residency. The STAR Program enables physicians at the fellowship/residency level a unique pathway to an advanced research degree (PhD or MS). MSTP graduates who join the STAR Program integrate their clinical fellowship with postdoctoral research training. For other trainees, especially those in one of the three K12 programs, the K30 program, the 29 T32 programs, or 11 R25 programs (see **Table 1**), this is an opportunity to receive research training through the Master of Science in Clinical Research Program.

The Robert Wood Johnson Foundation Clinical Scholars Program (CSP), which has been continuously funded for 41 years and currently focuses on training physicians in community-partnered approaches for T3/T4 translation, is a model program that the CTSI-ED will build from to develop the needed community-oriented curriculum to support T3 and T4 translation across the K12, K30, and T32 programs at CTSI partners. This program is funded at 3.4 million dollars a year, and currently has 21 clinical scholars from surgery, neurology, psychiatry, pediatrics, family medicine, internal medicine, radiology, obstetrics/gynecology, ophthalmology, and emergency medicine. In conjunction with **CERP**, CTSI-ED will expand the curricular and mentoring approach from this program to a much broader set of trainees across the partners (see **Specific Aim 2**). Our partnership with CERP will foster future interdisciplinary collaborations and should greatly enhance our capacity to conduct community-based clinical trials. Many of these trials will employ cutting-edge methods of comparative effectiveness research. Dr. Carol Mangione, the director of CTSI-ED, is a CSP co-director and therefore is well positioned to lead the building of and increasing access to the highly successful CSP curriculum for the broader set of CTSI-affiliated trainees. Also, the "clinician scientist track" in the MS degree in the School of

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Public Health for the CSP provides many required courses for the new CTSI T32 PhD program in Clinical and Community-Partnered Translational Research (see **section 6.1.5.**).

5.1. Programs contributing to the mission and aims of the CTSI-ED. Précis of ongoing programs directly impacted by CTSI-ED are described here and summarized in **Table 2.**

5.1.1. Subspecialty Training and Advanced Research (STAR) Program. The STAR Program is an institutionally funded K12-type of program (approximately 2 million dollars per year) that enables fellows and residents entering clinical training to:

- Earn a PhD in one of 10 basic science programs (Track 1)
- Earn a PhD in health services through the School of Public Health or the RAND Graduate School, where scholars have the option of focusing on community-partnered methods (Track 2)
- Earn an MS in Clinical Research (Track 3, supported in part by the K30 Program)
- For MD/PhD graduates, to set aside protected time for postdoctoral training (Track 4).

The STAR Program has an exceptional record, with over 81% of graduates (79) actively continuing in academic medicine and research, and is a target for expansion through institutional support to trainees across the CTSI and for improvement by the CTSI-ED.

5.1.2. K30 Program. The recently renewed NCRR-funded K30 provides outstanding educational opportunities in clinical research for scholars with any professional degree. Approximately 300 K30 scholars are trained annually throughout the CTSI. This program provides much of the curriculum for translational and clinical research education in the CTSI. In 2010, Drs. Salusky and Kaplan were awarded a supplement to the K30 to develop curriculum designed to teach state-of-the-art methods of comparative effectiveness research (CER). CTSI-ED Leader Dr. Mangione (professor at DGSOM and in the UCLA School of Public Health), will be key in helping develop and implement of this new CER curriculum in the K30 and throughout the appropriate new training programs in this application. Track I is an auditing option of all K30 courses. Track II provides a 2-year fellowship in translational investigation leading to a certificate of completion. Track III is a 2-year program leading to an MS in Translational and Clinical Research from UCLA or CDU. The K30 provides key courses for many mentored training programs (see **section 6.3.1**). The CTSI-ED also will increase the scope and capacity of the K30 to accommodate expansion of new and current CTSI training programs. Partnered with the CTSI **CTT**, CTSI-ED will add curriculum in systems biology approach to research, bioengineering, bioinformatics, and nanotechnology. Partnered with **CERP** and the Regulatory Knowledge and Support, Industry Relations and Research Ethics Program (**Regulatory Program**), CTSI-ED will develop new lectures for existing courses to enhance training in methods for conducting community-partnered research; communication, leadership, and science skills; and an expanded curriculum in the ethics of patient-oriented research. The ethics curriculum also will include important topics related to genetics, stem cell research, and issues around scientific misconduct. With the **BIP**, the CTSI-ED will transform these didactic lectures into webcasts, live videoconferences and other tools to enable trainees from across the CTSI to enroll, participate and attend courses in between or after their research and clinical duties.

Table 1. CTSI-ED Transformation of Training Programs Active at the CTSI Institutions

Ongoing CTSI-Related Training Programs 2009-2010	Transformative Contributions of CTSI-ED
~820 Trainees: PhD Programs in Biosciences (N=14) and in Public Health (N=9) and other T3/T4-related disciplines	Dr. Sun on behalf of the CTSI-ED will identify the 5 programs who we will work with intensively to transform their programs in a multi-disciplinary translational way. Create new courses and a T32 program that will provide increased access to T1 to T4 didactic education. Promote co-mentoring via clinical, basic science faculty, and community mentors available through CTSI-ED.
88 Trainees: Short-Term Training Program (STTP) for MD students during training	Provide resources through the CTSI-ED Office for students to find mentors for their research interests. Increased options for community-oriented research projects and CER projects potentially linked to the Healthy Community Initiative in partnership with CDU.
88 Trainees: MSTP Program	Provide increased career opportunities for MDs and PhDs via expansion of STAR and K12 Programs. Increase number of T1 to T4 courses for training in team-based science, CER, and community-oriented research. Increase opportunities for T1 to T4 education at the PhD level via new CTSI T32 in clinical and translational research. Enhance research and training opportunities in systems biology.

Ongoing CTSI-Related Training Programs 2009-2010	Transformative Contributions of CTSI-ED
366 Trainees: School of Public Health professional master's programs	Develop a new executive master's program with course elements from the CTSI-ED and existing programs in Public Health and Health Sciences to enable leaders in the community to receive an educational program for T3/T4 research training with a focus on CER and updated policy courses that prepare these organizations for changes attributable to health care reform. Expand access to the community-partnered clinician scientist track in the Public Health MSHS degree currently used by RWJF CSP for K12 trainees interested in T3/T4 research.
250 Trainees: K30 Track I (auditing option)54 Trainees: K30 Track II (2-year Fellowship)35 (25 UCLA, 10 CDU): K30 Track III (MS Clinical Research)	Provide support to increase capacity and scope of K30 courses and programs and thus facilitate the development of physician scientists via the STAR, K12, and other mentored training programs. Use the didactic courses as a base for the CTSI-ED Curriculum Tree. Enhance the teaching and mentoring in CER, health policy oriented research, community-partnered research, communication of science and leadership skills.
13 Trainees: GCRC K30 Summer Program	Enhance dissemination of this training opportunity.
25 Trainees: STAR Track 1&2/ Clinical fellow-Ph.D 10 Trainees: STAR Track 3/ Clinical fellow /MS 6 Trainees: STAR Track 4/ Clinical Fellow/ Post-Doc	Increase capacity by providing increased institutional support for training in new areas of clinical and translational medicine across all CTSI institutions. Expand translational and clinical research programs and courses for STAR scholars.
228/136 Trainees: Available slots on UCLA Bioscience T32s (N = 57) (Predoctoral/Postdoctoral)	Create a rigorous new T32 interdisciplinary program for PhD students that will train scholars in CER, health policy oriented research, and community-partnered translational research. Partner with the 5 most translational T-32s to develop curricular and mentoring linkages with the CTSI.
17 Trainees: K12 Programs (non-NCRR); Pediatrics, BIRCWH Center, and Women's Reproductive Health (3 separate programs)	Provide integration via shared leadership of the CTSI-ED. Include all PIs of K12 programs on the CREST Committee. Facilitate course accessibility/access to career development tools via the CTSI-ED Office of Education and Curriculum Tree. Add courses in CER methods, community-partnered research and add community mentors to the interdisciplinary research teams of specific projects in need of this input. Invite K12 awardees to the CTSI monthly interdisciplinary work-in-progress and seminars in T1/T2 translation. Create the needed IT infrastructure for web-based participation in these sessions at the CTSI institutions.
65 Trainees: R25, P50, P30 Departmental Research Fellowships	Provide increased training opportunities and didactic courses in T1 to T4 translation. The CTSI-ED Office will provide centralized information for courses and career development tools and priorities for each program.

5.1.3. Non-NCRR K12 Programs. There are three active K12 programs in the CTSI, and to coordinate them all K12 directors will participate in the CREST Committee (see **Table 4** for PI names). They are:

- Building Interdisciplinary Research Careers in Women's Health (BIRCWH): K12 HD001400
- Pediatric Research, Innovation, and Mentoring Experience (PRIME) Program: K12 HD034610
- UCLA Women's Reproductive Health Research Center: K12 HD001281

5.1.4. PhD Programs. There are 14 bioscience PhD programs and 9 PhD programs in public health, public policy, nursing, and dentistry at UCLA-Westwood and RAND. These link to training programs in clinical and translational research, including MSTP, STAR Program, and CSP. These programs have over 740 trainees and provide core curriculum and scholars who participate in multiple T32 programs. However, few if any of these programs focus on the didactic content that is most needed to create scientists who conduct novel T3/T4 research. In collaboration with **CERP** and the Health Services Research (HSR) faculty, CTSI-ED will develop an innovative T32 PhD program in Clinical and Community-Partnered Translational Research that teaches CER methods.

Table 2. NIH Training-Related Awards Active at CTSI Institutions

Number	Award Type	Funding FY10
10	D43	\$1,493,120
65	F31 (43), F32 (22)	2,368,551
17	K01	2,262,433
3	K02	418,145

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Number	Award Type	Funding FY10
2	K05	237,924
4	K07	586,504
34	K08	4,262,502
7	K12	1,834,481
8	K22	868,985
37	K23	4,998,239
4	K24	632,500
2	K25	263,984
1	K30	300,000
3	K99	269,500
496	PO1 (109), P20 (8), P30 (106), P41 (219), P50 (52), P60 (1), PN2 (1)	129,229,437
23	R24 (8), R25 (15)	6,389,553
3	SO6 (2), S21 (1)	5,361,868
73	T15 (3), T32 (65), T34 (1), T35 (1), T42 (2), T90 (1)	17,735,227
143	UO1 (55), U10 (8), U19 (27), U24 (7), U2R (2), U48 (3), U54 (35), U56 (3), U58 (2), U79 (1)	119,822,917
933	Total N	\$299,335,870

Among our current predoctoral T32 programs, the following five have the strongest orientation toward translational research:

- Fundamental Clinical Research Training Program (T32 DE007296)
- Pulmonary & Critical Care Training Program (T32 HL072752)
- Tumor Immunology Institutional Training Grant (T32 CA009120)
- Training for Academic Hematology (T32 HL066992)
- Drug Abuse Research Training Center (T32 DA007272)

Table 3 catalogs 256 trainees and their mentors in these programs from 2005 to present, including former trainees' current positions.

Past & Current Trainees (Mentor)	Pre/Post	Training Period	Prior Academic Degree		Title of Research Project		Current Position (If Graduated)
PO: Wong, David T32 DE007296 Fundamental Clinical Research Training Program							
Alstein, Lily (David Elashoff)	Pre	'07	BA	'03	Brown Univ	Statistics and bioinformatics: genomic and proteomic science and cancer	Graduate Student, UCLA
Bae, David (Cun-Yu Wang)	Pre	'08-	BA MS	'05 '07	UC Berkeley UCLA	YAP, A Regulator of Tumorigenesis	Predoctoral trainee
Calhoun, Colonya (Robert Chiu)	Post	'04-05	DDS	'97	Univ of MI	Cancer signal transduction	Asst Professor, Oral & Maxiofacial Surgery, CDU
Chaichansakul, Nini (Sotirios Tetradis)	Pre	'06-	BS	'07	UCLA	Generating deletion and modification constructs method to study the effect of <i>cis</i> -regulating element between <i>Hox</i> genes	Predoctoral trainee
Cowan, Catherine (Benjamin Wu)	Post	'04-07	MS PhD	'99 '07	CSUDH UCLA	Biomedical tissue engineering strategies	Research Scientist, Abbott Vascular
Giang, An (Cun-Yu Wang)	Pre	'09-10	BS MS	'06 '08	UCLA UCLA	Head and neck squamous cell carcinoma (HNSCC)	Predoctoral trainee

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Past & Current Trainees (Mentor)	Pre/Post	Training Period	Prior Academic Degree		Title of Research Project	Current Position (If Graduated)	
PO: Wong, David T32 DE007296 Fundamental Clinical Research Training Program							
Kamath, Meghna (David Elashoff)	Post	'04-06	BS PhD	'00 '06	College of St. Elizabeth UCLA	Dvlp and validation of statistical methods for mass-spectrometry proteomic data analysis	Statistician, Genetech
Kaplan, Chris (Wenyun Shi)	Pre Post	'05-09	BS PhD	'99 '07	Cal Poly SLO UCLA	Oral bacterium fusobacterium nucleatum: a causative agent of periodontal disease	Scientist, Biomedical Research
Kim, Jeffrey (David Wong)	Pre	'05-09	BS DDS	'02 '08	Cal Poly Pomona UCLA	P12 in Oral Cancer	Recipient of F31 Award
Kim, Reuben (No-Hee Park)	Post	'03-06	DDS PhD	'03 '08	UCLA UCLA	Role of HPV in oral carcinogenicity	Asst Prof, UCLA Dentistry
Kim, Yong (David Wong)	Post	'03-06	PhD	'98	Univ of Rochester	molecular alterations in oral cancer development	Asst Prof, UCLA Dentistry
Kreymer, Anna (Susan Haake)	Pre	'08-	BS MS	'05 '08	UCLA UCLA	Molecular biology of fusobacterium nucleatum	Predoctoral trainee
Lee, Yu-Hsiang (David Wong)	Post	'08-10	BS MS PhD	'98 '03 '06	Tunghai Univ. USC USC	TBA	Postdoctoral Trainee
Lillejoh, Peter (Chih-Ming Ho)	Pre	'09-	BS MS	'06 '07	Johns Hopkins UCLA	A microfluidic lab-on-a-chip for rapid diagnosis of oral diseases	Predoctoral Trainee
Litrell, Romie (Benjamin Wu)	Pre	'08-09	BA	'03	UC Berkley	Engineering a Bone Mimetic Platform for Quantitative Determination of Remodeling Imbalance	Predoctoral Trainee
Maksaereekul, S. (David Wong)	Post	'08-09	BS PhD	'01 '09	UC Davis UC Davis	Detection of Biomarkers for Early Screening and Monitoring of Cancer from Saliva Samples	Postdoctoral Trainee
McHardy, Ian (Wenyun Shi)	Pre	'08-	BS	'05	UCLA	Mechanisms of virulence in Treponema denticola: a global approach	Predoctoral Trainee
Mehrazarin, Shebli (Mo Kang)	Pre	'08-	BS	'08	UCLA	Loss of DSP, DMP-1 and osteocalcin expression during senescence of human dental pulp stem cells	Predoctoral Trainee
Merrit, Justin (Wenyuan Shi)	Pre Post	'03-07	BS PhD	'97 '04	Univ of Miami UCLA	Pathogenesis research in oral disease	Asst Prof, Univ of OK
Park, Noh-Jin (David Wong)	Post	'05-07	PhD	'04	UCLA	MRNA in saliva as a diagnostic tool	Research Scientist, Quest Diagnostics
Pathmanathan, D (Kang Ting)	Post	'07-08	DMD/ PhD	'06	Univ of CT School of Dentistry	Osteoblast Regulations	Resident, UCLA Sch of Dentistry
Pirih, Flavia (Sotirios Tetradis)	Post	'03-06	DDS	'99	Univ Federal do Parana, Brazil	Regulation and function of NGF ¹ -B nuclear orphan receptors	Postdoctoral Trainee Univ of MI
Ramachandran, Prasanna (Joseph Loo)	Pre	'06-08	B Pharm PhD	'97 '09	Birla inst of tech & Science, India UCLA	Identification of glycoproteins	Postdoctoral Fellow Univ of WA

Principal Investigator/Program Director (Last, First, Middle): Dubinett, Steven, MD

Past & Current Trainees (Mentor)	Pre/Post	Training Period	Prior Academic Degree		Title of Research Project	Current Position (If Graduated)
PO: Wong, David T32 DE007296 Fundamental Clinical Research Training Program						
Siu, Ron (Kang Ting)	Pre	'07-10	MS	'05	Stanford Univ	Nell-1 protein and its function in tissue regeneration Graduate Student UCLA
Siyahian, Arpi (Sotirios Tetradis)	Pre	'05-08	BS PhD	'06 '08	UC Riverside UCLA	Parathyroid hormone (PTH) and its effects on NGFI-B Lecturer UCLA
St John, Maie (David Wong)	Post	'05	PhD MD	098 099	Yale Univ	Salivary diagnostics for oral cancer detection Asst Prof UCLA, Surgery
Tang, Eric (Cun-Yu Wang)	Post	'07-09	MD PhD	'05 '05	Univ of MI	Mechanisms underlying production of interferon in response to bacteria and viruses Postdoctoral Trainee UCLA
Wang, Jianghua (David Wong)	Post	'05-08	MD PhD	'88 '00	Xi'an Med Univ, China	Gene therapy using salivary glands Student, UCLA School of Dentistry
Woo, Stacey (Sotirios Tetradis)	Pre	'03-08	BA DDS PhD	'01 '05 '08	Stanford Univ UCLA UCLA	The regulation of E4BP4 by glucocorticoids Postdoctoral Trainee Univ of MO, Kansas City
Yochim, Hin-Min (No Hee Park)	Post	'04-05	BS MS PhD	'93 '98 '03	Kyung-Pook Natl Univ USC	Innovative Therapeutic Modes for the treatment of Human Oral Cancers Student Univ of FL
Kumar, Anjuli (Jonathan Braun)	Post	'08	MD	'03	Cornell Univ	Utility of proteomic analysis in the characterization of intestinal transplant dysfunction Postdoctoral Trainee UCLA
Tachdijian, Raffi (Tallal Chatila)	Post	'04-07	MPH MD	'94 '01	Univ of AL Morehouse Univ	Role of IL-4 receptor α cjaom Q576R polymorphism in asthma pathogenesis Asst Clinical Prof, UCLA Pediatric Pain Program
Ching, John (Pinchas Cohen)	Post	'06-07	MD	'03	St George's Univ, Grenada	Humanin: a novel growth factor and its role in development Postdoctoral Trainee UCLA
Randhawa, Ruvdeep (Pinchas Cohen)	Post	'05-06	MD	'00	Loma Linda Univ	Role of Igf2 in fetal growth restriction Private Practice Orange, CA
Hoftman, Alice (Richard Gatti)	Post	'04-07	MD	'01	Northwestern Univ	Lupus nephritis: identification of auto-antibodies and genes Private Practice Orange, CA
Thao, Phuong (Kuk-Wha Lee)	Post	'08-	MD		Univ of Medicine of Ho Chi Ming City, Viet Nam	Role of humanin in beta cell survival Postdoctoral Trainee UCLA
Chow, Emilie (Michael Lovett)	Post	'04-05	MD	'93	Univ of IL	Chronic infection with leptospira interrogans Clinical Prof, UC Irvine Internal Medicine
Brasket, Melinda (Ed McCabe)	Post	'07-	MD	'01	Columbia Univ	Pathways of allergic disease in pediatric liver transplant patients treated with Tacrolimus Postdoctoral Trainee UCLA
Chen, Karin (Ed McCabe)	Post	'08-	MD	'04	UC Irvine	Development of a newborn screening test for severe combined immunodeficiency Postdoctoral Trainee UCLA
Martinez, Julian (Ed McCabe)	Post	'05-06	MD	'00	Yale Univ	Characterization of glycerol kinase loci in Drosophila melanogaster Asst Prof, UCLA Human Genetics
Kahana, Doron (Martina Martin)	Post	'06-08	MD	'03	Tel Aviv Univ, Israel	Role of enteroendocrine cells in nutrient assimilation and absorption Asst Clinical Prof, Harbor-UCLA, Pediatrics

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Past & Current Trainees (Mentor)	Pre/Post	Training Period	Prior Academic Degree		Title of Research Project		Current Position (If Graduated)
PO: Wong, David T32 DE007296 Fundamental Clinical Research Training Program							
Cheng, Jerry (Kathleen Sakamoto)	Post	'04-07	MD	'01	UC San Diego	CREB in normal and aberrant hematopoieses	Staff Physician, Kaiser Permanente
SooHoo, Linda (Julian Whitelegge)	Post	'09-	BS PhD	'09	UC San Diego	Identification of Human Salivary Cystatins as Biomarker for Pancreatic Cancer	Postdoctoral Trainee UCLA
Eshraghi, Aria (Ken Bradley)	Pre	'08-	BA	'04	UC Berkeley	Characterizing interactions between Aggregatibacter actinomycetemcomitans cytolethal distending toxin and host cells	Predoctoral trainee
Tremayne, Jarrod (David Wong)	Post	'09-	BS PhD	'08	Univ. Nebraska Med. Center	Mechanism of the presence of biomarkers in saliva	Postdoctoral Trainee UCLA
Yang, Jeiping (David Wong)	Post	'09-	BS MS PhD	'07	Indiana Univ.	Explore the cellular and mechanism mechanisms of salivary biomarker profile change during tumor progression	Postdoctoral Trainee UCLA
Khalid, Omar (David Wong)	Post	'10-	BS PhD	'09	Univ. So. Calif	Role of p12 in stem cells and oral cancer	Postdoctoral Trainee UCLA
Yoshizawa, Janice (David Wong)	Post	'10-	BS PhD	'09	UC Irvine	Identifying salivary transcriptome biomarkers for early detection of gastric cancer	Postdoctoral Trainee UCLA
Lau, Chang Shun (David Wong)	Post	'10-	BA BS PhD	'10	UC Riverside	Determining whether exosomal trafficking are responsible for distinct salivary biomarkers in cancer	Postdoctoral Trainee UCLA
Chang, Insoon (Cun-Yu Wang)	Pre	'10-	BS MS	'10	UC Los Angeles	Molecular regulation of cancer therapy resistance of head and neck cancer	Predoctoral trainee
Kang, Ben (Sotirios Tetradis)	Pre	'10-	BS MS	'08	Cal State Los Angeles	Bisphosphonate related osteonecrosis of the jaws.	Predoctoral trainee
PI: Dubinett, Steven M. T32 HL072752 Pulmonary & Critical Care Training Program							
Rivera, Seth (Ganz, Tomas)	Post	'03-06	MD	'98	USC	Role of Hecpidin in Anemia	Asst Professor UCLA
Dalwadi, Hamisha (Steven Dubinett)	Post	'03-05	PhD	'02	UCLA	COX-2 and non-small cell lung cancer	Researcher, Amgen
Mestas, Javier (Robert Strieter)	Post	'04-06	PhD	'03	UC Irvine	Regulation of tumor suppression and angiogenesis	Researcher, La Jolla Inst for Allergy & Immunology
Hwang, Dennis (Donald Tashkin)	Post	'04-06	MD	'99	Univ of IL	One-airway theory and asthma	Faculty, NYU Sleep Disorder Center
Peebles, Kathrine (Steven Dubinett)	Post	'05-07	PhD	'05	UCHSC, Denver	IL-1 β and IL-6 levels in lung cancer	Researcher Univ of AZ
Weigt, S. Stephen (John Belperio)	Post	'05-08	MD PhD	'01	Creighton Univ	Clinical and translational studies in lung transplantation	Asst Professor, UCLA
Pak, Cindy (Tomas Ganz)	Post	'05-07	MD	'01	Chicago Medical School	Elucidating the role of hepcidin on anemia of cancer	Clinical Instructor Kaiser Permanente
Walser, Tonya (Steven Dubinett)	Post	'06-09	PhD	'00	Univ of MD	Epithelial to mesenchymal transition (EMT)	Asst Professor UCLA

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Past & Current Trainees (Mentor)	Pre/Post	Training Period	Prior Academic Degree			Title of Research Project	Current Position (If Graduated)
Harui, Airi (Michael Roth)	Post	'06-09	PhD	'06	UCLA	Lung cancer vaccine development by utilizing Adenoviral Vectors (AdV) with therapeutic gene	Asst Researcher UCLA
Palchevskiy, Vyacheslav (John Belperio)	Post	'07-10	PhD	'07	USC	Inflammation and lung transplant	Postdoctoral fellow, UCLA
Fung, Eileen (Tomas Ganz)	Post	'07- 10	PhD	'07	UCLA	Identifying hepcidin antagonists in AI	Postdoctoral fellow, UCLA
Yangawa, Jane (Steven Dubinett)	Post	'07-09	MD	'04	Baylor College of Medicine	Inflammation in lung carcinogenesis	Surgical Fellowship UCSD
Kim, Airie (Tomas Ganz / Seth Rivera)	Post	'07-	MD	'04	Baylor College of Medicine	Mechanism of anemia of cancer	Current T32 Trainee
Derhovnessian, Ariss (John Belperio)	Post	'08-	MD	'05	UCLA	Mechanism of primary graft dysfunction	Current T32 Trainee
Hu, Scott (John Belperio)	Post	'09-	MD	'06	Ohio State University	Inflammation and lung transplant	Current T32 Trainee
Kim, Yan (Neil Wenger)	Post	'10-	MD	'05	Univ of Virginia	Quality of Life and Cost Effectiveness based calculated per QALY's in ICU patients	Current T32 Trainee
Shino, Michael (John Belperio)	Post	'10-	MD	'06	Cornell University	Role of plasma biomarkers in predicting outcomes in idiopathic pulmonary fibrosis	Current T32 Trainee
Kachroo, Puja (Steven Dubinett)	Post	'10-	MD	'07	Ross University	Inflammation in lung cancer pathogenesis	Current T32 Trainee
PI: Dubinett, Steven M. T32 CA009120 Tumor Immunology Institutional Training Grant							
Cho, John (Sherie Morrison)	Pre	'04-07	BS	'01	Univ of MD	Regulating the regulators: overcoming regulatory T cell suppression in cancer and identifying inhibitors of inflammation using RNA interference	Postdoctoral Researcher, UCLA Dermatology
Balaton, Cynthia (Michael Teitell)	Pre	'04-08	BS	'00	Santa Clara Univ	Investigations in TCL1-mediated lymphomagenesis involving polyneucleotide phosphorylase and STK39 hypermethylation	Science Writer, Amgen
Lee, Thomas (Ke Shuai)	Post	'06-07	PhD	'04	Univ of Mass	Regulation of STAT and NF- κ B signaling by PIAS1	Staff Research Assoc Genetech
Morris, Lila (James Economou)	Post	'06-08	MD	'04	UCLA	Role of FOXP3 transcription in tumor antigen-specific CD8+ cells	Staff Research Assoc UCLA, Surgery
Prasad, Sridhar (Steven Dubinett)	Post	'06-07	MD	'98	Boston Univ	Statin regulated signaling pathways in kras mutated human bronchial epithelial cells	Pulmonology, San Rafael Medical Center

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Past & Current Trainees (Mentor)	Pre/Post	Training Period	Prior Academic Degree			Title of Research Project	Current Position (If Graduated)
PI: Dubinett, Steven M. T32 CA009120 Tumor Immunology Institutional Training Grant							
Steward, Kristopher (John Timmerman)	Pre	'07-09	BS	'02	UCSD	Targeting tumor antigens to dendritic cells via FC receptors	GSR, UCLA Hematology/Oncology
Rickabaugh, Tammy (Beth Jamieson)	Post	'07-09	PhD	'04	UCLA	Effect of age on CD31 expression and naïve CD4+ T cells	Postdoctoral Researcher, UCLA Hematology/Oncology
Alva, Jackelyn (April Pyle)	Post	'07-08	PhD	'06	UCLA	Investigating the mechanisms that cause human embryonic stem cell transformation and the use of hESCs as a tumor model system	Postdoctoral Fellow UCLA, MIMG
Lee, Gina (Steven Dubinett)	Post	'07-10	MD	'02	Univ of Minn	Inflammation and tobacco-specific carcinogens in the pathogenesis of lung cancer	Current T32 Trainee
Nazarian, Ramin (Roger Lo)	Post	'07-	PhD	'07	UCLA	To discover genetic determinants of human melanoma sensitivity to Graf V600E inhibition by PLX4032 using siRNA knockdown screen	Current T32 Trainee
Sarmiento, Corina (Robert Reiter)	Post	'07- '09	PhD	'07	Yeshiva Univ	Gaining a deeper understanding of the role of N-cadherin in castration resistant prostate tumors	Postdoctoral Fellow, UCLA Urology
Walsh, Nicole (Michael Teitell)	Pre	'08-	BS	'04	Mt. Holyoke College	Investigating a role for LKB1 in the B cell germinal center reaction and lymphomagenesis	Current T32 Trainee
Laing, Rachel (Caius Radu)	Pre	'09-	MS	'06	Univ of Oxford	PET Imaging of metabolic pathways in immune cells and in cancer	Current T32 Trainee
Liu, Su-Yang (Genhong Cheng)	Pre	'09-	BS	'04	Brown Univ	The role of retinoid-X-receptors in innate immune response against virus	Current T32 Trainee
Tahk, Samuel (Ke Shuai)	Post	'08-	PhD	'08	UCLA	PIAS1 regulates self-renewal and differentiation of tumor-initiation cells through selective epigenetic gene silencing	Current T32 Trainee
Daniels, Tracy (Marisol Penichet)	Post	'08-09	MD	'02	Univ of Minn	The potential role of LEDGF/p75 in prostate cancer	Postdoctoral Researcher, UCLA Surgery
Epeldegui, Marta (Christel Uittenbogaart)	Post	'09- '10	PhD	'07	UCLA	Role of B cell activation by HIV-1 <i>in vivo</i> in the genesis of AIDS-NHL	Current T32 Trainee
Nguyen, David (Gang Zeng)	Post	'09-	PhD	'08	Penn State Univ	The use of tumor associated antigens as modulators of the immune system	Current T32 Trainee
Williams, Kevin (Steven Bensinger)	Post	'09-	PhD	'08	UCLA	Examining the impact of molecular sterol metabolism on tumor immunotherapy	Current T32 Trainee
Diana Moughon (Lily Wu)	Pre	'10-	BA	'08	UC Berkeley	Investigating the impact of the mTOR signaling pathway on cancer-associated inflammation	Current T32 Trainee

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Past & Current Trainees (Mentor)	Pre/Post	Training Period	Prior Academic Degree			Title of Research Project	Current Position (If Graduated)
PI: Marder, Victor T32 HL 066992 Training for Academic Hematology							
Bucher, Nora (Carolyn Britten)	Post	'06-08	MD	'01	Univ of IL	Phase 1 trials in malignancy	Private Practice Los Angeles
Kaluza, Vesna (Sven De Vos)	Post	'05-07	MD	'01	UC San Diego	Inducing and targeting EBV lytic antigens in EBV-associated lymphoma	Private Practice Long Beach
Dolezal, Milana (Judith Gasson)	Post	'03-05	MD	'99	Thomas Jefferson Univ	Notch signaling in hematopoiesis	Asst Medical Director BioOncology, Genetech
Garon, Edward (H Phillip Koeffler)	Post	'04-06	MD	'99	Washington Univ	<i>In vitro</i> and <i>in vivo</i> analysis of nanoelectropulse therapy; utility of quantum dots for labeling and tracking leukemic cell lines, human bone marrow, and CD34+ umbilical cord blood	Asst Professor, UCLA Hematology/Oncology
Sadeghi, Saeed (Victor Marder)	Post	'03-05	MD	'99	St Louis Univ, MO	Non-myeloablative bone marrow transplantation	Asst Professor, UCLA Hematology/Oncology
Stewart, Daphne (Victor Marder)	Post	'03-05	MD	'98	Columbia Univ	Plasmin: a novel thrombolytic agent	Assoc Director, Bone Marrow TX, Cedars Sinai Medical Center
Kengla, Alice (Charles Sawyers)	Post	'05-07	MD	'01	Albert Einstein College of Med	Identifying serum biomarkers in cancer	Kaiser Permanente
Eradat, Herbert (Michael Teitell)	Post	'07-08	MD	'02	Chicago Medical School	Regulation of B-CLL cell survival	Clinical Instructor UCLA, Hem/Oncology
Rojas, Ana Maria (Mary Territo)	Post	'07-'09	MD	'03	Wake Forest Univ	Ex-vivo-expanded hematopoietic stem cells in transplantation	Private practice, Orange County
Liao, Mickey (Gary Schiller)	Post	'07-'09	MD	0-2	Jefferson Medical College	Multiple myeloma at UCLA	Trainee in Geriatric Oncology
Kim, Benjamin (Victor Marder)	Post	'08-'11	MD	03	Feinberg School of Medicine, Northwestern University	ADAMTS 13 mismatches in renal allograft rejection	Current
Andorsky, David (John Timmerman)	Post	'07-'09	MD	02	Harvard Medical School	Immunotherapy of lymphoma	Private practice, Colorado
Ontiveros, Evelena (Sven De Vos)	Post	'08-'10	MD, PhD	04	Roy J and Lucille A Carver College of Medicine/University of Iowa	The PIM1 oncogene accelerates TCL1-driven lymphomagenesis in a double-transgenic murine model	Research Instructor, Iowa University
Koppel, Ahrin (Gary Schiller)	Post	'08-'10	MD	04	Sackler School of Medicine	Stem cell transplantation in acute myeloid leukemia	Private practice, California
Eshaghian, Sharooz (Gary Schiller)	Post	'10-	MD	06	Albert Einstein College of Medicine/Yeshiva University	To be determined	Current

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PI: Marder, Victor T32 HL 066992 Training for Academic Hematology							
Ngarmchamnanrith, Gataree (John Timmerman)	Post	'10-	MD	02	Chulalongkorn University, Thailand	Immunotherapy of lymphoma	Current
Aribi, Ahmed (Philip Koeffler)	Post	'09-	MD	96	University of Al Fateh, Libya	SNP analysis in AML	Current
PI: Rawson, Richard T32 DA007272 Drug Abuse Research Training Center							
Safa, Parsa (James Boulter)	Pre	'02-06	BA	'97	Stanford Univ	Molecular neurobiology of nicotine addiction	Marketing Application Scientist, Molecular Devices Corp
Gyawali, Sandeep (Christopher Evans)	Pre	'04-05	BS	'99	Univ of IL	Genetic manipulation of animal models to study effects of drugs on neural development and behavior	Research Associate, Weill Cornell Medical College
Helmus, Todd (Martin Iguchi)	Post	'03-05	PhD	'02	Wayne State Univ	Contingency management for drug abuse treatment; substance abuse in the military	Behavioral Scientist RAND Corp
Wong, Eunice (Martin Iguchi)	Post	'03-06	PhD	'03	UC Santa Barbara	Culturally diverse patient populations and treatment matching; evaluation of substance abuse treatment and prevention	Behavioral Scientist RAND Corp
Xu, Jiansong (Edythe London)	Post	'02-05	PhD	'99	Medical College of Ohio	Cigarette smoking, cognition an dfMRI; social cognition and methamphetamine	Research Scientist Yale Univ
Jacobson, Jerry (Douglas Longshore)	Post	'04-06	PhD	'04	RAND	Substance abuse policy; politics of place and treatment centers	Central America and Panama CDC and Prevention
Taylor, Didra Brown (Douglas Longshore)	Post	'03-05	PhD	'00	CA School of Prof. Psychology	Malt beverage use in minority communities and environmental relationships with risk behavior	Asst Professor, CDU Urban Public Health
Shoblock, James (Nigel Maidment)	Post	'03-06	PhD	'03	Albany Medical College	Neuropharmacology; role of inverse agonism at the muopod receptor in mediating endogenous hedonic tone	Senior Scientist Johnson & Johnson
Jackson, Brian (Thomas Newton)	Pre	'04-05	BS	'02	Univ of Pittsburgh	Neurobiology of addiction	Law Student Univ of Pittsburgh
Corbit, Laura	Post	'03-04	PhD	'03	UCLA	Safety of different pharmacotherapies for the treatment of stimulant abuse/dependence	Postdoctoral Fellow UC San Francisco
Gonzales, Rachel (Richard Rawson)	Pre	'03-05	MPH	'99	UCLA	Adolescent smoking and drug use, environment and behavior	Asst Research Psychologist, UCLA
Dang, Jeff (Steven Shoptaw)	Pre	'04-06	MPH	'02	UCLA	Applied biostatistical improvements to research in tobacco smoking and methamphetamine abuse	Graduate Student UCLA

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Past & Current Trainees (Mentor)	Pre/Post	Training Period	Prior Academic Degree			Title of Research Project	Current Position (If Graduated)
PI: Rawson, Richard T32 DA007272 Drug Abuse Research Training Center							
Campos, Michael (Steven Shoptaw)	Post	'05-07	PhD	'03	Washington State Univ	Multi-person interventions for substance abuse; adaptation of the multifamily psycho-educational group therapy for schizophrenia	Asst Research Psychologist, UCLA
Sodano, Ruthlyn (Richard Rawson)	Post	'08-10	PhD	'08	Univ of Albany, SUNY	NIDA-funded study evaluating 3 methods of training South African counselors to administer Cognitive Behavioral Therapy for stimulant dependence	Assistant Clinical Professor, UC San Diego
Domier, Catherine (Richard Rawson)	Post	'08-	PhD	'08	Claremont Graduate Univ	Phase 2, Double-Blind, Placebo-controlled trial of Bupropion for methamphetamine dependence	Postdoctoral Fellow UCLA
Spear, Suzanne (Martin Iguchi)	Pre	'08-	MA	'96	Univ of New Orleans	TBD	Graduate Student UCLA
Chim, David (Walter Ling)	Post	'08-09	DO	'03	Western Univ of Health Sciences	Optimizing outcomes using Suboxone® for Opiate dependence	Clinical Assistant Professor, Family Medicine, Community Medicine, and School of Public Health, the University of Hong Kong
Hara, Motoaki (Michael Seltzer)	Pre	'08-10	MA	'03	UCLA	Center for Advancing Longitudinal Drug Abuse Research Cross-Project Analyses	Graduate Student UCLA
Padwa, Howard (Christine Grella)	Post	'10-	PhD	'08	UCLA	TBD	Postdoctoral Fellow UCLA
Lanza, Haydee Isabella (Christine Grella)	Post	'10-	PhD	'10	Temple University	TBD	Postdoctoral Fellow UCLA
Lui, Camillia (Martin Iguchi)	Pre	'10-	MPH/MA	'03	UCLA	TBD	Graduate Student UCLA
Lu, Nu (French, Samuel)	Post	09-10	MD	'04	John A. Burns School of Medicine	Identification of novel proteins and post translational modifications associated with hepatocellular carcinoma	Postdoctoral Fellow UCLA
Callahan, Rena (Slamon, Dennis)	Post	09-	MD	'04	University of Pennsylvania School of Medicine	Safety and tolerability of targeted breast cancer therapy	Postdoctoral Fellow UCLA
Chun, Patrick (Cunningham, William)	Post	09-	MD	'04	Michigan State University College of Human Medicine	The Role of COX-2 in the development of intestinal adenomas	Postdoctoral Fellow UCLA
Kirimis, Evangelia (Glaspy, John)	Post	09-	MD	'05	University of Southern California	Prolactin and breast cancer	Postdoctoral Fellow UCLA
Singh, Arun (Radu, Caius)	Post	09-	MD	'05	UMDNJ New Jersey Medical School	Adoptive cell transfer (ACT) and TCR gene therapy in ovarian cancer	Postdoctoral Fellow UCLA

Past & Current Trainees (Mentor)	Pre/Post	Training Period	Prior Academic Degree		Title of Research Project	Current Position (If Graduated)	
PI: Ribas, Antoni T32 CA09297 Academic Training in Medical Oncology							
Lu, Nu (French, Samuel)	Post	09-10	MD	'04	John A. Burns School of Medicine	Identification of novel proteins and post translational modifications associated with hepatocellular carcinoma	Postdoctoral Fellow UCLA
Callahan, Rena (Slamon, Dennis)	Post	09-	MD	'04	University of Pennsylvania School of Medicine	Safety and tolerability of targeted breast cancer therapy	Postdoctoral Fellow UCLA
Chun, Patrick (Cunningham, William)	Post	09-	MD	'04	Michigan State University College of Human Medicine	The Role of COX-2 in the development of intestinal adenomas	Postdoctoral Fellow UCLA
Kirimis, Evangelia (Glaspy, John)	Post	09-	MD	'05	University of Southern California	Prolactin and breast cancer	Postdoctoral Fellow UCLA
Singh, Arun (Radu, Caius)	Post	09-	MD	'05	UMDNJ New Jersey Medical School	Adoptive cell transfer (ACT) and TCR gene therapy in ovarian cancer	Postdoctoral Fellow UCLA

5.1.5. Medical Scientist Training Program (MSTP). The UCLA MSTP is a joint venture with the California Institute of Technology (Caltech) and is currently training 88 scholars for careers as physician scientists. The MSTP has 128 graduates to date, of whom approximately 50% are still in training (residencies, postdoctoral and clinical fellows, clinical instructors), 35% are in academic medicine positions, and 10% are in clinical practice, 4% are in industry, and 1% are lost to follow-up.

5.1.6. Public Health Programs. The UCLA MS programs in the School of Public Health provide training for many programs in health service and community research. For example, fellows in the Clinical Scholars Program complete a Master's in the Science of Health Services (MSHS) in a clinician-scientist track that trains students to develop and evaluate community-participatory interventions and conduct health services focused on comparative effectiveness and health policy research in underserved communities. Clinical Scholars also have the option of pursuing PhD-level training. This existing MS curriculum provides the core for the new CTSI T32 in Clinical and Community-Partnered Translational Research. Also, in collaboration with **CERP**, the CTSI will develop a Community Translational Research track in the Executive MS Program to provide expertise in translational research for community and faculty leadership. Given the recent enactment of H.R.3590 – Patient Protection and Affordable Care Act, CTSI-ED will develop new curricula and recruit the most knowledgeable scientists and teachers in the UCLA/RAND environment to prepare our community partners for what should be a substantial change in the organization and financing of health care in the US.

5.1.7. Interdepartmental and Community Collaborations at UCLA. There are many training programs in the UCLA community that cross departments and utilize multidisciplinary basic science, clinician, and community investigator mentorship teams to facilitate T1 to T4 translational and patient-oriented research training. There are also programs that link the CTSI partners to each other and the community, such as:

- **The RWJF CSP** trains postdoctoral fellows from many specialties (medicine, surgery, pediatrics, radiology, neurology, obstetrics and gynecology, and family medicine) and engages clinical, public health, social science, and community mentors to create interdisciplinary teams needed to conduct innovative community-partnered research. Scholars receive intensive training in health care issues and methods of positive change at clinical practice, community, and policy levels. Scholars conduct T3/T4 translational research projects such as development and evaluation of a primary-care program to treat hepatitis C among homeless persons²³, and a randomized trial of an icon-based tool to enhance medication adherence for low-literacy patients discharged from a safety-net hospital.²⁴ The CSP projects require high-level community engagement and partnerships, implementation of novel designs, and a comparative effectiveness framework to assess the impact of organizational and therapeutic interventions. All of them have recruited and enrolled participants who are underrepresented in medical research. The CSP provides a transformational model for how to engage

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community in design of CTSI-ED translational research projects that will enhance recruitment of minority participants into research and will enhance the relevance of research for communities with the greatest health disparities. The new CTSI K12 scholars will work closely with our community mentors to develop leadership and communication skills needed to advance translational research nationally. As a co-director of CSP, Dr. Mangione has the experience needed to lead this effort.²⁵

- **The NCRR-funded RCMI Translational Research Network (RTRN) at CDU**, directed by Dr. Keith Norris, a CTSI Associate Director and Leader of a **CERP**, provides opportunities for clinical and translational research among minority and other collaborating institutions throughout the US. Dr. Mangione is a member of the RTRN External Advisory Committee and has partnered with Dr. Norris for over 12 years across nearly 10 NIH funded grants in areas such as innovative intervention studies to reduce health disparities, training of minority faculty, and community engagement activities. By providing computer-based tools for analyzing and managing clinical research data, recruiting for clinical trials, and sharing information with patients, the RTRN enables clinical and translational researchers to collaborate more efficiently with each other and their communities. The CTSI-ED will facilitate partnerships between the RTRN and the CTSI training programs by creating the infrastructure needed to develop a new generation of scientists grounded in the principles of interdisciplinary research teams to address complex translational research challenges and ultimately improve health outcomes. The CTSI-ED will align with the RTRN to expand diversity within the translational research environment, and enhance training across the UCLA CTSI and RTRN institutions.
- **The Brain Research Institute's (BRI) Kindergarten through 12th grade (K–12) Science Outreach Program**: Stimulates interest in neuroscience for children and young adults through a hands-on learning experience emphasizing brain function and implications of neuronal plasticity and drug use.
- **The CDU biomedical sciences and health professional pipeline program spans pre-K–12**: Includes the Lincoln-Drew Magnet Elementary School and the CDU Magnet High School with a specialized Medicine and Science college preparatory program that is partially supported through a NIH-NLM grant. A highlight of the pipeline is a standalone weekend preparatory program, called the Saturday Science Academy. Initiated in 1990, this program provides additional exposure to science and research topics to children from pre-K through 12th grade. Another highlight is the CDU/NIH STEP-UP Program, a NIH National High School Student Summer Research Program. This National Institute of Diabetes and Digestive and Kidney Disease (NIDDK)-funded program has been at CDU since 2000 and focuses on addressing the critical shortage of minorities in the biomedical sciences across the country. The CTSI-ED will partner with BRI and CDU to expand and support these model programs designed to address the minority health care workforce shortage.
- **Harbor-LA BioMed and Cal State Partnership**: Harbor-LA BioMed has partnered with California State University, Dominguez Hills (CSUDH) since 1998 to provide opportunities for under-represented undergraduate and graduate students in the College of Natural and Behavioral Sciences to participate in biomedical research, including clinical and translational research, through National Institute of General Medical Sciences (NIGMS)-funded programs (Undergraduate Student Training in Research [U-STAR] (active), Research Initiative for Scientific Enhancement [RISE] (active), Initiative for Maximizing Student Diversity [IMSD]) (no longer active, although individual Master's students can choose to conduct their thesis research with LA BioMed Faculty). These programs match well funded investigators (MDs and PhDs) at Harbor-LA BioMed with students from traditionally under-represented groups at CSUDH, providing them rich and diversified laboratory or translational research experiences and one on one mentoring. The program also provides structured training in Human Subjects Protection, Use of Animals in Research, Basic Biostatistics, Access to Biomedical Informatics Resources and Advice on Applications and Interviews for PHD and MD programs. More recently, an agreement is about to be signed to allow undergraduates in the CSUDH School of Health and Human Services to intern for a semester with researchers working in the areas of health care services and community health.
- **Harbor-LA BioMed Summer Student Fellowship**: Funded by corporate sponsors, this program provides top graduating high school seniors from Los Angeles Basin with a compensated intense eight week immersion in basic, translational, and clinical research. Students are embedded within active basic and clinical research teams and learn science from the ground up. The program, in its 33rd year, attracts candidates from high schools across the Los Angeles and most recently accepted 15 fellows from an applicant pool of 95.

6. APPROACH

6.1. Specific Aim 1. Establish novel infrastructure (CTSI-ED office) to optimize cross-disciplinary training and integrate community input into training via team-based, interdisciplinary, patient-oriented research throughout the CTSI.

6.1.1. Leadership of the CTSI-ED.

Carol Mangione, MD, MSPH is CTSI-ED Leader and will direct the operations of the CTSI-ED Office. She is a general internist, whose federally funded research has focused on health system and patient-level approaches to improving diabetes care for adults. She directs the P30 UCLA Research Centers for Minority Aging Research (RCMAR), where she mentors minority faculty at the UCLA Schools of Nursing, Medicine, Public Health, Arts and Letters, and at CDU and RAND. As Co-Director of the RWJF CSP, she has extensive experience with mentoring young physician-scientists. Co-leaders of the CTSI-ED, include:

Ronald Edelstein, EdD is the CDU Leader and co-leader for the CTSI-Ed Core and all of its educational programs such as the CTSI K12 and the new T32. Dr. Edelstein works to enhance participation of CDU trainees in all of the allied health professions in CTSI-Ed educational and training opportunities. He also assists with the recruitment of minority scholars into all programs.

Leon Fine, MD, a Pilot/ Collaborative Program Co-leader, is the Cedar-Sinai co-leader for the proposed CTSI-Ed Core and the CTSI K12 Program.

Antoni Ribas, MD, PhD is the Clinical Research Co-leader for the CTSI-ED program co-directs the CTSI K-12 program.

Isidro Salusky, MD, a CCRR Program Leader, is the PI/PD of our NCRR K30 Program. He works closely with Dr. Mangione to assist with coordinating access to the K30 courses for all CTSI affiliated trainees.

Ren Sun, PhD is PI of a PO1, RO1, T32 on virology and gene therapy and a co-PI of a Fogarty training program, Chair of Education for California NanoSystems Institute. He is our liaison to the graduate programs and is the Basic Science Co-leader for the CTSI-ED.

Christina Wang, MD, CTSI Associate Director and CCRR Program Leader, directs the research education programs for graduate students, pre- and post doctoral trainees at Harbor-LA BioMed. She is a co-investigator of the UCLA K30 grant to support training in translational and clinical research. She will be the Harbor-LA BioMed liaison for the proposed CTSI K12 Program and is a Co-leader for the CTSI-ED program.

Table 4. Program and Administrative Leadership of the CTSI-ED and CREST Committee.

CTSI Faculty	Leadership Role	Credentials and Qualifications
Arleen F. Brown, MD, MSPH Martin Shapiro, MD, PhD Susan Ettner, PhD William Cunningham, MD, MPH	CREST Members; Dr. Cunningham is Chair of Recruitment and Admissions Subcommittee.	Dr. Brown, Chair of CERP, will work with the School of Public Health leadership to direct the new Executive MS in Community Research Dr. Shapiro, will lead development of the new translational research seminar series Drs. Ettner and Cunningham will co-direct the new PhD track in Clinical and Community-Partnered Translational Research. Both are jointly appointed Professors in Medicine and Public Health who have chaired numerous translational dissertation committees
Pamela Davidson, PhD	CREST Member/Co-Chair of Assessment and Outcomes Subcommittee	CTSI Co-Director, Chair of CTSI Evaluation and Tracking Unit; research interests include organizational development, medical leadership, and medical care access; teaches health program evaluation
Sherin Devaskar, MD Gautam Chaudhuri, MD, PhD	CREST Member, leaders of CTSI K12 Programs	Drs. Chaudhuri and Devaskar direct the 3 existing K12 programs that will be affiliated with the CTSI. Dr. Devaskar's laboratory is involved in determining the molecular and cellular basis of metabolic fueling of tissues during fetal and neonatal phases of development. Dr. Chaudhuri is the Chair of Obstetrics and Gynecology

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CTSI Faculty	Leadership Role	Credentials and Qualifications
Ronald Edelstein, EdD	CTSI-ED Co-Leader, CREST Committee Member, CDU Representative	Dean of Academic Affairs at CDU
Robert Elashoff, PhD	Co-Director of MS Clinical Research, CREST Committee Member	Vice Chair of the Department of Biomathematics; Chair of the Biostatistics, Study Design, and Clinical Data Management Program; and a nationally recognized master biostatistician with vast experience in clinical trials design and data analysis
Christopher Evans, PhD	CREST Committee Member	Basic researcher (T1 experience), directs a NIDA P50 and the UCLA Brain Research Institute, which administers the Neuroscience graduate and undergraduate training programs (430 students total), key faculty in CTSI K30 and K12 programs
Leon Fine, MD	CTSI-ED Co-Leader, CREST Committee Member, Cedars-Sinai Representative	Chair of the Department of Biomedical Sciences at UCLA-Westwood, Director of Research Graduate Education at Cedars-Sinai, and Emeritus Professor of Medicine, University College, London, Liaison to the CTSI-ED core for faculty appointed at Cedars-Sinai
Joy Frank, PhD	CREST Committee Member/Co-Chair, Director of STAR Program, Co-Director of MS Clinical Research	T1 researcher in atherosclerosis, Director of the highly successful STAR Program since 1997, extensive administrative experience as Associate Dean for Research at UCLA-Westwood
Loretta Jones, MA	CREST Committee Member/CTSI-ED Community Lead	Founder and Executive Director of Healthy African American Families (HAAF), Co-Chair of the RWJF CSP Institutional Policy and Community Board, community representative to the UCLA IRB, RCMAR Board Member and faculty, community representative to CTSI Executive Oversight Committee
Carol Mangione, MD, MSPH	CTSI-ED Co-Leader, CREST Committee Chair, Director CTSI-ED Office, Course Coordinator	Community HSR T3/T4 researcher, PI of P30 Resource Center for Minority Aging Research (RCMAR), Co-Director of RWJF Clinical Scholars Program, Proposed co-director of the new CTSI K12 Program
Antoni Ribas, MD, PhD	CTSI-ED Co-Leader and Co-Director of CTSI K12	Associate Professor of Medicine and Surgery, Director, Tumor Immunology Program Area, Jonsson Comprehensive Cancer Center. Principal investigator of a T32. A physician-scientist conducting laboratory-to-patient research in cancer.
Kathleen Sakamoto, MD, PhD	Pediatrics Lead, CREST Committee Member	T1 to T4 pediatrics researcher, Chief of Division of Pediatric Hematology/Oncology and Vice Chair of Translational Research in Pediatrics at Mattel Children's Hospital, currently PI on two R01 projects and one T32
Isidro Salusky, MD	CTSI-ED Co-Leader, CREST Committee Member, PI of NCRR K-30	T1 to T4 pediatrics researcher, CTSI Co-Leader, Director of the CCRR at UCLA-Westwood; Director of the NCRR K30 Program overall, and critical liaison to that program's course offerings
Ren Sun, PhD	CTSI-ED Co-Leader (Basic Science Lead), CREST Committee Member	Professor of Molecular and Medical Pharmacology and Associate Dean of Graduate Studies at DGSOM
Michael Teitell, MD, PhD	CREST Committee Member, Co-Director of the new CTSI K12 Program	Professor of Cellular and Molecular Pathology, proposed Basic Science Co-Director of the new CTSI K12 Program
Laura Trejo, MPA, MSG	CREST Committee Member/Community Co-Investigator	Chair of the RCMAR Community Action Board, General Manager of the Los Angeles County Department on Aging, experienced developer of programs for elderly with an emphasis on cultural competence, mental health, health, Alzheimer's disease, and rehabilitation
Christina Wang, MD	CTSI-ED Co-Leader, CREST Committee Member Harbor-LA BioMed Representative	Director of the CCRR at Harbor-LA BioMed, CTSI Co-Director, Chair of <u>CCRR Program</u> , extensive experience with training of underrepresented undergraduate and graduate students, critical liaison for faculty appointed at Harbor-LA BioMed

CTSI Faculty	Leadership Role	Credentials and Qualifications
LuAnn Wilkerson, EdD	CREST Committee Member/Co-Chair of Assessment and Outcomes Subcommittee	Senior Associate Dean for Medical Education, Chair of the Faculty Fellowship in Medical Education, and Director of the Center for Education Development and Recruitment at David Geffen School of Medicine; oversight of the full range of medical student curricular activities, including curricular revision, faculty development, and program evaluation

6.1.2. CREST Committee Oversight of CTSI-ED. The CREST Committee provides a forum to fulfill the broad missions of the CTSI-ED. The CREST Committee is composed of the leadership of all the CTSI-ED programs, including the three active K12 programs at UCLA-Westwood, the NCRR K30 Program, the NCRR-funded RCMI Translational Research Network at CDU, our proposed new CTSI K12 and T32, and other institutionally supported training programs.

Two subcommittees assist the CREST Committee in specific tasks: the Assessment and Outcomes Subcommittee and the Recruitment and Admissions Subcommittee. The subcommittee chairs will work closely with CTSI-ED Office staff to analyze programs, including student recruitment, mentor performance, and course assessment data. Each subcommittee also will have a community representative. With assistance from the subcommittees and the CTSI-ED Office, the CREST Committee will:

- Provide administrative support for the proposed CTSI K12 Scholars Program.
- Develop and implement curricula on communication of science and leadership in science for all CTSI K12 trainees and affiliated programs.
- Develop a list of core competencies to provide a framework for training under the CTSI.
- Formulate and optimize training initiatives via ongoing evaluation of courses and programs.
- Facilitate career development and provide an on-call advisory group for trainees and mentor education;
- Reduce redundancy in and assess curricula needs.
- Form trainee interdisciplinary team-science committees to encourage collaboration among trainees at all levels and to support them and their mentors with CTSI resources (see **CCRR**) Initial efforts will focus on the 2010 recipients of the CTSI K12 awards, and trainees in the new CTSI T32 in community-oriented translation.
- Improve recruitment into CTSI programs and clinical and translational research feeder programs.
- Organize seminars in team-based interdisciplinary translational research in collaboration with the team of CTSA HSR researchers described in **CERP**.
- Organize work-in-progress seminars that will be attended by CTSI T1, T2, T3 and T4 scientists.
- Guide the activities of the CTSI-ED Office to effectively accomplish the missions of the CREST Committee and to provide the CTSI-ED with a physical and virtual home.
- Co-host select **CERP** Community Research Symposia with the K12 and K30 directors.
- With **CERP** create and sustain a CTSI community mentor pool and add mentors to specific projects.

6.1.3. Specific Functions of the CTSI-ED Office. The CTSI-ED Office will be contiguous with the CTSI Office of the Institute (see **Overall and Governance**). It will be the primary contact point and information source for trainees, mentors, community participants, and program administrators concerning CTSI-related programs and activities. The CTSI Virtual Home will be developed with **BIP**. The Virtual Home will provide online access to a suite of translational research tools and will enable training and experience with these tools. Other UCLA CTSI Programs, such as **CERP** and **CTT** will use the CTSI-ED Office to accomplish their educational objectives. The responsibilities of the CTSI-ED Office are summarized in **Figure 1**. The CTSI-ED Office, using resources provided by **BIP**, will maintain an up-to-date, detailed database for trainee guidance and program evaluation. This will include information on translational and clinical training grants, program curricula, faculty and community mentors, and trainee opportunities within the four CTSI partner institutions, and select community organizations. The CTSI-ED Office will collaborate with the Telemedicine Program at UCLA to deploy resources for research education of trainees at distant sites whenever possible.

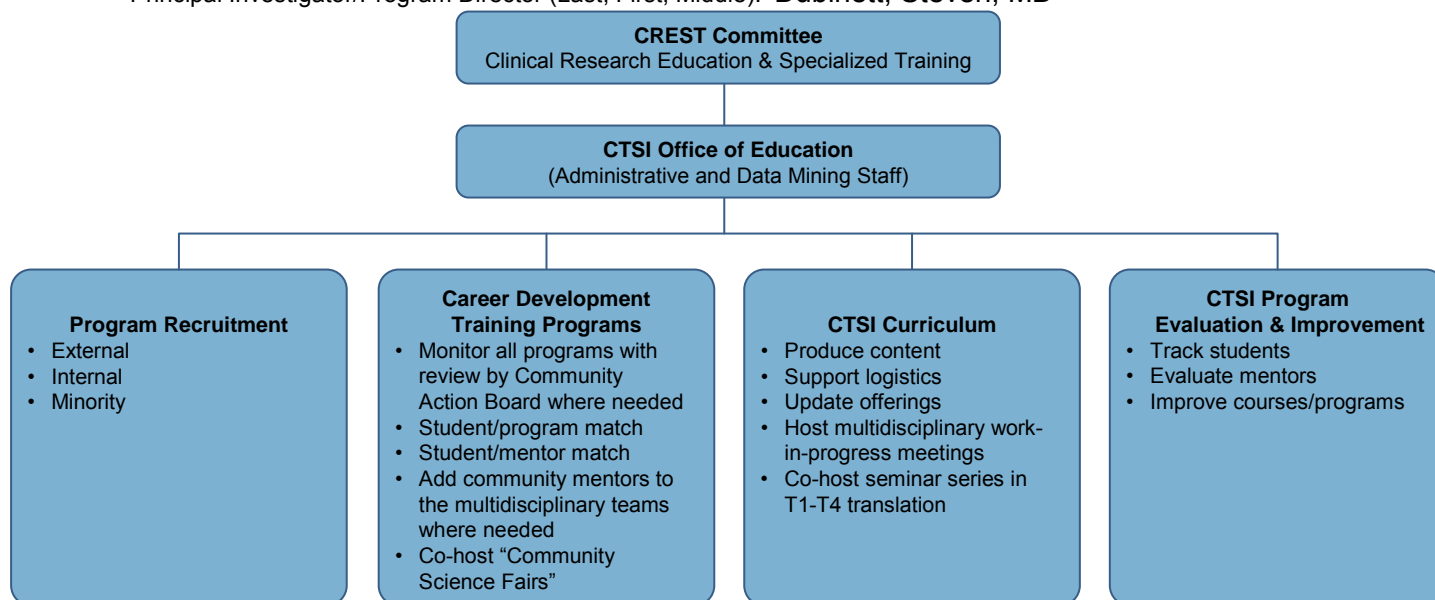


Fig. 1: Primary Functions of the CTSI-ED Office of Education

6.1.4. Overall Recruitment Strategies. Data presented by Ley and Rosenberg²⁶ suggest that nearly half of NIH-funded MD scientists are above 50 years old, double the percentage from 20 years ago. Despite an 82% increase in graduating MDs during this period, only 2 of every 1,000 medical school graduates have NIH-funded research careers. These discouraging data suggest that strategies to recruit MD graduates to clinical, basic, or translational research careers have not been successful. The CTSI-ED will actively recruit young investigators, focusing on both attracting underrepresented minority scholars and men and women from majority populations, and will provide incentives for these individuals to remain involved in academic clinical and translational research. Each of the central element programs of the CTSI-ED (STAR, K30, MS in Clinical Research, K12s, and the new PhD track in Community-Partnered Translational Research) has developed an admissions committee, which will supply data to the CTSI-ED Office for analysis by the Recruitment and Admissions Subcommittee. This subcommittee will ensure that all criteria are available for evaluation of applicants and will offer advice to enhance both minority and general recruitment across all of the programs.

6.1.5. Underrepresented Minority Recruitment Strategies. Current minority programs and long-term strategies in place to enhance minority recruitment to the CTSI institutions include the following:

- **Minority Elementary, High School, and College Student Biomedical Research Programs.** One of our long-term goals is to increase the pool of minority students entering medicine and biomedical research. To this end, we are working closely with the UCLA ACCESS Program, which has been cited nationally for its successes.²⁷ Also, Harbor-LA BioMed since 1998 has formed a collaborative partnership with California State University at Dominguez Hills (with 75% underrepresented minority students) to train undergraduate and graduate students in biomedical research via NIGMS-funded programs.
- **Minority Medical Students and graduate students from UCLA and CDU.** Participation of CDU is a strong asset to CTSI minority recruitment efforts. A recent study confirmed that the majority of CDU/UCLA graduates fulfill their commitment to practicing in medically disadvantaged communities at a rate twice that of their UCLA counterparts (68.5% vs. 28%)^{28,29,30} who are themselves above the national average. Forty percent (40%) of CDU graduates have been African American and 35% have been Latino. More than one-third of all underrepresented minority doctors practicing in Los Angeles County received training at CDU. Many of these students are provided with summer research experience, via the Short-Term Training Program (STTP) and 1-year paid research fellowships from institutional funds. Promising students will be actively recruited as CTSI-ED program scholars. The new Program in Medical Education Urban Rural Underserved (PRIME UR-US) at UCLA-Westwood, funded by the State of California, enrolled its first class of 18 medical students in 2008. In the first three cohorts of this program, fifty-five percent of these students are Latino, 17% are African American, and 89% come from under-privileged backgrounds. The goal of the program is to increase the number of physicians prepared to provide leadership in addressing health

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disparities. In 2009, under the direction of the Dean's office and Dr. Mangione, UCLA CSP scholars initiated a one-on-one mentorship program for the PRIME UR-US students. This provided the students with an important opportunity to conduct research in minority communities and to be mentored by physicians from minority backgrounds who were further along in the academic pipeline. With CTSI-ED resources we plan to greatly expand this mentorship program by linking a greater number of our medical students interested in academic careers with our CTSI postdoctoral and junior faculty trainees.

- **Residents, Fellows, and Junior Faculty.** To identify qualified minority candidates early in their training, residency program directors will work with the members of the CTSI-ED admissions and recruitment subcommittee directed by Dr. Cunningham. Potential candidates will be directly contacted, interviewed, and encouraged to apply to UCLA programs. A number of these students are being mentored by our postdoctoral fellows in the Robert Wood Johnson Clinical Scholars Programs under Dr. Mangione's direction, where they are working on community-based T3/T4 translational research projects. Many programs to enhance minority recruitment are underway. For example, in 2008 the UCLA Department of Medicine created a visiting elective scholarship program for medical students from underrepresented groups. This program provides institutional support for 10 fourth-year minority medical students interested in applying for the Department of Medicine's clinical electives. The goal of the program is to expose these students to our Internal Medicine training program and promote student interest in applying to UCLA for internship and residency.

The RWJF Clinical Scholars Program at UCLA has been highly successful at recruiting and training minority scholars. Among the 75 alumni or current scholars, 16% are African American, and 9% are Latino. These minority alumni include Dr. David Satcher, former US Surgeon General; Dr. David Carlisle, Director of the Office of Statewide Health Planning and Development for the State of California; and a number of tenured professors at UCLA, including Dr. Arleen F. Brown, **CERP** leader and Dr. William Cunningham, the proposed co-director for the new CTSI T32. At the junior faculty level, the NIA-funded RCMAR/CHIME has successfully recruited 27 minority faculty, most of whom were at the assistant professor level at the time of their awards. To date, 10 have been promoted with tenure and 10 are currently in tenure-track positions. An unplanned benefit of RCMAR is that the funded minority faculty have created a community to support and advance their careers by peer mentoring each other in meetings multiple times a year. These meetings have proven vital in combating the isolation that minority and women faculty report as a barrier to their success in traditional academic medical settings.³¹ The CTSI-ED expects to have the needed "critical mass" of minority faculty and trainees for this type of supportive co-mentoring arrangement as the minority scholars matriculate in their programs. With resources from the CTSI-ED, Dr. Mangione will take what she has learned from the RCMAR trainees and expand peer mentoring programs for CTSI-affiliated T1 to T4 trainees. Given the multi-institutional structure of the CTSA, this will be accomplished by adding a "trainee only" social hour with a light dinner at the end of the monthly translational research seminar series meetings for trainees to network and advise each other. CTSI-ED will also partner with **BIP** to develop a translational research trainee blog and user group that will be maintained by the CTSI-ED office staff.

- **Attendance at Minority Career Opportunity Symposia.** We will join the efforts of the UCLA ACCESS Program, which annually sends its director and a manager to several minority career opportunity symposia sponsored by the Association of Minority Health Professional Schools, the Society for Advancement of Chicanos and Native Americans, and the California Minority Coalition.
- **Brochure and Web Site.** Brochures and a comprehensive web site have been created to advertise our K30 Program and many others. The web site URL is given to all applicants, distributed on interview day, and disseminated to training programs. A brochure and website will be created for all CTSI-ED programs highlighting the new CTSI K12 and T32 programs in translational research.
- **Trainee Support to Provide Role Models.** It is the aim of our program to provide strong support of minority scholars and ensure future role models for aspiring students. Minority scholars are counseled and encouraged to participate in research endeavors at all levels. Specifically the CTSI-ED will facilitate linkage of minority scholars funded by CSP, K30, RCMAR, EXPORT and CTSI K12 programs to the UCLA PRIME students for longitudinal mentorship.

6.1.6. Program Retention of Minority Students. Retention and career development of minority trainees is a concern for the CTSI at all levels of education. One example of the dedication of CTSI partners to improving minority representation in biomedical research is a Cedars-Sinai and Harbor-LA BioMed collaboration in 2000 that created the Minority High School Clinical Scholars Program, an accredited semester course for motivated 12th-grade students in the ethnic minority-enriched Long Beach Polytechnic High School (LBPHS). We anticipated that early exposure to clinical research would encourage students to consider careers in biomedical research. The 14-week curriculum, which will be an elective of the CTSI-ED Curriculum Tree, is split between a mentor-supervised, hands-on experience in one of our CTSI CRRs or in community settings where translational research is underway, and a formal course in high school. The curriculum culminates with a student poster presentation at the academic health center and high school sites. Under the CTSI, we will track our graduating high school students by survey every 2 years, through college and graduate school, to determine whether our early intervention had any effect on their eventual career choices. As part of this CTSA application, we propose to expand this program from one to three high schools in Los Angeles by leveraging existing partnerships between UCLA and the Los Angeles Unified School District.

6.1.7. Career Development. The CTSI-ED Office will provide a resource and comprehensive guidance center to facilitate career development for all affiliated scholars besides that provided by the individual programs. Knowledgeable staff familiar with training programs will direct faculty or trainees to appropriate virtual and hard-copy resources maintained by the office. The CTSI-ED staff will have a contact faculty list of CREST Committee members and faculty experts in specific areas of training to provide more specific guidance. Additionally, Drs. Mangione, Ribas, Salusky, and Sun will triage these requests to the most appropriate faculty mentors. The office will keep up-to-date information regarding program opportunities, faculty and community expertise, and mentor qualifications and evaluations. The CTSI-ED also will disseminate specific courses on the Curriculum Tree for career advancement and survival, such as the Academic Advancement Seminar in the Division of Geriatrics that has been taught 2 hours a month over the past 8 years.

6.1.8. Mentoring

6.1.8.1. Mentors. A large, diverse group of federally funded mentors will participate in the CTSI-ED programs. For example, Dr. Mangione, in partnership with Dr. Keith Norris and others, has implemented a multimodal mentoring program for junior faculty from underrepresented groups in the RCMAR and EXPORT Programs. This mentoring program trains faculty from the Schools of Medicine, Nursing, Public Health, and Arts and Sciences at UCLA-Westwood, RAND, and CDU and is a model for minority faculty development throughout CTSI-ED. In 2005, Dr. Mangione was awarded the Society of General Internal Medicine Mid-Career Research Mentor Award based on the successes of her mentees. Since arriving at UCLA in 1994, she has been the primary researcher mentor for 46 trainees, and 52% of these were from underrepresented minority groups, 90% of whom have either been promoted or are currently in academic medicine tenure-track positions.

Faculty from all four CTSI partners will have access to a robust CTSI web portal. The domains of the portal will be divided into curricular, mentoring and structured faculty development programs such as the CTSI K12, T32 and K30 programs, and interdisciplinary collaborative opportunities in translational science. The mentoring/faculty development section will have a brief biographical description of each CREST Committee member and each pre- and postdoctoral program. Once the faculty member has had an opportunity to review the materials, there will be an email portal where the faculty member can request a one-on-one consultation with the CTSI-ED Leader or the appropriate Co-Leader ([Sun for basic lab-based research, Ribas for clinical research, Salusky (T1 to T4 Pediatrics) and Mangione for translational research that spans from bedside to communities, T3/T4]), consultations can also be requested from the CTSI-ED co-investigators who are the leaders of each of the major career development opportunities affiliated with the program. These include Dr. Frank for those who are considering participation in STAR and Dr. Etnner for those who are interested in the T32. Eligibility criteria, deadlines, and all application materials for the faculty development training programs will be available on the CTSI portal. Announcements and RFAs for each funded program will be sent out on the four institution listserves to a very broad group of trainees and scientists.

In accord with the CTSA RFA, we have selected for our K12 Program 30 highly experienced mentors with excellent training records and training resources. Biosketches for these 30 mentors are included in this application. **Table 5** summarizes their areas of research experience and success in mentorship. It is important to note, however, that these key mentors are only a subset of the highly qualified mentors available in our

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academic community. Our mentors represent a broad array of scientific disciplines in basic and clinical research or community-oriented research, and they each have stellar track records in teaching and mentoring.

6.1.8.2. Mentor-Trainee Pairing and Evaluation. If a trainee is participating in laboratory-based investigations, he or she will have a basic science and clinical investigation mentor. This will ensure constant instruction in translational aspects of their patient-oriented investigations. Selected laboratory-based investigations with potential for development of clinical therapeutics and virtually all clinical- and community-based investigators also will have a community mentor on the team. CTSI-affiliated K12 trainees will present their work at least annually in one of the monthly CTSI work-in-progress meetings. There they will receive feedback from senior faculty across the full translational research spectrum. The new CTSI K-12 scholars will present at work-in-progress sessions quarterly to their multidisciplinary mentorship teams and to selected members of the CREST Committee. As part of the communication and leadership curriculum for these scholars, the CREST Committee community and academic mentors will also guide the scholars in the preparation of presentations of their projects to community venues. In collaboration with CERP, the CTSI-ED will hold an annual community research forum where each scholar will present his or her research to a wide array of people without specific scientific training. This exercise has been highly successful in the RCMAR and EXPORT Centers and serves two purposes: (1) heighten awareness of scientific studies in the community, and (2) provide a mentored experience in communication to communities. We consider this team-based approach to mentorship essential for successful clinical and translational research, consistent with policy of the CTSI Pilot Program. Mentorship quality will be measured by trainee evaluations, trainee accomplishments, and peers' and co-mentors' evaluations. Successful researchers do not always make successful mentors; thus, mentors will also be evaluated and guidance available to them throughout the program. Mentor evaluation criteria will include capacity for providing scientific guidance; experience in research design; technical skills; scientific communication to peers and community members; interaction with personnel; ethical behavior; advice on career development; and fostering pathways to team-based and independent pursuits. Evaluation materials for CTSI program mentors will be reviewed by the CREST Committee, and in the event of perceived poor mentoring the CREST Committee will decide on the nature of the intervention and if mentoring should continue or be contingent on mentor education.

6.1.8.3. Mentor Recognition. UCLA is addressing faculty and community credit in team-based science. We recognize that the facilitation of team-based science will require an academic reward system in which promotion does not depend solely on individual productivity. Recently, the specific criteria for promotion have changed at UCLA in response to the need to reward individuals for team-based efforts (see Overview and Governance). However, there is a continuing need to inform faculty about presenting CVs and writing letters for evaluation of those involved in team-based science. The CTSI-ED website at the Virtual Home will contain information on preparation of promotion materials for team scientists, focusing on descriptions of the individual's role in manuscripts and grants, and the essential elements these faculty provide to complete clinical or translational studies. The CTSI-ED also will provide a short seminar course for mentors, community partners, and program directors, beginning in Year 2. This will include developing leadership skills and effective administrative infrastructure, information technology (IT) resources provided by the CTSI-ED (courses, Web-based career opportunities and program descriptions, data analysis of training programs), and addressing ethical issues, with an emphasis on establishing criteria for credit in team science. Based on our experience in the RWJF CSP, this last issue is of critical importance for T3/T4 projects with community partners. The CREST Committee will also work on a longer-term goal of obtaining academic appointments at UCLA for community members who contribute in substantive ways to research and teaching. Dr. Norris has succeeded in accomplishing this at CDU where, along with others, Ms. Loretta Jones, Chief Executive Officer of Healthy African American Families, was appointed in June 2010. The CREST Committee will partner with Dr. Norris to design a process at UCLA to accomplish this important goal.

6.2. Specific Aim 2: Transform translational education through new curricular elements and create new programs (K12, K30, T32, and others) incorporating community engagement and interdisciplinary methodologies and technologies.

Rationale: The CTSI-ED will build on established clinical and translational research training programs that have proven records of excellence, including our STAR Program, three K12 Programs, RWJF CSP, and the RCMAR. Many of the STAR, K12, and other mentoring programs rely on a didactic infrastructure created by the recently renewed K30 Program, which includes the MS Program in Clinical Research and the Certificate in

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Translational Investigation. These programs will be enhanced by strengthening the training in systems biology, translation of technology and therapeutics, bioinformatics, comparative effectiveness, and development of community interventions. Along with selected courses from the IMED program, these enhancements will provide the needed curriculum for the new CTSI K-12 Program. The RWJF CSP scholars matriculate a “clinician scientist track” in an MSHS degree from the Department of Health Services in the School of Public Health. The required courses in this track will provide a considerable portion of the curriculum for the new CTSI T32 PhD in Community-Partnered Translational Research. Overlaid on this didactic core will be a set of electives that will provide high-level expertise in specific areas such as community-partnered interventions, advanced methods for comparative effectiveness research, health economics, or health behaviors. The CTSI-ED also will develop a new Executive MS Program in Community Research with **CERP** faculty, and new curricula for all scholars designed to improve communication of science, and theory and practice of community engagement with a strong focus on developing needed leadership skills to take promising T1/T2 translation findings and disseminate and evaluate their effectiveness in T3/T4 projects. A major function of the CTSI-ED Office for these new and existing programs will be to develop the needed IT infrastructure to consolidate courses into a single Curriculum Tree to allow ready assembly of rigorous and evaluated didactic components for our programs.

6.2.1. Expand the Scope of Preexisting Mentored Training Programs

6.2.1.1. Expand the STAR Program to Trainees at All CTSI Institutions. The highly successful Subspecialty Training and Advanced Research (STAR) Program was developed at UCLA in 1994 and its educational goals overlap extensively with those of the CTSI. Accordingly, we propose to expand this program as one of the central elements for translational physician-scientist training. The STAR Program in collaboration with the CTSI-ED will be enhanced by:

- Expanding training opportunities to a greater number of clinical departments via increased institutional commitment
- Providing increased educational opportunities for clinical research training.

Overview: Conceived and implemented entirely at UCLA, the STAR Program enables clinical fellows, residents, or MSTP students to obtain a graduate degree or to receive mentored postdoctoral research training. Fiscal constraints inherent to continued training represent a great barrier to recruiting and retaining translational physician scientists. Addressing this disincentive, guaranteed salary and tuition coverage under the STAR Program provides financial stability to individuals who have already dedicated many years to education. Thus, advanced training in basic, clinical, translational, or community-based research takes place in a structured, rigorous, and financially secure setting. By integrating formal research training with the clinical fellowship or residency, the STAR Program provides a unique entry point into academic medicine, producing outstanding physician scientists who often continue to educate future translational researchers.

Training and Career Development under the STAR Program: Through the STAR Program, we offer four research tracks:

- **Track 1:** PhD in basic biomedical science (for MD graduates)
- **Track 2:** PhD in health services/outcomes (for MD graduates)
- **Track 3:** MS in Clinical Research/Clinical trials (for MD graduates)
- **Track 4:** Protected postdoctoral research training (for MSTP graduates).

UCLA CTSI faculty, those from Caltech, and the RAND Graduate School can be mentors for STAR trainees.

Leadership: Dr. Joy Frank directs the STAR Program and as a member of the CREST Committee, will provide a critical bridge to the CTSI-ED that will ensure an enriched base for the STAR Program—including recruitment, maintained excellence of didactic education provided by the CTSI-ED Curriculum Tree, services of the centralized Office for Education providing evaluation materials for program improvement, information on mentors, training program and internal/external career development information, and funding opportunities.

STAR Program Outcomes: The productivity of STAR graduates clearly demonstrates the program’s remarkable success and the basis for which support and expansion of this program is proposed by the CTSI-ED. 98 scientists have graduated since the program’s inception in 1994, with 79 currently involved in research in academic or industry settings. Current appointments include 13 clinical instructors, 41 assistant professors,

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15 associate professors, 3 professors, 2 of whom are currently UCLA division chiefs. 7 STAR graduates currently work in either government or industry. The STAR fellows are a diverse group, from Medicine, Pediatrics, Pathology, Surgery, OB/GYN, Ophthalmology, and Family Medicine. Of the 79 graduates of the program, 22% have been women and 6.3% are underrepresented minorities.

Enhancement of the STAR Program by the CTSI-ED: Resources to expand STAR will derive from a combination of additional institutional funds committed to CTSI-ED by the DGSOM and increased opportunities for NIH-funded institutional training programs identified via the CTSI-ED Office. The STAR trainees will benefit from the CREST Committee-organized seminar series that will expose trainees to the CTSI Program of sponsored monthly symposia that will bridge T1 to T4 translation. Additionally, the CTSI-affiliated STAR fellows will participate in the monthly CTSI sponsored cross-disciplinary work-in-progress meetings. New courses in the CTSI-ED Curriculum Tree will expand didactic opportunities for STAR trainees. The CTSI-ED, through institutional funds and the restructured K30, will support faculty salaries and increase computer laboratory space for the biostatistics and data management courses required for Track 3 STAR Fellows who rely on the MS in Clinical Research for their curriculum. Enhancements also will be added for translational researchers who want to develop expertise in comparative effectiveness, the implementation and evaluation of community-based clinical trials and health system-level organizational interventions designed to improve the delivery of clinical care. Much of this curriculum will be derived from existing seminar series and courses in the UCLA School of Public Health and the new curriculum that will be developed as part of the recently awarded K30 CER grant. STAR fellows will continue to be encouraged to apply for pilot study funding through the UCLA Society of the CTSI Scholars Program launched during Spring 2008 [see **Pilot and Collaborative Research Studies Program (Pilot Program)**] and the proposed CTSI K12 Program (see **section 6.2.2.1.**).

6.2.1.2. K12/T32 Mentored Interdepartmental Clinical Pharmacology Research Scholars Program. This program, currently funded by the NIGMS T32 (2 scholars) and previously funded by an NCRK K12 (6 scholars), provides formal training to post-specialty MDs through mentored fellowships in clinical pharmacology and therapeutics. Successful elements of the previously funded K12 training program will be incorporated and expanded in the new CTSI K12 (see **section 6.2.2.1.**). The newly proposed version of this K12 program under the auspices of the CTSI-ED will add courses and mentored research in a systems biology approach to disease, providing a training interface with the CTT and will add courses in comparative effectiveness. The proposed CTSI K12 will create a more comprehensive academic infrastructure, thereby facilitating education, training, and career development of junior faculty in new areas of research excellence at UCLA-CTSI. Additionally, the newly proposed 4 institution CTSI K12, through patient care, physician education, and service, will reach into the community to improve access to therapeutics and health care.

The NCRK T32 program is directed by Dr. Barbara Levey (see **Table 4**). As a member of the CREST Committee, Dr. Levey will be able to share her wealth of knowledge from directing this program with Drs. Ribas, Mangione, Salusky, and Teitell, the proposed co-directors of the new CTSI K12 Program. The courses in these programs are shared with the CTSI-ED Certificate/MS in Clinical Research programs, which comprise our K30 Program. The K12 Program in Clinical Pharmacology is a translational research program to build from because of its strong multi-institutional connection with CDU and because of its strong orientation toward extending scientific findings from bench to bedside and into the community to improve therapeutic outcomes. The newly proposed CTSI K12 program will retain many of the successful elements of this existing program.

6.2.2. Develop Novel Programs that Facilitate Integrated Training in Patient-Oriented Research

Training at UCLA-Westwood of clinicians to become effective research scientists is well developed and provides opportunities at all levels. The CTSI-ED will place additional emphasis on mechanisms for basic scientists and community professionals to acquire skills necessary for T1 to T4 translational research. Three components in the CTSI-ED will address this area:

- Development of new didactic courses targeting conduct of translational research.
- Development of new training programs requiring new didactic courses in translational research and mentors in clinical, community-oriented, and basic science.
- Creation of a program taught on weekends that emphasizes community research for training of community-based and academic professionals.

The proposed programs will:

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- Develop a CTSI K12 Interdisciplinary Translational Therapeutics and Technologies Research Program
- Develop a unique PhD track in translational systems biology in collaboration with the CTSI Technology Program that interfaces with the expanded CTSI-ED K12/T32 program in clinical pharmacology.
- In collaboration with **CERP**, create the Executive MS Program in Community Research by combining curricula from the CTSI-ED Curriculum Tree and the School of Public Health.
- Develop the new T32 Training Program in Clinical and Community-Partnered Translational Research to provide a mentoring and didactic environment for developing team-based T3/T4 scientists with special skills in the conduct of community-oriented CER.

6.2.2.1. CTSI K12 Mentored Interdisciplinary Translational Therapeutics and Technologies Research.

Rationale: The next generation of clinicians will develop and rely upon increasingly complex technologies that may span multiple disciplines in the engineering and physical sciences, besides the life sciences, to advance patient care. The CTSI-ED has identified the training of clinical fellows and newly hired faculty at the interface of technology development and translational/community medicine as an emerging, national unmet need that is being addressed through a highly innovative, mentored TTTRP. This new 4-institution K12 program will provide a program in patient-oriented investigation, emphasizing the diseases that disproportionately affect minority populations.

Overview: As a K12 training program within the CTSI, the TTTRP has a unique, shared leadership structure of four senior investigators with proven track records in basic, translational, and community-oriented research. This leadership format provides representation in each aspect of trainee activity, to ensure a balanced, innovative and technology-enabled approach to important problems in clinical medicine. TTTRP trainees are selected from all medical training specialties at the level of clinical fellow or early, first-time faculty appointment with at least 80% protected research time. There are 3 educational foci that each TTTRP trainee will undertake to varying extents based on identified interests:

- Systems Biology
- Clinical Pharmacology
- Translational Community-Partnered Interventions with an emphasis on advanced methods for CER.

Trainees drawn from clinical programs at the four CTSI institutions will focus on a clinical problem and develop the required technological skills to approach the problem with the guidance of a specially assembled translational and scientific mentoring team that is project oriented (see **Table 5**, CTSI-ED K12 Mentors). The TTTR also addresses several identified practical needs of emerging academic physicians including cutting-edge interdisciplinary training to expand potential lab research topics, time to develop critical thinking skills, time to generate additional preliminary data, guidance for competitive grantsmanship, academic advancement, leadership, and communication of science skills.

Table 5. Thirty Mentors selected for the CTSI-ED K12 Program.

Mentor Positions and Affiliations Mentor Expertise	Trainees Past 10 Years	Current Positions of Top Trainees over Past 10 Years	Mentor Funding FY10
Lori Altshuler, MD , Professor of Psychiatry Director of Mood Disorders Research Program, Semel Institute of Neuroscience, UCLA Mood Disorders, Neuroimaging STAR, K30, T32, Systems Biology PhD, MS Community Research	32	1. Mark Frye, MD, Professor of Psychiatry, Mayo College of Medicine, Rochester, MN 2. Natalia Rasgon, MD, PhD, Professor of Psychiatry and Obstetrics and Gynecology, Stanford University 3. Carrie Bearden, PhD; Assistant Professor of Psychiatry and Biobehavioral Sciences, UCLA	\$1,611,256

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Mentor Positions and Affiliations Mentor Expertise	Trainees Past 10 Years	Current Positions of Top Trainees over Past 10 Years	Mentor Funding FY10
Jonathan Braun, MD, PhD , Professor and Chair of Pathology; Professor, Department of Molecular Pharmacology, UCLA Inflammatory Bowel Disease STAR, K30, Systems Biology PhD, MS Community Research	22	1. Dean Felsher, MD, PhD, Associate Professor, Oncology, Stanford University 2. Rick M. Fairhurst, MD, PhD, Staff Physician, NIH, Bethesda, MD 3. John S. Tomlinson, MD, PhD, Assistant Professor, Department of Surgery, UCLA	\$290,551
Arleen Brown, MD, PhD , Associate Professor UCLA Division of General Internal Medicine and Health Services Research, Department of Medicine, Center for Health Sciences, UCLA Medical Center Health disparities, chronic disease management, neighborhood influences on health, community partnered participatory research	12	1. Kenrik Duru, Assistant Professor; UCLA Division of General Internal Medicine and Health Services Research 2. Jason Fish, MD, Clinical Instructor, General Internal Medicine, UCLA 3. Ozlem Equils, MD, Assistant Professor, Department of Pediatrics, Cedars-Sinai	\$316,846
Yvonne J. Bryson, MD , Professor of Pediatrics and Chief of Pediatrics Infectious Diseases, UCLA Mother-to-child transmission of HIV STAR, K30, Systems Biology PhD, MS Community Research	16	1. Karin Nielsen, MD, Associate Professor, Pediatrics, UCLA 2. Michael Lamacchia, MD, Vice President of Clinical Services, Department of Pediatrics, Maimonides Hospital, Brooklyn, NY 3. Ozlem Equils, MD, Assistant Professor, Department of Pediatrics, Cedars-Sinai	\$3,130,868
Gautam Chaudhuri, MD, PhD , Professor of Pharmacology, Professor and Executive Chair of Obstetrics and Gynecology, UCLA Vascular Biology, Breast Cancer STAR, K30, Systems Biology PhD, MS Community Research	17	1. Robin Farias-Eisner, MD, PhD, Professor and Chief, Obstetrics and Gynecology, UCLA 2. Rajan Singh, MD, PhD Assistant Professor of Medicine, CDU 3. Lauren Nathan, MD, Professor, Department of Obstetrics and Gynecology, UCLA	\$1,100,914
Judith Currier, M.D. , Professor of Medicine; Chief, Division of Infectious Diseases; Associate Director, Center For Clinical AIDS Research and Education UCLA Treatment Optimization for HIV, Metabolic Complications of ART, and Maternal Health STAR, T32, K24	12	1. Mario Raviglione, MD, Director STOP TB, World Health Organization, Geneva 2. Obiamiwe Umeh, MD, MSc, Sr. Director – Clinical Research, Cubist Pharmaceuticals, Lexington MA 3. Matthew Leibowitz, MD, Assistant Clinical Professor of Medicine Division of Infectious Diseases, UCLA	\$4,134,963
Sherin Devaskar, MD , Professor of Pediatrics and Interim Chair, UCLA Perinatal/Neonatal Metabolism STAR, K30, Systems Biology PhD, MS Community Research	50	1. Vedang Londhe, MD, Assistant Professor of Pediatrics, UCLA 2. Stephen Shew, MD, Assistant Professor of Surgery, UCLA 3. Valencia Walker, MD, Neonatology Postdoctoral Fellow, UCLA	\$1,596,411
Steven M. Dubinett, MD , Professor of Medicine and Pathology, UCLA Lung Cancer Research STAR, K30, Systems Biology PhD, MS Community Research	27	1. Sherven Sharma, PhD, Assistant Researcher, Pulmonary and Critical Care Medicine, UCLA 2. Nathalie Heuzé-Vourch, PhD, Assistant Professor, University of Tours, France 3. Karen Reckamp, MD, Assistant Professor, City of Hope Medical Center, Los Angeles	\$1,308,158
John Edwards, Jr., MD , Chief of Division of Infectious Diseases; Professor of Medicine, Harbor-UCLA Medical Center Opportunistic Fungal Infections STAR, K30, Systems Biology PhD, MS Community Research	30	1. Brad Spellberg, MD, Assistant Professor of Medicine, Harbor-UCLA Medical Center 2. Gunter Rieg, MD, Assistant Professor of Medicine, Harbor-UCLA Medical Center 3. Don Sheppard, MD, Assistant Professor, Department of Microbiology and Immunology, McGill University, Quebec, Canada	\$651,882
Susan Ettner, PhD , Professor of Medicine and Public Health, DGSOM and UCLA School of Public Health STAR, K30, Proposed CTSA T32 Director, PhD Program, MS Community Research	25	1. Kevin Heslin, PhD, Assistant Professor, Drew Medical College 2. Will Shrank, MD, Assistant Professor, Harvard University 3. Mitchell Wong, MD, PhD, Associate Professor, UCLA	\$372,850

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Mentor Positions and Affiliations Mentor Expertise	Trainees Past 10 Years	Current Positions of Top Trainees over Past 10 Years	Mentor Funding FY10
Daniel Geschwind, MD, PhD , Professor of Human Genetics, Neurology, and Psychiatry, UCLA Neurogenetics and Development STAR, K30, T32, Systems Biology PhD, MS Community Research	28	1. Sarah Spence, MD, PhD, Staff Researcher, NIH Autism Program, Bethesda, MD 2. Maricela Alarcón, PhD, Assistant Professor, Department of Neurology, UCLA 3. Joseph Dougherty, PhD, Postdoctoral Associate, Rockefeller University, New York	\$14,040,217
Bevra Hahn, MD , Professor of Medicine; Vice Chair of Department of Medicine; Chief of Division of Rheumatology, UCLA Lupus and Autoimmunity STAR, K30, Systems Biology PhD, MS Community Research	10	1. Gabriela Riemakasten, MD, Professor of Rheumatology, Charite Hospital, Berlin, Germany 2. Ram Raj Singh, MD, Professor of Medicine, Director of Translational Research in Division of Rheumatology, UCLA 3. Nan Shen, MD, Vice Chief, Associate Professor, Shanghai Medical Center, China	\$453,538
Aldons Lusic, PhD , Professor of Medicine, Cardiology, and Microbiology, UCLA Microbiology and Molecular Genetics STAR, K30, Systems Biology PhD	36	1. Weibin Shi, PhD, Associate Professor, Cell Biology, University of Virginia 2. Brad Aouizerat, PhD, Assistant Professor, Department of Nursing, UCSF 3. Hooman Allayee, PhD, Assistant Professor, Institute for Molecular Medicine, University Southern California	\$4,951,830
Carol Mangione, MD, MSPH , Professor of Medicine and Public Health, UCLAT3/T4 Translation in Diabetes STAR, K30, MS Community Research	36	1. Arleen Brown, MD, PhD, Associate Professor of Medicine, UCLA 2. Catherine Sarkisian, Associate Professor of Medicine, UCLA 3. David Ganz, MD, PhD, Assistant Professor of Medicine, UCLA	\$1,988,603
Shlomo Melmed, MD , Professor of Medicine, UCLA; Senior Vice President for Academic Affairs, Cedars-Sinai Endocrinology T32, K08	30	1. Ning-Ai Liu, MD, PhD Assistant Professor of Medicine, UCLA; Director Zebrafish Core, Cedars-Sinai 2. Run Yu, MD, PhD, Asst Professor of Medicine, UCLA; Medical Director, Carcinoid and Neuroendocrine Tumor Center, Cedars-Sinai 3. Christoph Auernhammer, MD, Privat Dozent, Director of Neuroendocrine Unit, Klinikum Grosshadern, University of Munich, Germany	\$478,109
Keith Norris, MD , Professor and Interim President, CDU Improving Outcomes for Kidney Patients STAR, K30, MS Community Research	19	1. Kalpana Ganesan, MD, Internal Medicine and Geriatrics, UCLA; Associate Professor, CDU 2. Merlyn Asuncion, MD, Internal Medicine and Geriatrics, UCLA; Associate Professor, CDU 3. David Martins, MD, Internal Medicine and MSCR Program; Assistant Professor, CDU	\$23,202,368
Adeline Nyamathi, PhD, ANP , Professor and Associate Dean for Academic Affairs, School of Nursing, UCLA Effectiveness of AIDS Prevention Program STAR, K30, MS Community Research	20	1. Sheryl Tyson, PhD, Assistant Professor, Psychosocial and Community Health, University of Washington, Seattle 2. Elizabeth Dixon, MSN, MPH, Project Director for the Center for Vulnerable Populations Research, School of Nursing, UCLA 3. Tonia Jones, RN, FNP-C, PhD, Researcher, Veterans Affairs Center, Los Angeles	\$1,995,176
Antoni Ribas, MD, PhD , Associate Professor of Medicine and Surgery, Director, Tumor Immunology Program Area, Jonsson Comprehensive Cancer Center STAR, T32	24	1. Jennifer Wargo, MD, Assistant Professor, Massachusetts General Hospital and Harvard University 2. Robert Prins, PhD Assistant Professor in Dermatology, UCLA. 3. Bartosz Chmielowski, MD, PhD, Assistant Professor in Medicine, UCLA	\$1,425,000
Jerome Rotter, MD , Professor of Medicine, Director of Research and Co-Director of the Medical Genetics Institute, Director of the Division of Medical Genetics, and Director of the Common Diseases Genetics Program, Cedars-Sinai Genetics of common diseases, specifically cardiovascular, diabetes, lipid disorders, and inflammatory bowel diseases STAR, K23	9	1. Maricela Alarcon, MD, Researcher, Neurobehavioral Genetics, UCLA 2. Kazuhito Sugimura, MD, Niigata University Graduate School of Medicine and Dental Science, Japan 3. Mark Goodarzi, MD, PhD, Assistant Professor of Medicine, Associate Director of Division of Endocrinology, Diabetes and Metabolism, Medical Genetics Institute, Cedars-Sinai	\$2,326,981

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Mentor Positions and Affiliations Mentor Expertise	Trainees Past 10 Years	Current Positions of Top Trainees over Past 10 Years	Mentor Funding FY10
Isidro Salusky, MD , Professor of Pediatrics, UCLA Kidney Disease STAR, K30, Systems Biology PhD, MS Community Research	17	1. C. Sanchez, MD, Associate Professor of Pediatrics, University of Wisconsin, Madison 2. F. Can, MD, Professor of Pediatrics, University of Catolica, Chile 3. K. Wesseling, MD, Assistant Professor of Pediatrics (K23 awardee), UCLA	\$1,071,634
Ronald Swerdloff MD , Professor of Medicine, Chief Division of Endocrinology, Harbor-UCLA medical Center, David Geffen School of Medicine at UCLA and Harbor-LA BioMedical Research Institute Male Reproductive Endocrinology; Pituitary dysfunction; Endocrine Dysfunction in Traumatic Brain Injury; Regulation of Apoptosis; Mouse models for sex chromosome aneuploidy	40	1. David Handelsman MD, PhD, Anzak Research Institute, University of Sydney, Australia; Professor and Chair 2. Peter Liu, MD, PhD, Associate Professor, ANZAC Research Institute, University of Sydney, Australia 3. Vahid Mahabadi, MD, Assistant Professor, Division of Endocrinology, Department of Medicine, Olive View Medical Center, David Geffen School of Medicine at UCLA	\$2,023,000
Michael Teitell, PhD, MD , Professor of Pathology and Laboratory Medicine, Chief of Pediatric and Developmental Pathology, UCLA Cancer Biology, Nanotechnology, and Pediatric and Developmental Pathology STAR, K30, Systems Biology PhD, MS Community Research	15	1. Samuel French, MD, PhD, Assistant Professor, Department of Pathology, UCLA 2. David Dawson, MD, PhD, Assistant Professor, Department of Pathology, UCLA 3. Daphne Weihs, PhD, Assistant Professor, Technion University, Haifa, Israel	\$721,280
Arthur Toga, PhD , Professor of Neurology, UCLA Neuroimaging and Informatics STAR, K30, T32, Systems Biology PhD, MS Community Research	62	1. Paul M. Thompson, PhD, Associate Professor of Neurology, UCLA 2. Anne Blood, PhD, Research Staff, Neuropsychology, McGill University, Montreal, Canada 3. Ahmad Hariri, PhD, Director, Developmental Imaging Genomics Program, University of Pittsburgh	\$17,345,135
Christina Wang, MD , Professor of Medicine, Harbor-LA BioMed Male Reproductive Endocrinology STAR, K30, Systems Biology PhD, MS Community Research	24	1. Yu Gui Cui, MD, Professor of Endocrinology, Nanjing Medical University, Nanjing, China 2. Peter Liu, MD, PhD, Associate Professor, ANZAC Research Institute, University of Sydney, Australia 3. Vahid Mahabadi, MD, Assistant Professor, Division of Endocrinology, Department of Medicine, Olive View Medical Center	\$487,445
James Weiss, MD , Chief of Division of Cardiology, Director of Cardiovascular Research Laboratory, UCLA Cardiac Electrophysiology STAR, K30, Systems Biology PhD, MS Community Research	17	1. Kalyanam Shivkumar, MD, PhD, Associate Professor of Clinical Medicine (Cardiology), UCLA 2. Zhilin Qu, PhD, Assistant Professor of Medicine (Cardiology), UCLA 3. Aman Mahajan, MD, PhD, Associate Professor of Clinical Anesthesiology, UCLA	\$3,813,936
William Cunningham, PhD , Professor of Medicine, School of Medicine; Professor of Health Services, School of Public Health Mental health, diabetes, HIV	44	1. David Zingmond, MD, PhD, Assistant Professor, DGSOM at UCLA 2. Diana Tisnado, PhD, Adjunct Assistant Professor, DGSOM at UCLA 3. Nina Harawa, PhD, MPH, Adjunct Assistant Professor, UCLA School of Public Health	\$134,601
Kenneth Wolf, PhD , Professor of Otolaryngology, Associate Dean for Educational Affairs, CDU Cultural Competence, Research Ethics STAR, K30, MS Community Research	17	1. Junko Nishitani, PhD, Assistant Professor of Otolaryngology, CDU 2. Jimmy Brown, MD, Associate Professor of Otolaryngology, CDU 3. Sofia Avitia, MD, Chief Resident in Otolaryngology, CDU	\$0
Lily Wu, MD, PhD , Professor of Molecular and Medical Pharmacology, UCLA Pediatrics, hematology/oncology, adenovirus biology, transcription regulation, gene therapy STAR, K30, Systems Biology PhD, MS Community Research	13	1. Makoto Sato, PhD, Assistant Researcher, Department of Urology, UCLA 2. Ebba Brakenhielm, PhD, Assistant Professor, Rouen University, France 3. Marxa L. Figuieredo, PhD, Assistant Researcher, Department of Urology, UCLA	\$287,595

Mentor Positions and Affiliations Mentor Expertise	Trainees Past 10 Years	Current Positions of Top Trainees over Past 10 Years	Mentor Funding FY10
Ernest M. Wright, PhD , Professor of Physiology, UCLA; Fellow of the Royal Society Membrane Transporters STAR, K30, Systems Biology PhD, MS Community Research	9	1. Dr. Eskandari, PhD, Associate Professor of Biology, California State University, Pomona 2. Dr. Diez-Sampedro, PhD, Assistant Professor of Physiology and Biophysics, University of Miami 3. Dr. Meinild, PhD, Assistant Professor, August Krogh Institute, University of Copenhagen, Denmark	\$784,257
Stephen Young, MD , Professor of Medicine and Human Genetics, UCLA Lipid Metabolism STAR, K30, Systems Biology PhD, MS Community Research	15	1. MacRae F. Linton, MD, Professor of Medicine, Vanderbilt University 2. Robert V. Farese, MD, Professor of Medicine, UCSF 3. Martin Bergo, PhD, Associate Professor, University of Goetheberg, Sweden	\$4,791,374

Training and Career Development under the K12 Program: This new CTSI K12 program with focus on: systems biology, clinical pharmacology and translational community-partnered interventions to prepare trainees for team science across disciplines and for all populations and across the life cycle. These trainees will have a curriculum and mentorship committee that is broader than those traditionally assembled for graduate programs, to gain insight into the molecular or systems basis of disease, incorporating the current state of medical care, and learning and applying novel technologies to improving the practice of medicine in communities and grounding in state-of-the-art methods for studying comparative effectiveness. Research topics will be disease-based and individualized to each trainee, and sufficient flexibility will be provided for the trainee to tailor his or her educational program as necessary. Moreover, an interactive environment to promote collaborations among fellows and faculty members will be fostered to help accomplish a team science and education program, as increasingly specialized researchers are required to work together to achieve a larger, common goal. If a trainee's topic fits into one of the proposed CTSI clusters, he/she will be invited to join the cluster and fully participate in all team science activities related to the cluster. The transition from K award funding to R funding can be particularly challenging for soon to be mid-level faculty. To facilitate success with this transition, all scholars will obtain intensive training in grant writing, career guidance, and will be integrated into teams of scientists who are developing larger proposals such as program project grants where an individual may be able to "nest" their project in addition to submitting proposals as a PI. The program will rely on the DGSOM Curriculum, the K30 Program, and the CTSI Curriculum Tree (see **Table 9**) for courses.

Trainees focusing on clinical pharmacology and therapeutics will experience a unique program emphasizing foundational concepts of bench to bedside to community translation, the main focus of the UCLA CTSI. This course of mentored investigation will also employ courses and mentored research in a systems biology approach to disease, providing a training interface with the CTSI Technology Program. A proposed increase in scope will create a more comprehensive academic infrastructure, thereby facilitating education, training, and career development of junior faculty in new areas of research excellence at UCLA. The precursor of this program is the NCCR-funded K12 Program in Clinical Pharmacology that began in 2002. This K12 is notable for the distinctive interdisciplinary nature of its trainees and the focus on vulnerable populations. *The new CTSI K12 will retain this important focus in the program.* The NCCR K12 trained faculty and clinical fellows in anesthesiology, head and neck surgery, immunology, gastroenterology, obstetrics and gynecology, pediatric hematology, psychiatry, and transplantation surgery. In its most recent cohort, six fellows were based at UCLA-Westwood and two at CDU. The CTSI-ED will expand this program to include scholars from all CTSI partners.

Recruitment and Selection of Trainees: The CTSI K12 Admissions Committee will select three K12 trainees for admission each year into a 3-year program, with the potential to leave the program early if the trainee has obtained individual NIH career development funds (K08, K23). A rich pool of highly qualified potential scholars is available among young specialty and subspecialty physicians among CTSI partners. To recruit scholars to this program, we will replicate what we learned from a 2008 pilot study program called the UCLA Society of the CTSI Scholars Program. This program was designed and implemented by the CREST Committee with multi-institutional support. It provided four recently appointed translational research faculty with \$25,000 per year for 3 years to conduct pilot studies considered highly probable to lead to federally funded translational research. Launching this program provided an opportunity to develop and electronically circulate an RFA to all four CTSI partners. Within 3 weeks we had 44 letters of Intent across a wide array of disciplines with representation from all four partners. The 12 highest ranked applicants were

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interviewed by two CTSI and/or CREST Committee members, we then convened a selection committee with representation from the four partners and four awards were made. The recipients included:

- Mukti “Mina” Patel-Chamberlin, MD, Division of Nephrology Fellow, Harbor-UCLA Medical Center; Project: Identification of Biomarkers to Predict Progression of Renal Disease.
- Tamara Horwich, MD, Assistant Professor of Medicine, DGSOM; Project: Management of Diabetes with Metformin in Patients with Chronic Heart Failure.
- Xiao Hu, PhD, Assistant Professor of Medicine, DGSOM; Project: Development of Noninvasive continuous Monitoring of Brain Physiology in NICU Patients.
- Christine S. Walsh, MD, MS, Assistant Professor of Obstetrics and Gynecology, Cedars-Sinai Medical Center; Project: Role of Cyclin E in Ovarian Cancer.

This small program targeted many of the same scholars who could be eligible to participate in the K12. The large number of highly qualified applicants provides strong evidence that the CTSI can reach out to junior faculty at all four CTSI partners and can collaboratively select and mentor these scientists. The highly successful approach used to recruit these scholars will be replicated for the K12 program. Additionally, our Master’s of Clinical Research, STAR, and K30 Certificate Programs will continue to be effective “feeder” programs, and will be potential sources for future applicants. Strategic mechanisms generate a pipeline of ethnically diverse trainees for minority recruitment, as described in **section 6.1.5**. In the coming year, the UCLA Society of the CTSI Scholars Program will move beyond pilot phase and will annually award 12 senior postdoctoral or recently appointed faculty up to \$50,000 per year for three years to conduct studies under a team of transdisciplinary mentors. The CTSI **Pilot Program** now administers it.

Curriculum: A curriculum encompassing skills common to all areas of clinical research will enhance the scientific foundation for the proposed CTSI K12 Program. **One track** in the TTTRP is partially based upon the highly successful graduate training program in the IMED, which provides a translational PhD track in systems biology offered by the Department of Molecular and Medical Pharmacology and the Department of Cellular and Molecular Pathology. **A second track** will provide academic clinicians with the skills needed to conduct research at the interface of T1/T2 and T3/T4 translation. **A third track** will provide physician scientists with skills needed to conduct T3/T4 translation. The curricular focus for trainees in the third track will include selected courses that are required in the Clinician Scientist Track of the MSHS degree in the School of Public Health such as HS266A/B Theory and Practice of Community Partnered Research and graduate-level courses in implementation research and cost effectiveness analysis. Scholars in this track will take a CTSI special seminar series that focuses on the most robust study designs and statistical methods for comparative effectiveness research. Participants will select a 3-person lead mentor team (basic/clinical/community) that will closely guide their research projects and a research career guidance committee (with basic, clinical, and community representation) from a diverse pool of potential mentors (**Table 5**). The training objectives of the TTTRP program are much broader than a traditional PhD program and include gaining insight into the molecular or systems basis of disease, understanding the current practice of medicine, and learning, developing, and applying novel technologies to improve the practice of medicine in communities. Hence, a non-traditional education philosophy is implemented for TTTRP trainees. Research topics will be disease-based and individualized to each clinical fellow or new faculty member, so sufficient flexibility is provided for the trainee to tailor his or her education program as needed. The unique features of the TTTRP curriculum include the following:

- Toolbox courses on advanced technologies.
- A course on successful examples in translational medicine.
- Interdisciplinary research environment and mentoring triads.

Leadership: Dr. Michael Teitell (Departments of Pathology and Laboratory Medicine, and Pediatrics) provides basic T1 program leadership. He is a practicing physician scientist and member of the California NanoSystems Institute. Dr. Antoni Ribas (Departments of Medicine and Surgery) provides T1 to T3 translational leadership. He is a medical oncologist and physician-scientist conducting bench-to-bedside research and the principal investigator of a T32 training grant in academic Oncology. Dr. Isidro B. Salusky (Department of Pediatrics) provides T1 translational leadership. He is Associate Dean for Clinical Research at DGSOM, Director of the UCLA GCRC, PI/PD of the K30 Program, and is critical in the coordination of the overall clinical research infrastructure across the UCLA Health System. Dr. Carol Mangione (Departments of Medicine and Health

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Services in the School of Public Health) provides T3/T4 health services and community program leadership. Programmatic decisions are reached by a consensus process among the four leaders.

Programmatic Support by the CTSI-ED: CTSI-ED also will provide administrative infrastructure to electronically advertise the program and select the fellows and resources for courses, including those listed in the CTSI-ED Curriculum Tree. Additionally, CREST committee members will participate as mentors on the K-12 awardee's multidisciplinary mentorship teams.

6.2.2.2. New Translational Graduate Training Track in Molecular Medicine with an emphasis on systems biology.

Rationale: The CTSI Technology Program has identified systems biology as an area of research growth and excellence at the CTSI institutions. The proposed PhD Track in Molecular Medicine will offer a novel translational educational curriculum and mentoring program for developing future clinical and translational researchers. As a capstone to the CTSI training efforts in systems biology, our newly proposed CTSI K12 Program will include systems biology approaches to disease.

Overview: In the Fall of 2010, a unique PhD track in Molecular Medicine will be initiated, jointly offered by the Department of Molecular and Medical Pharmacology and the Department of Pathology and Laboratory Medicine. The PhD track fulfills a need for training in a rapidly evolving area of emphasis at UCLA and provides a nucleus for a more extensive educational and research program in translational systems biology described in the CTT. The training objectives of this new PhD program is broader than traditional graduate programs and includes gaining insight into the molecular or systems basis of disease, understanding the current practice of medicine, and learning and applying novel technologies to improve the practice of medicine. Thesis research topics will be disease-based and individualized to each trainee, and sufficient flexibility will be provided for the trainee to tailor his/her educational program as necessary. Moreover, an interactive environment to promote collaborations among faculty members and trainees will be fostered to help accomplish this "team science and education" program.

Curriculum: The PhD track in Molecular Medicine will incorporate a new curriculum and be integrated with the School of Medicine curriculum, as shown in the CTSI Curriculum Tree (see **Table 9**). A number of unique features in this new PhD program will include the incorporation of a predetermined set of medical school courses and the creation of two new courses: "Systems Biology of Disease" and "Advances in Translational Medicine". In the first year, all Molecular Medicine track PhD students will be required to take Block 1, an 8-week series of lectures on the foundations of medicine, which integrates pathologic processes, genetics, molecular/cellular biology, immunology, and critical appraisal. By exposure to studies of diseases and organ systems, PhD trainees will be better prepared for selection of a disease-focused research topic. In the second year, trainees will choose another problem-based learning block pertinent to the disease/organ system of his/her thesis research as an elective. The trainee will be required to take at least two elective courses, choosing amongst options that include (a) coursework on advanced technologies (Years -01 or -02); (b) a course on translational medicine (Year -02); (c) exposure to clinical medicine (Year -03 or -04); and (d) exposure to topics in T3/T4 translation and community engagement with science (all years).

Interdisciplinary Research Environment: The following program components will be implemented specifically to foster the team science and educational environment. First, trainees will be co-mentored by a basic science thesis advisor and a secondary clinical science advisor to broaden both perspectives. Second, the UCLA School of Medicine has explicitly created the IMED, with 22,000 sq. ft of newly renovated research space on the third floor of the Center for the Health Sciences building, to support interdisciplinary translational research. A particularly novel concept within IMED is an *Incubator Laboratory*, which is a single 5,300-square-foot fully-equipped open lab. Each basic and clinical faculty member with an established collaborative project will place one of their trainees (e.g., PhD students, postdoctoral or clinical fellows, or junior physician-scientists) in the incubator space. The Molecular Medicine PhD students will spend a significant portion of their training time in this cross-disciplinary environment. Third, to foster enthusiasm for strong translational science, trainees will be required to attend the weekly IMED seminar series lecture. The extraordinary scholarship of this seminar series (where ~50% of speakers in the 2008 academic year are HHMI investigators or National Academy members, including one Nobel laureate) has truly galvanized the UCLA health sciences community interest in medical translational sciences. In addition to meeting with speakers over lunch every week, trainees in this program will host one speaker of their choosing for an annual student-sponsored

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Molecular Medicine lectureship. Fourth, to further strengthen program identity and camaraderie, students and mentors will participate in quarterly student research presentations and an annual retreat on the UCLA main campus.

Leadership: Dr. Lily Wu (Depts. of Molecular & Medical Pharmacology, Urology, and Pediatrics) and Dr. Michael Teitell (Departments of Pathology and Laboratory Medicine, Pediatrics, and Bioengineering) are the Co-Directors of this program. Both are MD, PhD clinician-scientists who are running active research groups in translational medicine mainly focused on cancer pathogenesis, therapeutics, and technology development.

Programmatic Support by the CTSI-ED: CTSI-ED will provide resources for courses, including those listed in the CTSI-ED Curriculum Tree. The CTSI has committed institutional support for 8–12 PhD/postdoctoral positions, effectively providing a CTSI-ED institutional T32 program.

6.2.2.3. Executive Master's of Public Health (EMPH) Program in Community Research

Rationale: The School of Public Health currently offers a successful 2-year EMPH, with courses on Friday evenings and Saturdays to allow participation by community-based professionals. The CTSI-ED proposes to add a track to this program that will focus on community research.

Overview: The CTSI-ED, in collaboration with **CERP** and the School of Public Health, will develop an Executive Master's program for community-based health care leaders and providers, and academic researchers, interested in conducting community-based clinical research. The program will equip working professionals with the knowledge, skills, networks, and credentials to assume leadership in management and policy positions in community health and health care research. This innovative program will serve the dual purpose of bringing a substantive community perspective to translational research projects and providing the community mentors with first-hand experience working collaboratively with scientists at UCLA.

Curriculum: The curriculum for the CTSI EMPH Community Research will be based on the existing infrastructure of the accredited UCLA EMPH and combined with courses from the CTSI-ED Curriculum Tree in translational research. An introductory methods course in comparative effectiveness and health policy analysis will be included with a special emphasis on changes in benefit design and care delivery that are key elements in the new health care reform legislation. The program requires supervised research experience and group projects on translation of basic research findings to community settings. One of the requirements will be a written research proposal that is of value to the student's parent institution.

Mentoring and Career Development: Each student will organize an interdisciplinary research team for their project to advise all phases of their protocol (research questions, design, methods, analysis, budget). The research advisors must include: ■ one CTSI faculty member (as primary research mentor) with expertise in the student's area of interest who will help identify/assemble the rest of the committee ■ one CTSI faculty research methods mentor ■ the key academic partner for the community partner students, or the key community partner for the academic faculty or students.

Leadership: The Directors of the EMPH Programs are Drs. Fred Hagigi and Aram Dobalian, both experienced professors in the Department of Health Services of the School of Public Health at UCLA. Dr. Hagigi's research focuses on organizational performance measurements, and marketing strategies within public and private organizations. In 2005, the Public Health Student Association (PHSA) awarded him the Distinguished Teaching Award. Dr. Dobalian directs an Health Services Research & Development Center of Excellence for the Study of Health Care Provider Behavior at the VA Greater Los Angeles Health Care System. He is also the Associate Director of the Executive Education Programs in Health Services.

Programmatic Support by the CTSI-ED: The CTSI-ED will provide courses as well as logistic and financial support for the new executive MS program. Institutional commitment will include a contribution to the salaries for faculty teaching this new track and support of two fellowships per year for the first 5 years of the program for the founding community partners of the CTSI.

6.2.2.4. CTSI T32 Program in Clinical and Community-Partnered Translational Research.

Rationale: Advances in basic science have stimulated rapid changes in the nature of medical care. New therapies may dramatically change the way health care is delivered. However, in U.S. health care system costs have been uncontrollable, placing even the most rudimentary treatments beyond the reach for many people.

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There are complex patient, clinician, and system-level barriers to the delivery of high-quality, evidence-based care in most communities. Overall, there is a significant shortage of people trained in community-partnered health services research, and in health economics. Further, individuals trained in these fields often do not get exposure to the biomedical sciences that they evaluate.

Overview: Most health economists are trained in an economics department and have had little or no exposure to biomedical research or to the practice of medicine. Alternatively, despite the few available programs nationwide, few physicians gain exposure to health services research. To address these critical deficiencies, the CTSI-ED leadership, in collaboration with CERP and HSR faculty, proposes a unique interdisciplinary T32 program that will train predoctoral students in clinical and community-partnered health services research with an emphasis on advanced methods in comparative effectiveness. Projects conceived under this T32 Program will identify and study critical barriers for the translation of new effective treatments into communities. The program's goal is to provide a positive early exposure to translational research in underserved communities that ultimately will increase the number of scientists who pursue careers in T3/T4 translation fields. The objectives of the CTSI Clinical and Community-Partnered Translational Research program will be to:

- Train PhD-level scientists in community-partnered health services and outcomes research
- Provide professional students (medical, dental and others) with a 2-month introduction into the principles and practice of community-partnered translational research
- Engage faculty across the UCLA Schools of Medicine and Public Health in these training activities.

Leadership: Overall, UCLA is well positioned to collaboratively implement this T32 because of the diverse set of faculty engaged in extramurally funded translational research who are appointed in the Schools of Medicine, Nursing, and Public Health and are CREST members (see **Table 3**). Dr. Susan Ettner, Professor of Medicine and Public Health, will lead the T32. Dr. Ettner is an MIT-trained economist who has conducted numerous collaborative extramurally funded translational research projects with physicians in the fields of mental health and diabetes. As a jointly appointed faculty member in the departments of Medicine and Health Services who has taught in the core curriculum for the PhD program in health services for 12 years, she is uniquely qualified to lead this program. She has chaired eight dissertation committees, and served as the methodologist on 7 additional committees in areas such as the affects of system-level factors on cardiovascular outcomes, influence of organizational context on receipt of colorectal cancer screening, adherence to prescription drugs and adverse outcomes for persons with chronic illnesses. Dr. William Cunningham, Professor of Medicine and Public Health, will co-direct this program. Dr. Cunningham works in the area of HIV prevention and treatment and has conducted extensive community-partnered projects. He also is jointly appointed to the departments of Medicine and Health Services and has successfully mentored over 40 graduate students, medical students, or postdoctoral fellows over the past 11 years. He will direct the 2-month introduction to community-partnered translational research for the professional students funded by this program. Dr. Jack Needleman, Professor of Public Health and Director of the PhD program in HSR, will also be a co-director for the T32, since the four students per year in this track will need to be accepted into the Department of Health Services PhD program. Dr. Needleman is committed to working closely with Drs. Ettner and Cunningham to coordinate the selection of graduate students for this program.

Proposed Training for the PhD Candidates: PhDs from this program will be awarded by the Department of Health Services in the School of Public Health. The T32 will also utilize parts of the CTSI-ED Curriculum Tree for its training, with shared mentorship by clinical, health services, and community-partnered faculty to ensure the translational nature of dissertation projects. The goal is to provide predoctoral trainees with an understanding of both investigative skills required to create new knowledge about health services and the theory and methods of community-partnered research. The trainees will also be given intensive training in the basics of medicine and health care. To achieve this goal, students will engage in the following activities:

- Didactic coursework in research methodology, outcomes research, and methods of community-partnered research.
- Participation in original community-partnered translational research, culminating in a dissertation.
- Practical experience in development of public policy relevant to health and health care.

The PhD Program requires 17 courses. Each student is expected to take a didactic qualifying examination and successfully complete a dissertation. The student's dissertation committee will include at least four members,

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the chair, who will be a senior faculty translational researcher jointly appointed in the Department of Health Services (the PhD granting department) and the School of Medicine (many of these are CREST Committee members), a community mentor, and a social scientist from the student's cognate department. Students will have the option to concentrate in the development and evaluation of community-based interventions, health economics, social determinants of health, comparative effectiveness methods, or measurement of health outcomes. Four predoctoral candidates will be supported by the T32 for 4 years. The first 2 years will involve completing the required curriculum and developing the dissertation research project and the second 2 years will involve conducting research and writing up the results.

Mentors: As part of our preparation for this new T32, we have assembled a preliminary list of UCLA faculty who have expressed interest in serving as mentors in this program. All are highly experienced mentors with excellent training records and training resources, and considerable experience in federally funded community-partnered research. As a special track in the Health Services PhD Program, the department faculty played a key role in the T32 planning effort so our mentors list to date is well populated with faculty who have strong ties to the Department of Health Services, as indicated in **Table 6**.

Table 6. Proposed Mentors for the CTSI-ED T32 in Clinical and Community-Partnered Translational Research.

Mentor Positions and Affiliations Mentor Expertise	Trainees Past 10 Years	Current Positions of Top Trainees over Past 10 Years	Mentor Funding FY10
Ronald Andersen, PhD , Wasserman Prof Emeritus of Health Services, School of Public Health, Professor Emeritus	30	Health Services Research, Evaluation of Health Programs	\$100,000
Kathryn Atchison, DDS, MPH , Professor of Health Services, School of Public Health; Professor of Public Health and Dentistry, School of Medicine; Vice Provost, Intellectual Property and Industry Relations.	45	Outcomes assessment and quality of care issues	\$0
Roshan Bastani, PhD , Professor of Health Services and Associate Dean for Research, School of Public Health; Co-Director UCLA Kaiser Permanente Center for Health Equity; Director for Cancer Disparities Research, Associate Director Cancer Prevention and Control, Jonsson Comprehensive Cancer Center	30	Access to care in underserved groups, community-based collaborative intervention research	\$1,950,000
Robert Brook, MD, ScD , Vice President, RAND Corporation; Director, RAND Health; Professor of Medicine, School of Medicine; Professor of Health Services, School of Public Health	25	Development and use of health-status measurements in health policy; Efficiency and effectiveness of medical care; Quality assessment and assurance; Variation in the use of medical services across geographic areas	\$517,089
Arleen Brown, MD, PhD , Associate Professor, Division of General Internal Medicine and Health Services Research, Department of Medicine, Center for Health Sciences, UCLA Medical Center	14	Health disparities, chronic disease management, neighborhood influences on health, community partnered participatory research, behavioral economics	\$466,864
E. Richard Brown, EdD , Professor of Health Services, School of Public Health; Director, UCLA Center for Health Policy Research; Principal Investigator, California Health Interview Survey	12	Health policy research, health care reform	\$9,664,789
William Cunningham, MD, MPH , Professor of Medicine, School of Medicine; Professor of Health Services, School of Public Health	44	Mental health, diabetes, HIV	\$134,601
Susan Etner, PhD , Professor of Medicine, School of Medicine; Professor of Health Services, School of Public Health	25	Mental health, diabetes, HIV	\$372,850

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Mentor Positions and Affiliations Mentor Expertise	Trainees Past 10 Years	Current Positions of Top Trainees over Past 10 Years	Mentor Funding FY10
Lillian Gelberg, MD , Professor of Medicine, School of Medicine	61	Health status, access to care, quality of care, and health promotion/disease prevention interventions for homeless and other vulnerable populations	\$706,048
Gerald Kominski, PhD , Professor of Health Services, School of Public Health	9	Cost and cost-effectiveness of medical programs and technologies	\$6,374,645
Mark Litwin, MD, MPH , Professor of Urology, School of Medicine; Professor of Health Services, School of Public Health	17	Health care delivery systems, medical outcomes research, quality-of-life assessment, and clinical urology	\$4,961,345
Carol Mangione, MD, MSPH , Barbara A. Levey MD & Gerald S. Levey MD Endowed Chair, Professor of Medicine, School of Medicine; Professor of Health Services, School of Public Health	36	Diabetes in minority populations, health knowledge and behaviors, quality of life, managed care and vision quality of life, and diabetes interventions in minorities	\$1,988,603
William J. McCarthy, PhD , Adjunct Professor of Health Services, School of Public Health; Adjunct Professor of Psychology	10	Theory and practice in health-related lifestyle change to help healthy individuals improve their daily food choices, increase their daily physical activity, and reduce their exposure to tobacco smoke. Special focus on low-income Latino adults and residents of transitional shelters for the homeless.	\$3,476,937
Jack Needleman, PhD , Professor of Health Services; Director of Health Services PhD and MSHS Programs	8	Quality of care, health workforce, health care finance, payment and insurance, health policy	\$100,000
Thomas Rice, PhD , Distinguished Professor of Health Services, School of Public Health	2	Health economics, health services research	\$0
Stuart Schweitzer, PhD , Professor and Vice Chair, Department of Health Services, School of Public Health	4	Health Economics	\$160,000
Martin Shapiro, MD, PhD , Professor of Medicine, School of Medicine; Professor of Health Services, School of Public Health	27	Health service research, HIV	\$1,128,483
Kenneth Wells, MD, MPH , Kenneth Wells, MD, MPH, Professor of Psychiatry and Behavioral Science, David Geffen School of Medicine; Professor of Health Services, UCLA School of Public Health; Director, Health Services and Society, Jane and Terry Semel Institute for Neuroscience and Human Behavior; Affiliated Adjunct Staff, The RAND Corporation	11	Community-based participatory research methods for mental health services improvement in disadvantaged communities.	\$5,577,357
Frederick J. Zimmerman, PhD, MS , Professor and Chair of Health Services, School of Public Health	13	Health Economics	\$40,000

Selection of Predoctoral Trainees: We will solicit applications from candidates through annual mailings to mentors and graduate programs. The T32 directors will work closely with Dr. Needleman, to develop an application process that meshes with the existing structure in Health Services. Students will indicate an interest in translational research to the Health Services PhD program. Those who are interested in applying to this T32 will be asked to describe their interest and background in translational research in their personal statements. Among the training project proposals that are translational, training fellowships will be awarded based on the average priority rankings of an admissions committee consisting of CREST and Public Health faculty. Strategies for minority recruitment have been noted earlier (see **section 6.1.5.**).

Proposed Training for Professional Students: Under Dr. Cunningham's leadership, the T32 will create a 2-month didactic- and project-oriented program for 10 of the 18 UCLA medical students in the new PRIME UR-US program. PRIME UR-US was funded by the State of California to address the physician workforce shortage in urban and rural communities with the greatest health disparities. The mission of PRIME UR-US is to train leaders for communities, some of whom will conduct research to mitigate health disparities.

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Participation in the T32 during the summer between the first and second year of medical school will provide the PRIME UR-US students with an early exposure to the practice of interdisciplinary, community-partnered translational research. Each student in the program will attend a weekly seminar where they will hear about topics such as community-partnered research methods, ethics of conducting community-oriented research, study design, measurement of outcomes in communities, introduction to comparative effectiveness and cost effectiveness analyses, and introduction to health disparities research. Each student in this program will be paired with a senior faculty mentor who conducts either clinical or community-partnered research and will be expected to work on a project. Findings from this work will culminate in a CTSI-sponsored poster session.

Selection of Professional Students: In partnership with the CTSI-ED and the directors of the PRIME UR-US, the directors of the T32 will develop a brief online application for students who are interested in applying to this program. Students will be asked to provide a brief summary of a research idea or area of interest, any relevant background, and future goals. Those who are eligible will be interviewed by two faculty. The T32 directors will convene a selection committee with CREST members to select students for the program. Priority will be given to the PRIME UR-US students, but students from the non-PRIME UR-US slots in the medical school and other professional schools also will be considered.

6.3. Specific Aim 3: Provide mechanisms to integrate patient-oriented research training through a course menu, expansion of didactic programs (the CTSI-ED Curriculum Tree), and an integrated assessment program providing a sophisticated, computer-based learning-management system.

6.3.1. Expansion of the Curriculum provided by the K30 Program. Our recently renewed NCRR K30 program provides the didactic framework for the integrated programs of clinical and translational research education described in **sections 6.2.1.** and **6.2.2.** Under the CTSI-ED, the Track II Certificate Program in Translational Investigation and the Track III MS in Clinical Research, which provide key courses for multiple mentored training programs, will be expanded in scope and capacity. New curricula include:

- A clinical research curriculum for senior medical students.
- New modules on community-engaged research, comparative effectiveness methods, and molecular medicine/systems biology.
- Workshops and laboratories on statistical procedures applied to clinical investigation.

We also will extend the audience for K30 Program presentations using real-time teleconferencing to link all four partner institutions. The courses developed for the K30 programs will form the core of the CTSI-ED Curriculum Tree. The CTSI-ED in partnership with the BIP will provide the critical IT infrastructure and support for greater multi-institutional faculty involvement that permits the critically needed collaborative expansion of this program to scientists in training at the four CTSI partners. The K30 Program directed by Dr. Salusky has developed a broad-based, innovative curriculum involving all CTSI affiliates with elements to individualize training. Overall, the K30 is designed to stimulate passion for collaborative scientific discovery and provide training and mentoring that will enable health professions students, residents, fellows, postdoctoral, and faculty participants to conduct innovative clinical and translational research. The 3 tracks and summer program are geared to accommodate the diverse needs of our large and heterogeneous pool of potential participants:

- **Track I: an auditing option of all K30 courses** providing trainee access to multiple training programs that require course material developed for the K30 (see **section 6.2.3.3**)
- **Track II: a 2-year fellowship in Translational Investigation leading to a certificate of completion** that is essential for mentored training programs and will be an option for selected CTSI K12 awardees
- **Track III: the MS in Clinical Research from UCLA or CDU**, which provides a mechanism to train clinicians and faculty in skills necessary to conduct clinical trials research
- **A K30 Summer Program**, which provides skills on the preparation of an NIH proposal and introduction to different aspects of patient-oriented research. The Translational and Clinical Research Certificate Program (CTSI-ED Certificate Program) and the MS in Clinical Research accommodate the varied didactic requirements of many of our trainees, allowing them to gain expertise in core elements of clinical research, to obtain federal funding, and transition toward independent research careers.

6.3.1.1. CTSI Fellowship in Translational Investigation Certificate Program (Track II). This program trains a diverse group of basic and clinical scientists with wide-ranging backgrounds at different stages of their careers. In addition to rigorous courses in competencies required for clinical-translational research, the

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program shifts the focus of academic translational scientists away from individual efforts and toward cross-disciplinary research teams. Courses are geared to ensure competence in working with special populations such as children, women, and underrepresented minorities. The program emphasizes mentoring, training, and professional development of scholars who are members of underrepresented groups. This 2-year, 24-credit-hour program shares several components with the Track III Master of Science (MS) degree but allows trainees flexibility in determining depth of involvement (auditing versus enrollment in coursework) and choice of focus.

a) Training and Career Development under the CTSI-ED Certificate Program: A brief description of the coursework included in the CTSI-ED Certificate Program is provided in **Table 7**, with a more detailed description of the courses provided in **Table 9**. Under the CTSI-ED, the selection of courses available to the program will be expanded to include Pathways to Clinical Goals (covering the principles and examples of T1/T2 translational research), How to Succeed in Academics (a Saturday workshop survival guide for junior faculty) and two new community-focused modules, Development and Implementation of Community-Based Effectiveness Interventions and Engaging Community-Academic Partnered Research. Ethics in Patient-Oriented Research is required in this program. Scholars must take one of the pharmacology courses, biostatistics, and three of eight currently available modules.

Table 7. Curriculum for CTSI Certificate Program in Translational Investigation.

Required Courses	Quarter	Course Coordinator
Introduction to Biostatistics	Fall	D. W. Gjertson, PhD
Ethics in Patient-Oriented Research	Fall	Stanley Korenman, MD
Controversies in Clinical Trials	Winter	R. M. Elashoff, MD, and J. A. Frank, PhD
Introduction to Biostatistics (Problem Sets)	Spring	Ron Brookmeyer, PhD
Statistical Methods in Clinical Trials	Spring	Martin Lee, PhD
UCLA Clinical Pharmacology, <i>or</i>	Spring	Barbara Levey, MD
NIH Principles of Clinical Pharmacology	7 Months	NIH Clinical Center
Monthly Meetings - Fellows are required to participate in three presentations.	Duration of Fellowship	Barbara A. Levey, MD
Additional Courses (3 of 6 Required)		
NIH Grant Preparation	Fall	John Adams, MD
Health Services Research	Fall	Martin Shapiro, MD, PhD
Gender-Related Issues in Medicine	Fall	Carla Janzen, MD
Brain Mapping for Translational Investigators	Winter	Jeff Alger, PhD
Safety and Regulatory Issues in Patient-Oriented Research	Winter	Barbara Levey, MD
Role of Genetics in Clinical Research	Spring	Deborah Krakow, MD
Optional Coursework		
Biostatistics	Winter	Thomas A. Belin, PhD
NIH Introduction to Principles and Practices of Clinical Research	5 Months	NIH Clinical Center
Essentials of Clinical Investigations: Developing a Research Proposal	Summer	Isidro Salusky, MD
New CTSI-ED Courses		
Pathways to Clinical Goals	TBA	Antoni Ribas, MD
How to Succeed in Academics	TBA	Allison Moore, MD
Development and Implementation of Community-Based Effectiveness Interventions in a CER framework	TBA	Carol Mangione, MD and colleagues
Engaging Community-Academic Partnered Research.	TBA	Arleen Brown, MD and colleagues

b) Recruitment and Selection of Trainees: The CTSI-ED Certificate Program has averaged 20–30 trainees per year. A large pool of highly qualified applicants have included participants in our STAR Program who wish to pursue careers in clinical investigation; mentored clinical research scholars from our K12 and T32 training

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programs, for whom participation in the K30 may be required; participants in our Robert Wood Johnson Foundation Clinical Scholars Program; current K23 grantees; current and past students in ongoing programs and lectures (auditing courses); participants in our existing summer CCRR Program course on clinical research; and participants in our training grants. The large number of UCLA NIH-funded training grants is an asset to the Certificate Program because it ensures a large pool of potential applicants. Therefore, we are confident that we will continue to be able to select at least 50 highly qualified applicants in future years, and that this function will be enhanced by the increased visibility of the program and increased options for courses that will be provided by the CTSI-ED. A key transformational element that would not be possible without the CTSI-ED resources is the utilization of biomedical informatics tools and telemedicine to facilitate expansion of this program across the CTSI institutions and aggressive, coordinated, well-planned strategies to enhance the ethnic and racial diversity of the participants.

6.3.1.2. MS in Clinical Research. Two degree programs are offered as part of the K30 Track III. **The UCLA Master of Science in Clinical Research (MSCR)** was established in the Department of Biomathematics at DGSOM in 2002, during the first cycle of K30 funding. The UCLA program is co-directed by Robert Elashoff, PhD, Vice Chair of Biomathematics and an internationally recognized biostatistician with vast experience in clinical trials; and Joy Frank, PhD, Vice Chair of Research Training in the Department of Medicine and Director of the STAR Program. The CDU Master of Science in Clinical Research degree was developed in 2005, in part to complement the in-depth biostatistical orientation of the UCLA MS degree program by providing a curriculum explicitly geared to the study of vulnerable populations and health disparities, with attention on community engagement. Both MSCR programs are synergistic and constitute important additions to clinical research training accessible to all four institutional partners, with each program offering a different scientific focus and targeting a different trainee population. With the new teleconferencing capacity at all four K30 partner institutions, we anticipate an increase in the numbers of “cross-fertilizing” trainees from across the partners in both MSCR programs, including the number of UCLA students remotely attending the CDU program, and vice versa. With 35 current students and 11 graduates, this program provides formal instruction in modern clinical investigation for fellows, residents, and established faculty.

a) Training and Career Development: This program provides a rigorous curriculum equipping students with the tools needed to design and conduct clinical trials and observational studies, analyze and interpret data, compete successfully for NIH funding, present research at scientific meetings and in peer-reviewed journals, and critique and interpret the research of others. For MSCR scholars, coursework and an orally defended research thesis are completed within 2 years. Students then prepare manuscripts for publication and apply for K23 funding to aid transition into faculty positions during the third year. Junior, mid-level, and senior faculty have also enrolled in the Master’s in Clinical Research Program and can extend the time to degree completion to accommodate their clinical schedules. The curriculum is contained within the CTSI-ED Curriculum Tree and includes courses in clinical trials, observational studies, and biostatistics and data analysis, research ethics, clinical pharmacology, and other graduate-level electives (**Tables 8 and 9**). The CTSI-ED will work with Drs. Frank and Elashoff to add a core curricula to this master’s degree to cover the theory and practice of community-partnered interventions.

Table 8. Curriculum for MS Program in Clinical Research.

Required Courses	Quarter	Course Coordinator
First-Year Curriculum		
Computer-Based Introduction to Biostatistics	Fall	Jeff Gornbein, PhD
Intermediate Biostatistics	Winter	David Elashoff, PhD
Advanced Biostatistics	Spring	Chi-Hong Tseng, PhD
Data Analysis 1 (SAS software)	Winter	Arun Karlamangia, MD, PhD

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Required Courses	Quarter	Course Coordinator
First-Year Curriculum		
Data Analysis 2 (SAS software)	Spring	Arun Karlamangia, MD, PhD
Observational Studies	Fall	Teresa Seeman, PhD
Controversies in Clinical Trials	Winter	Robert Elashoff, PhD
Methodology in Clinical Research 1	Spring	Sara Hurvitz, MD, Carolyn Britten, MD, David Reese, MD, Bonnie Bhaduri, MD
Second-Year Curriculum		
Methodology in Clinical Research 2	Fall	Steven Pianadosi, MD, PhD
Ethics in Research	Fall	Stanley Korenman, MD
Clinical Pharmacology	Fall	Elliot Landaw, MD
Advanced Clinical Trials	Spring	Robert Elashoff, PhD

b) K30 Program Outcomes: The productivity of graduates of the K30 MS and Certificate Programs clearly demonstrates success since its launch in September 2000. Among 164 trainees enrolled in Tracks II and III to date, there has been a 97% retention rate. As of June 2009, 89 trainees (Track II Certificate $N = 49$, and Track III Master of Science $N = 40$) have completed the program, 68 (76%) of whom currently are faculty in academic institutions. Twenty-five graduates (28%) have been awarded at least one NIH grant (41 awards in total, including 16 K23s, 2 K08s, 2 R21s, 2 R01s, and 1 SC1), and 60 (67%) have peer-reviewed publications, ranging between 1 and 80 publications per graduate. Current trainees ($N = 70$) in Tracks II and III already show great promise of independent careers as translational scientists. Among them are 9 K23 awardees, 3 K08 awardees, and 1 P20 awardee. The research accomplishments thus far of the K30 participants demonstrate the program's effectiveness.

c) Enhancement of the MS and Certificate Programs by the CTSI-ED: Courses required for the MS in Clinical Research and CTSI-ED Certificate Program will be strongly supported under the CTSI-ED with specific, immediate investment in computer laboratories to increase capacity of biostatistics classes. Courses will be funded by a combination of K30 and institutional funding. The CTSI-ED Office will enhance trainee recruitment, standardize course evaluations, and provide resources for trainee placement and career development. Directors of programs Drs. Salusky and Frank will ensure communication for integration of the program as members of the CREST Committee.

6.3.2. Creation of the CTSI Curriculum Tree

Overview: A key integrating process of the CTSI-ED will be to identify and nurture courses that are most relevant to the training and education within the CTSI-ED programs and create a Curriculum Tree to service all CTSI-ED programs. At UCLA there are over 11,000 courses in the general catalogue; hundreds could be utilized by clinical or translational training programs. The objectives of creating the Curriculum Tree are not to be all-inclusive but to provide a set of outstanding uniformly evaluated courses specifically targeting the training mission and needs of the CTSI-ED. The CTSI-ED Curriculum Tree will:

- Provide a framework of rigorous courses for established and evolving CTSI-ED programs.
- Increase access and dissemination of translational and clinical research courses.
- Provide a mechanism for other CTSI programs to develop training initiatives.
- Reduce didactic redundancy and organize courses according to requirements of multiple programs.
- Collate uniform evaluation criteria to determine need and a basis for improvement.
- Provide a mechanism for CTSI-ED trainees to take courses to fulfill their individual needs.

The CREST Committee representing the leadership of the CTSI-ED will continuously develop and improve the CTSI-ED Curriculum Tree. Through a series of evaluations and the proposed learning management system, the CREST Committee will:

- Formally establish a set of educational goals that underlie the CTSI-ED program
- Decide which classes to include on the Curriculum Tree and in which categories based on how well they address these goals

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- Prioritize programmatic participation in specific classes when class enrollment is capped
- Develop new classes to fulfill didactic needs
- Prioritize necessary investment of CTSI resources in teaching efforts (computing facilities, video-recording lectures, compensation, etc).

In addition, course material will be uploaded for electronic access for key classes, particularly those in the core curriculum. The CTSI-ED Office will closely monitor courses, faculty, and trainees based on how well these goals are met, and subsequently the CTSI-ED Assessment and Outcomes Subcommittee will provide collated feedback to the CREST Committee (for program and course review, see Section 6.3).

Courses developed for the successful K30 and K12 programs, MS in Clinical Research Program, MS programs in the School of Public Health, and RWJF Clinical Scholars Program will provide the framework for the CTSI Curriculum Tree. The CTSI Curriculum Tree (detailed in **Table 9**) will have 4 major categories. A menu of Core Courses will cover fundamental subjects, whereas Modules, Electives, and Seminars will convey more specific material. Modules will consist of specialized courses such as “Imaging” and “Women’s Health.” Electives will cover program-specific courses. The CTSI-ED Office will track-relevant seminars and disseminate this information to all CTSI faculty and students via the monthly electronic bulletin. The CTSI-ED Office will integrate didactic resources according to matter, class size, and faculty participation. The CTSI-ED Office will organize the CTSI Curriculum Tree, institute evaluation mechanisms, and, in collaboration with departmental efforts, assign qualified instructors to the appropriate courses. We anticipate that the CTSI Curriculum Tree will contribute to the unification of all CTSI clinical and translational research programs and provide opportunities for trainees at all levels of education.

Core Branch: Core Courses will introduce key concepts in translational research and will cover essential subjects, including ethics, biomathematics, and safety and regulatory issues. The CTSI-ED Program will cooperate extensively with other CTSI Programs to design and optimize the core curriculum. For example, the Regulatory Program will oversee courses addressing traditional and modern ethical issues (e.g., stem cell research, genotyping, and shared databases). “Safety and Regulatory Issues in Patient-Oriented Research” covers important safety issues in clinical research and the complexities of the IRB approval process. The Core Curriculum also offers three biomathematics courses, covering elementary through advanced concepts.

Modules Branch: CTSI Modules address specific translational research issues in depth as workshop/lecture series. Current modules include the Role of Genetics in Clinical Research (Coordinator: Deborah Krakow); Health Services Research (Coordinator: Martin Shapiro); Research in Women’s Health (Coordinator: Carla Janzen); Brain Mapping for Translational Investigators (Coordinator: John Mazziotta); NIH Grant Preparation (Coordinator: John Adams); and Development and Implementation of Community-Based Effectiveness Interventions (Coordinator: Carol Mangione). The CTSI Short Course will introduce trainees to the steps in development of clinical research studies through the preparation of a grant application. The course is offered as an intensive two-week seminar. Participants are separated into small working groups and guided through developing a grant application on a specific topic (Coordinator: Isidro B. Salusky). Additional modules will include systems biology, addressing the new PhD track in this area, and the expanded K12 mentored program in clinical and systems pharmacology.

Electives Branch: Electives are designed for completion of specific training programs within the CTSI. Specialized didactic training courses for programs will also be classified as electives. An innovative new elective will focus on experiential training and will utilize the UCLA clinics and scientific cores as “classrooms” for cross-training in basic, clinical, and community research. Also included in the category will be the academic courses designed for high school and college students in programs such as the Minority High School Clinical Scholars Program, to encourage students to pursue research-oriented careers in medicine.

Seminars Branch: Seminar series are important educational elements already in place at UCLA. The CTSI-ED Office will disseminate information on relevant seminars and series to all CTSI Program participants. In addition, leading clinical and translational investigators will be invited by the CREST Committee to speak at the CTSI-wide, biweekly seminar series in team-based interdisciplinary clinical-translational research and the monthly seminars on T1 and T2 translation sponsored by the HSR Program.

Table 9. CTSI Curriculum Tree: Core, Module, Elective, and Seminar Branches.

Course Coordinator(s) / Lecturers	Course Logistics (Training Level)	Topics Covered
Pathways to Clinical Goals (new course for CTSI-ED) Antoni Ribas, MD Carol Mangione, MD	10-week course 1-hour lecture with discussion/week (MS and above)	Provides an overview of translational investigation from discovery to clinical trials, and community-based trials after FDA approval. Experts from the academic community, industry, and government will present appropriate topics. The course is designed around the flow diagrams.
Ethics in Patient-Oriented Research (established) Stanley Korenman, MD	10-week course 2-hour lecture with discussion/week (MS and above)	Covers ethical issues in human research. Topics include IRB approval, HIPPA, research with human subjects, conflicts of interest, data and safety monitoring, international research, and misconduct.
Methodology in Clinical Research II (established) Robert Elashoff, PhD	10-week course 2x2-hour/week (requires MD, PhD, or DDS)	Presents the principles and practices of major disciplines underlying clinical research methodology, such as biostatistics, epidemiology, and pharmacokinetics.
Computer-Based Introductory Biomath for Medical and Biological Experimenters (established) Jeff Gornbein, PhD	10-week course 2x2-hour lecture with discussion/week (MS and above)	Emphasizes experimental design and data analysis using statistical software packages. Topics include descriptive statistics, <i>t</i> -tests, confidence intervals, linear regression and correlation, analysis of variance, nonparametric statistics, experimental design, and sample size determination.
Statistical Methods in Clinical Trials (established) Martin Lee, PhD	10-week course 2x1.5-hour lecture with 1-hour discussion/week (MS and above)	Covers advanced topics in experimental design. Topics include: pre-clinical models; randomization; historical controls; p-values; cohort size; stratification; choosing controls; prognostic factors; survivorship studies; design of prognostic studies; clinical trials administration; comparability; protocols; clinical standards; data collection and management.
NIH: Introduction to the Principles and Practices of Clinical Research (NIH IPPCR) (established) NIH Webcast	2 lectures a week for 17 weeks Broadcast from NIH Clinical Center	Introduces the Principles and Practice of Clinical Research (IPPCR). The program trains researchers in how to design a successful clinical trial by focusing on epidemiologic methods, study design, protocol preparation, patient monitoring, quality assurance, and FDA issues. Other areas covered include data management and ethical issues, including protection of human subjects.
Safety and Regulatory Issues in Patient-Oriented Research (established) Barbara Levey, MD	1-day course 5 1-hour lectures	Summary of regulatory oversight in patient-oriented investigation. Topics include IRB, FDA, data safety monitoring boards, and regulatory issues in clinical trials.
Principles of Clinical Pharmacology (NIH PCP) (established) NIH Webcast	1 lecture a week for 31 weeks at UCLA Broadcast from NIH Clinical Center	Provides an in-depth review of quantitative pharmacokinetics, drug metabolism and transport, assessment of drug effects, drug therapy in special populations, and contemporary drug development.
How to Succeed in Academics (established) Faculty TBD	Full day Saturday workshop, taught twice a year	This course covers all aspects of an academic career, including establishing personal goals; selecting a training environment and a position in academia; finding grant opportunities; writing a grant; understanding the grant review process; preparing abstracts, posters, and talks for scientific meetings and job interviews; selecting a journal, preparing a manuscript, and responding to reviews; dealing with power abuse; developing leadership skills; and gauging success. The central theme is the role of mentoring in career development.
CTSI Curriculum Tree Module Branch: Module courses are designed to cover areas of interest to subsets of trainees or faculty with specific training goals in mind.		
NIH Grant Preparation (established) John S. Adams, MD	2-day course 5 1-hour lectures	Introduces trainees to the NIH grant review process, from the logistics of preparing an application to submission and review: preparing a NIH grant; UCLA offices of contracts and grants; NIH study sections; non-NIH funding sources.
Essentials of Clinical Investigation: Developing a Research Plan (established) Isidro B. Salusky, MD	2-week seminar; 30 hrs of class	Covers initial steps in development of a clinical research study through the preparation of a grant application. Students develop a grant application on a specific topic.
Health Services Research (established) Martin Shapiro, MD, PhD	2-day course 4 1.5-hour lectures (MS and above)	Provides trainees with an overview of health services research. This includes health outcomes, assessments of quality of care, and cost effectiveness. Workshops include Introduction to the Assessment of Costs and Cost-Effectiveness of Care, Science of Measuring the Quality of the Processes of Medical Care, Comprehensive Approach to the Measurement of Health.

Course Coordinator(s) / Lecturers	Course Logistics (Training Level)	Topics Covered
CTSI Curriculum Tree Module Branch: Module courses are designed to cover areas of interest to subsets of trainees or faculty with specific training goals in mind.		
Health Services Research (established) Martin Shapiro, MD, PhD	2-day course 4 1.5-hour lectures (MS and above)	Provides trainees with an overview of health services research. This includes health outcomes, assessments of quality of care, and cost effectiveness. Workshops include Introduction to the Assessment of Costs and Cost-Effectiveness of Care, Science of Measuring the Quality of the Processes of Medical Care, Comprehensive Approach to the Measurement of Health.
Gender-Related Issues in Medicine (established) Carla Janzen, MD	2-day course 4 1-hour lectures (MS and above)	Covers the impact of gender and pregnancy on drug action and metabolism. Topics include gender differences in clinical research, physiology of pregnancy, drug transport across the placenta, fetal medicine.
Systems Biology of Disease (new course for CTSI-ED) Thomas Graeber, PhD and Michael Teitell, MD, PhD	5-week course 1.5-hour workshop per week (PhD and above)	Teaches trainees the power and necessity of a systems biology approach to understanding the complex changes in cell signaling and metabolism circuitry that accompany the evolution of disease. The curriculum will introduce systems biology conceptually along with the promise of genome-wide quantitative biological analysis (1 session). Next the most striking successes of systems biology will be taught. In each case relevant biology will be introduced with emphasis on how the new approaches introduced by the authors expand our ability to interrogate and understand disease (2 sessions). The course will then cover representative examples of the mathematics and computation required for systems biology, and introduce computational programs that have mathematical engines buried within them and empower researchers to incorporate their data into systems algorithms (2 sessions).
Development and Implementation of Community-Based Effectiveness Interventions (new course for CTSI-ED) Carol Mangione, MD, Kenneth Wells, MD, and others	5-week course 1.5-hour workshop per week (MS and above)	Provides trainees with an overview of the methods used to design, implement, and evaluate community-based effectiveness trials. This module is composed of the following: an introduction to community-based intervention development, methods for assessing health priorities and partnering with communities; two sessions on a comprehensive review of study designs and their statistical trade-offs for community-based interventions; a review of best practices for the recruitment and retention of vulnerable populations in community-based research; and a review of evaluation tools in a comparative effectiveness framework to determine the impact of community-based interventions on the health of the community.
Brain Mapping for Translational Investigators (established) Jeff Alger, PhD	8-week course 8 1.5-hour lectures (MS and above)	Provides an introduction to brain mapping techniques. Techniques covered include magnetic resonance imaging (structural, functional, spectroscopic, diffusion and perfusion approaches), positron emission tomography, optical intrinsic signal imaging for use in the operating room, computed tomography angiography. Examples will be provided of their applications in clinical neuroscience (e.g., neurology, neurosurgery, and psychiatry) as well as in research. A laboratory where course participants can perform an actual brain mapping experiment will also be provided.
Clinical Pharmacology (established) Barbara Levey, MD, FACP	10-week course 1-hour lecture/week (MS and above)	Clinical pharmacology is a broad-based discipline, bridging basic pharmacology and all other areas of clinical medicine. A working knowledge of clinical pharmacology is an essential element for sound therapeutics and translational investigation. The application of clinical pharmacology principles to advances in contemporary medicine, e.g., targeting, gene therapy, and genomics, will lead to more effective individualized therapies and fewer adverse events. The clinical pharmacology course will provide an overview of this area.
Role of Genetics in Clinical Research (established) Deborah Krakow, MD	3-week course 5 1-hour lectures (MS and above)	Introduce concepts of disease inheritance, diagnosis of genetic diseases, and underlying biology. Topics include thoughtful and careful clinical observations, role of genetics in understanding common disease, using rare genetic disorders to dissect mechanisms of disease, application of new genetic techniques to solve old problems, understanding genetic techniques in research.

Course Coordinator(s) / Lecturers	Course Logistics (Training Level)	Topics Covered
CTSI Curriculum Tree Module Branch: Module courses are designed to cover areas of interest to subsets of trainees or faculty with specific training goals in mind.		
Engaging Community-Academic Partnered Research (new course for CTSI-ED) Steve Shoptaw, PhD Cathy Reback, PhD Arleen Brown, MD	10-week course 2-hour lecture per week Friday/Saturday (MS and above)	Serves as a foundation for the engagement of community agencies and professionals in translational research across the spectrum of community settings. This will range from large-scale engagement—one or more UCLA faculty member(s), health care, or governmental agencies (e.g., Kaiser Permanente, State and County Health Departments)—to a modest scale in which a UCLA faculty member partners with a clinician or administrator at his/her community-based agency, to a smaller scale engaging providers or clinics in their office setting. Student will learn to recognize and implement the steps necessary to develop and sustain productive community-academic research partnerships; to listen and respond to academic partners when selecting designs, when choosing funding sources, when determining the timing for the study, and when conducting other tasks involved in conducting community-academic partnered research; to act ethically when conducting community-academic partnered research by including the community partner in all aspects of the research, from idea generation through findings dissemination.
CTSI Curriculum Tree Elective Branch: Electives are designed for completion of specific training programs within the CTSI-ED.		
Advanced Topics in Clinical Pharmacology (established) Elliot Landaw, MD	10-week course 1-hour lecture/ 1-hour discussion/week (MS and above)	Reviews pharmacokinetics, drug metabolism and transport, assessment of drug effects, drug therapy in special populations, and contemporary drug development.
Topics in Applied Regression (established) Jeff Gornbein, PhD	10-week course 3-hour lecture/discussion 1-hour lab/week (MS and above)	Covers advanced topics in multiple linear regression, including applied multiple regression models, regression diagnostics and model assessment, factorial and repeated measure analysis of variance models, nonlinear regression, logistic regression, propensity scores, matching versus stratification, Poisson regression, and classification trees.
Controversies in Clinical Trials (established) Robert Elashoff, PhD and Joy A. Frank, PhD	10-week course 1-hour lecture/ 1-hour discussion/week MS trainee and above	Discusses and analyzes eight published and well-known clinical trials with students, one invited clinical faculty member, and course director. Development of critical ability to evaluate trial design and pitfalls.
Advances in Translational Medicine (New course for CTSI-ED) Lily Wu, MD, PhD Michael Teitell, MD, PhD	10-week course 2 hours per week (PhD and above)	Discusses the major advances in medicine based on molecular investigation. The historical perspective of advancement will be covered. The discussion may include primary scientific literature that led to many advances. Topics covered will include cancer, neurological diseases, cardiovascular diseases, inflammatory and infectious diseases. The objective is to learn from the most successful approaches in translational science and apply winning strategies to advance the future of molecular therapeutics and diagnostics.
Translational Neurobiology of Psychiatric and Neurological Disorders (New course for CTSI-ED) Tyrone Cannon, MD David Jentsch, PhD	10-week course 2-hour lecture/week (PhD and above)	Addresses translational animal and human research in multiple domains: neuroanatomy and neurochemistry, electrophysiology and cellular physiology, developmental molecular biology, and systems neuroscience, in relation to human diseases of the nervous system, including schizophrenia, bipolar disorder, learning disabilities, Alzheimer's disease, attention deficit hyperactivity disorder (ADHD), mania, conduct disorder, substance abuse and dependence, depression, anxiety disorders, and autism. Courses will include content related to clinical trials methodology and prevention.
Molecules to Community: Research Realities (New course for CTSI-ED) Michael Irwin, MD Chris Evans, PhD	15 hours Either volunteering in a clinic, or participating in research core, or animal techniques, or radioactivity training sessions.	Provides a follow-up experiential course for the core course "Pathways to Clinical Goals" and will utilize CTSI clinics as well as scientific cores and resources for experiential training. Trainees in basic science will be expected to experience clinical settings and course completion will require documentation to include a description of the disease symptoms, issues important to the patients, issues important for the caregivers, priorities for disease treatment. Clinical trainees will leverage the extensive in place training programs offered by scientific cores (including confocal microscopy, flow cytometry, EM, animal behavior, immunocytochemistry, histology, microarrays, bioinformatics, mass spectrometry) and regulatory/aptitude training (radiation, animal procedures, animal barrier training).

Course Coordinator(s) / Lecturers	Course Logistics (Training Level)	Topics Covered
CTSI Curriculum Tree Elective Branch: Electives are designed for completion of specific training programs within the CTSI-ED.		
Molecules to Community: Research Realities (New course for CTSI-ED) Michael Irwin, MD Chris Evans, PhD	15 hours Either volunteering in a clinic, or participating in research core, or animal techniques, or radioactivity training sessions.	Provides a follow-up experiential course for the core course "Pathways to Clinical Goals" and will utilize CTSI clinics as well as scientific cores and resources for experiential training. Trainees in basic science will be expected to experience clinical settings and course completion will require documentation to include a description of the disease symptoms, issues important to the patients, issues important for the caregivers, priorities for disease treatment. Clinical trainees will leverage the extensive in place training programs offered by scientific cores (including confocal microscopy, flow cytometry, EM, animal behavior, immunocytochemistry, histology, microarrays, bioinformatics, mass spectrometry) and regulatory/aptitude training (radiation, animal procedures, animal barrier training).
Intermediate Biostatistics David Elashoff, PhD	10-week course 4-hour lecture/week (MS and above)	Course covers simple linear regression, multiple regression, regression model selection, analysis of variance, logistic regression and survival analysis.
Advanced Biostatistics Li-Jung Liang, PhD	10-week course 4-hour lecture/week (MS and above)	Same topics as Intermediate Biostatistics but more advanced.
Data Analysis 1 (SAS software) Arun Karlamangia, MD, PhD	10-week course 4-hour lecture and discussion/week (MS and above)	Topics include developing testable hypotheses, data management, operationalization of variables, and selection of analysis of techniques.
Data Analysis 2 Arun Karlamangia, MD, PhD	10-week course 4-hour lecture and discussion/week	Continuation of Data Analysis 1.
Observational Studies Teresa Seeman, PhD	4-hour lecture (MS and above)	Studies and Design, Case-Control Studies and Design.
Electives for High School Students	14-week summer course	The course is divided between a mentor-supervised, hands-on experience in one of the CTSI PCIR sites (formerly, GCRCs), and a formal course in high school covering translational and clinical research. The curriculum culminates with a student poster presentation at both the academic health center and high school sites.
Colloquium on Economic and Econometric Issues in Novel Care (New course for CTSI-ED) Emmett Keeler, PhD	2–3 hours/monthly	The HSR Program will develop advanced training, including syllabi, in medical economics, utilizing a range of CTSI investigators engaged in economic or econometric analyses. Other CTSI investigators will present periodically to keep CTSI health economists apprised of the areas of greatest need for scholarly work on cost, financing, and cost-effectiveness.
CTSI Curriculum Tree Seminar Branch: Seminar series are ubiquitous elements required in most training programs, and many series are already in place at UCLA. The CTSI will coordinate the CTSI-wide bi-weekly seminar series and disseminate information on lectures of interest to the CTSI investigator community		
CTSI-wide Bi-Weekly Seminar Series CREST	Every other week.	Will cover team-based interdisciplinary translational and clinical research.
CTSI-wide Monthly Work-in-Progress Series CREST Committee	Monthly	All CTSI affiliated trainees will be encouraged to present their research at least once a year. Sessions will be attended by CREST members and faculty and community mentors. Participation will be mandatory for scholars funded in the CTSI K12, T32, and Pilot Study Program.
Seminars in T1 to T4 Translation Program 3: HSR	Monthly	Will cover a broad array of topics by pairing T1 to T4 speakers who work with similar diseases. . Participation will be mandatory for scholars funded in the CTSI K12, T32, and Pilot Study Program.

CTSI-ED Curriculum Tree in Development of New Programs: Several new CTSI-ED programs are proposed in this application: The K12 in Mentored Interdisciplinary Translational Therapeutics and Technologies Research, the Executive MS in Community Research, the Systems Biology PhD program, and the T32 in Clinical and Community-Partnered Translational Research. The CTSI-ED Curriculum Tree will contribute to these programs and benefit from courses developed for these programs by providing additional opportunities (see **Table 10**). Molecular Medicine faculty will be leading the effort to develop several new courses for their PhD programs and that will enrich other CTSI-ED programs (the CTSI-ED K12 Program). The

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combined infrastructure provided by the CTSI-ED Office and the Curriculum Tree will become a foundation for the development of new training initiatives by other programs in the CTSI. For example, the CTSI Community Engagement and Research Program has proposed training to educate and train CTSI investigators to conceptualize, design, conduct, and utilize community-academic partnered research. Development of these courses and seminars will require logistics, resources, and knowledge bases that will be provided by the proposed CTSI-ED infrastructure.

6.3.3. Assessment and Outcomes

6.3.3.1. The CREST assessment and outcomes subcommittee. The CREST **Assessment and Outcomes Subcommittee** will continuously evaluate all CTSI-ED programs. The CTSA RFA calls on grantees to include a detailed self-evaluation plan to assess implementation of the short-term and long-term CTSA goals with a special focus on research education, training and career development. The Assessment and Outcomes Subcommittee will be co-chaired by Drs. Pamela Davidson, **Evaluation and Tracking (E/T)** Program leader, and LuAnn Wilkerson, both of whom are highly experienced in program evaluation. Members of the subcommittee will include: (1) Lianna Anderson, Assistant Dean of Life Sciences and Director of the UCLA Education Training Office, who has extensive experience in educational program assessment and will direct data mining; (2) Dr. Deborah Koniak-Griffin from the UCLA School of Nursing, who is an E/T Co-leader with extensive experience in designing and assessing clinical research training programs; (3) Dr. Denise Aberle, a BIP investigator who will build the Web-based CTSI-ED Database and Program Management System.

6.3.3.2. CTSI-ED Database and Program Management System (DPM System). A CTSI-ED DPM System will be adapted in close collaboration with **Dr. Ali Sayed, from the Adaptive Systems Laboratory at the UCLA School of Engineering**, who has developed the EE-web system for UCLA engineering students and is now adapting the system for health professions education programs at UCLA. He is also an E/T investigator. Dr. Sayed's system evaluates and tracks faculty, students, and coursework for their achievement of specified learning objectives, competencies, and educational outcomes. We will adapt Dr. Sayed's prototype to the needs of the CTSI-ED program with the foundation of this system being competency-based curriculum and a complete set of program monitoring indicators, including, trainee and program characteristics, recruitment, participation and mentoring, program quality ratings, and trainee short- and long-term outcomes. Additionally, we will obtain annual feedback from current and former trainees to help identify weaknesses in the training programs and to provide suggestions for program improvements. This system will enable the CTSI-ED to efficiently develop rigorous evaluation standards and statistical metrics to monitor trainees, scholars, and their mentors through the coursework, projects, and interpersonal training activities as to how well they attain the goals of the CTSI-ED program.

Table 10. CTSI Curriculum Tree Core Branch.

CTSI CT Courses	K30 MS Clinical Research	K30 Cert	STAR Tracks 1-3	CTSI K12 (TTTR)	PhD Track Molecular Medicine	CTSI T32 Clinical and Comm. Research	Executive MS Comm. Research	K12, T32, R25, and P30/50 Programs
Core Courses	Required	Required	Available	Required	Available/ Required	Required	Required	Available/ Required
Module Courses	Available	3 Modules Required	Available	3 Modules Required		Available	Required	Available/ Required
Elective Courses	Available	Available	Available	Available	Required	Required	Required	Available/ Required
Seminars	Encouraged	Required	Encouraged	Required	Encouraged	Required		Available/ Required

6.3.3.3. Trainee Recruitment. Success of the CTSI-ED programs depends on recruiting and selecting applicants with the potential to succeed in clinical and translational science research. The pool of applicants will be drawn from the 4 UCLA CTSI institutional partners and the 6 UCLA professional schools. Similar to the evaluation and tracking approach used by the Clinical and Translational Science Institute (CTSI) at UCSF, our database will include documented characteristics of applicants, current participants, and graduates including diversity of the applicant pool and trainees selected (age, ethnicity, gender), and academic and professional experience (previous training, academic discipline, specialty department, academic rank, etc.). These data will

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derive from application forms and we will develop a pre-enrollment survey as part of the online DMP System. See **Table 11** for description and definition of measures, data sources, and timing for data collection. After each recruitment period, summaries of the tracking data will be reported to the Recruitment and Admissions Subcommittee, chaired by Dr. William Cunningham. These data will be used to review admissions criteria, effectiveness of publicity in the performance sites, professional schools and various medical departments, and enrollment of high-quality, diverse participants.

Table 11. Trainee Characteristics.

Component Timing/Source	Measure: Description/Definition	Data
Monitor applicant pool and trainees recruited	Diversity of pool of applicants and trainees, including age, ethnicity, gender, career stage, and previous training; academic discipline, specialty, department, academic rank, etc.	Trainee Applications Annual Web Survey

6.3.3.4. Program Quality Ratings. The CTSI-ED DPM System will allow trainees, mentors, and instructors to rate the quality of the CTSI-ED program and offer suggestions for program improvement. See **Table 12** for description and definition of measures, data sources, and timing for data collection. Participants will assess quality of curricula and effectiveness of instructors at the completion of each course. Course and faculty evaluation forms will be based on those used for the UCLA medical students. The forms will be delivered using the online DPM system for ease of completion and analysis. The DPM system will include pictures of faculty members to be evaluated to assist in recall for multi-instructor courses. It has been our experience that online systems increase the number and quality of learners' narrative comments and that having access to these comments in typed form increases review of results by faculty. Items assessed include course organization, materials, and assignments. Faculty items include clarity of presentations, effectiveness in guiding discussion, and provision of feedback. The online system will generate reports immediately after course completion, and will forward these to the program directors, subcommittee members, course chairs, and individual instructors. In interviews, scholars will be asked for general comments, suggestions for areas to be expanded or truncated, and for new topics for inclusion in the program. The CTSI-ED Office will provide course evaluations for both the CTSI Program Assessment and Outcomes Subcommittee and the faculty members responsible for program components. This strategy provides constant feedback and has led to effective curriculum changes and development of new courses in the past. The CTSI-ED Program Assessment and Outcomes Subcommittee and the CREST Committee will determine appropriate steps to correct student dissatisfaction while maintaining rigorous training.

Table 12. Program Quality Ratings.

Component	Measure: Description/Definition	Data Source (Timing)
Quality of didactic courses	Course evaluations: evaluation of lectures, lecturers, course director/faculty, readings, homework, and overall course using structured items (1-5) and open-ended qualitative comments	Student Web Survey (Course Completion)
Quality of mentoring	Structured ratings of quality of mentoring on multiple domains (e.g., accessibility, expertise) and qualitative evaluation of mentoring quality	Trainee Web Survey (Annual)
Sufficiency of mentoring team	Adequacy of mentoring team to provide needed resources and interdisciplinary approaches	Trainee Web Survey (Annual)
Quality of training program	Structured rating of quality of components of each degree or training program (i.e., curriculum, mentor selection process, research support, training faculty, program directors, etc.)	Trainee Web Survey (Annual)
Helpfulness of program in building CTS competence	Structured rating of the extent to which the program strengthened their capacity in a variety of CTS skills.	Trainee Web Survey (Annual)
Sufficiency of program Trainees components	Qualitative evaluation of extent to which program provided expertise needed and gaps	Interviews (Annual)

6.3.3.5. Trainee Participation and Mentoring. The CTSI-ED DPM System will allow trainees and mentors to rate the participation and mentoring components of the CTSI-ED program. **Table 13** shows the description and definition of measures, data sources, and timing for data collection.

Table 13. Trainee Participation and Mentoring.

Component	Measure: Description/Definition	Data Source (Timing)
Mentoring team, faculty advisor	Nature of mentoring team for each trainee Nature of faculty advisory	Admin Records (Annual)
Participation in didactic courses	Number of trainees completing research education courses and participating in various workshops, workshop seminars by topic	Admin Records (Annual)
Use of Shared Resources	Number of trainees utilizing shared facilities and resources (e.g., statistical or grant writing support)	Admin Records (Annual)
Amount of mentoring received	Number of meetings and other contracts with mentors	Trainees (Annual)
Participation in pilot research	Ability to complete pilot research (funded by respective program)	Trainees, Mentors (Annual)
Faculty and researchers participate in education and training	Number of faculty and research staff completing research education programs or didactic courses	Admin Records (Annual)
Completing all program requirements	Number of trainees completing all program components, including number earning certificate or degree and monitoring if minority groups or persons from underrepresented departments complete programs at the same rate	Admin Records (Exit Interviews)

6.3.3.6. Trainee Outcomes. To track scholars after completion of the program, we will implement a three-pronged approach that has been used successfully by our K30 Program: (1) Scholars from all CTSI-ED affiliated programs (CTSI K12, T32, K30, STAR, etc.) will be interviewed in the second, fifth, and tenth year following program completion. Areas of assessment will include current research involvement, level of research funding, and academic career status. Additionally, the interview will explore how the program has helped scholars to advance their research careers. An e-mail survey will be sent to scholars who are not available for interviews. (2) Scholars' CVs will be collected annually to determine positions held, publications, and research accomplishments. (3) When necessary, the CTSI-ED Office will query publicly available electronic resources, such as Web of Science and PubMed, to obtain current publication records. The CTSI-ED Office will identify federally funded projects involving our scholars through the Computer Retrieval of Information on Scientific Projects (CRISP), on a yearly basis. Post-graduation data will be used to assess program effectiveness and drive optimization of our CTSI programs. **Table 14** shows the description and definition of measures, data sources, and timing for data collection using the DPM System.

Table 14. Trainee Outcomes.

Component Timing/Source	Measure: Description/Definition	Data Source (Timing)
Short-term trainee outcomes		
Competence/Trainees:	Self-reported competence in 10 baseline domains using a CTS inventory	Trainees Web Survey (Annual)
Productivity in interdisciplinary teaching activities, manuscripts, publications, translational research	Research products: number of abstracts, presentations, manuscript publications, CV citations, index/Baseline	Trainees and translational research and grant activities reflecting scientific impact of publications (Annual)
	Mentor reported assessment of the trainees' competencies using inventory and open-ended questions	Mentors Web Survey (Annual)
Success in CTS Research	Satisfaction with various facets of research activities	Trainees Web Survey (Annual)
Long-term career outcomes (after completing or exiting program)		
Academic position	Current position, institution/setting, discipline	Trainees CV at 2, 5, 10 yrs
Professional activities, patient care, teaching, research	Percent effort in CTS research	Trainees CV Admin Records, Web Survey at 2, 5, 10 yrs
CTS research participation	Engagement in clinical/translational research, nature of research (T1-T2 community), research products.	Trainees CV Web survey at 2, 5, 10 yrs

Component Timing/Source	Measure: Description/Definition	Data Source (Timing)
Long-term career outcomes (after completing or exiting program)		
Research leadership	Number of research projects as PI or Co-PI role	Trainees CV at 2, 5, 10 yrs
Mentoring others	Extent of mentoring others	Trainees CV, Web survey at 2, 5, 10 yrs
Long-term program effectiveness	How well program prepared them for their current position and how the program could have better prepared them	Trainees Web Survey at 2, 5, 10 yrs

7. INVESTIGATORS

The outstanding Leaders of CTSI-ED and CREST are listed in **section 6.1.1**. Mentors and leaders of specific training and educational programs are identified throughout this key function. CREST subcommittee members are identified in section 6.3.3

8. INTEGRATION OF UCLA CTSI KEY FUNCTIONS

CTSI-ED creates the infrastructure and resources for the educational and training missions of every CTSI Program. The CTSI-ED Office provides a physical home and, collaborating with **BIP**, a Virtual Home with tools for aiding career development. The CTSI-ED collaborates with **CTT** on the new PhD in systems biology, with **CERP** on a new MS in Community Research Program, and with **CERP** and HSR on the new T32 in Clinical and Community-Partnered Translational Research. Programs will contribute back to the missions of the CTSI-ED by providing didactic courses. The CTSI-ED is designed not only to develop educational and training initiatives proposed in this application but also for developing a base for future CTSI initiatives.

9. EXTRA-UCLA COLLABORATIONS

Our leadership and mentors have numerous collaborations with other CTSA sites. For example, CTSI-ED Leader Dr. Mangione is co-PI with Dr. Michael Ong on a \$10-million, 3-year randomized controlled study supported by the AHRQ comparing two interventions to usual care on reducing hospital readmissions for heart failure patients. Four collaborating CTSA institutions are UC Davis, UC Irvine, UC San Diego and UC San Francisco. Dr. Mangione's RCMAR center has mentored faculty from UCI (Quyen Ngo-Metzger, Associate Professor of Medicine), and from University of Southern California (USC) (Dr. Isabel Lagomasino, Associate Professor of Psychiatry). Drs. Mangione and Etner have also mentored Dr. Shaista Malik (Assistant Professor of Medicine at UCI) as Chair and members of her dissertation committees. Drs. Mangione and Samet (Director of the USC Ed Core) have met during the preparation phase of this application and have all intentions to use teleconferencing for sharing curricular opportunities for trainees at both of our institutions. Dr. Mangione also has a close research collaboration with Dr. Carl Kesselman (Director of the USC informatics core) on AHRQ funded research designed to create a federated data system for the State of California.

CTSI-ED Co-leader Dr. Salusky is collaborating with researchers at Harvard University, a CTSA site, on two studies. One examines the effects of vitamin D therapy on bone mineralization defects in dialyzed patients. The second seeks to define the relationship between parathyroid hormone and bone formation across the spectrum of kidney disease.

BARRIERS, OPPORTUNITIES, AND TRANSFORMATIONS

Table 15. CTSI-ED Program Barriers, Opportunities, and Transformation Process.

Barriers / Opportunities	Transformation Process
Overcome existing training program silos	Address Aim 1 by forming an oversight leadership committee (CREST) and an Office of Education and immediately instating a centralized operational infrastructure to foster training program evaluation, improvement and career development (Aim 1).
Career opportunities	Develop in Years 1 and 2 an Office of Education providing a physical and virtual home for training requirements/opportunities within the multiplicity of T1 and T2 translational research programs at UCLA and the partner institutions.

Barriers / Opportunities	Transformation Process
Expand and improve existing training programs to reflect expertise of CTSI faculty	Provide infrastructure and support for the key didactic CTSI-ED programs (the MS and Fellowship in Clinical Translational Research). Reorganize and increase institutional support for successful CTSI-ED programs, including the MS, STAR, K30, and K12 training programs. (Aim 2.1)
Lack of didactic opportunities for basic scientists to acquire knowledge and skills in T1/T2 research	Create new courses such as Pathways to Clinical Goals to provide information on the process of T1 and T2 research and make available such courses to the training programs. Develop a new K12 program, PhD track in systems biology and a novel T32 training program in clinical and community partnered research. Develop an Executive MS Program for education of community and health sciences leadership. Provide resources for other CTSI resources programs to develop educational and training programs to enhance their missions. (Aim 2.2)
Inertia to readily develop new programs and courses crossing basic science to community	Create and maintain a CTSI-ED Curriculum Tree (Aim 3) of rigorously evaluated courses and a well-staffed Office of Education to provide elements and logistic aid to develop new cross-disciplinary programs.

10. IMPLEMENTATION PLAN

The RFA includes a special focus on research education, training and career development. Detailed plans and evaluation methods are provided in this program including the organization of the CTSI-ED Assessment and Outcomes Subcommittee. Once the CTSI-ED degree and career development programs are operational, we will implement annual continuous evaluation that is standardized across all of the programs to measure milestones and a follow-up plan to track scholars after program completion. **Table 16** presents the CTSI-ED implementation plan and the E/T milestones and measures that will be monitored years -01 to -05.

Table 16. CTSI Education Program Implementation Plan

Years	Key Activities	Milestones and Measures
Current Activity: Prepare for transition to CTSI.		
	<ul style="list-style-type: none"> • CTSI Education Office with institutional support managing K12, K30 • Streamline and prepare to expand existing programs, e.g., K30 • CREST Committee formed • Multi-institutional, transdisciplinary translational research seminar series • Pilot program to fund 4 CTSI-CTS Scholars 	<ul style="list-style-type: none"> • CREST Committee formed • Seminar series launched • RFA and 4 Scholars selected • K30 successfully renewed
Aim 1. Establish novel infrastructure (CTSI-ED office) to optimize cross-disciplinary training and integrate community input into training via team-based, interdisciplinary, patient-oriented research throughout the CTSI.		
1-5 1-2 1-5 1 1-5 1-3 1-2 1-5	<ul style="list-style-type: none"> • Convene monthly meeting of the CREST Committee • Develop and implement curricula in communication of science and leadership in science for all K12 trainees • Implement URM recruitment, retention, career development strategies • Develop list of core competencies to provide a training framework • Formulate and optimize training initiatives via ongoing evaluation • Initiate career development and advisors for trainees and mentor education • Reduce redundancy in curricula and assess curricula needs • Form trainee committees to encourage collaboration among trainees • Improve recruitment into CTSI programs and CTS feeder programs • Organize seminars in team-based interdisciplinary translational research • Organize work-in-progress seminars for CTSI T1 and T2 scientists • Co-host <u>Community Program</u> Symposia with K12 and K30 directors • With <u>Community Program</u> create and sustain a CTSI community mentor pool and add mentors to specific projects 	<ul style="list-style-type: none"> • CTSI Office of Education established (Yr 1) • CTSI-ED virtual home operational (Yr 2) • Select CTS Competency Model as the foundation for CTSI-ED web (Yr 1) • Curriculum mapping to CTS competency model (Yr 2) • Mentor/mentee database created (Yr 1) • Semi-annual trainee and mentor assessments and feedback via CTSI-ED web (Yr 2) • Number of CTS seminars and symposia, attendance, and participant evaluations (Yrs 1-5) • Initiation and expansion of community mentor pool (Yrs 1-5)

Years	Key Activities	Milestones and Measures
Aim 2. Transform translational education through new curricular elements and create new programs (K12, K30, T32, and others) incorporating community engagement and interdisciplinary methodologies and technologies:		
1-5 1-2 1-3 1-5 1-3 4-5 2-3 3-4	<ul style="list-style-type: none"> Expand and integrate scope of Preexisting Mentored Training Expand and integrate the STAR Program and the RWJF Clinical Scholars Program to Trainees at all CTSI Institutions Develop new K12 Mentored Interdisciplinary Translational Therapeutics and Technologies Research Program (TTTRP) Develop T32 PhD Training Program in Clinical, Comparative Effectiveness, and Community-Partnered Translational Research Expand and integrate K30 training paths in systems biology; clinical pharmacology; community-oriented clinical and translational research; biomedical engineering; nanotechnology and other emerging technologies Develop New Translational Graduate Training Track in Molecular Medicine with systems biology emphasis Develop new PhD Track of Molecular Medicine with an emphasis in Translational Systems Biology Develop new Executive MS with a concentration in Community Translational Research Develop new EMPH Program in Community Research 	<ul style="list-style-type: none"> Implementation Reports to monitor new and expanded programs, new curricula, and curricular revisions (Yrs 1-5) CTSI-ED web to track educational programs, trainees, mentors, and CTS research projects, and other career development activities (Yr 2) New K12 fully operational (Yr 2) New T32 fully operational (Yr 2) New PhD Track in Molecular Med (Yr 5) New Exec MS in Community Translation Research operational (Yr 3) New EMPH in Community Research operational (Yr 4)
Aim 3. Provide mechanisms to integrate patient-oriented research training through course menu, expansion of didactic programs (CTSI-ED Curriculum Tree), and an integrated assessment program providing a sophisticated, computer-based learning-management system.		
1-3 1-2 1-5 1-3 1-5	<ul style="list-style-type: none"> Expand and integrate didactic course structure including expanded K30 Program and the Curriculum Tree Develop Fellowship in Translational and Clinical Research Certificate Program Develop Training and Career Development under the CTSI-ED Develop CTSI-ED Curriculum Tree Enhance the MS and Certificate Programs Convene monthly meetings of the CREST assessment and outcomes subcommittee Collaborate with CTSI E/T and BIP to design CTSI-ED online program management/assessment system 	<ul style="list-style-type: none"> Fellowship in Translational and Clinical Research Certificate Program (Yr 2) CTSI Curriculum Tree completed and ready for expansion (Yr 1) CTSI-ED web fully operational (Yr 2)

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Evaluation and Tracking (E/T)



PROGRAM TEAM

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Martin Shapiro, MD, PhD – Leader
Ronald Andersen, PhD – Co-Leader
Mohsen Bazargan, PhD – Co-Leader
Richard Casaburi, PhD, MD – Co-Leader
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Deborah Koniak-Griffin RN, EdD – Co-Leader
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Gerald Kominski, PhD – Investigator
Kumar Rajaram, PhD, MBA – Investigator
Ali Sayed, PhD – Investigator

Abbreviations:

BIP – Biomedical Informatics Program; C&G – Contracts and Grants; BSD-CDM – Biostatistics, Study Design and Clinical Data Management Program; CAHME – The Commission on Accreditation of Healthcare Management Education; CDU – Charles Drew University; CCRR – Clinical and Community Research Resources Program; CERP – Community Engagement & Research Program; CTS – Clinical Translational Science; CTSI-ED – Research Education, Training and Career Development Program; CTT – Center for Translational Technologies; DGSOM – David Geffen School of Medicine; DTMI – Duke Translational Medicine; EMPH – Executive Masters of Public Health; EOC – Executive Oversight Committee; E/T – Evaluation and Tracking; HSR – Health Services Research; IRB – Institutional Review Board; OIA – Office of Industry Alliances; OIS – Office of Investigator Services; PARO – Post-Approval Research Oversight; Pilot/Collaborative Program – Pilot and Collaborative Translational and Clinical Studies Program; Regulatory Program – Regulatory Knowledge and Support, Industry Relations and Research Ethics Program; RSA – Research Subject Advocate; SPA – Service Planning Areas; TRC – Translational Research Clusters

1. OVERVIEW

The Evaluation and Tracking Program (E/T) conducts self-evaluation activities for the UCLA CTSI and participates in the evaluation of the national CTSA program. E/T evaluates the scientific and administrative operations of UCLA CTSI and provides reports to the CTSI leadership on program functioning, implementation and accomplishments to guide improvements. Our duties include close monitoring of the quality, productivity and equitable distribution of resources across CTSI institutional and community partners. We belong to the Greater Los Angeles CTSA Coalition with the University of Southern California and the University of California, Irvine.

In prior review, E/T was reviewed with CTSA Staffing, Governance, Institutional Commitment, Local and National Collaboration, Data Sharing, Dissemination and Evaluation Plan. Reviewers praised our outstanding leadership team, our “exceptional” approach to ensuring operational effectiveness, and our comprehensive, well-designed evaluation and tracking plans. No substantive weaknesses were identified.

We are nonetheless adding exciting new improvements to this application. First, we are launching an Improvement Sciences Program to increase efficiency and stimulate innovation. We have recruited **Moira Inkelas, PhD**, an Associate Professor in the UCLA School of Public Health, to co-lead this program. She will design and lead improvement projects and will provide coaching in process improvement. Dr. Inkelas conducts outreach and engagement activities in collaboration with the National Children’s Study neighborhoods within Los Angeles and contributes to the development of metrics and dashboarding within community research centers sponsored by CTSI **Community Engagement in Research Program (CERP)** that involve child health interventions.

Second, we are creating a **UCLA CTSI Center for Evaluation and Health Services Research (HSR)** to accelerate the speed and efficiency of translational research for improving organizational effectiveness and population health. We have strengthened our HSR expertise by recruiting **Martin Shapiro, MD, PhD**, Professor of Medicine and Health Services and Chief of the Division of General Internal Medicine at UCLA. Dr. Shapiro is a recognized leader in the areas of health care access and disparities. His accomplishments include leadership of a large US study of HIV treatment patterns and outcomes. His initial focus is on developing and implementing a CERP/HSR research agenda.

Third, we are expanding our national collaboration by participating in the cross-cutting CTSA initiative, “Research Metrics and Dashboarding.” This initiative, spearheaded by the University of California, San Francisco (UCSF CTSI), is a national model of transparency and accountability to improve clinical and translational research and research administration in CTSA networks across the nation. Substantive changes to this application since our last submission are indicated in the left margin.

2. SPECIFIC AIMS

The UCLA CTSI provides the operations and governance necessary to facilitate successful transdisciplinary clinical and translational research. The overarching **mission** of the UCLA CTSI is to *transform our academic-clinical-community partnership into a borderless institute that brings our combined innovations and resources to bear on the most pressing health needs in our diverse community*. E/T will longitudinally track CTSI progress, integration, and operations. Our team has carefully aligned the UCLA CTSI goals, initiatives, program aims and outcomes to focus our evaluation efforts and resources most efficiently. In this application we have emphasized five crosscutting CTSI Initiatives designed to enhance program integration, demonstrate UCLA CTSI goal achievement, and align with the National CTSA Consortium goals. Additionally E/T collaborated with all the program leaders to develop 9 Implementation Plans summarizing specific aims, implementation strategies, milestones and measures for assessing the formation of the institute and its programs, processes, and outcomes in project years 1-5. The implementation plans are summarized in two locations: in the final section of each CTSI Program and in **Implementation Phases and Milestones**, available elsewhere in this application.

Specific Aim 1: Longitudinally track and evaluate Initiative and program outcomes.

Aim 1.1. Develop an Evaluation and Tracking (E/T) System for monitoring progress and performance across the CTSI;

Aim 1.2. Conduct implementation evaluation, provide ongoing progress reports, and suggest high priority

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improvement sciences initiatives; and

Aim 1.3. Monitor implementation of 5 CTSI Initiatives to assess CTSI goal achievement.

Specific Aim 2: Implement an Improvement Sciences Program with the intent of increasing efficiency, stimulating innovation, and improving operational effectiveness in the CTSI and its community research centers.

Specific Aim 3: Create the UCLA CTSI Center for Evaluation and Health Services Research to accelerate the speed and efficiency of translational research for improving organizational effectiveness and population health.

Specific Aim 4: Collaborate with local, regional, and the CTSA National Consortia and participate in the National Process and Outcome Evaluations.

3. PROGRESS TO DATE

E/T has achieved a number of important and transformative goals during the pre-award period. We have updated our comprehensive plans for a uniform data collection and analysis system to inform decision-making across CTSI programs and to guide institutional transformation and integration. Our data system will integrate uniform measures and metrics monitored in the national CTSA evaluation studies, as well as measures and metrics unique to our regional CTSA.

In 2009-10 we completed a pilot project that will be expanded to build our **Research Education, Training and Career Development Program (CTSI-ED)** Internet based assessment and program management system. EE-web (Electrical Engineering), a sophisticated course management system with embedded assessment, was adapted to our Executive Masters in Public Health (EMPH) program. We conducted a feasibility study including plan and budget for building and maintaining the Web-based system including hardware, software, and technical requirements. Additionally, EE programmers developed a platform containing the critical components of the multilevel system required for program, department, and/or school level analysis including accreditation requirements, constituencies, overall program objectives, educational outcomes and competencies. The Commission on Accreditation of Healthcare Management Education (CAHME) characterized the adapted EMPH-Web system as a “national best practice.” In 2010-2011, we will expand the existing structure to create the CTSI-ED curriculum tree and to build in a series of assessment and analysis tools (See **CTSI-ED**, elsewhere in this application).

We conducted a formative evaluation to assess a September 2010 retreat convened to review research agendas proposed by our CTSI Translational Research Clusters. The Clusters bring together basic, clinical and community researchers from a range of disciplines to address the leading causes of morbidity and mortality in Los Angeles County. The Clusters are the centerpiece of our transformative clinical and translational science grants program featured in **Pilot and Collaborative Translational and Clinical Studies (Pilot Program)**, available elsewhere in this application). The survey response rate was 63.5%. Among respondents, 85% were enthusiastic/very enthusiastic to attend 2-3 additional cluster retreats in the next 12 months. Almost 80% agreed a shared conceptual framework should be adopted to guide the research clusters in the future, in terms of team formation, conceptual and analytical thinking, research agenda and future research. Sixty-five percent (65%) thought the research clusters generated novel ideas and ways of thinking about translational research. The CTSI will use this information to refine the concept and structure of our Translational Research Clusters and to improve program performance.

4. E/T ORGANIZATIONAL STRUCTURE: SIGNIFICANCE & UNIQUE ENVIRONMENT

The E/T Team will be composed of a leader and co-leaders from all four institutional partners and five of the UCLA professional schools involved in the CTSI (medicine, nursing, public health, engineering, and management). It is a core function within the UCLA CTSI and will be organized within the CTSI Office of the Institute (see **Overview and Governance**, elsewhere in this application). E/T will be led by Dr. Pamela Davidson with Dr. Deborah Koniak-Griffin serving as Co-Leader and will provide weekly reports to the CTSI Executive Oversight Committee (EOC), to ensure Institute operations are effective and efficient. **Figure 1.** shows the E/T organizational chart will include the Program Monitoring Committee (**Specific Aim 1**), an Improvement Sciences Program (**Specific Aim 2**), and a Center for Evaluation and Health Services Research (**Specific Aim 3**).

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The **Program Monitoring Committee (Specific Aim 1)** will have the primary charge of ensuring the generation, quality, and monitoring of E/T data to make certain all programmatic milestones are met. **Figure 1.** (below) indicates responsibilities of each Program Monitoring Committee member. Members will engage in ongoing communication with all CTSI key function leaders to collect information and provide feedback on program progress. Additionally, we will provide expertise and E/T services to the **CTSI Office of Education**, housed in the CTSI Office of the Institute. Drs. Bazargan, Davidson, Koniak-Griffin, and Sayed will participate on the **CTSI-ED Assessment and Outcomes Subcommittee**. The Subcommittee will provide support to design the **CTSI-ED** web-based program management and assessment system (designed by Dr. Sayed in collaboration with the CTSI Bioinformatics Program). This internet based system will enable the **CTSI-ED** Program to measure core competencies, map curriculum, develop rigorous evaluation standards and statistical measures to monitor trainees, scholars, and their mentors, assess translational research clusters, research projects, interdisciplinary training activities, and career development (see **CTSI-ED**, elsewhere in the application).

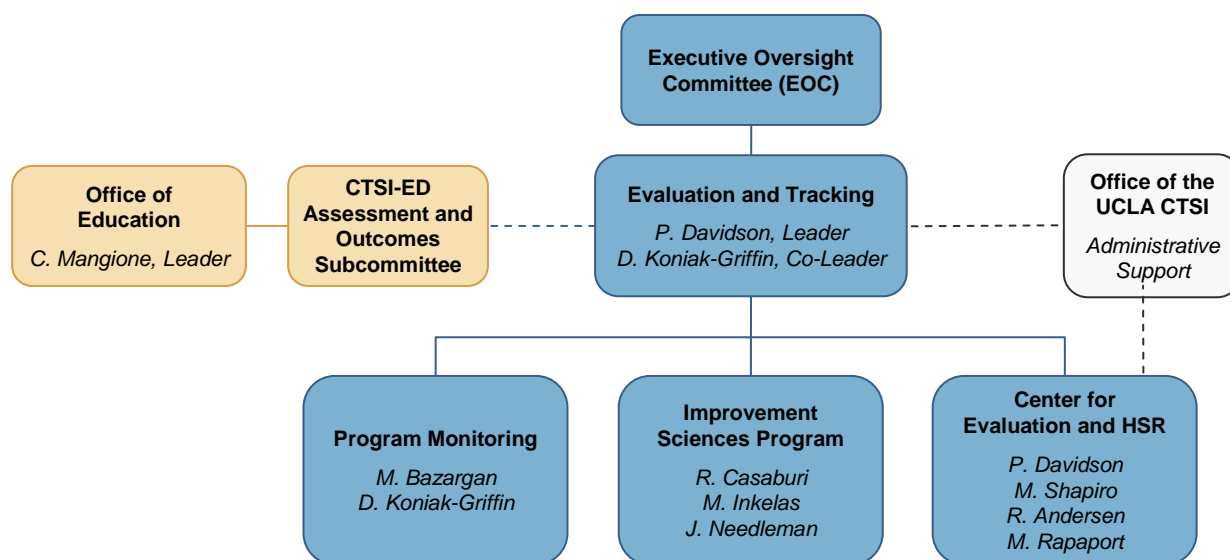


Figure 1. Evaluation and Tracking Organizational Structure

The **CTSI Improvement Sciences Program (Specific Aim 2)** has the aim of increasing efficiency, stimulating innovation, improving operational effectiveness, and building organizational capacity for process improvement. Data obtained through special projects implemented through the Improvement Sciences Program will be used to formulate strategies to reduce delays, inefficiencies, and rework pervasive in the research enterprise and to stimulate innovation and improve operational effectiveness. The Improvement Sciences Program will be led by Drs. Casaburi, Inkelas, and Needleman (see **section 6.2.**).

The **Center for Evaluation and Health Services Research (HSR)** will have the purpose of facilitating and conducting evaluation and HSR studies and improving the science and methods of evaluation research (Aims 3-4). The Center will receive operating expenses through institutional support and extramural funding for conducting studies to accelerate the speed and efficiency of translational science occurring at all three potential blocks (T_1 , T_2 , and T_3) designed to improve organizational effectiveness and population health (see **section 6.3.3.**). The principal architects of this novel initiative will be Drs. Shapiro and Andersen, who will lead the HSR Core, and Drs. Davidson and Rapaport, who will lead the Evaluation Core. The Center will involve E/T and HSR investigators across the CTSI and UCLA and Charles Drew University (CDU) campuses. **Section 7** (below) provides a summary of the E/T leadership qualifications and responsibilities.

5. INNOVATION: EVALUATION APPROACHES AND CONCEPTUAL FRAMEWORK

We will deploy a range of approaches to comprehensively monitor and evaluate activities in the CTSI. Additionally, we will advance the science of evaluation and facilitate and conduct evaluation and HSR in clinical

Principal Investigator/Program Director (Last, First, Middle): Dubinett, Steven, MD and translational science (CTS). The evaluation approaches will include contextual,¹⁻⁶ formative,^{7,8} implementation,⁹ quality and performance improvement monitoring,¹⁰⁻¹⁴ and summative evaluation studies.¹⁵⁻¹⁶ Contextual evaluation will be used to assess the policy, regulatory, and industry environment and the characteristics of communities, hospitals, health care providers, researchers and patients/populations associated with CTS (e.g., recruitment, participation rates, technology utilization and cost). Formative evaluation will be used to collect data in the early phases of implementation to refine program plans and to provide recommendations for improving structures and processes. Implementation evaluation will be ongoing and used to monitor progress against plan. Quality and performance improvement needs will be addressed and monitored and E/T data will be used to identify and spread effective improvement strategies. Summative evaluation studies will be used to measure the extent to which program aims are achieved and the short- and longer-term program impacts over time.

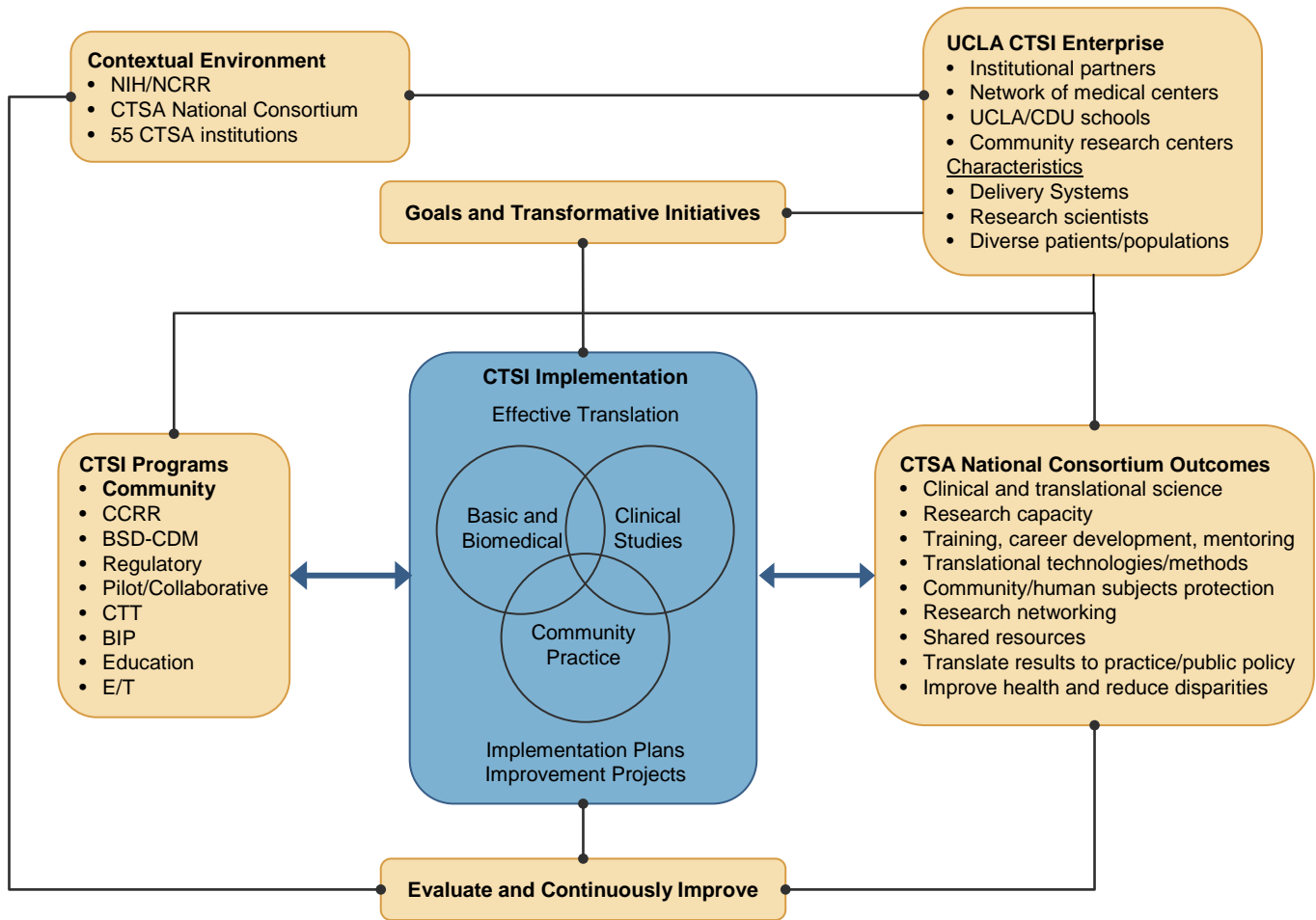


Figure 2. UCLA CTSI Evaluation Framework

Figure 2. shows the UCLA CTSI Evaluation Framework that has been adapted from our previous evaluation research.^{2-4,16,17} The conceptual framework provides the rationale for the evaluation and is central to defining the objectives and expected outcomes. The major purposes for developing a framework are to guide data collection and analysis, facilitate effective communications, and enable a bi-directional exchange of information with CTSI leaders and stakeholders. The framework shows the contextual environment for conducting CTS research includes the NCRR, and its current network of 55 medical research institutions in 28 states. When fully implemented, the program will support approximately 60 CTSA's across the nation and host a multitude of opportunities for national, regional, and local collaborations.

Within this national context is the UCLA CTSI enterprise wide organizational structure and characteristics of the healthcare delivery systems, research scientists, and our diverse Los Angeles communities, patients, and research participants. The UCLA CTSI enterprise includes four CTSI institutional partners, the UCLA, Cedars-Sinai, and Harbor-LA Biomed medical centers, UCLA and CDU professional schools, and community research

Principal Investigator/Program Director (Last, First, Middle): Dubinett, Steven, MD centers (see **Overview and Governance**, elsewhere in this application). The **CERP** and the integrated research infrastructure proposed in this application will allow us to engage and partner with these communities to develop and implement a collaborative CTS research agenda to address community needs.

The UCLA CTSI has proposed 5 overall CTSI goals and initiatives (see **Table 3**). These goals and cross-cutting Initiatives are implemented through the **CTSI programs** and the **Office of Investigator Services (OIS)**. The framework shows core functions of E/T are to assess and improve CTSI **implementation processes and outcomes**. E/T will function within all programs spanning the entire CTSI enterprise from laboratory based discoveries through clinical trials, and translating results to evidence-based practice adopted by the community and influencing public policy to improve health. We will continuously monitor implementation and improve programs by identifying and addressing barriers, sharing lesson learned, and disseminating best practices. Our CTSI leaders and E/T team have identified key structure, process, and outcome measures directly associated with all key function areas and aims. **Improvement projects** will be used to reduce delays, inefficiencies, and rework that are pervasive in research. Over the past three decades much has been learned from experience in a wide range of industries and settings about improving organizational processes and performance. Since the 2000 Institute of Medicine report *To Err is Human: Building a Safer Health System*,¹⁸ these methods have been increasingly applied in health care delivery and clinicians have become more familiar with them. It is time to apply them to biomedical, clinical, and public health research. We have initiated this process by emphasizing key analytic and design concepts in our Improvement Sciences Program (see **section 6.2.**).

E/T investigators will apply the most rigorous feasible evaluation design to monitor implementation and outcomes of CTSI initiatives, programs, and improvement projects. **CTSI outcomes** are categorized according to priorities reflected in the CTSA National Consortium Strategic Goals and the National Evaluation Feasibility Study. **Figure 2** illustrates how evaluation results will feedback to continuously improve CTSI performance and outcomes. Performance and performance improvement will be measured using a CTSI Dashboard that employs a multidimensional set of cascading measures aligning program with institutional performance. Used to translate strategic and organizational goals into metrics and provide feedback about internal operational processes and external outcomes,¹⁹⁻²⁷ the balanced scorecard (or dashboard) is increasingly used in research environments, such as the Duke Translational Medicine Institute (DTMI) and the UCSF CTSA.

6. APPROACH

6.1. Specific Aim 1: Longitudinally track and evaluate CTSI initiatives and program outcomes. Our E/T priorities are to: **Aim 1.1.** - Develop an Evaluation and Tracking (E/T) System for monitoring progress and performance across the CTSI; **Aim 1.2.** - Conduct implementation evaluation, provide ongoing progress reports, and suggest high priority improvement initiatives; and **Aim 1.3.** - Monitor implementation of 5 CTSI Initiatives to assess CTSI goal achievement.

6.1.1. Develop an Evaluation and Tracking (E/T) System for monitoring progress and performance across the CTSI. The RFA specifies that an evaluation plan should be developed for each key function area. Our plan includes the objectives of the evaluation and tracking activities, the principal measures or indicators, and the potential data sources. The **E/T System**, hosted by the CTSI Virtual Home, (i.e. UCLA CTSI Web Portal) will contain both quantitative indicators contained in the **E/T Database** and the semi-structured qualitative summaries of program progress contained in the **Implementation Reports** (see **section 6.1.2.1.**) based on Implementation Phases and Milestones (summarized elsewhere in this application). Technical support and expertise will be provided by Biomedical Informatics Program (**BIP**) to co-design the internet based E/T System that will be shared and integrated with other CTSI Program reporting. We will execute the following 10 activities:

- a. Co-design components of the **E/T Database** with CTSI Leaders (see **section 6.1.1.1.**).
- b. Collect existing baseline measures from 2005 forward and identify gaps in data collection.
- c. Develop a uniform format for periodically monitoring progress and providing feedback.
- d. Ensure data validity, reliability, and efficiency of data collection and entry.
- e. Develop the **CTSI Online E-Grant application and monitoring system** with the **Pilot Program** (see **section 6.1.1.2.**).

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- f. Collaborate to develop the **CTSI Virtual Home Users' Evaluation** for assessing and improving the internet portal (see **section 6.1.1.3.**).
- g. Conduct **CTSI Periodic Surveys** including needs assessments and satisfaction (see **section 6.1.1.4.**).
- h. Develop a **CTSI Dashboard** for measuring and managing performance (see **section 6.1.1.5.**).
- i. Design the **Contextual Variables** database (see **section 6.1.1.6.**).
- j. Design the **Evaluation/HSR Data Repository** starting with the **CERP** research agenda (**Aim 3**).
- k. Respond to emerging data needs of leadership and the CTSA National Consortium Evaluations.

6.1.1.1. Evaluation and Tracking (E/T) Database. The E/T Database will consist of quantifiable measures drawn from existing data sources and newly constructed measures required for monitoring core program activities and operations. We will include uniform measures suggested in the CTSA National Consortium Process Evaluation conducted by Westat and those suggested in the national "Research Metrics and Dashboarding" initiative (**Aim 4**), in addition to those unique to our UCLA CTSI. E/T will prepare a data dictionary containing variable definitions and data formatting for each measure and metric. The CTSI and E/T leaders will agree on a uniform set of measures to be monitored across performance sites, programs, and community research centers. We will determine the appropriate time interval for collecting each variable and report longitudinal data to monitor progress against plan and trends. **Table 2** (below) presents sample measures, indicators, and data sources that will be used by E/T to monitor progress longitudinally over the 5 year project period. Quantifiable indicators will be collected in the internet based E/T database for each CTSI program for both program management and evaluation and monitoring functions. Examples of E/T variables include the number and type of services utilized through the CTSI Office of Investigator Services and the level of satisfaction with services provided.

6.1.1.2. CTSI internet based E-Grant application and monitoring system. We will review 30-40 grants per year and provide more than \$18 million over 5 years for clinical and translational research. A team of reviewers will be selected to peer review these competitive proposals. E/T will closely monitor the peer review process and the outcomes of the **Pilot Program**, found elsewhere in this application. E/T will co-design the CTSI Web-Based E-Grant application and monitoring system with the complete application process for each of the pilot grant programs available at the CTSI Virtual Home portal. E/T will use the same system and database to monitor grant activities. We will track investigator productivity using the NIH Annual Progress Reports (3 page) and abstract format, reprints of publications, and research supported in whole or in part by the CTSI. The E-Grant database will contain aggregate information on the number and type of CTS grants funded, dollar amount, the number and type of peer-reviewed publications, and subsequent larger scale research projects that were initially funded through the CTSI pilot grants programs. In addition, more intensive monitoring will be conducted to examine the productivity and career trajectories of CTSI scholars to track CTS research projects and longitudinal career development (see **CTSI-ED**, available elsewhere in this application). In terms of the peer review process itself, we will monitor: the equitable appointment of leadership and members to the review committees, use of both scientific and community representatives when appropriate, attendance at the meetings, the merit review process itself, and the rating of grant applications. Additionally, in-line with our CTSI mission, we will determine the extent to which the awarded proposals address the leading causes of morbidity and mortality in Los Angeles County and an economic valuation of the potential impact of the research products on improving policy, delivery system, and population health.

6.1.1.3. CTSI Virtual Home Users' Evaluation. The **Bioinformatics Program (BIP)** aims are focused on establishing the virtual home and research data repository and educating and training clinical and translational researchers and new biomedical informaticians (see **BIP** section). **BIP** will facilitate interdisciplinary team science from bench to bedside to community by designing, implementing, evaluating, and providing training on new biomedical informatics methodologies, tools, and technologies that advance translational research, and by promoting awareness of and access to a broad range of functions and capacities. The CTSI Virtual Home will create a powerful technology toolbox, information system, and internet based gateway to allow scientists, clinicians, administrators, and community affiliates to view and access the comprehensive services and resources available across the CTSI. This internet based system will incorporate and integrate activities of all CTSI programs. Many approaches are available for evaluating, critiquing, and benchmarking usage of an Internet site or a web resource. E/T will collaborate with **BIP** leaders to ensure the CTSI Virtual Home

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highlights defined goals and communication strategies, easily guides visitors through the site, effectively communicates site offerings, and provides a mechanism to facilitate a two-way relationship with site visitors. Our phased approach to E/T includes: Phase 1: We will conduct interviews and surveys of CTSI leaders and program directors, researchers, trainees, and community partners to obtain direct feedback for each service available through the Virtual Home portal, utility of this information, and ease of use, access, and navigation. We will augment these basic web usage statistics including counts of page visit, download and web-page based submissions of queries and forms. If personnel and budget resources permit, we will augment the basic counts with more sophisticated data mining focused on navigation routes to frequently visited pages or downloaded materials to improve navigation tools for users.³⁵ These results will be incorporated into an annual report on user satisfaction with the internet based services and plans for changes and continuous improvement. Phase 2: Based on the Phase 1 analysis and comparison of the UCLA CTSI internet site to other relevant web sites, we will design updates and refinements of CTSI virtual home content, design, navigation tools and in-bound links. Prior to implementing major changes, these will be tested in prototype with key potential users, and once implemented subject to the same ongoing review outlined in Phase 1.

6.1.1.4. CTSI Periodic Surveys. Internet based surveys will be administered periodically to assess needs, availability and utilization of resources, and to track satisfaction with CTSI programs and services. For example, E/T and BIP conducted the first CTSI IT Investigators Survey using an internet based interface to assess biomedical information technology needs for investigators, administrators, and trainees across the UCLA CTSI. We incorporated items from previously validated surveys and conducted a pilot test before administering the BIP Survey. Over 900 respondents provided information on their professional activities, importance and availability of information resources, usefulness of information services, use of clinical information, computer sophistication, size of working group, and interest in designing the CTSI BIP and Virtual Home. In concert with CTSI leadership we will continue to conduct periodic surveys of CTSI investigators and community stakeholders to inform the next cycle of planning and decision making.

6.1.1.5. CTSI Dashboard. Our intent is to develop or adapt a uniform set of core measures with uniform variable definitions to be used in all CTSI partner institutions, programs, and community research centers. This will allow us to monitor activities across programs and performance sites, as well as roll-up measures to monitor overall CTSI-level performance. We will use a dashboard with the five domains shown to influence productivity and stakeholder satisfaction in multicenter research consortia: extent of collaboration and quality of communication, performance of programs and infrastructure, data quality, scientific productivity, and impact on member organizations.²⁷ Our dashboard will also reflect uniform metrics outlined in the national CTSI crosscutting initiative, "Research Metrics and Dashboarding" (Aim 4). For example, one important indicator of scientific productivity is the number of K awards and other early career awards that we will include in our dashboard. We will collect this information in all four partner institutions and in the UCLA and CDU health sciences and professional schools. The dashboard design process will include the following: (i) Select initial domains for the scorecard with the CTSI Director and Executive Oversight Committee (EOC), and the CTSI Office of the Institute; (ii) Recruit a standing subcommittee of the EOC to review and approve measures that will enable comparison and benchmarking; (iii) Create the CTSI dashboard and data dictionary; (iv) Provide initial orientation sessions to the EOC about the dashboard and how to employ it to improve performance; and (v) Update the dashboard and performance goals periodically to track progress against strategic and operational goals.

6.1.1.6. Contextual Variables. Data on environmental, organizational, community and population characteristics will be collected and analyzed to understand the factors influencing performance and outcomes in CTSI evaluation and HSR. Variables constructed from administrative and/or external data sources will include, for example, type of center, patient mix, number of beds, number of investigators and trainees, total research funding, utilization census by site and by each core, and census data showing population characteristics by geographic area in Los Angeles County (e.g., percentages by age, race/ethnicity, income, and educational attainment), and other data sources reporting health, demographic, and/or social characteristics by population subgroups, such as key indicators of health by Service Planning Areas (SPAs) reported by the Los Angeles County, Department of Health Services, the Los Angeles Children's Planning Council, and the California Health Interview Survey. E/T and HSR investigators have conducted studies to evaluate the influence of environmental, organizational, and population characteristics on policies, programs, processes, and outcomes.¹⁻⁶

6.1.2. Conduct implementation evaluation, provide ongoing progress reports, and suggest high priority improvement initiatives. The E/T team worked closely with the Leaders of all the CTSI Programs and the Office of the Institute to develop Implementation Plans to summarize program aims, activities, and the 5-year deliverables including milestones and measures. Monitoring implementation and preparing monthly progress reports will become a standard operating procedure. Specific activities will include:

- a. **Engage in ongoing implementation planning** with CTSI Program Leaders. Create detailed implementation plans and monthly, quarterly, and annual progress reports.
- b. **Refine and expand evaluation and tracking data sources** as needed.
- c. **Continuously monitor progress against plans** within the CTSI and provide reports to EOC and the CTSI Program Leaders.
- d. **Work with the EOC to prioritize operational planning**, track overall progress of CTSI, and identify strategic issues, opportunities, and concerns.
- e. **When implementation falls short**, work with CTSI leadership to formulate strategies to remediate the problem including intensified project management and/or improvement projects.
- f. **Report longitudinal data to monitor progress against plans and trends.**
- g. **Provide annual progress reports to NCRR and CTSI annual retreat.**

6.1.2.1. Implementation Reports. The implementation plans and milestones summarized in the final section of each program and in the **Implementation Phases and Milestones** narrative (elsewhere in this CTSA application), form the foundation for the Implementation Reports data source. The E/T **Program Monitoring Committee** will have the primary charge of ensuring the generation, quality, and monitoring of E/T data to make certain all programmatic milestones are met. The Program Monitoring Committee will be led by Drs. Bazargan and Koniak-Griffin and will include other E/T leaders presented on **Table 1**. Committee members will attend relevant program meetings and communicate at least monthly with the program leaders, and more often if necessary, to assess program progress against plan. The E/T Program Monitoring Committee will meet monthly to review the program implementation plans and milestones to confirm program activities are focused and achieving aims. Remedial action will be taken when necessary, for example, if a CTSI Program Leader is unable to meet performance and productivity milestones, the EOC will discuss options to accelerate activities to meet the specified time schedule, e.g., provide supplemental project management support, programmatic expertise, and/or other resources to resolve challenges and realign program activities to meet specified time lines. At the end of each project year, E/T will conduct a brief semi-structured interview with the Leader of the each CTSI Program to discuss progress against plans and to begin the next cycle of detailed program and implementation planning.

Some key elements of the assessment will include: (1) What changes if any, were made to the original design or implementation plan, and why were the changes made? (2) What challenges and opportunities to the development or implementation of the activity were encountered and how were these addressed, resolved, or optimized? (3) What individual, organizational, or other factors facilitated or impeded development or implementation? (4) What are the lessons learned and best practices for designing or implementing other activities? (5) For those activities fully implemented, have we identified the appropriate measures for E/T?

Table 1. Evaluation and Tracking Program Monitoring Committee

Program Monitoring Committee	Community	CCRR	Biostatistics	Regulatory	Pilot Studies	Technology	BIP	Education**	E/T	HSR
Deborah Koniak-Griffin, EdD, RN, FAAN	X					X		X	X	
Ronald Andersen, PhD	X		X						X	X
Mohsen Bazargan, PhD*	X	X	X					X	X	
Richard Casaburi, PhD, MD*		X		X					X	
Pamela Davidson, PhD					X			X	X	X
Moira Inkelas, PhD	X								X	X
Gerald Kominski, PhD						X			X	X
Jack Needleman, PhD				X			X		X	X
Mark Rapaport, MD**		X			X				X	X
Ali Sayed, PhD							X	X	X	
Martin Shapiro, MD, PhD	X								X	X

*Drs Bazargan, Casaburi, and Rapaport are E/T Associate Chairs who will lead the E/T at their respective CTSI partner institutions (CDU, Harbor LA-Biomed, and Cedars-Sinai); **Through the UCLA CTSI-ED Program Assessment and Outcomes Subcommittee.

6.1.2.2. Education Assessment and Outcomes Subcommittee to monitor and evaluate the interdisciplinary CTSI-ED Program. The RFA calls on grantees to include a detailed self-evaluation plan to assess implementation of the short- and long-term CTSA goals. The RFA includes a special focus on research education, training and career development. Detailed plans are provided in the **CTSI-ED** (available elsewhere in this application), starting with the organization of the **CTSI-ED** Assessment and Outcomes Subcommittee. The E/T plans describe the methods for evaluating **CTSI-ED** to determine success and a follow-up plan to track scholars after completion of the program. This will include information on program publications, grant proposals and awards, and the career trajectory of the scholars. To facilitate ongoing evaluation of training activities, a CTSI internet based program management and assessment system will be adapted by Dr. Sayed, from the UCLA School of Engineering, in collaboration with the **BIP**. Dr. Sayed will adapt his web-based system with a full set of program monitoring indicators including trainee characteristics, recruitment, participation and mentoring, program quality ratings, CTS research projects, and longitudinal career development (see **CTSI-ED**, available elsewhere in this application).

Once the CTSI-ED degree and career development programs are operational, we will implement annual continuous evaluation that is standardized across all of the programs to measure milestones in the following domains: (1) Ability to recruit and enroll participants as estimated by the number of applicants per cycle, the number admitted, and the % minority faculty and students in each program; (2) Continuous evaluation of our ability to construct transdisciplinary mentorship teams for each scholar and project; (3) Continuous evaluation of the courses taken by trainees coupled to a mapping of those courses on the identified core competencies so that we can see where we have gaps in the curriculum and address these in real time; (4) Continuous evaluation of the mentors who participate in the program; and (5) Rigorous tracking of participant productivity in terms of scientific presentations, peer-reviewed publications, grants obtained, and success with the promotion process. Most of this information will be in the annual progress reports that each program must provide to their funder. We will engage the BIP to help us pool this information for our own CTSI implementation and evaluation assessments. **Table 2** provides an overall summary of sample measures and data sources we will monitor and use to improve Programs.

Table 2. Sample Measures, Indicators and Data Sources

UCLA CTSI and Programs	Sample Measures and Indicators	Data Sources
Overview and Governance	<ul style="list-style-type: none"> Office of the Institute for translational research Levels of Institutional Support (space, faculty, staff) Partnerships w/ institutions, industry, and communities \$ in CTS research investment/public and private sources 	Implementation Reports Social Network Analysis CTSI Balanced Scorecard
Community Engagement and Research Program (CERP)	<ul style="list-style-type: none"> Number of lay health workers trained to work in underserved communities Needs assessment to identify the high priority research training needs in partnered research Number and type of community centers established Number of novel study designs for reproduction Number and type of new health education, health care navigation, and evidence-based policies Number of pilot/seed grants and larger awards to conduct community partnered research Number of reports and peer-reviewed publications 	Implementation Reports CTSI E-Grant E/T Database
Clinical and Community Research Resources (CCRR)	<ul style="list-style-type: none"> Number of investigators and publications Number of Protocols and \$ grants supported Number collaborative proposals Number underserved research participants Mobile units initiated and fully operational Number of multicenter projects CCRR modules utilization Harmonized CCRR utilization application and justification 	E/T Database CCRR Database CCRR Census Implementation Reports
Biostatistics, Study Design, and Clinical Data Management	<ul style="list-style-type: none"> CTSI design and statistical cores established -Publicize Network through CTSI Virtual Home Implement biostatistical services Number PhD students recruited to the CTSI Number CTSI investigators using statistical services Number hours/satisfaction with statistical consultation Number research projects w/ bio data analysis methods Number methodological papers in peer-reviewed journals Number methods/statistical studies in statistical journals 	Implementation Reports E/T Database Periodic Satisfaction Surveys E/T Database
Regulatory Knowledge and Support, Industry Relations, and Research Ethics Program	<ul style="list-style-type: none"> Number approved research applications-Completion time for cross-institutional IRB protocols Number discoveries, patents, and licenses Number startup companies formed Number Industry-sponsored agreements/clinical trials Office of Investigator Services (OIS) operational Volume and type of OIS services/resources utilized % investigators satisfied with OIS services/resources % investigators satisfied with BIP services/toolbox 	E-IRB Office of Industry Alliances (OIA) database Implementation Report E/T Database CTSI Periodic Survey
Pilot and Collaborative Translational Clinical Studies	<ul style="list-style-type: none"> Number/Type of new translational faculty recruited Think tank research agendas Annual grants programs funding reports Annual progress report on each funded project Number and \$ amount extramural grants funded Semi-annual CTSI mentor assessment 	Implementation Reports CTSI E-Grant CTSI-ED web
Center for Translational Technologies	<ul style="list-style-type: none"> Number and type of technology consults Number and type of CTT Service Core services Number and type of lab and technology cores requested Satisfaction with CTT Service Core \$ amount in cost recovery/sharing for resource/utilization Number, type, and \$ amount of grants/awards funded Number of pilot studies resulting in R01s and \$ amt Annual progress reports from grantees 	E/T Database CTSI Periodic Surveys E/T Database CTSI E-Grant

UCLA CTSI and Programs	Sample Measures and Indicators	Data Sources
Biomedical Informatics	<ul style="list-style-type: none"> Number of queries, number enrolled in SSO system Numbers and outcome of collaborations facilitated and grant applications submitted that used BIP resources Web statistics and survey reported Volume of use and satisfaction with tools Number of protocols available to potential subjects Number of users and usage levels for Curriculum Tree and social networking services Number of seminars and trainees Number of investigators and staff trained as Super-users Number of graduate students enrolled in new courses 	Web statistics Periodic user surveys Web statistics Implementation reports CTSI-ED web
Research Education, Training and Career Development (CTSI-ED)	<ul style="list-style-type: none"> Applicant pool and trainees recruited to CTSI programs Number of CTS mentors and trainees Number of K awards and other early career awards Program Quality (courses, mentoring, training) Effectiveness of CTS competency development Participation in translation research clusters and projects Productivity in interdisciplinary teaching, publications Satisfaction w/ mentor-mentee relations 	CTSI-ED web hosted on the CTSI on-line portal

6.1.3. Monitor implementation of 5 CTSI Initiatives to assess CTSI goal achievement. Beyond the overall monitoring activities of the CTSI Programs, we have selected 5 initiatives that reflect the directions of the CTSI overall goals. While we have chosen to highlight these 5 Initiatives, the reviewers should note many other new and novel, innovative, forward-looking, and transformative initiatives are proposed throughout the CTSI (see **Overview and Governance**, elsewhere in this application) and these will be highlighted in our annual reports. **Table 3** indicates CTSI key personnel responsible for leading and evaluating each of the CTSI Initiatives. Over the 5-year project period, the E/T leaders will monitor implementation and outcomes using both quantitative and qualitative data sources.

Table 3. CTSI Goals, Initiatives and Leaders

UCLA CTSI: Five Goals	Initiatives	Program	E/T Leaders
Goal 1: Create an academic home for clinical and translational science that integrates and builds on the many strengths of UCLA and its partners.	Office of Investigator Services (OIS)	Regulatory: Korenman, Toga,	Casaburi; Needleman
Goal 2: Build transdisciplinary research teams to accelerate and translate discovery to improve health.	Translational Research Clusters	Pilot and Collaborative: Rome	Davidson; Rapaport
Goal 3: Transform educational and career development programs to promote the next generation of clinician investigators and translational scientists.	CDU Integrated Life Sciences	Research Education: Mangione	Bazargan; Koniak-Griffin
Goal 4: Build and expand strong bi-directional academic-community partnerships to ensure that new scientific discovery is relevant to community needs.	Healthy Community Neighborhood Initiative – “70 Block Project”	Community Engagement: Brown	Andersen; Koniak-Griffin; Inkelas; Shapiro
Goal 5: Serve as a national resource for collaborative research through regional, statewide and national CTSA consortia.	National, Regional, and Local CTSA Consortia	UCLA CTSI PI: Dubinett	Shapiro; Davidson

6.1.3.1. The first CTSI initiative is associated with CTSI Goal 1: Create an academic home for clinical and translational science research that integrates and builds on the many strengths of UCLA and its partners. **CTSI Initiative 1** is the “**Office of Investigator Services**” that will be led by the **Regulatory Knowledge and Support, Industry Relations, and Research Ethics Program**. The Research Facilitators guide investigators to resources and expertise necessary to conduct clinical and translational research. This is a cross-cutting CTSI initiative that involves all of the key function leaders to improve investigators’ access to domain expertise and research resources. **Table 4** summarizes the implementation and E/T plan.

Table 4. CTSI Initiative 1, Implementation and Evaluation

Initiative 1	Yrs	Implementation / Milestones	Data Sources/Measures
Develop pre- and post-approval regulatory support services through deployment of an Office of Investigator Services (OIS) and creation of a UCLA system-wide "one-stop-shop" for approval of CTSI-supported science	1-3	Recruit/train and identify existing facilitators to provide comprehensive array of services, market services and provide investigator support	<ul style="list-style-type: none"> • Number Facilitators hired and trained • Number and type of services utilized; satisfaction • Number of proposals completed, submitted, funded • Log of obstacles identified and overcome
	1-5	Provide assistance with FDA approvals and compliance	
	1-5	Collaborate with BIP to design the CTSI Virtual Home	
	2-5	Develop operations and procedure manual	
	2-5	Evaluate and continuously improve services; Develop reporting system for obstacles	
	3-5	Enhance databases	

6.1.3.2. The second CTSI initiative is related to CTSI Goal 2: Build transdisciplinary research teams to accelerate and translate discovery to improve health. CTSI Initiative 2 is the Translational Research Cluster Grants Program funded through **Pilot Program** (see elsewhere in this application). These grants support transdisciplinary team-based research addressing major health problems in our Los Angeles communities. These investigators will generate ideas and interventions that will lead to improved health. **Table 5** summarizes the implementation and E/T plan.

Table 5. CTSI Initiative 2, Implementation and Evaluation

Initiative 2	Yrs	Implementation / Milestones	Data Sources/Measures
Transform research through our comprehensive <u>Translational Research Grants Program</u> to support the full range of translational team science.	0	Launch the first 6 research clusters to address the leading causes of morbidity and mortality in Los Angeles County	<ul style="list-style-type: none"> • Assess research agenda and responsiveness to community needs • Assess cost effectiveness of competing interventions • Annual grants programs funding reports • Annual progress report on each funded project • Number and \$ amount extramural grants funded
	1-5	Develop and vet research agenda and seek pilot funding through the CTSI pilot grants program	
	1-5	Ensure relevant stakeholder representation in the research clusters including community, industry, policy, comparative effectiveness research (CER)	
	1-5	Conduct evaluation and HSR to improve the Translational Research Clusters program and impact on improving population health	

6.1.3.3. The third CTSI initiative is related to CTSI Goal 3: Transform educational and career development programs to promote the next generation of clinician investigators and translational scientists. CTSI Initiative 3 is the UCLA/CDU Faculty Innovation Awards, a coordinated educational effort to create interdisciplinary translational researchers of the future that involves Charles Drew University (CDU). The CTSI is committed to enhancing its collaborative relationship with its partner CDU to assist in creating the requisite environment to enhance faculty recruitments, faculty scientific career development, and to create a culture of the highest level of scholarship. The County of Los Angeles has recently committed over \$350 million to re-open the Martin Luther King (MLK) Jr. Hospital with support from the University of California Regents. The need for collaborative academic support from UCLA and CDU will be critical to transforming the health of South Los Angeles. The UCLA/CDU Faculty Innovation Program will serve to increase the CTSI interdisciplinary translational research capacity at CDU in anticipation of the new MLK medical campus. **Table 6** summarizes the implementation and E/T plan. The program will be monitored through our CTSI-ED Assessment and Outcomes Subcommittee and led by Dr. Bazargan (CDU).

Table 6. CTSI Initiative 3, Implementation and Evaluation

Initiative 3	Yrs	Implementation / Milestones	Data Sources/Measures
Leverage CTSI resources and services to advance Charles Drew University (CDU) translational research to improve health in underserved communities	1-2	Identify mentors from existing UCLA faculty for a joint appointment at CDU	Implementation Reports <ul style="list-style-type: none"> • CDU faculty recruitment and selection CTSI E-Grants <ul style="list-style-type: none"> • Number pilot grants • Number of K awards and other early career awards CTSI-ED web <ul style="list-style-type: none"> • Number of mentors and trainees • Satisfaction w/ mentor-mentee relations
	1-4	Establish an inter-institutional compensation agreement between UCLA and CDU	
	2-4	Recruit new CDU faculty who will be focused on translational sciences	
	1-5	Expand CDU translational research training and apply for CTSI pilot studies	
	3-4	Develop and monitor mentoring relations	
	4-5	Sustain scholars dedicated to translational research to improve health in underserved communities	

6.1.3.4. The fourth CTSI initiative is related to CTSI Goal 4: Build and expand strong bi-directional academic-community partnerships to ensure that new scientific discovery is relevant to community needs. CTSI Initiative 4 is the “70 Block Project” led by the CERP collaborating with our HSR investigators (see CERP, elsewhere in this application). **Table 7** summarizes the implementation and evaluation plan.

Table 7. CTSI Initiative 4, Implementation and Evaluation

Initiative 4	Yrs	Implementation / Milestones	Data Sources/Measures
Healthy Community Neighborhood Initiative (HCNI) Partner with the Los Angeles Urban League’s (LAUL) “70 Block Project” in a pilot project to reduce racial/ethnic health inequities via patient-centered and community feasible strategies	1-5	Expert consultation by CERP on needs assessment	<u>Implementation Reports</u> <ul style="list-style-type: none"> • Summary Survey Report • LA County Health DHS statistics on 70 block area • Number of health education sessions • Percent adherence to nationally endorsed clinical guidelines • Time Comparisons of Utilization of Health Services • Percent increase in healthy behaviors related to physical activity, diet, smoking
	1-2	Household health assessment survey as part of HCNI	
	3-5	Coordinate UCLA-wide community engagement activities (e.g., Health education, Lay health workers, <i>Promotora</i> services, Mobile nurse units)	
	1-5	Follow residents in 70-blocks with chronic conditions	
	3-5	Develop and distribute health education materials	
	2-3	Adapt set of existing patient-centered decision aids	

CERP: Community Engagement and Research Program; Members of the CTSI, LAUL and residents will jointly develop E/T methods.

6.1.3.5. The fifth CTSI initiative is related to CTSI Goal 5: Serve as a national resource for clinical and translational science research through regional, statewide and national CTSA collaborations. We are transcending institutional barriers and collaborating in education, training and clinical trial recruitment through our membership in the Los Angeles and West Coast CTSA consortia. We are committed to sharing our innovations and resources as members of the national CTSA. In the pre-award period E/T is monitoring several UCLA CTSI consortia activities, such as: ■ **Greater Los Angeles CTSA Coalition** (areas of proposed collaboration include training, core competencies in translational science, community outreach and engagement); ■ **University of California CTSA-sponsored Biomedical Research committee** (convening a UC-Wide Biomedical Research Acceleration Initiative Retreat to plan for a UC health campus wide collaboration to accelerate clinical and translational research); ■ **Biospecimen Repository** (collaboration with investigators from multiple CTSA and the NCI intramural program with oversight by D. Aberle of 23 centers and 19,000 patients). We will report results of our CTSA consortia collaborations in our annual reports to the NCRR.

6.2. Specific Aim 2: Implement an Improvement Sciences Program with the intent of increasing efficiency, stimulating innovation, and improving operational effectiveness in the CTSI and its community research centers.

Improving processes and engineering systems to optimize productivity will require leadership commitment, staff training, support of process improvement work, and integration of these methods throughout the organization. Therefore, the CTSI leadership is committed to: (1) provide training in process redesign and quality improvement; (2) train administrators, researchers, and staffs of CTSI institutions and programs; (3) develop process maps for critical CTSI operational processes; (4) identify high-priority projects; and (5) work with each of the CTSI programs to ensure quality improvement is integral to operations.

To integrate and improve research and teaching programs in the four partner institutions via process improvement, we will adhere to the key analytic and design concepts of this field, including adopting a systems view and process orientation (identifying processes occurring within units and as work is handed off or shifted from one process center to the next with the goal of eliminating unneeded steps, increasing the efficiency of each step, and reducing errors or delays in handoffs), approaching analysis of operations and operational failure from the perspective of multiple causation, focusing on identifying solutions that achieve the three “rights” (right actions in the right place at the right time) and assure process optimization, making effective and routine use of analytic tools, such as CQI, Lean tools, and statistical analysis, and implementing systematic testing of alternatives. The Executive Oversight Committee will establish improvement priorities, assure vision alignment, and support steady commitment to improving programs and processes. We have designed an implementation plan to increase training and experience in the use of quality improvement and operations management methods. Our phased implementation will include the following activities:

- **Strengthen top management commitment:** Our entire CTSI leadership team participated in the first one-day training program in March 2007, to prepare them to champion improvement.
- **Identify a short and mid-term improvement agenda:** We will work with the CTSI programs to ensure projects are well conceived and consistent with the broader priorities of the CTSI.
- **Benchmark current processes:** While constructing metrics and mapping processes for key CTSI functions, we will encourage each partner to access these resources.
- **Build training and project resources:** Researchers and staff will learn process improvement techniques through the following resources:
 - **Training:** Trainers available from the senior staff will be augmented by project staff from other divisions. This trainer cadre will train researchers, teams, and trainees.
 - **Incentives:** Staff will be encouraged to participate via incentive programs and recognition events designed to increase energy and share innovations.
 - **Self-paced instruction materials:** Materials will be made available to complement formal training on-line along with toolkits to download.
 - **Data:** Improvement teams will establish metrics and monitor process enhancements as well as respond to requests for data repositories.
 - **Process maps:** We will provide support in process mapping and develop maps across sectors of the CTSI and interfacing organizational components.
 - **Resource support:** We will provide leadership, ongoing training, project facilitation, and funding for training, participant incentives, and project support.

We have identified four initial improvement projects consistent with priorities to: (a) achieve visible success early, (b) involve institutional and community partners, (c) strengthen our leaders and investigators, and (d) improve the research and training processes (see **Table 8**). Improvement projects will be proposed by CTSI key function leaders and competitively reviewed by the Executive Oversight Committee. Institutional funds will support the improvement projects and their E/T. Each Improvement team of 5 to 7 engaged staff will be sponsored by involved senior leaders, receive initial training, be assigned a project leader, and have outcomes monitored by E/T. Improvement Projects 1-2 propose to increase efficiency in the UCLA CTSI CCRR and CERP. Project 3 is centered on the CTSI web-portal developed by the **Biomedical informatics Program (BIP)**. Improvement Project 4 propose to improve overall operational effectiveness. Data obtained

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through special projects implemented through the Improvement Sciences Program will be used to formulate strategies to reduce delays, inefficiencies, and rework pervasive in the research enterprise and to stimulate innovation and improve operational effectiveness. The Improvement Sciences Program will be led by Drs. Casaburi, Inkelas, and Needleman.

6.2.1.1. Improvement Project 1: Improve Collection, Transport, and Analysis of Biological Samples. The vision of the UCLA-CTSI CCR is to create a geographically dispersed but highly coordinated, seamless, user-friendly, and community accessible infrastructure for clinical and translational research to serve and reach the diverse populations of LA County. Current protocols for collection, processing, transport, analysis, and reporting of results from biological samples vary among institutions and clinical sites. This variation is inefficient and not supportive of accurate research. Challenges need to be overcome to improve quality, including: (1) improve cooperation among research staff; (2) implement a highly reliable transport system; and (3) establish a secure and anonymous, cross-institution laboratory data log through the CTSI web portal. **Goal:** Improve services to collect, process, transport, analyze, and use biological sampling to fulfill our mission of inclusion of research participants spanning all ages throughout the CTSI and community research centers (described elsewhere in this application). The Improvement Sciences leaders will work with operational staff to design and implement clear, consistent, economical, and state of the art processing that will be written into protocols and implemented throughout the CTSI.

6.2.1.2. Improvement Project 2: Establish Mobile Nurse Units to Reach into the Community. Currently researchers from the CTSI partner institutions individually hire and deploy nurses and research support staff to support community-based studies. These personnel are recruited, trained, and supported for short-term work related to each project, are used inefficiently, and rarely travel into the community. **Goal:** Establish an infrastructure within **CERP** and **CCRR Programs** with 4 new full-time well-trained nurses, with properly equipped vans and drivers. These nurses will be trained in clinical research by **CCRR** and in community engagement methods by community research partners. They will have knowledge and skill in community-based research methods and delivery of culturally competent care in addition to the clinical expertise required for specific studies. They will establish effective and collaborative working relationships with research participants in the community to facilitate successful projects. They will attend community forums and group discussions organized by the **CERP** to provide feedback from the community partners and the community research participants to the **CCRR**.

6.2.1.3. Improvement Project 3: Assess the new CTSI Virtual Home (web portal) by user feedback. Investigators cannot effectively identify resources, including investigators working in complementary areas, and relevant data that span all the CTSI sites and community research centers. Meeting the managerial and regulatory requirements of all the sites is difficult and wasteful. User needs vary. **Goal:** Initial and ongoing feedback from users, will enable us to develop and refine internet resources to guide researchers in identifying and obtaining information on relevant regulatory and institutional requirements specific to the research they are designing, menu of technology and lab resources, nursing and bionutrition infrastructure support, biostatistics and study design, a searchable database of current researchers and institutional resources (Cores), list of investigators, research projects, community based participatory research projects, and mentors (see **section 6.1.1.3.**). The BIP and E/T will effectively work with IT personnel to create and refine the CTSI Virtual Home.

6.2.1.4. Improvement Project 4: Improve research enterprise operational effectiveness. Investigators and their direct reports are not familiar with a process oriented view, importance of capacity planning and effective scale of management, putting the service profit chain to work, managing variability, estimating customer service times, the product process matrix, high volume business in the service industry, and competing on service excellence. **Goal:** Following didactic education, 6 teams of 8 individuals will address specific improvement projects, preferably of high visibility, high priority or of critical importance to CTSI operations, resources, customer satisfaction, cost management or some other area of strategic value.

Table 8. CTSI Improvement Projects, Implementation and Resources

Improvement Projects	Sponsors ¹	Implementation / Outcomes	Key Resources Allocated
IP1. Collect, transport, & analyze specimens	<ul style="list-style-type: none"> Nurse manager Lab director IT project manager Operations director 	<ul style="list-style-type: none"> Control limits for time from sample collection to results Metrics for error measures Transport time 	Richard Casaburi, MD, PhD, CCRR operations expert
IP2. Mobile nurse units	<ul style="list-style-type: none"> Academic Researcher Physician clinician Research Nurse Community researcher Educator 	<ul style="list-style-type: none"> Nurse community involvement Number of related positions Assessment of Community work among CTSI institutions 	Moira Inkelas, PhD, process improvement expert with substantial community experience <ul style="list-style-type: none"> Access to human resources and training development 3 RNs, vans and drivers funded by the DGSOM Dean's office
IP3. Assess CTSI Web Portal	<ul style="list-style-type: none"> Bio-informatics Office of Investigator Services (OIS) Researchers Regulatory leader 	<ul style="list-style-type: none"> User need survey System usage Feedback system Workflow diagrams 	Jack Needleman, PhD, Quality Improvement and Information Technology expert
IP4. Improve operational effectiveness	<ul style="list-style-type: none"> CTSI leaders and their direct reports 	<ul style="list-style-type: none"> Team agendas Operations improvement 	Kumar Rajaram, PhD, MBA, leading expert in Operations Engineering

6.2.1.6. Improvement Sciences Projects Data Source. Data will be used to: (1) identify issues and processes that may require improvement, and (2) diagnose problems and assess whether improvement has been made. The data to carry out these functions may be part of the existing E/T data sources or may require developing new information. For example, a critical issue for investigators is the time required to recruit human subjects. Existing data sources provide information for comparing actual recruitment time to projected time, but additional information would be required to make the process more efficient. An improvement project would require additional information, such as a process map with each task identified. Appropriate improvement experts would identify the time required for each task, and the reengineering of the process to eliminate tasks, decrease the time to complete specific tasks, and/or increase recruitment rates. All improvement projects will be jointly developed by the E/T and CTSI programs and E/T will be responsible for identifying appropriate measures, as well as developing a data collection and analysis plan.

6.3. Specific Aim 3: Create the UCLA CTSI Center for Evaluation and Health Services Research (HSR) to accelerate the speed and efficiency of translational research for improving organizational effectiveness and population health. The Center for Evaluation and HSR will reside in the CTSI Office of the Institute and will conduct and be responsible for all evaluation and tracking and HSR operations and supervision and development of analytic personnel. The Center for Evaluation and HSR will be responsible for 3 major operational functions to support CTSI leadership: (a) planning, development, and continuous monitoring of key function areas implementation and outcomes (Aim 1), (b) primary and secondary data collection, analysis, and reporting for evaluation and HSR (Aims 1-4), and (c) providing the infrastructure for the development of HSR throughout the CTSI and our community research centers (see **CERP Specific Aim 4**, elsewhere in this application).

The principal architects of this novel initiative will be Drs. Shapiro and Andersen, who will lead the HSR Core, and Drs. Davidson and Rapaport, who will lead the Evaluation Core. The Center will involve E/T and HSR investigators across the CTSI and UCLA and Charles Drew University (CDU) campuses.

6.3.1. Partner with UCLA and CDU professional schools and research centers to provide access to relevant evaluation and HSR resources and expertise across the CTSI. A wealth of evaluation resources and HSR expertise is available to E/T. A sampling is listed here.

Multidisciplinary Methods Core of Research Center in Minority Institutions (CDU). Addresses health disparities experienced by racial/ethnic minorities and the socio-economically disadvantaged.

Health Economic and Evaluation Research (HEER) Program (Center for Health Policy Research). Examines economic and financial impacts of national, state and local-level health care interventions to increase understanding of the costs of health care interventions and to improve programs/policies.

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Vulnerable Population Research (School of Nursing). Conducts biostatistical and community-based research, methods, measurement and analysis strategies.

National Center for Research on Standards (Graduate School of Education) Advances in evaluation design, multi-method evaluations of program quality, technology, evaluation practice, special populations

Center for Health Policy Research (School of Public Health) Program evaluation course designed to teach community based research to community partners.

Electrical Engineering Department (Engineering and Applied Science) Web interface to monitor learning outcomes with all the features of a typical course management system; prototype for CTSI-ED program

Statistical Consulting Group (Academic Tech Services) Assistance in applied statistics, data analysis, statistical computing, and research methodology

California Center for Population Research (LS, SOM, Public Affairs) Basic/applied research and training in demography: economics, policy, community health sciences, epidemiology, medicine.

Human Complex Systems (Computational Social Science) Relevant methodological expertise includes systems analysis, phenomenological research, modeling.

Center for Healthier Children, Families, and Communities (Mattel Children's Hospital, Dept. of Pediatrics, SPH). Conducts evaluation of communities attempting to improve availability and quality of early child development services and systems.

Biostatistics, Analytical Support, Evaluation (Jonsson Cancer Center). Biostatistical resource in basic science and clinical research design, data analysis and modeling.

Fieldwork Qualitative Data Res Laboratory (Psychiatry and Bio-behavioral Science) Laboratory offers training and consultation in fieldwork and qualitative data in medical, mental health, and social science.

Institute for Social Science Research (UCLA) Strength in conducting large-scale, interdisciplinary, quantitative research.

Network Research Lab (Computer Science) Network communication, measures, protocols, modeling/analysis.

6.3.2. Engage and train CTSI academic and community investigators to incorporate evaluation and HSR design and methods into initiatives, programs, and projects. Initially, we will focus our efforts on engaging CTSI program leaders to design the E/T System and other data sources to generate information for monitoring progress and ongoing improvement efforts. Additionally, our HSR team will collaborate with the Community Program leaders and investigators to collect and analyze HSR data for translational research initiatives involving community-partnered research (see **CERP**, elsewhere in this application). When the E/T data sources are operational and refined, we will reach out to CTSI investigators and community research centers to provide expertise on evaluation design and HSR methods. We will convene a 1-day conference to promote evaluation and HSR resources available on the UCLA campus and invite our partner institutions and community research centers to identify the high priority E/T and HSR needs. Following the conference, we will conduct a web-based survey to collect systematic data on evaluation and HSR resource needs. This information will be used to develop a tailored CTSI training program on evaluation design and HSR methods that will be offered through the Center.

6.3.3. Seek extramural funding to conduct evaluation and HSR studies to accelerate the translation process and to advance the science of evaluation. Figure 3 shows the **Clinical Translational Science: HSR and Evaluation Continuum** adapted from Rubenstein and Pugh (2006)²⁸, Khoury et al. (2007)²⁹, and Kleinman and Mold (2009).³⁰ The first transition (T1) is from basic biomedical research to human research. The second transition (T2) is from human to evaluation/intervention research. The emphasis here is on the degree to which human research is translated into practice and community based studies of both personal and public health services. The third transition (T3) is the diffusion of evaluation/intervention research to routine application in health systems and medical practice and the translation of the results into public policy. Within the CTSI programs we will investigate evaluation approaches for accelerating translational science, such as mechanisms for: (1) increasing translation of basic research into human research; (2) involving community clinicians and other partners in translational research, and (3) improving bidirectional feedback from human

Principal Investigator/Program Director (Last, First, Middle): Dubinett, Steven, MD and evaluation/intervention research to basic research. We will collaborate with CTSA investigators to seek extramural funding through the Center for Evaluation and HSR to investigate translational science occurring at all three transitions (T₁, T₂, and T₃) and to evaluate strategies designed to accelerate the speed and efficiency of translation (see **Figure 3**).

6.4. Aim 4: Collaborate with local, regional, and the CTSA National Consortia and participate in the National Process and Outcome Evaluations. The NCRP has implemented a phased approach to evaluate the National CTSA Consortium and CTSA network across the US. The phased approach includes the feasibility study conducted by the Madrillon Group and a Process Evaluation conducted by Westat, to be followed by an Outcome Evaluation. We will collect and provide all requested information to Westat and subsequent national evaluation teams. When our CTSA is funded, we will participate on the National CTSA Evaluation Key Function Committee and its six interest groups (shared resources, social network analysis, definitions, and IRB issues, bibliometrics, and the liaison group). Additionally, we have recently communicated with the University of California San Francisco (UCSF), and propose to expand our national CTSA collaboration by participating in the proposed CTSA crosscutting initiative, “**Research Metrics and Dashboarding**,” a national initiative to promote transparency and accountability to improve clinical and translational research and research administration in CTSA networks across the nation.

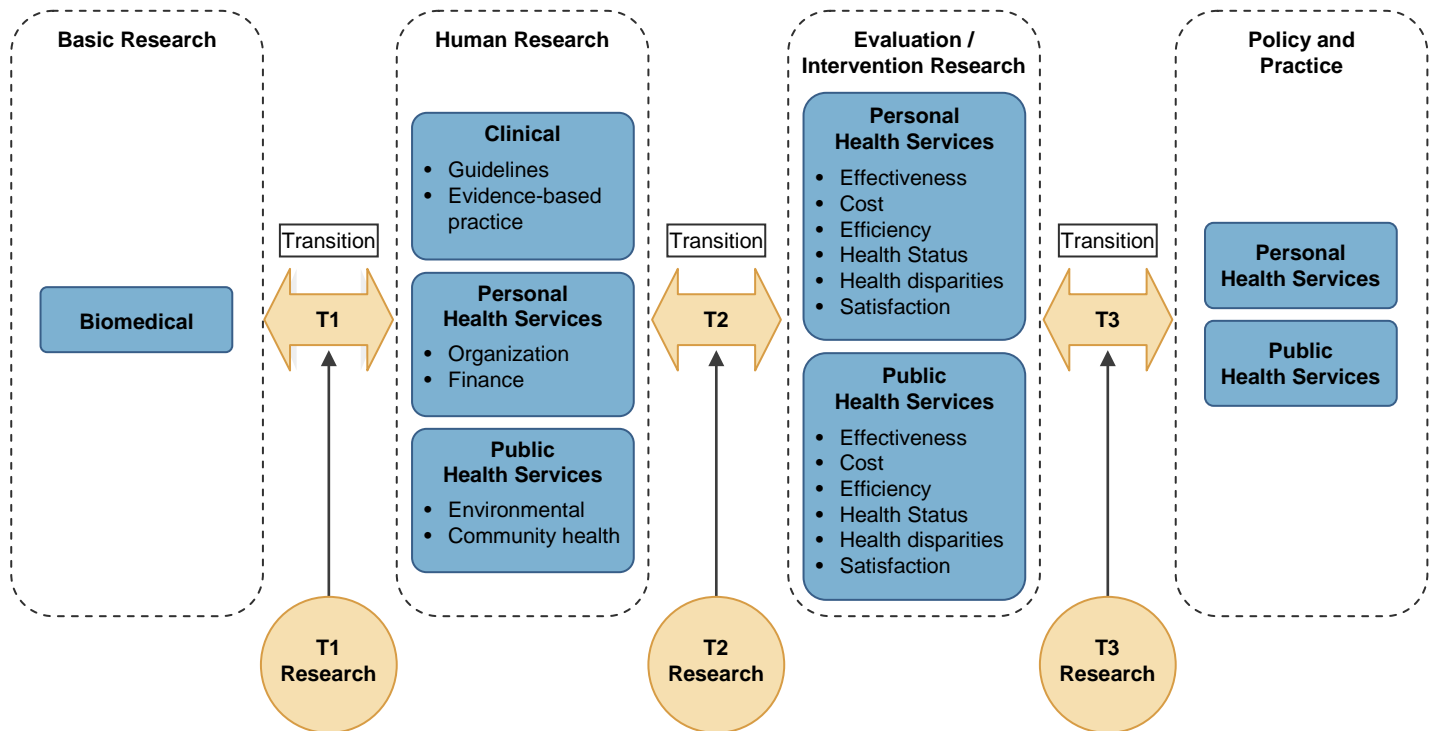


Figure 3: Clinical Translational Science HSR and Evaluation Continuum

6.4.1.1. Institutional Review Board Approval. In the earliest phases, the primary purposes of E/T will be to generate valid information that can be used to guide management decision-making, and to improve the conduct of translational research and the performance of research support, education and training programs. However, NIH and the NCRP expect this project to “develop or contribute to generalized knowledge” about the conduct of research activities so the lessons learned by the CTSA awardees can be widely disseminated within the field. As such, there is a research component to the CTSA Initiative, and we will seek IRB approval to allow data generated by E/T to be used in a research context, and work with the IRB to identify mechanisms consistent with three distinctive elements of CTSA as a focal point of research. First, most of the data that will be obtained and available to E/T for management use will be collected in the ordinary course of institutional activities. These include non-human subjects’ data such as number of grants or number of trainees, performance indicators such as those reported on the dashboard, and data such as course evaluations, which are anonymous. In general, a project using only these data would be exempt and the data collection would proceed even without a research goal. Second, this is a minimal risk study, that is, the risks are no greater than

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those encountered in the ordinary course of normal life. This should allow for expedited review, and openness by the IRB to considering variations in the form by which consent is documented. Third, only select elements of the project should require informed consent.

7. E/T INVESTIGATORS: LEADERSHIP AND RESPONSIBILITIES

The E/T Team will be composed of a leader and co-leaders from all four institutional partners and the UCLA schools of medicine, nursing, public health, engineering, and management. E/T will be led by Dr. Pamela Davidson with Dr. Deborah Koniak-Griffin serving as Co-Leader and will provide weekly reports to the CTSI Executive Oversight Committee (EOC), to ensure Institute operations are effective and efficient. **Figure 1** (above) shows the E/T organizational chart will include the Program Monitoring Committee (**Aim 1**), the Improvement Sciences Program (**Aim 2**), and the Center for Evaluation and Health Services Research (**Aim 3-4**). The leadership is listed below with the Program areas they track for the Program Monitoring Committee.

Pamela Davidson, PhD (Leader) is the director of the UCLA Health System Patient Safety Institute and Associate Professor in the UCLA Schools of Nursing and Public Health. She oversees all E/T activities and represents E/T to the National CTSA Consortium. (**Pilot Program, CTSI-ED, E/T, HSR**)

Mohsen Bazargan, PhD, (Co-Leader, Aim 1) is an Associate Professor of Medicine, Charles Drew University (CDU), School of Medicine. (**CERP, CCRR, BSD-CDM, CTSI-ED, E/T**)

Richard Casaburi, PhD, MD (Co-Leader, Aim2) is Professor of Medicine and Director of the Rehabilitation Clinical Trials Center at Harbor-LA BioMed and a seasoned clinical and translation investigator. (**CCRR, Regulatory, E/T**)

Deborah Koniak-Griffin, EdD, RNC, FAAN (Co-Leader, Aim1) is Professor, UCLA School of Nursing and Chair. (**CERP, CTT, CTSI-ED, E/T**)

Mark Rapaport, MD (Co-Leader, Aim 3) is Chair of the Department of Psychiatry and Behavioral Neurosciences at Cedars-Sinai and Professor and Vice-Chair of Psychiatry at the David Geffen School of Medicine. (**CCRR, Pilot Program, E/T, HSR**)

Ronald Andersen, PhD, (Co-Leader, Aim3) is an internationally recognized leader in medical sociology and health services research and a pioneer in modeling use of health services. He leads the Center for Evaluation and HSR. (**CERP, BSD-CDM, E/T, HSR**)

Gerald Kominski, PhD, (Investigator, Aim 3) is a Professor of Health Services in the SPH and Associate Director of the UCLA Center for Health Policy Research. (**CTT, E/T, HSR**)

Jack Needleman, PhD, (Co-Leader, Aim 2) is Professor in the UCLA School of Public Health and directs the Department of Health Services PhD and MS programs. (**Regulatory, BIP, E/T, HSR**)

Kumar Rajaram, PhD, MBA, (Investigator, Aim 2) is a Professor of Operations and Technology Management at the UCLA Anderson School of Management

Ali Sayed, PhD (Investigator, Aim1) is Professor of Electrical Engineering and Director of the Adaptive Systems Laboratory in the School of Engineering and Applied Science at UCLA. (**BIP, CTSI-ED, E/T**)

Moira Inkelas, PhD (Co-Leader, Aim 2), is an Associate Professor of Health Services, SPH (**CERP, E/T, HSR**)

Martin Shapiro, MD, PhD, (Leader, Aim 3) is a Professor of Medicine and Health Services and Chief of the Division of General Internal Medicine at UCLA. (**CERP, E/T, HSR**)

8. IMPLEMENTATION PLAN

Table 9 presents the implementation plan summarizing Evaluation and Tracking specific aims, timelines, implementation activities, and milestones.

Table 9. Implementation Plan

Year(s)	Implementation Activities	Milestones
Prepare for transition to CTSI		
Pre-Award Planning & Operations	<ul style="list-style-type: none"> • Conduct CTSI IT Investigators Survey • Develop Implementation Plans • Join CTSA Evaluation Key Functions 	<ul style="list-style-type: none"> • CTSI E/T Office operational
Specific Aim 1: Longitudinally track and evaluate Initiative and program outcomes		
1-2 1-5	<ol style="list-style-type: none"> 1. Develop the E/T System 2. Conduct implementation evaluation 3. Monitor 5 CTSI Initiatives 4. Convene monthly meetings of the E/T Program Monitoring and Education Assessment/Outcomes Subcommittee 	<ul style="list-style-type: none"> • E/T System functional (Y1) • Monthly progress reports (Y1) • CTSI-ED web functional (Y2)
Specific Aim 2: Implement an Improvement Sciences Program with the intent of increasing efficiency, stimulating innovation, and improving operational effectiveness		
1-2 2-3 1-2 3-5	<ol style="list-style-type: none"> 1. Improve Collection, Transport, and Analysis of Biological Samples 2. Mobile Nurse Units to Community 3. Assess new CTSI Virtual Home by establishing user feedback 4. Improve research enterprise operational effectiveness through leadership development 	<ul style="list-style-type: none"> • Improved PCIR lab services (Y2) • Mobile nurses trained (Y3) • IT standards shared at CCRR sites (Y3) • Operational effectiveness education (Y3)
Specific Aim 3: Create the UCLA CTSI Center for Evaluation and HSR		
1-5 3-5	<ol style="list-style-type: none"> 1. Plan, develop, and prepare continuous monitoring reports 2. Collect and analyze primary and secondary data for Evaluation and HSR 3. Providing the infrastructure for the development HSR throughout the CTSI (See CERP, Aim 4) 4. Partner with UCLA/CDU professional schools and research centers 5. Engage and train CTSI institute and community investigators 6. Seek extramural funding 	<ul style="list-style-type: none"> • Center functional (Y1) • Conference/ web survey (Y3) • At least 1 proposal/year
Specific Aim 4: Collaborate with local, regional, and the CTSA National Consortia and participate in the National Process and Outcome Evaluations		
1-5	<ol style="list-style-type: none"> 1. Conduct CTSI evaluation self-study 2. Participate in national evaluations 3. Participant in the CTSI crosscutting initiative, "Research Metrics and Dashboarding" 	<ul style="list-style-type: none"> • Annual progress reports to NIH

CTSI-ED web-based program management and assessment system is described in [Education, Training, and Career Development Program](#), elsewhere in this application; CERP: Community Engagement and Research Program.

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Implementation Phases & Milestones



Abbreviations:

BIP – Biomedical Informatics Program; C&G – Contracts and Grants; BSD-CDM – Biostatistics, Study Design and Clinical Data Management Program; CDU – Charles Drew University; CCRR – Clinical and Community Research Resources Program; CERP – Engagement & Research Program; CTS – Clinical Translational Science; CTSI-ED – Research Education, Training and Career Development Program; CTT – Center for Translational Technologies; DGSOM – David Geffen School of Medicine; EOC – Executive Oversight Committee; E/T – Evaluation and Tracking; HSR – Health Services Research; IAB – Internal Advisory Board; IRB – Institutional Review Board; OIA – Office of Industry Alliances; OIS – Office of Investigator Services; PARO – Post-Approval Research Oversight; Pilot Program – Pilot and Collaborative Translational and Clinical Studies Program; Regulatory Program: – Regulatory Knowledge and Support, Industry Relations and Research Ethics Program; RSA – Research Subject Advocate.

1. OVERVIEW

Implementation Phases & Milestones presents the critical path for implementing the UCLA CTSI and its integration into our inter-organizational strategic plan including the integration of CTSA resources with other complementary resources available to our institutions and community research centers. In collaboration with our CTSI and Program Leaders we propose a time line of milestones for the CTSI goals and aims with alternatives should those milestones not be reached. In prior review, Implementation Phases & Milestones was reviewed with "Significance, Approach, Innovation, Environment, and Implementation Plans" and received a score of "1". Reviewers described our plans for implementation as outstanding, well developed, well described, and reasonable, yet exceptionally ambitious, and found the tracking elements across the components comprehensive and practical. No weaknesses were identified in the section. We are nonetheless adding exciting new improvements to this application. For this resubmission, we have updated the implementation phases and milestones to reflect improvements proposed in the CTSI. ***Owing to the extent of the changes made throughout the Implementation Phases and Milestones section, we do not highlight specific changes in the text.***

2. IMPLEMENTATION PLANNING

We consider the implementation plan in two phases: first, the pre-award planning and operations, and second, launching the UCLA CTSI.

2.1. Implementation Approach. The development of the proposal was originally initiated by our former UCLA Vice Chancellor for Medical Sciences and Dean of the DGSOM, Gerald Levey. Following Dr. Levey's retirement in 2009, Dr. Gene Washington was recruited to UCLA as the new Vice Chancellor for Medical Sciences and Dean of the DGSOM. Viewing the National CTSA initiative as a mission critical achievement, Vice Chancellor Washington immediately launched the application revision and recruited Dr. Steven M. Dubinett the CTSI Director and Associate Vice Chancellor for Translational Science.

Dr. Dubinett has been a faculty member at UCLA for 22 years and has led major translational research programs in lung cancer including those funded by the NCI SPORE program, the Early Detection Research Network and the Department of Defense. He has extensive experience in academic administration, translational investigation, research mentorship and peer review. Along with the leadership of Drs. Washington and Dubinett, in 2010, UCLA appointed Dr. James S. Economou as Vice Chancellor for Research. This set in motion a leadership team with extensive experience in translational investigation and academic research administration to guide the clinical and translational research enterprise and mission at UCLA. Dr. James Economou is the Beaumont Professor of Surgery and Chief of the Division of Surgical Oncology. He has joint appointments in the departments of Microbiology, Immunology, and Molecular Genetics and Molecular and Medical Pharmacology. Dr. Economou's extensive experience in translational investigation includes research in genetic therapy of cancer. As Vice Chancellor for Research, Dr. Economou continues to maintain an active program in translational cancer therapy in the Jonsson Comprehensive Cancer Center. Dr. Economou has been a faculty member at UCLA for more than 20 years. For more than a decade he has collaborated closely with Dr. Dubinett in developing a variety of clinical and translational infrastructures such as the cellular GMP suite; T32 and K12 programs in Gene Medicine; the Gene Medicine seed grant program and joint, transdisciplinary training for high school and undergraduate students. Their close, collaborative working relationship has now continued in their new roles.

These three leaders implemented a plan that continued the integration of GCRC infrastructure and operations. The integration of the GCRCs has enabled UCLA and its partner institutions to forge a uniquely transformative, novel and integrative clinical research entity. The PCIR without walls is now referred to as the **Clinical and Community Research Resources (CCRR)** consistent with its capacity to leave the inpatient-based infrastructure and move to affiliated community research centers as needed for individual research projects. The CTSI leadership has continued to meet as a unified Executive Oversight Committee (EOC). The leadership structure has been defined such that all of the program areas and Associate Directors participate as voting members of the EOC. This Executive Oversight Committee has launched several important initiatives under the direction of the Director, Dr. Steven Dubinett.

The new UCLA CTSI governance structure includes all of the CTSI partner institutions: Cedars-Sinai, Charles Drew University and Harbor-LA Biomed, in addition to the UCLA-Westwood campus. All four

partner institutions are represented on the Executive Oversight Committee (EOC). This ensures the administrative and academic research services are highly coordinated and responsive to both the investigators and community needs. In designing the governance structure, the leadership has benefitted from consultation with more than 20 CTSA sites across the country. We have also been guided by the CTSA Consortium Governance Manual. Utilizing this governance structure, including an active weekly meeting of the EOC, the leadership of the UCLA CTSI has accomplished the following: 1) distribution and assignment of budgetary benefits and responsibilities; 2) wide-spread agreement and support of key leadership positions, their responsibilities and scope of authority; 3) structure and partners to be included in the overall UCLA CTSI; 4) selection of initiatives to begin funding and supporting; 5) procedures and priorities for harmonizing CTSI-wide processes and organizational structure; 6) establishing a pilot CTSI scholars program; 7) the announcement of a new Translational Research Cluster Team grant mechanism initiated with institutional support via Catalyst funding; 8) Town Hall research meetings at the partner institutions with the CTSI leadership; 9) videoconferencing for trainees and group meetings; 10) initiation of a CTSI-wide Translational Research retreat; 11) surveys of investigators to assess high priority needs; 12) establishment of a new Virtual Home with regular group meetings with BIP working groups and the EOC for updates; and 13) initiated a new transdisciplinary Committee on Maternal, Child and Adolescent Health (CMCAH) to guide new integrated research strategies, provide advice to the EOC, and develop new transdisciplinary training opportunities.

2.2. Phase 1: Pre-Award Planning & Operations. Recently with the appointment of the new leadership of Vice Chancellors Washington and Economou, the appointment of Dr. Dubinett has served to create a leadership team with career focus in clinical and translational investigation. The implementation of a fully operational CTSI at UCLA is the highest priority on the agenda for both the School of Medicine and the UCLA Campus at large. This team, in consultation with Chancellor Gene D. Block, PhD, has continued to meet on a regular basis and oversee operations of the Executive Oversight Committee. Drs. Economou and Washington will lead our Internal Advisory Board (IAB).

The pre-award planning and operations has included the development of Translational Research Clusters in: HIV, addiction; mental health and cognition; diabetes and obesity; cardiovascular disease and stroke; as well as cancer. These are transdisciplinary research groups that have formed to address major health problems in Los Angeles County. The culmination of their initial planning was demonstrated in a CTSA-wide retreat in September 2010, at which the groups presented their translational research agendas. Based on interactions and discussions at the retreat and a survey that followed, planning is now underway for an additional retreat and further development of the Translational Research Cluster program. In addition, the Vice Chancellor for Research, Dr. Economou, has been instrumental in working with Dr. Dubinett to identify funds to continue organizing the UCLA CTSI Office of the Institute. Drs. Economou and Dubinett continue to meet weekly to discuss the emerging needs of this office to plan for its full implementation. The accomplishments in this pre-award operations period have moved the group significantly toward transformation in team-based translational investigation in the area of discovery, training and administration. The UCLA CTSI will continue the activities initiated under the direction of the program director, Dr. Dubinett and the Executive Oversight Committee. Our program leaders, investigators, and administrators have enthusiastically embraced Dr. Dubinett's leadership and vision for accelerating the translation of innovation and discovery to address the leading causes of morbidity and mortality in our Los Angeles community.

2.3. Phase 2: Launching of the UCLA CTSI. At the time that NCRR funding for the CTSA is received, the leaders of the CTSI will continue the infrastructure set in place with regularly scheduled meetings, seminars, videoconferencing sessions, and clinical translational research and community engagement. The implementation phase will transition smoothly to launching the UCLA CTSI because activities will be continued throughout this year in anticipation of launching full activities in year one. The CTSI has reached out to other CTSA nationally, has held conference calls with the West Coast CTSA Consortium, and has formed a unique link with The Greater Los Angeles CTSA Coalition. Collaboration among these consortia will continue and expand when the CTSI is funded.

Table 1. Community Engagement and Research (CERP)

CTSI Milestones	Pre-Award	Year 1	Year 2	Year 3	Year 4	Year 5
Pre-Award Period and Transition to CTSI						
<ul style="list-style-type: none"> Stimulate networking and collaborations through research symposia and follow-up working groups 	X	X	X	X	X	X
Aim 1: Promote and sustain bi-directional knowledge sharing between community and academia						
<ul style="list-style-type: none"> Prepare a community workforce for receiving and sharing knowledge with underserved communities 		X	X	X	X	X
<ul style="list-style-type: none"> Build academic and community researcher skills in partnered research, regulatory compliance, ethics and organizational and practice change 		X	X	X	X	X
<ul style="list-style-type: none"> Exploit innovative networking and information dissemination technologies 			X	X		
Aim 2: Strengthen community infrastructure for sustainable partnered research						
<ul style="list-style-type: none"> Establish centers in communities that support community engagement and research 		X	X	X	X	X
<ul style="list-style-type: none"> Promote novel study designs 			X	X	X	X
<ul style="list-style-type: none"> Strengthen incentives and motivation for research participation of community healthcare providers 			X	X	X	X
Aim 3: Drive innovation in community engagement that accelerates the volume and impact of partnered research						
<ul style="list-style-type: none"> Foster strategic demonstration projects that enhance CERP's community reputation and capabilities 		X	X	X	X	X
<ul style="list-style-type: none"> Implement comprehensive community-partnered research initiatives, such as the "70 Block Project" 		X	X	X	X	X
Aim 4: Build health services research (HSR) methods into partnerships to accelerate evidence-based practice						
<ul style="list-style-type: none"> Form HSR teams and conduct 2-4 methods studies annually, e.g., compliance, CER, implementation, diffusion 		X	X	X	X	X
<ul style="list-style-type: none"> Collect and analyze HSR data for translational research initiatives of community-partnered research 		X	X	X	X	X
<ul style="list-style-type: none"> Expand HSR to analyze high priority delivery system, population, programmatic, cost concerns to inform policy 				X	X	X
Aim 5: Establish a governance and operations structure that strengthens existing partnerships and builds new bridges						
<ul style="list-style-type: none"> Formalize CERP governance including leadership, working groups and conflict resolution procedures 	X	X	X	X	X	X
<ul style="list-style-type: none"> Create a Community Research Liaison Office 	X	X	X	X	X	X

3. MILESTONES

The **Overview and Governance** (see elsewhere in this application) describes the UCLA-CTSI Initiatives and programs that were built around the Institute's 5 key goals. **Evaluation and Tracking (E/T)** worked with each of the program leaders to develop implementation plans that summarize the specific aims, time lines, measurable objectives, and milestones in each program (available elsewhere in this application). CTSI program plans are ambitious and proposed accomplishments substantial. The CTSI Initiatives and program plans demonstrate the level of integration already being achieved. The combined set of 9 implementation plans found in the final section of each program and the milestones tables presented in this Implementation Phases and Milestones document will be used as the foundation for ongoing implementation monitoring and reporting. The milestones tables will be used as a guide to focus our efforts on the critical path and the implementation strategies that will enable us to achieve each milestone. Additionally, we have proposed an **E/T** plan with multiple data sources, both quantitative and qualitative, that will provide the foundation for data-driven executive and management decision making across the CTSI.

3.1. Community Engagement and Research (CERP). CERP is the primary link to our diverse Los Angeles community. It strengthens and builds strong bi-directional partnerships that help CTSI scientists identify research relevant to community needs. CERP builds community capacity to engage in research; communicates research findings; and facilitates opportunities for health services and comparative effectiveness research. CERP has been active, engaging our community partners and academic faculty. A number of projects have been undertaken, notably the 70-Block Project, led by the Charles Drew University

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(CDU). Community representatives have been active in the CTSI's key committees, ensuring the voice and input of the community at all levels of decision-making in the CTSI (**Table 1**).

3.2. Clinical and Community Research Resources (CCRR). CCRR, formerly the PCIR, supports and supervises human studies and clinical trials. Its transforming, flexible, mobile research units bring scientific teams to our population. Our new mobility and community emphasis has led to the change in our name for this program. This Program has fostered the development of harmonization protocols in CTS processes and procedures between the partner institutions, identified improvement projects, and tracking across sites. We have initiated new collaborations with Engineering and the UCLA Wireless Health Institute to use the internet and mobile phones to bring transformational change to clinical research. One of our junior faculty in Pediatrics has recently been funded to work with collaborators in the School of Engineering in research facilitated by **CCRR (Table 2)**.

Table 2. Clinical and Community Research Resources (CCRR)

CTSI Milestones	Pre-Award	Year 1	Year 2	Year 3	Year 4	Year 5
Preparing for transition to CTSI						
<ul style="list-style-type: none"> Construction of a new ambulatory CCRR facility and "home" to the CTSA at UCLA (to open in January 2011) Launch of the statewide California Telehealth Network to create a digital highway for healthcare and research Initiation of monthly conference calls with the other UC CTSIs to plan CTSI West Coast Consortium joint research Successful development of the CTSI Virtual Home Creation of CTSI-wide forms and agreement from Harmonization Initiative Regular meetings of the nursing and bionutrition staff with the CERP to coordinate CCRR services Establish strong relationships between participating centers, their respective communities and providers 	X	X				
	X					
	X					
	X					
	X					
	X					
	X					
Aim 1: Broaden the range of clinical, translational and community research by implementing the CCRR without walls						
<ul style="list-style-type: none"> Cross-training research staff so that they can support research in the inpatient, outpatient and community environments Initiating Mobile "Chaperone" Services to link the CTSI partners and communities Assess and modernize CCRR staffing to provide an appropriate workforce mix to meet research needs Initiate a Promotora program to enhance recruitment and communication with participants Continue standardizing nursing and bio-nutrition operating procedures across all sites 		X	X	X	X	X
			X	X		
		X	X	X	X	X
		X				
		X	X	X	X	X
Aim 2: Promote clinical collaborations across the CTSI by facilitating the performance of research at all CTSI institutions						
<ul style="list-style-type: none"> Increase interaction among investigators through the CTSI virtual home and Office of Investigator Services (OIS) Share common protocols, SOPs, and teaching materials Centralize labs that follow Good Laboratory Practice standards Ease research approval barriers at partner institutions Maximize access of Promotora Program in LA County 		X	X	X	X	X
		X	X			
		X	X	X		
		X	X	X		
				X	X	X
Aim 3: To recruit young professionals into careers in translational clinical research						
<ul style="list-style-type: none"> Expand training and career development activities to encourage health care professionals to consider careers in clinical research Provide hands-on exposure to clinical research Lead CTSI efforts in training research staff to ensure research is performed by certified staff 		X	X	X		
		X	X			
		X	X	X	X	X

3.3. Biostatistics, Study Design, and Clinical Data Management (BSD-CDM). The Biostatistics Program leverages our existing strengths and resources to provide one-stop biostatistical design and data management services to CTSI research teams. It fosters development of novel clinical trial designs and biostatistical methodologies; operates a secure, user-friendly CDM system; and offers expanded translational science courses in clinical trials methodology and new methods in biostatistics and modeling. We have significantly expanded the number of statisticians in this program. Training and per-project instruction in study design and methodologies available to all CTSI investigators includes clinical, genomic,

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and community epidemiology, and adaptive clinical trials and methodologies to deal with the challenges of genomic and proteomic data. A novel, biostatistical grand rounds will be held four times a year in which a biostatistical consulting problem will be presented and discussed in an open forum (**Table 3**).

Table 3. Biostatistics, Study Design and Clinical Data Management (BSD-CDM)

CTSI Milestones	Pre-Award	Year 1	Year 2	Year 3	Year 4	Year 5
Aim 1. Provide coordinated biostatistics consulting and services						
• Investigator Access to the CTSI Biostatistics Program		X				
• Publicize Network through Virtual Home; Implement biostatistical services and biomedical studies		X	X			
• Review protocols of the <u>CTSI CCRR</u>		X	X	X	X	X
• Train study staff and new investigators in CDM systems		X	X	X	X	X
Aim 2. Develop novel statistical applications and methodologies						
• Conduct statistics/design research in clinical trials		X	X	X	X	X
• Develop methods in high-throughput Bio data analysisA		X	X	X	X	X
• Support weighted gene co-expression network analysis		X	X	X	X	X
• Conduct studies in community methodologies		X	X	X	X	X
Aim 3. Provide Biostat education and training						
• Continue biostatistical training		X	X	X	X	X
• Expand Master of Science in Clinical Research (MSCR)		X	X	X	X	X
• Bio-statistical collaboration in Dissertation Committees		X	X	X	X	X

CCRR: Community and Clinical Research Resources

3.4. Regulatory Knowledge and Support, Industry Relations, and Research Ethics. The Regulatory program ensures that our research is in full regulatory compliance and meets the highest quality assurance standards. Through its Office of Investigator Services, it functions as a gateway to CTSI investigator resources and provides a one-stop shop for submission to CTSI-specific IRBs. It actively seeks and encourages industry alliances and offers ethics counseling and research. In collaboration with the new leadership at UCLA we have continued to expand the Regulatory Program. This program has undertaken a Harmonization Initiative with the aim of originating and effectuating process harmonization among the CTSI partners in IRB functions and specific aspects of Contracts and Grants (C&G). The leader of this program, Dr. Korenman will attend the CTSA-sponsored national meeting on ethics in the fall of 2010. Dr. Dubinett has joined in conference calls with the University of California (UC) CTSA sites that have formed a group to examine IRB harmonization and contracting across the UC CTSA sites (**Table 4**).

Table 4. Regulatory Knowledge and Support, Industry Relations, and Research Ethics

CTSI Milestones	Pre-Award	Year 1	Year 2	Year 3	Year 4	Year 5
Aim 1. Harmonize regulatory mechanisms throughout the UCLA CTSI to promote easy access to translational research						
<ul style="list-style-type: none"> Complete multi-institutional MOU and Convene IRB Harmonization Committee among 4 partner institutions Join CTSA National Consortium Regulatory KFC Each institute appoints a CTSI C&G officer Convene ongoing C&G Harmonizing Committee Continue harmonizing oversight and monitoring between IRB and PARO Implement AAHRPP approval at the remaining partner site Achieve full IRB reciprocity within CTSI and UC Consortium Develop educational initiatives for community partners 	X	X X X	X X	X X X	X X	X X
Aim 2. Develop pre- and post-approval regulatory support services through						
<ul style="list-style-type: none"> deployment of an Office of Investigator Services (OIS) Continue periodic multi-institutional Post Approval Research Oversight (PARO) meetings Inventory similar and disparate research oversight processes and their rationales throughout CTSI Align processes across institutions to reduce or eliminate differences in workflow, requirements, and processes Harmonize and integrate the PARO processes OIS operational and core staff recruited and hired 		X X	X X	X X X	X X X	X X X
Aim 3: Create a new Office of Industry Alliances (OIA)						
<ul style="list-style-type: none"> Convene meetings of OIA; Develop collaborations Facilitate industry interactions by providing 1-stop shopping Assist faculty inventors/partners with technology transfer Push innovation by matching needs with tech innovations Develop verifiable system for judging COI matters Develop/conduct entrepreneur education program 		X X X X X	X X X X	X X X X	X X X X	X X X X
Aim 4. Develop a Research Ethics Consortium (REC) and Continuing						
<ul style="list-style-type: none"> Education (CE) System Identify and assemble REC; consultation service Begin development of research projects; consultations Develop a Continuing Education (CE) System to inventory, map, and expand educational resources/curriculum Use the CITI system to certify clinical investigators Develop database on completion and achievements in CE Set up system to simulcast; Integrate CE systems 		X X X	X X X	X X X	X X X	X X X

3.5. Pilot and Collaborative Translational and Clinical Studies. Our **Pilot Program** is the research engine of the UCLA CTSI. It delivers two key functions: First, it supports Pilot and Collaborative Translational and Clinical Studies among basic, clinical, community and population-based scientists. Second, it supports the development of the Novel Clinical and Translational Methodologies needed to sustain an environment of intellectual exploration. We offer the only campus-wide translational team science grants available at UCLA. A novel transforming funding mechanism—the Translational Research Cluster (TRC) Grant Program—leverages local funds to support transdisciplinary research addressing the most pressing health needs in Los Angeles County (**Table 5**).

3.6. Center for Translational Technologies. **CTT** links scientific teams with core technologies. We have developed and tested a pilot voucher system and we are initiating a survey for investigator input. An innovative on-line searchable database and the Office of Investigator Services (OIS) will provide a one-stop technology consulting service linking CTSI investigators with the cores or collaborators most relevant to their research project. **CTT** Technology Officers will vigilantly assess the need for laboratory and technology cores and emerging trends and novel developments to accelerate clinical translational science (**Table 6**).

Table 5. Pilot and Collaborative Translational and Clinical Studies Program

CTSI Milestones	Pre-Award	Year 1	Year 2	Year 3	Year 4	Year 5
Aim 1. Advance transformative collaborative translational research through broad-ranging funding mechanisms						
<ul style="list-style-type: none"> Establish CTSI Grants Review Committee Develop web-based E-Grant application system Create rigorous review and reporting processes Develop and implement new Grants Programs Develop new funding streams 		X	X	X	X	X
Aim 2. Develop novel clinical and translational technologies and methodologies						
<ul style="list-style-type: none"> Establish and conduct Novel Translational Technologies and Methodologies Grants awards program 		X	X	X	X	X
Aim 3. Create the Society of the CTSI						
<ul style="list-style-type: none"> Establish CTSI Society bylaws and procedures Form a network of senior CTSI faculty advisors Establish formal mentoring relationships Conduct annual CTSI scientific meeting Initiate and activate think-tank program Evaluate advisor-mentor pairings/satisfaction 		X	X	X	X	X
Aim 4. Use multidimensional strategy to recruit at least 30 new CTSI translational research faculty over the next five years						
<ul style="list-style-type: none"> Recruit approximately 6 new faculty members per year based on strategic plan to build translational science 		X	X	X	X	X

Table 6. Center for Translational Technologies

CTSI Milestones	Pre-Award	Year 1	Year 2	Year 3	Year 4	Year 5
Aim 1. Implement a system for providing centralized access to and ongoing performance monitoring of Translational Technology Resources (TTRs)						
<ul style="list-style-type: none"> Create searchable on-line database to connect translational researchers with core services Provide streamlined core access to CTSI clients through a voucher system Conduct ongoing needs/trends assessments of TTRs Develop SOP for cost recovery and cost sharing Organize non-CTSI supported TTRs using Technology Affinity Groups 		X	X	X	X	X
Aim 2. Create an efficient mechanism for developing promising new technologies into functional TTRs						
<ul style="list-style-type: none"> Promote trans-disciplinary interaction that will catalyze development of new technologies Create a structured process to evaluate, prioritize and test viability of emerging technologies 		X	X	X	X	X
Aim 3. Conduct personalized counseling and continuing education programs to facilitate collaboration and assist translational investigators in selection and optimal use of TTRs						
<ul style="list-style-type: none"> Hire and train Technology Officers to advise individual Investigators and facilitate networking and core utilization With the Pilot Studies Program, provide seed funding on a competitive basis to foster TTR collaborations TAGs develop training module for young investigators Create didactic series (seminars, workshops, and interdisciplinary lectures) to foster innovation 		X	X	X	X	X

3.7. Biomedical Informatics Program (BIP). Informatics is key to the NIH Roadmap and through informatics the CTSA program will achieve advances in the understanding of disease and its translation to improvements in health. **BIP** leverages our expertise and resources in data management to provide databases, tools, resources and infrastructure for the acquisition, storage and analysis of data. It provides the online infrastructure and support for the Virtual Home. We have made significant progress in re-designing our Virtual Home. The UCLA CTSI Biomedical Informatics Program (**BIP**) seeks to integrate informatics throughout the lifecycle of translational research to ensure CTSI investigators appropriately apply novel tools capable of transforming their studies and the training of the next generation of translational scientists (**Table 7**).

Table 7. Biomedical Informatics Program

CTSI Milestones	Pre-Award	Year 1	Year 2	Year 3	Year 4	Year 5
Preparing for transition to CTSI						
<ul style="list-style-type: none"> • Planning meetings of BIP key investigators to design implementation methods. • Preliminary design of Virtual Home and RDR • Survey biomedical informatics needs of all CTSI personnel 	X					
	X					
	X					
Aim 1: Virtual Home						
<ul style="list-style-type: none"> • CTSI Web Portal implemented with Virtual Home modules • Registry of CTSI Researchers and Research Partners • Implement SSO • Initial list of biomedical informatics mentors and projects • RAP and Project Registry, Center for Translational Technologies Resources Directory, and Protocol Templates • Make available clinical trials protocols and contact information to potential research subjects through public systems 		X				
Aim 2: Research Data Repository						
<ul style="list-style-type: none"> • Prototype for RDR, including RDR services, CTS • Initial Registry of Research Databases for Westwood campus • Registry of Research Databases expanded to all partner sites • Full implementation of RDR, including CTS, Record Locator Service, and Clinical Research Applications, Clinical Trials Management System, and biospecimen repository (e.g., caBIG) 		X				
		X	X			
			X	X	X	X
				X	X	X
Aim 3: Education and Training						
<ul style="list-style-type: none"> • Informatics training seminars outside degree programs • Workshops on CTSI infrastructure tools • Develop new biomedical informatics course on domain ontologies, controlled vocabularies, data models, data curation, and clinical/biological data/text mining that draws in part on data repository experience 		X	X	X	X	X
			X	X	X	X

3.8. Research Education, Training, and Career Development. CTSI-ED houses all our research and training activities. It builds on collaborations with other CTSI programs to identify training and education needs and opportunities (Table 8). It ensures CTSI trainees acquire the core competencies needed to conduct transdisciplinary research, and to integrate community priorities and input into research. CTSI-ED leaders were able to successfully renew our inter-institutional K30 program and recently received a K30 supplement to develop curriculum to teach state-of-the-science methods of comparative effectiveness research (CER).

Table 8. Research Education, Training and Career Development (CTSI-ED)

CTSI Milestones	Pre-Award	Year 1	Year 2	Year 3	Year 4	Year 5
Preparing for transition to CTSI						
<ul style="list-style-type: none"> Clinical Research Education and Specialized Training (CREST) Committee formed Seminar series launched 4 Scholars funded in the CTSI Pilot Scholars Program K30 successfully renewed 	X					
Aim 1. Establish novel infrastructure (CTSI-ED office) to optimize cross-disciplinary training and integrate community input into training via team-based research						
<ul style="list-style-type: none"> CTSI-ED office and virtual home operational CTS Competency Model selected for CTSI-ED web Complete curriculum mapping to CTS competency model Mentor/mentee database created Semi-annual trainee and mentor assessments Initiation and expansion of community mentor pool 		X	X			
		X	X			
		X	X	X	X	X
		X	X	X	X	X
Aim 2. Transform translational education through new curricular elements and create new programs (K12, K30, T32, and others) incorporating community engagement and interdisciplinary methodologies and technologies						
<ul style="list-style-type: none"> CTSI-ED web operational to track programs, trainees, mentors, CTS research projects, and career development New K12 fully operational New T32 fully operational New PhD Track in Molecular Med New Exec MS & EMPH training in Community Research 			X	X	X	X
			X	X	X	X
			X			X
				X	X	
Aim 3. Provide mechanisms to integrate patient-oriented research training through a course menu, expansion of didactic programs (the CTSI-ED Curriculum Tree), and an integrated assessment program providing a sophisticated, computer-based learning-management system						
<ul style="list-style-type: none"> Expand the Curriculum provided by the K30 Program Create the CTSI Curriculum Tree and didactic courses for training clinical and translational researchers CREST Assessment and Outcomes Subcommittee Develop CTSI-ED web Assess and improve programs and career development 		X	X	X	X	X
		X	X	X	X	X
		X	X	X	X	X
		X	X	X	X	X

3.9. Evaluation and Tracking (E/T). E/T conducts self-evaluation activities for the UCLA CTSI and participates in the evaluation of the national CTSA program. E/T evaluates the scientific and administrative operations and provides reports to the CTSI leadership on program functioning, implementation and accomplishments to guide improvements. Our duties include close monitoring of the quality, productivity and equitable distribution of resources across CTSI institutional and community partners. Our Center for Evaluation and Health Services Research conducts studies to accelerate the speed and efficiency of the translation process and to advance the science of evaluation. With Catalyst funding we organized a meeting to discuss team based research in CER for conducting cost analysis to invest in efficient medical interventions with the greatest potential impact on improving patient/population health.

3.10. Addressing failing to meet milestones. Evaluation and Tracking (E/T) will longitudinally track CTSI progress, integration, and operations. E/T Program Monitoring Committee will be in continuous communication with Program Leaders regarding progress against plan. When Program Leaders fail to meet milestones and timelines the CTSI Director and the Executive Oversight Committee will be notified and options will be developed with the Program Leaders to accelerate activities to meet the specified time schedule. These may include providing supplemental administrative and/or project management support, programmatic expertise, and/or other resources to resolve challenges and realign program activities to meet specified time lines. If inadequate progress is made at the time of the annual report, the CTSI Director and other relevant leadership will meet with the Program Leader and Co-Leaders to address barriers to progress and to create solutions to accelerate progress. The CTSI executive leadership reserves the option of replacing Program Leaders who are unable to effectively lead the program with a Co-Leader who has demonstrated leadership competencies.

Table 9. Evaluation and Tracking

CTSI Milestones	Pre-Award	Year 1	Year 2	Year 3	Year 4	Year 5
Preparing for transition to CTSI						
• CTSI E/T Office operational	X					
Aim 1: Longitudinally E/T initiative and program outcomes						
• Develop the E/T System		X	X			
• Conduct implementation evaluation		X	X	X	X	X
• Monitor 5 CTSI Initiatives		X	X	X	X	X
• Convene monthly meetings of the E/T Program Monitoring and Education Assessment/Outcomes Subcommittee		X	X	X	X	X
Aim 2: Implement an Improvement Sciences Program						
• Improve Collection, Transport, Analysis of Biological Samples		X	X			
• Mobile Nurse Units to Community			X	X		
• Assess new CTSI Virtual Home with user feedback		X	X			
• Improve research enterprise operational effectiveness through leadership development				X	X	X
Aim 3: Create the UCLA CTSI Center for Education and HSR						
• Plan, develop, and prepare continuous monitoring reports		X	X	X	X	X
• Collect and analyze data for Education and HSR				X	X	X
• Provide the infrastructure for the development of HSR throughout the CTSI (See CERP, Aim 4).				X	X	X
• Partner with UCLA/CDU schools/research centers				X	X	X
• Engage and train institute and community investigators				X	X	X
• Seek extramural funding				X	X	X
Aim 4: Collaborate with local, regional, and the CTSA National Consortia and participate in the National Evaluations						
• Conduct CTSI evaluation self-study		X	X	X	X	X
• Participate in national evaluations		X	X	X	X	X
• Participate in the CTSI crosscutting initiative, "Research Metrics and Dashboarding"		X	X	X	X	X