National Cancer Institute

Office of Cancer Complementary and Alternative Medicine

ANNUAL REPORT ON Complementary and Alternative Medicine

FISCAL YEAR 2009

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

The research the National Cancer Institute (NCI) supports, both in our own laboratories and at institutions worldwide, is focused on the ultimate goal of helping cancer patients. That mission – achieved through rigorous science – extends to NCI's program on complementary and alternative medicine, also known as CAM.

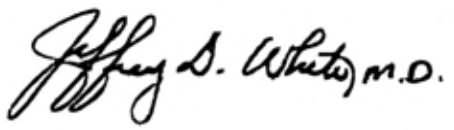
It is with great pleasure and pride that we once again provide NCI's research partners, physicians, the advocacy community, policymakers and cancer patients with this fifth annual review of NCI's extensive accomplishments in advancing evidence-based CAM interventions and therapies.

Fiscal year (FY) 2009, marked the 10th anniversary of the establishment of NCI's Office of Cancer Complementary and Alternative Medicine (OCCAM). Since its creation, OCCAM has held the job of coordinating and fostering the Institute's CAM research portfolio and partnerships with extramural researchers as well as within NCI's intramural programs.

Over the past ten years, NCI's portfolio of CAM research grew from about $20 million to around $120 million. This growth has been due to the hard work of hundreds of cancer researchers around the world as well as many individuals throughout the NCI, including OCCAM's efforts in developing new funding opportunities, enhancing CAM technical assistance to grant applicants, and creating collaborative partnerships. There also has been substantial growth in the number of clinical trials relevant to CAM therapies, including landmark studies which for the first time provided solid evidence that improvements in lifestyle and dietary interventions are feasible and can impact the recurrence of certain cancers.

NCI's commitment to CAM research and clinical practice has been steadily supported, coordinated, and expanded by OCCAM over the years. That mission is continuing with the identification of new research priorities for NCI's CAM office. OCCAM's new priorities will expand NCI's ability to extend the search for effective therapies into areas outside the mainstream of conventional biomedical research.

I hope you find this report helpful and informative. I also hope that it will generate an enhanced dialogue – especially between patients and health care professionals – about the appropriate uses of CAM interventions in conjunction with conventional medicine. Cancer patients deserve credible, unbiased information about any intervention or treatment regimen that they are considering. It is our duty to conduct and support the science that makes wise and informed decisions possible.



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Office of Cancer Complementary and Alternative Medicine
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The following acronyms are used throughout this report:

NCI	National Cancer Institute
CAM	complementary and alternative medicine
OCCAM	Office of Cancer Complementary and Alternative Medicine
FY	fiscal year
NIH	National Institutes of Health
DCB	Division of Cancer Biology
DCCPS	Division of Cancer Control and Population Sciences
DCP	Division of Cancer Prevention
DCTD	Division of Cancer Treatment and Diagnosis
CCR	Center for Cancer Research
DCEG	Division of Cancer Epidemiology and Genetics
ARRA	American Recovery and Reinvestment Act
DOC	Divisions, Offices and Centers
TCM	Traditional Chinese Medicine
MOU	Memorandum of Understanding
NPB	Natural Products Branch
DTP	Developmental Therapeutics Program
CSC	cancer stem cells
RDSP	Research Development and Support Program
PA	program announcement
CCOP	Community Clinical Oncology Program
CARRA	Consumer Advocates in Research and Related Activities
COP	Communications and Outreach Program
PAP	Practice Assessment Program
BCS	Best Case Series
CIS	Cancer Information Service
PDQ	Physician Data Query
SQF	Sheng Qi Formula
ND	Naturopathic Doctor
FOA	funding opportunity announcement
CDC	Centers for Disease Control and Prevention
PMID	PubMed Identifier

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FIGURE 1. MAJOR CATEGORIES OF CAM THERAPIES

ALTERNATIVE MEDICAL SYSTEMS

DEFINITION: Alternative medical systems are built upon complete systems of theory and practice. Often, these systems have evolved apart from and earlier than the conventional medical approach used in the United States.

EXAMPLES: Acupuncture, Ayurveda, Homeopathy, Naturopathy, Traditional Chinese Medicine, Tibetan Medicine

ENERGY THERAPIES

DEFINITION: Energy therapies involve the use of energy fields. There are two types:

- **Biofield therapies** are intended to affect energy fields that purportedly surround and penetrate the human body. The existence of such fields has not yet been scientifically proven.

EXAMPLES: Qi gong, Reiki, Therapeutic touch

- **Electromagnetic-based therapies** involve the unconventional use of electromagnetic fields, such as pulsed fields, magnetic fields, or alternating current or direct current fields.

EXAMPLES: Pulsed electromagnetic fields, Magnet therapy

EXERCISE THERAPIES

DEFINITION: Exercise therapies include health-enhancing systems of exercise and movement.

EXAMPLES: T'ai chi, Yoga asanas

MANIPULATIVE AND BODY-BASED METHODS

DEFINITION: Manipulative and body-based methods in CAM are based on manipulation and/or movement of one or more parts of the body.

EXAMPLES: Chiropractic, Therapeutic massage, Osteopathy, Reflexology

MIND-BODY INTERVENTIONS

DEFINITION: Mind-body medicine uses a variety of techniques designed to enhance the mind's capacity to affect bodily function and symptom.

EXAMPLES: Meditation, Hypnosis, Art therapy, Biofeedback, Imagery, Relaxation therapy, Support groups, Music therapy, Cognitive-behavioral therapy, Aromatherapy

NUTRITIONAL THERAPEUTICS

DEFINITION: Nutritional therapeutics are an assortment of nutrients and non-nutrients, bioactive food components used as chemo-preventive agents, and specific foods or diets used as cancer prevention or treatment strategies.

EXAMPLES: Macrobiotic diet, Vegetarianism, Gerson therapy, Kelley/Gonzalez regimen, Vitamins, Soy phytoestrogens, Antioxidants, Selenium, Coenzyme Q10

PHARMACOLOGICAL AND BIOLOGIC TREATMENTS

DEFINITION: Pharmacological and biologic treatments include the off-label use of prescription drugs, hormones, complex natural products, vaccines, and other biological interventions not yet accepted in mainstream medicine.

EXAMPLES: Antineoplastions, 714X, Low dose naltrexone, Immunoaugmentative therapy, Laetrile, Hydrazine sulfate, Melatonin

COMPLEX NATURAL PRODUCTS

DEFINITION: Complex natural products are an assortment of plant samples (botanicals), extracts of crude natural substances, and un-fractionated extracts from marine organisms used for healing and treatment of disease.

EXAMPLES: Herbs and herbal extracts, Mistletoe, Mixtures of tea polyphenols, Shark cartilage

SPIRITUAL THERAPIES

DEFINITION: Spiritual therapies are therapies that focus on deep, often religious beliefs and feelings, including a person's sense of peace, purpose, connection to others, and beliefs about the meaning of life.

EXAMPLES: Intercessory prayer, Spiritual healing

Each year, Congress requests a report of the National Cancer Institute's (NCI) annual expenditures in complementary and alternative medicine (CAM)* research. To give more meaning to the numbers provided to Congress, a more detailed account of the Institute's investment in CAM has been produced for the last four years. The reports, (including last year's *NCI's Annual Report on Complementary and Alternative Medicine: Fiscal Year 2008*), are intended as a way for NCI to communicate its progress in this area of medical research, not only to Congress but also to other interested stakeholders including cancer researchers, CAM practitioners, health care providers, advocacy organizations, cancer patients, and the general public.

The NCI's Office of Cancer Complementary and Alternative Medicine (OCCAM) is proud to present the latest such report, *NCI's Annual Report on Complementary and Alternative Medicine: Fiscal Year 2009*. Similar to the previous reports, this publication provides an overview of the NCI-supported work in this field along with details on certain selected projects in the areas of cancer CAM relating to communication, training and conferences, and research.

This report highlights projects, grants, and cooperative agreements supported by each of the Institute's extramural grant funding divisions – Division of Cancer Biology (DCB), Division of Cancer Control and Population Sciences (DCCPS), Division of Cancer Prevention (DCP), and the Division of Cancer Treatment and Diagnosis (DCTD), along with projects from NCI's intramural laboratories – Center for Cancer Research (CCR) and the Division of Cancer Epidemiology and Genetics (DCEG). These projects represent a variety of CAM categories, cancer types, research types, and grant mechanisms. This report includes summaries of selected training grant awards, as well as a breakdown of NCI's CAM research portfolio. In fiscal year (FY) 2009, NCI's research expenditures for CAM were an estimated $114,441,501 for the funding of 429 CAM research projects. In addition, during FY 2009, NCI used $21,637,877 in funds from the American Recovery and Reinvestment Act (ARRA) to award 104 CAM research grants.

As this report on cancer CAM indicates, we at the NCI are committed to an integrated approach to marshalling all of the many resources and approaches necessary to make cancer a condition that is – at worst – a manageable, chronic illness similar to heart disease and diabetes. We believe that evidence-based CAM techniques, systems, and products can have an important role in helping us reach that worthwhile goal.

* CAM is often defined as any medical system, practice, or product that is not thought of as "western medicine" or standard medical care. Complementary medicine means it is used along with standard medicine, also called conventional medicine. Alternative medicine is used in place of standard treatments. CAM treatments may include dietary supplements, megadose vitamins, herbal preparations, acupuncture, massage therapy, magnet therapy, spiritual healing, and meditation (See Figure 1, on page 4 for the major categories of CAM therapies).

Office of Cancer Complementary and Alternative Medicine

NCI's Office of Cancer Complementary and Alternative Medicine (OCCAM) is a coordinating office responsible for: identifying gaps in the science and creating corresponding funding opportunities for cancer CAM research; partnering with NCI program staff and other governmental and nongovernmental organizations to increase the testing of CAM approaches for cancer prevention, diagnosis, treatment, symptom management, and rehabilitation; developing communication products for various audiences concerning the investigation and use of these approaches; and helping to build bridges between CAM practitioners and the cancer research community.

OCCAM is part of the NCI Division of Cancer Treatment and Diagnosis (DCTD). The division's mission is to improve the lives of the American public by discovering better ways to diagnose, assess, treat, and cure cancer through stimulating, coordinating, and funding a national program of cancer research. OCCAM's programs and activities complement DCTD's mission and are enhanced by the other major programs and branches within DCTD.

During FY 2009, OCCAM announced its new research priorities:

- Identifying novel therapeutics in the pharmacopeia of traditional medical systems as defined by the World Health Organization
- Using complementary approaches to improve the therapeutic ratio of standard and investigational anti-cancer therapies
- Research on lifestyle modifications (e.g., diet, exercise, mind-body approaches) for their impact on cancer outcomes (e.g., response to conventional cancer therapy, survival)

The new priorities were developed after OCCAM became part of the NCI Division of Cancer Treatment and Diagnosis (DCTD) in FY 2007. This move allowed OCCAM to develop a new focus on cancer treatment research in addition to its historical role of supporting the growth of CAM research in all of NCI's divisions, offices, and centers (DOCs). The three research priorities identified by OCCAM represent areas of special opportunities in the CAM field that do not overlap with the DOCs' existing research projects.

FOCUSING ON BOTANICALS RESEARCH

BOTANICALS AND CANCER RESEARCH: CLINICAL TRIALS WORKSHOP

In July 2009, OCCAM convened a meeting attended by more than 100 researchers, policymakers, and experts for a two-day workshop designed to tackle the topic of botanicals and clinical cancer research. Based on the type of expertise, the attendees were assigned to one of the following six working groups:

- Targets, Pathways, and Networks of Pre-Clinical Models;
- Botanical Drug Issues;
- Clinical Trial Design and Implementation I;
- Clinical Trial Design and Implementation II;
- Role of Industry in Botanical Drug Development; and
- Obtaining Grant Funding for Botanical Drug Research.

Each working group was tasked to answer a series of questions about the challenges as well as the opportunities related to the current state of botanicals and cancer research.

A number of ideas emerged about how to establish an effective and organized clinical trial research infrastructure in the United States. The image of a pathway was used by some at the workshop as a way to describe how a botanical could move through the entire development spectrum: from discovery and reliable harvesting, into preclinical research at the bench, through to animal testing and human clinical trials, and ultimately to approval by the U.S. Food and Drug Administration (FDA) as a cancer treatment in humans. The discussions from this meeting are being used by OCCAM to better assess how to grow research in this topic and to improve technical assistance to grant applicants.

For more information, visit http://www.cancer.gov/cam/attachments/workshop_agenda_09.pdf.

NCI SIGNS RESEARCH AGREEMENT WITH CHINESE BOTANICAL INSTITUTE

After the United States government signed a research agreement with China to foster collaboration between researchers studying integrative and Traditional Chinese Medicine (TCM) in both countries, one of the first and most promising of these projects is a partnership between the Kunming Institute of Botany (KIB) of China Academy of Sciences and two groups at NCI.

OCCAM began to oversee the growing collaboration after a Memorandum of Understanding (MOU) was signed between KIB and NCI in October 2008. KIB is supplying unique natural compounds from Chinese plants, while NCI's Natural Products Branch (NPB) of the Developmental Therapeutics Program (DTP) will screen them for anticancer activity in NCI's system of 60 human cancer cell lines. If any of the botanical compounds show promise, more drug analysis and development will follow.

OCCAM SUPPORTS INTRAMURAL RESEARCH

During FY 2009, OCCAM financially supported two research projects within NCI's Center for Cancer Research (CCR). One research project led by William Farrar, Ph.D., head of the CCR Cancer Stem Cell Section, identified two phytochemicals – parthenolide and gossypol – that target prostate cancer stem cells (CSC) and may be used to eradicate CSCs in such tumors.

Thus far, parthenolide has been shown to affect:
1. tumor incidence and latency in animal studies;
2. signals associated with tumor proliferation and cancer cell invasion in micro-array studies; and
3. prostate cancer initiation, progression, and metastasis through altering transcription factor binding, which was found in protein/DNA array studies.

OCCAM COMPLETES ITS FIRST DECADE AT NCI

The beginning of FY 2009 marked the 10th anniversary of OCCAM's creation at NCI. During its first decade, OCCAM contributed to and documented the approximately $100 million growth of NCI's CAM research portfolio. There was also significant growth in the number of clinical trials of CAM interventions, including landmark studies which for the first time provided solid evidence that improvements in lifestyle and dietary interventions are feasible and can impact the recurrence of certain cancers. NCI's commitment to CAM research and clinical practice has been steadily supported, coordinated, and expanded by OCCAM over the years and that mission continues.

The following articles, that present the results of this research, were published in FY 2009 (PubMed Identifier (PMID) numbers are provided for the citations):

- Kawasaki BT, Farrar WL. Cancer stem cells, CD200 and immunoevasion. *Trends Immunology,* October 2008;29(10):464-8. Epub 2008 Sep 3. PMID: 18775673.
- Kawasaki BT, Hurt EM, Kalathur M, Duhagon MA, Milner JA, Kim YS, Farrar WL. Effects of the sesquiterpene lactone parthenolide on prostate tumor-initiating cells: An integrated molecular profiling approach. *Prostate,* June 1, 2009; 69(8):827-37. PMID: 19204913.
- Klarmann GJ, Hurt EM, Mathews LA, Zhang X, Duhagon MA, Mistree T, Thomas SB, Farrar WL. Invasive prostate cancer cells are tumor initiating cells that have a stem cell-like genomic signature. *Clinical & Experimental Metastasis,* 2009; 26(5):433-46. Epub 2009 Feb 17. PMID: 19221883.
- Mathews LA, Crea F, Farrar WL. Epigenetic gene regulation in stem cells and correlation to cancer. *Differentiation,* July 2009;78(1):1-17. Epub 2009 May 14. Review. PMID: 19443100.

In addition, for a third year, OCCAM has supported a CCR study on the Traditional Chinese Medicine (TCM) therapy called Sheng Qi Formula (SQF). O.M. "Zack" Howard, Ph.D., staff scientist and her team in the CCR Laboratory of Molecular Immunoregulation, Cancer and Inflammation Program conducted several studies during FY 2009 in follow up to work that was featured in a previous NCI CAM research annual report (An article on the earlier research is on page 35 of the FY 2007 CAM report which can be found at http://www.cancer.gov/cam/attachments/CAMAnnualReportFY2007.pdf).

These previous studies largely focused on the immunologic mechanisms of action of SQF. However, the CCR researchers' recent experiments have begun to explore the direct effects of the TCM therapy on cancer cells. The resulting data from this year's work indicate that the *in vitro* and *in vivo* effects of SQF on the 4T1 breast cancer model are due to the induction of apoptosis through the mitochondrial pathway.

OCCAM PROGRAMS

RESEARCH DEVELOPMENT AND SUPPORT PROGRAM

NCI sponsored 387 cancer CAM research projects in FY 2009, each of which are managed within the various Divisions and Centers of the Institute. OCCAM's Research Development and Support Program (RDSP) staff manages a portion of this portfolio and works with other program staff throughout NCI, assists investigators in identifying funding opportunities, and provides guidance in the pre- and post-review periods of grant application. The staff also coordinates programs and initiatives designed to stimulate research in cancer CAM as well as activities to develop the foundation of the science in cancer CAM research.

Isis Mikhail, M.D., M.P.H., Dr.P.H. was named as RDSP Program Director in November 2008. Dr. Mikhail received her medical degree from Cairo University Medical School. She then received her MPH and DrPH degrees in Epidemiology and International Health from the University of Alabama at Birmingham. Before coming to OCCAM, Dr. Mikhail was a program director, epidemiologist and acting branch chief at the Clinical and Translational Epidemiology Branch (CTEB) of the NCI Division of Cancer Control and Population Sciences (DCCPS).

Under Dr. Mikhail's leadership, OCCAM reissued the program announcement (PA) PA-09-167 "Developmental Projects in Complementary Approaches to Cancer Care and Treatment" in April 2009. This PA solicits grant applications to encourage and support the development of basic and clinical complementary cancer research projects (prevention, therapeutic, and palliative) through the exploratory/developmental research grant (R21) award mechanism.

For more information, visit http://grants.nih.gov/grants/guide/pa-files/PA-09-167.html.

In addition, OCCAM initiated a new small grant R03 funding opportunity announcement. This announcement, PA-09-168 offered R03 grant awards for researchers interested in starting small pilot and feasibility studies of CAM therapies and practices. Through this mechanism, studies can be funded that generate data needed for conducting larger scientific studies of CAM. OCCAM seeks to encourage investigators to initiate research in areas not typically explored in larger studies funded by other grant mechanisms, such as R01 and R21 awards. Outreach to international audiences was conducted for this PA.

For more information, visit http://grants.nih.gov/grants/guide/pa-files/PA-09-168.html.

Funding CAM Research with Stimulus Act Funds

OCCAM successfully proposed funding from the American Recovery and Reinvestment Act (ARRA) of 2009 for three new supplements to grants in its portfolio. The ARRA awardees were chosen, in part, because they were addressing highly significant areas of cancer research:

- Dr. Rakesh Srivastava "Chemoprevention of Pancreatic Cancer by EGCG" (3R01CA125262-02S1). University of Texas Health Center at Tyler.
- Dr. Fazlul Sarkar "A Novel and Targeted Approach to Inhibit Invasion and Angiogenesis" (R01CA131151-02S1). Wayne State University, Detroit, Michigan.
- Dr. Yung-Chi Cheng "Nucleoside Analogs as Anticancer Compounds" (3R01CA063477-14S1). Yale University.

OCCAM also provided an administrative supplement to the Radiation Therapy Oncology Group, Community Clinical Oncology Program (CCOP) Research Base (CA037422) to support components of a phase II/III study comparing acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) versus pilocarpine in treating early radiation-induced xerostomia (dry mouth).

COMMUNICATIONS AND OUTREACH PROGRAM

OCCAM's Communications and Outreach Program (COP) develops and disseminates information about NCI program initiatives and funding opportunities, workshops and other events, and educational materials through OCCAM's publications and Web site (http://www.cancer.gov/cam).

This program also assesses the opinions, interests, and informational needs of cancer researchers, CAM practitioners, and cancer patients regarding CAM research through surveys, public comment sessions, and focus groups. Results from these explorations are used to guide outreach efforts to these communities.

Assessing Cancer Patients Information Needs

In FY 2009, COP made a commitment to expand its outreach and communication efforts to cancer patients and produce additional resources that fill the existing gaps in patients' information needs.

In order to develop resources that best serve the needs of patients, OCCAM began a qualitative needs assessment to identify the CAM issues and topics most important to cancer patients. The needs assessment started by targeting health care professionals who work closely with patients, including patient educators, social workers, nurses, physicians, and CAM practitioners. The information collected in OCCAM's assessment will shape a dialogue about cancer patients' needs related to CAM. It will also help NCI determine high priority areas for new patient-focused publications and resources.

Other major communication activities in FY 2009 included:

- Redesign of Health Information and About Us sections of the OCCAM website, along with usability testing of entire website.
- Creating a Wikipedia entry on OCCAM http://www.cancer.gov/cam/newsletter/2009-fall/cam_information_occam_fall2009.html

COP also published the following publications in FY 2009:

- *NCI's Annual Report on Complementary and Alternative Medicine: Fiscal Year 2008* http://www.cancer.gov/cam/attachments/fy2008_CAM_annual_report.pdf
- *NCI CAM News* – Spring 2009 http://www.cancer.gov/cam/newsletter/2009-spring/home.html
- *NCI CAM News* – Fall 2009 http://www.cancer.gov/cam/newsletter/2009-fall/fall2009_OCCAM_newsletter_home.html

In addition to sending staff and publications to the numerous professional meetings listed below, COP improved OCCAM's outreach efforts by unveiling a new exhibit on NCI CAM research in FY 2009. This exhibit better promotes the mission of OCCAM and gives NCI a larger, more integral presence at key cancer CAM meetings, events, and symposia.

- Frontiers in Integrative Oncology; American College for Advancement in Medicine; Las Vegas, NV; October 15-19, 2008 (OCCAM staff attending: Shea Buckman)
- 5th International Conference of the Society for Integrative Oncology; Atlanta, GA; November 20-21, 2008 (OCCAM staff attending: Shea Buckman, Dr. Isis Mikhail, Dr. Dan Xi)
- Evidence-based Complementary and Alternative Cancer Therapies Conference; West Palm Beach, FL; January 8-10, 2009 (OCCAM staff attending: Shea Buckman)
- 8th Annual Oxford International Conference on the Science of Botanicals; Oxford, MS; April 2009 (OCCAM staff attending: Shea Buckman, Dr. Isis Mikhail)
- North American Research Conference on Complementary and Integrative Medicine; Minneapolis, MN; May 2009; (OCCAM staff attending: Shea Buckman, Commander Colleen Lee, Dr. Dan Xi)
- Oncology Nursing Society (OCCAM staff attending: Commander Colleen Lee)
- American Society of Clinical Oncology (OCCAM staff attending: Dr. Farah Zia)
- American Association of Family Physicians (materials only)

COP Collaborations

Each fiscal year, groups around NCI request the expertise of the COP staff. In FY 2009, COP:

- Assisted the NCI Office of Partnerships and Dissemination Initiatives' Multicultural Media Outreach Program with developing an article on CAM titled: "Interested in Complementary

and Alternative Medicine for Cancer? Talk with Your Doctor" for NCI's *Lifelines,* a biweekly column outreaching to Hispanic and African American community newspapers across the country. The CAM article was made available to the BlackPressUSA.com via the National Newspaper Publishers Association and Journey to Wellness, a radio media brand that provides health care and health literacy information through syndicated radio programming on public radio stations and on the CNN Radio network.

- Worked with the NCI Cancer Information Service's (CIS) to edit the CAM script for the recorded message on CAM offered through the 1-800-4-CANCER telephone line. The CAM script is one of six automated treatment messages.
- Provided content review of CAM articles written for the *NCI Cancer Bulletin* biweekly newsletter, which reaches approximately 52,000 subscribers. In FY 2009, COP participated in the following article reviews:
  - Harnessing the Biological Activity of Natural Products
  - Chemotherapy Provides Longer Survival than Enzyme Therapy for Pancreatic Cancer
  - Dietary Supplements and Cancer Treatment: A Risky Mixture
  - Researchers Urge Caution and Greater Scrutiny of Colon-related CAM Treatments.

In FY 2009, cancer patient advocates were involved in the review of NCI's CAM Annual Report. OCCAM solicited feedback from four Consumer Advocates in Research and Related Activities (CARRA) members who agreed to review a draft of the FY 2008 report. These members provided comments on whether the document was easy to read, contained relevant information to the cancer patient community, or omitted topics of patient interest. The feedback from these CARRA members improved the quality of the *NCI's Annual Report on Complementary and Alternative Medicine: Fiscal Year 2008*.

PRACTICE ASSESSMENT PROGRAM

OCCAM's Practice Assessment Program (PAP) reviews information on cancer patients treated with alternative therapies. PAP manages the NCI Best Case Series (BCS) Program, which provides an opportunity for CAM practitioners to submit retrospective case reports regarding cancer CAM treatments used in their settings. Practitioners are asked to submit patient records for evaluation by experts in clinical assessment and cancer treatment research. Results of the NCI BCS Program are used to inform decisions regarding NCI-initiated research and to share well-documented best cases with interested members of the scientific community in order to stimulate research.

In FY 2009, 29 cases of cancer patients treated with an alternative approach were submitted to the NCI Best Case Series Program and reviewed for eligibility. Two cases were found to fit the program criteria and reviews were completed on those cases (i.e., confirmation of pathological diagnosis of cancer, confirmation of radiological response to alternative treatment, and summary letter sent to submitters).

PAP is involved in an on-going collaboration with NCI's Community Oncology and Prevention Trials Research Group of the Division of Cancer Prevention, which is involved in all aspects of the design and implementation of NCI's large cancer prevention and symptom management clinical trials. PAP participates in concept and protocol reviews of trials utilizing CAM approaches, providing medical oncology and CAM research expertise and guidance.

During FY 2009, OCCAM staff published two articles about the NCI BCS Program and CAM practitioners:

- Zia F, White J. Letter to the Editor. *Integrative Cancer Therapies,* 2009; 8(2),113-114.
- Lee C., Zia F., Olaku O., Michie J., White J. Survey of CAM practitioners regarding cancer management and research. *Journal of the Society of Integrative Oncology,* Winter 2009; 7(1), 26-34.

On February 4, 2009, PAP hosted a talk given by Drs. Mary Tagliaferri and Emma Shtivelman, from Bionovo Inc. titled "Anti-tumor Effects of BZL 101 for Patients with Advanced Breast Cancer."

OCCAM'S PARTICIPATION AT MAJOR PROFESSIONAL CONFERENCES

OCCAM staff members are active in both domestic and international professional conferences through presentations and interactions with cancer CAM researchers, practitioners, and patient advocacy groups attending the conferences.

During FY 2009, this encompassed several important meetings (OCCAM staff attending):

- Cancer Patient Education Network Annual Meeting; October 20-22, 2008; Clearwater, FL; (Shea Buckman)
- Cancer Foundation of China: The Progress and Prospect of Traditional Chinese Medicine Cancer Therapy and Prevention; October 22-24, 2008; Zhangjiajie, China; (Dr. Libin Jia gave a presentation titled "Overview of the National Cancer Institute's Cancer CAM Research")
- 2nd International Congress of TCM and Integrated TCM-Western Medicine Oncology; October 24-26, 2008; Beijing, China; (Dr. Libin Jia was a session chairperson and gave a presentation titled "National Cancer Institute's Traditional Chinese Medicine Related Research")
- New York International Traditional Chinese Medicine Summit; New York City, NY; November 1-2, 2008; (Dr. Libin Jia gave a presentation titled "Cancer Research and Traditional Chinese Medicine: A Perspective from the U.S. National Cancer Institute")
- Institute of Medicine Summit on Integrative Medicine and the Health of the Public; Washington, D.C.; February 25-27, 2009; (Dr. Isis Mikhail, Lauren Rice, Vera Rosenthal)
- American Association for Cancer Research Annual Meeting; Denver, CO; April 18-22, 2009; (Dr. Isis Mikhail and Dr. Libin Jia participated in Meet-the-Expert sessions)

- City of Hope CAM Research Seminar; Duarte, CA; May 15, 2009; (Dr. Jeffrey D. White gave a presentation titled "Complementary and Alternative Medicine and Cancer Research")
- American Society of Clinical Oncology Annual Meeting; Orlando, FL; May 29-June 2, 2009; (Dr. Libin Jia participated in a Meet-the-Expert session)
- Cancer Guides™ II Cutting Edge Integrative Cancer Care; Washington, D.C.; June 11-14, 2009; (Dr. Isis Mikhail gave a presentation titled "Understanding OCCAM and Applying for Assistance" and Dr. Jeffrey D. White gave a presentation titled "Integrative Oncology: Thoughts Regarding Future Development")
- International Workshop on Bioinformatics and Systems Biology in Traditional Chinese Medicine Research; Shanghai, China; August 3-6, 2009; (Dr. Dan Xi was co-chair)
- 8th Meeting of the Consortium for the Globalization of Chinese Medicine; Nottingham, England; August 25-28, 2009, (Dr. Jeffrey D. White was co-chair of session titled "Clinical Trial I: Cancer and Liver Inflammation")
- 9th Annual Meeting of the Comprehensive Cancer Center of Wake Forest University Community Clinical Oncology Program Research Base; Ashville, NC; September 24-26, 2009; (Dr. Isis Mikhail gave a presentation titled "Complementary and Alternative Medicine at the NCI")
- HINTS Data Users Conference Partners in Progress; Silver Spring, MD; September 24-25, 2009; (Elizabeth Austin)

OCCAM STAFF LIST: FY 2009

Jeffrey D. White, M.D.	Director, OCCAM
Christina Armstrong	Administrative Program Specialist
Akia Samuda	Administrative Assistant
Isis Mikhail, M.D., Dr.P.H., M.P.H.	Director, Research Support and Development Program
Dan Xi, Ph.D.	Program Officer, Research Support and Development Program
Oluwadamilola Olaku, M.D., M.P.H.	Scientific Program Analyst
Libin Jia, M.D.	Scientific Program Manager
Akiko Nakayama, M.S.	Scientific Program Analyst
Juanita Cox, B.S.	NCI Administrative Career Development Intern
Farah Zeba Zia, M.D.	Director, Practice Assessment Program
CDR (U.S. PHS) Colleen Lee, M.S., AOCN®	Coordinator, Practice Assessment Program
Shea Buckman, M.A.	Coordinator, Communications and Outreach Program
Lauren Rice, M.S.	Communications Analyst
Vera Rosenthal, M.P.H.	Health Communications Intern
Elizabeth Austin, M.S.	Health Communications Intern

NCI CAM Communications Programs

NCI directs communications programs committed to providing current and credible information resources about CAM to its stakeholders.

PROVIDING INFORMATION ONLINE

OCCAM's Web site (http://www.cancer.gov/cam) serves as NCI's information hub on CAM issues. It provides a wealth of information resources and timely updates about the Institute's CAM research portfolio, grant opportunities, and other news.

Included on the OCCAM site are links to other information sources such as the Physician Data Query (PDQ®), which is NCI's comprehensive cancer database. PDQ produces summaries covering topics such as cancer treatment, prevention, screening, and CAM.

MOST FREQUENTLY ACCESSED PDQ CAM SUMMARIES

NCI tracks the number of page views of each PDQ CAM summary on Cancer.gov within both the patient and health professional versions. The number of page views is determined by the number of views to the first page of each PDQ summary.

In FY 2009, the patient version summary with the highest number of page views was Essaic/Flor-Essence, which had 31,002 page views. The second highest number of page views was for the patient version of Laetrile/Amygdalin, at 18,116. Third in the rankings was the Coenzyme Q10 patient summary, which had 17,462.

During FY 2009, the highest number of page views received for a health professional version of a PDQ CAM summary was 6,085 for Mistletoe Extracts. The second most page views for the health professional versions was for Coenzyme Q10 with 5,366. The third most page views was for the Aromatherapy professional summary, which received 4,869.

Figure 2 shows the total number of page views during FY 2009 for all of the PDQ CAM summaries in both the patient and health professional versions.

PDQ CAM CLINICAL TRIALS

NCI sponsors clinical studies on CAM approaches for cancer. The OCCAM Web site hosts a database which organizes CAM clinical trials by cancer types and types of symptoms. Clicking on an entry in the table triggers a search of the NCI's PDQ Cancer Clinical Trials Registry, which includes approximately 4,500 abstracts of protocols that are open and approved to accept patients. Many, but not all, of these trials are conducted with NCI support. The table also archives trials that are currently closed. The Registry is available on the NCI Web site at http://www.cancer.gov/clinicaltrials/search/.

In FY 2009, there were 80 NCI-supported CAM clinical trials (See appendix for the complete list).

For the current list of CAM clinical trials by cancer type and to access the CAM clinical trials table, go to http://www.cancer.gov/cam/clinicaltrials_list.html.

FIGURE 2. PDQ CAM SUMMARIES FY09

PATIENT SUMMARY PAGE VIEWS

	714X	Acupuncture	Antineoplastons	Aromatherapy	Cancell/Entelev	Cartilage	Coenzyme Q10	Essiac/Flor-Essence	Gerson Therapy
Totals	**4182**	**11662**	**9651**	**5745**	**17462**	**9347**	**31002**	**25581**	**16637**

HEALTH PROFESSIONAL SUMMARY PAGE VIEWS

	714X	Acupuncture	Antineoplastons	Aromatherapy	Cancell/Entelev	Cartilage	Coenzyme Q10	Essiac/Flor-Essence	Gerson Therapy
Totals	**1248**	**3191**	**1544**	**4869**	**827**	**1282**	**5366**	**3755**	**1879**

PRODUCING PUBLICATIONS

Various offices within NCI provide educational materials on CAM in print format to health professionals, people affected by cancer, and the general public.

NCI'S ANNUAL REPORTS ON CAM

OCCAM published *NCI's Annual Report on Complementary and Alternative Medicine: Fiscal Year 2008*, which documented NCI's participation in and support of a wide range of CAM activities. The report highlights the contributions of communications programs, training and conferences, and cancer CAM research in addressing the NCI strategic areas.

The report can be viewed and downloaded from http://www.cancer.gov/cam/attachments/fy2008_CAM_annual_report.pdf.

NEWSLETTER ON NCI'S CAM ACTIVITIES

OCCAM's twice-yearly newsletter *NCI CAM News* provides the latest information on NCI-sponsored research, funding opportunities, meetings and workshops, as well as educational information on cancer and CAM. *NCI CAM News* also includes features on cancer CAM projects representing the full range of NCI's activities as well as OCCAM program updates.

The following issues of *NCI CAM News* were made available online in FY 2009:

- Spring 2009 http://www.cancer.gov/cam/newsletter/2009-spring/home.html
- Fall 2009 http://www.cancer.gov/cam/newsletter/2009-fall/fall2009_OCCAM_newsletter_home.html

Note: NCI Web sites do not offer personalized medical advice to individuals about their condition or treatment, and the resources on the sites should not be used as a substitute for professional medical care.

Gonzalez Regimen	Hydrazine Sulfate	Laetrile/Amygdalin	Milk Thistle	Mistletoe Extracts	Newcastle Disease Virus	PC-SPES	Selected Vegetables/ Sun's Soup	Spirituality in Cancer Care
2066	**6300**	**18116**	**15571**	**16527**	**3674**	**5510**	**5957**	**7031**

Gonzalez Regimen	Hydrazine Sulfate	Laetrile/Amygdalin	Milk Thistle	Mistletoe Extracts	Newcastle Disease Virus	PC-SPES	Selected Vegetables/ Sun's Soup	Spirituality in Cancer Care
1296	**637**	**1848**	**2602**	**6085**	**1176**	**1918**	**1989**	**3507**

CAM IN NCI NEWSLETTERS AND PUBLICATIONS

The *NCI Cancer Bulletin* is a biweekly online newsletter designed to provide useful, timely information about cancer research to the cancer research community. During FY 2009, there were numerous cancer CAM studies featured in the *NCI Cancer Bulletin:*

- *Harnessing the Biological Activity of Natural Products,* September 22, 2009
- *Chemotherapy Provides Longer Survival than Enzyme Therapy for Pancreatic Cancer,* September 8, 2009
- *Weight Lifting Reduces Lymphedema Symptoms after Breast Cancer,* September 8, 2009
- *Review Finds No Firm Evidence that Green Tea Prevents Cancer,* August 11, 2009
- *Dietary Supplements and Cancer Treatment: A Risky Mixture,* August 11, 2009
- *Cutting Calories to Prevent Cancer,* July 14, 2009
- *Ginger Helps Reduce Nausea from Chemotherapy*, May 19, 2009
- *A Conversation with Dr. Rashmi Sinha,* April 7, 2009
- *Study Suggests Low, Moderate Alcohol Use Increases Cancer Risk,* March 10, 2009
- *Researchers Urge Caution, Greater Scrutiny of Colon-related CAM Treatments,* March 10, 2009
- *Compounds Found in Green Tea Block Bortezomib,* February 24, 2009
- *A Conversation with Dr. Richard Troiano*[diet and physical activity], January 27, 2009
- *Two Prevention Trials Show Antioxidants Do Not Cut Cancer Risk* December 16, 2008
- *Selenium and Vitamin E Fail to Reduce Prostate Cancer Risk,* November 4, 2008
- *Delving Deeper into Exercise and Breast Cancer Prevention,* October 21, 2008

Likewise, in FY2009, cancer CAM was the topic of stories in other NCI publications:

- *A Diet That Works: New Study Shows Early Response of Colon Cancer to Dietary Change,* CCR Connections, Volume 3, No.1, 2009
- *Dietary and Factors and Small Intestinal Cancer,* Linkage, March 2009

NCI FACT SHEETS ON CAM

The NCI "fact sheet" collection addresses a variety of cancer topics, including cancer CAM topics. The fact sheets are frequently updated and revised based on the latest cancer research. During FY 2009, NCI issued a new fact sheet on "Calcium and Cancer Prevention: Strengths and Limits of the Evidence." The document can be downloaded or printed from http://www.cancer.gov/cancertopics/factsheet/prevention/calcium.

See Table 1 for the list of the current NCI CAM fact sheets and the number of page views each fact sheet received during FY 2009. The NCI fact sheets collection can be found at http://www.cancer.gov/cancertopics/factsheet.

RESPONDING TO CAM CANCER INQUIRIES

The Cancer Information Service (CIS) serves as NCI's link to the public by interpreting and explaining research findings in a clear and understandable manner and providing personalized responses to specific questions about cancer. Highly trained cancer information specialists are available to answer questions via phone, live online chat, mail, and e-mail about cancer treatment and clinical trials, including CAM therapies. During FY 2009, CIS responded to 1,179 inquiries regarding CAM approaches for cancer.

Access the CIS by calling 1-800-4-CANCER (1-800-422-6237), or by using the LiveHelp instant-messaging service at https://cissecure.nci.nih.gov/livehelp/welcome.asp.

TABLE 1: NCI CAM FACT SHEETS PAGE VIEWS STATISTICS FY 2009

Fact Sheet Title	Total Views
Antioxidants and Cancer Prevention: Fact Sheet	71,513
Calcium and Cancer Prevention: Strengths and Limits of the Evidence	3,622
Garlic and Cancer Prevention: Questions and Answers	14,732
Physical Activity and Cancer: Fact Sheet	9,166
Questions and Answers About Beta Carotene Chemoprevention Trials	2,736
Red Wine and Cancer Prevention: Fact Sheet	18,769
Selenium and Vitamin E Cancer Prevention Trial (SELECT): Questions and Answers	1,885
Tea and Cancer Prevention: Fact Sheet	11,853
Vitamin D and Cancer Prevention: Strengths and Limits of the Evidence (New)	81
Complementary and Alternative Medicine in Cancer Treatment: Questions and Answers	24,353
	158,710

THE NCI FACT SHEET "COMPLEMENTARY AND ALTERNATIVE MEDICINE IN CANCER TREATMENT: QUESTIONS AND ANSWERS" WAS VIEWED 24,353 TIMES IN FY 2009.

TO VIEW THIS PUBLICATION, PLEASE VISIT HTTP://WWW.CANCER.GOV/CANCERTOPICS/FACTSHEET/THERAPY/CAM.

Training and Conferences

NCI provides a variety of training support programs on different aspects of CAM research including grant writing workshops and scientific conference sponsorships.

NCI LECTURES AND WORKSHOPS ON CAM

NCI provides educational opportunities for its staff, fellows, and the public on topics related to cancer. In FY 2009, the following seminars and lectures relevant to CAM research were held:

- **Epigenetics, Nutrition, and Disease Susceptibility – Randy Jirtle, Ph.D.**
  (Stars in Nutrition & Cancer Seminar Series, Division of Cancer Prevention)
  September 29, 2009

- **Natural Products as the Starting Point for New Discoveries – Zhu-Jun Yao, Jr. Ph.D.**
  (Center for Cancer Research)
  August 3, 2009

- **Soy Protein and Isoflavones Research: Challenges in Designing and Evaluating Intervention Studies**
  (Office of Dietary Supplements cosponsored by NCI and other NIH Institutes and Centers)
  July 28-29, 2009
  http://ods.od.nih.gov/News/Soy_ProteinIsoflavone_Research_Scientific_Workshop_July_2009.aspx

- **7th Annual Cancer Survivorship Series: Living With, Through and Beyond Cancer, Part III: Survivors Too: Family, Friends and Loved Ones – Managing the Fatigue of Caregiving**
  June 23, 2009
  http://www.cancercare.org/get_help/tew_details.php?tew=emotional_062309&ret=%2Fget_help%2Ftew_calendar.php

- **Seventh International Conference on Diet and Activity Methods – Chair: Amy F. Subar, PhD, MPH, RD**
  (Sponsored in part by the National Cancer Institute)
  June 5-7, 2009
  http://www.icdam.org

- **7th Annual Cancer Survivorship Series: Living With, Through and Beyond Cancer, Part II: The Importance of Nutrition and Physical Activity**
  May 19, 2009
  http://www.cancercare.org/get_help/tew_details.php?tew=medical_051909&ret=%2Fget_help%2Ftew_calendar.php

- **Selenium Redox Chemistry: Understanding Cancer Prevention and Therapy- Dr. Julian Spallholz**
  (Division of Cancer Prevention)
  May 11, 2009

- **Oxidative Damage, Free Radicals, Antioxidants and Space Flight**
  April 27, 2009
  http://calendar.nih.gov/app/MCalInfoView.aspx?evtID=19360

- **7th Annual Cancer Survivorship Series: Living With, Through and Beyond Cancer, Part I: Managing the Stress of Survivorship**
  April 14, 2009
  http://www.cancercare.org/get_help/tew_details.php?tew=emotional_041409&ret=%2Fget_help%2Ftew_calendar.php

- **Nanonutrition Frontiers: Lessons Learned from Imaging and Therapy- Martin Philbert, PhD (Stars in Nutrition & Cancer Seminar Series, Division of Cancer Prevention)**
  March 19, 2009
  http://prevention.cancer.gov/newsandevents/events/20090319

- **Nutrition and Cancer Prevention Research Practicum**
  (Division of Cancer Prevention)
  March 16-20, 2009
  http://prevention.cancer.gov/newsandevents/events/20090316-20

TRAINING OPPORTUNITIES AT OCCAM

During FY 2009, OCCAM hosted two Health Communications Interns, Vera Rosenthal, M.P.H., and Elizabeth Austin, M.S., who helped organize and execute a scientific conference; wrote articles for the newsletter *NCI CAM News*, *Annual Report on Complementary and Alternative Medicine*, and promotional materials; and assisted with the management of OCCAM's Web site. The interns also participated in professional meetings and NIH-sponsored training seminars.

CAM MONTHLY LECTURE SERIES AT NCI

The OCCAM Monthly Lecture Series informs the NCI community about recent and ongoing research projects in cancer CAM. These hour-long lectures feature a fifty-minute presentation on a cancer CAM topic and allow 10 minutes for questions. The lectures are open to the public and are archived as videocasts on the OCCAM Web site at http://www.cancer.gov/cam/news_lectures.html.

During FY 2009, the series included lectures on:

- Successful Combination of TCM and Chemotherapy: Immune and Oncological Effects of Sheng Qi Formula (SQF) on a Murine Model of Inflammatory Breast Cancer
- The Use of Curcumin and Flaxseed in Radiation Pneumonopathy
- Anti-tumor Effects of BZL 101 for Patients with Advanced Breast Cancer
- Role of NFkB in Activity of Benzyl Isothiocyanate Against Pancreatic Cancer
- Effects of Exercise on the Chronic Cardiac Dysfunction Associated with Doxorubicin
- Dietary Fat-Gene Interaction in Prostate Cancer
- Chemoprevention of Lung Cancer by Naturally-occurring and Synthetic Compounds
- Breast Cancer Prevention and Treatment with Noni Juice
- Metabolomics Approach to Understanding Metabolic Disorders and Traditional Chinese Medicine
- Phenolic Antioxidants as Tumor Radio/Chemosensitizers
- Evaluation of Resveratrol and Curcumin as Therapeutics Against High Risk Leukemia

SUPPORTING SCIENTIFIC CONFERENCES

In FY 2009, NCI supported the following conferences that included CAM content:

- American Psychosocial Oncology Society Annual Conference; Integrating Psychosocial Research and Practice into Quality Cancer Care: Setting the Standard
  February 5-8, 2009
  Charlotte, NC
  GRANT NUMBER: 1R13CA138133-01

- American Society of Pharmacognosy Annual Meeting
  June 27-July 1, 2009
  Honolulu, HI
  GRANT NUMBER: 1R13CA139768-01

- Translational Research in Acupuncture: Bridging Science, Practice, and Community
  March 18-21, 2010
  Chapel Hill, NC
  GRANT NUMBER: 1R13AT005565-01

- American Society of Preventive Oncology Annual Conference
  March 20-23, 2010
  Bethesda, MD
  GRANT NUMBER: 2R13CA094927-08

- Society for Behavioral Medicine
  April 7-10, 2010
  Seattle, WA
  GRANT NUMBER: 5R13CA091918-09

- PsychoNeuroImmunology Research Society Annual Conference: Mentoring Program
  June 3-6, 2010
  Breckenridge, CO
  GRANT NUMBER: 1R13CA139766-01
  (See related story page 28)

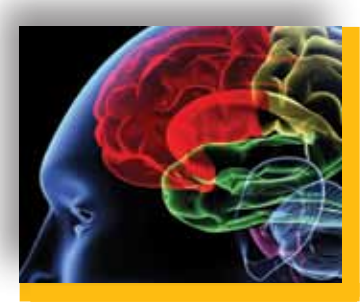
Highlights from NCI's CAM Training Projects

The highlights on the following pages are selected from the 33 CAM training projects that NCI supported during FY 2009 at laboratories and clinics throughout the United States and the world. NCI's programs allow students and professionals at all stages of their careers to develop the skills necessary to conduct basic, clinical, and cancer control research into CAM therapies and interventions.

Abstracts for the CAM training projects featured in the report can be found by searching the NIH RePORTer research trials database at http://projectreporter.nih.gov/reporter.cfm.

NCI Supports Mentoring Program in Psychoneuroimmunology Research

DIVISION OF CANCER CONTROL AND POPULATION SCIENCES



Every year for the past decade, the PsychoNeuroImmunology Research Society (PNIRS) invites 25 of the most promising pre- and post-doctoral research scientists to participate in the society's annual conference. Under an R13 training grant, funded primarily by NCI*, each PNIRS Trainee-Scholar receives $1,000 to cover airfare and hotel costs for the 3-day meeting.

The funds enable the younger scientists to participate in a PNIRS Educational Short Course, as well as a mentoring colloquium with senior faculty. These scientists also attend two workshops with junior faculty and NIH program staff, who provide advice on career building, grant writing, and funding opportunities in the growing research field of behavioral and neuroimmune interactions and their translational relevance for disease prevention and treatment.

"The program has been in place since 1999, and over the years, PNIRS has had more than 200 trainees at the annual conferences," recalled Andrew Miller, M.D., professor of psychiatry and behavioral sciences at Emory University and director of psychiatric oncology at the Winship Cancer Institute. "The scholar-trainee program is very competitive. In 2009, we had about 80 individuals applying for 25 slots."

The Educational Short Course provides a didactic framework on an emerging topic in psychoneuroimmunology research. "Each speaker is encouraged to provide some basic foundation for their areas of investigation, and typically the first talk is an introduction to this whole research field," Dr. Miller explained. During the 2009 conference he moderated a short course on his special interest of inflammation and its links to behavioral patterns in a variety of diseases including cancer.

After the short course, the 25 trainees participate in a Senior Faculty-Trainee Colloquium. "We have the trainees break up into several small groups of five trainees each," Dr. Miller said. "There are two senior faculty for each group. The trainees and faculty are carefully selected for each group, so the trainees will have faculty who are experts in the trainees' fields of interest."

Each trainee has three minutes in which they informally present their research projects to the faculty and peers. "After the trainees do their brief presentations everyone can ask questions," Dr. Miller noted. "The faculty makes various suggestions about how the research projects could be improved, what things might be missing, what are the strengths. It gives the students the opportunity to really focus their ideas, make presentations, and meet their peers in the same field as well as senior faculty investigators."

The PNIRS Trainee-Scholar program has demonstrated real benefits for the participants' scientific careers. Dr. Miller noted a PubMed survey of former trainees from the 2004 PNIRS conference that found they had published more than 60 publications in peer-reviewed journals since participating in the program.

"We also invite former trainee-scholars and other junior faculty members attending subsequent PNIRS meetings to a junior faculty workshop," he added. "It really fosters the networking and helps the trainees get to know peers who've made that transition from post-doc or graduate school into a post-doc, junior faculty status."

*** GRANT NUMBER: 1R13CA139766-01**

Mentoring Helps Researcher Pursue Study of Ginger for Preventing Colorectal Cancer

CENTER FOR CANCER TRAINING

For at least 2,000 years, people have used ginger as a medicinal herb. In Western herbal medicine, ginger is used mainly as a remedy for digestive disorders. However, the prevalence of foods such as ginger, garlic, and chilies in the diets of people in southeast Asian countries is thought to contribute to the reduced occurrence of several types of cancer, including colon cancer, in that region. Furthermore, studies in animals have shown that ginger can prevent the development of colon cancer, leading some researchers to ask whether ginger can help prevent colorectal cancer in humans.

One researcher hoping to answer that question is Suzanna Zick, N.D., M.P.H., an assistant research professor in the department of family medicine at the University of Michigan, Ann Arbor. With support from a 5-year Mentored Career Development Award* from NCI, Dr. Zick has been doing a series of preliminary studies that she hopes will lead to a large clinical trial examining ginger's ability to prevent colorectal cancer or prevent its recurrence in people at normal or high risk of developing the disease.

Dr. Zick's interest in the medicinal properties of ginger began with research she did on whether ginger could prevent nausea in adults who were receiving chemotherapy. As a member of a research group that studies cancer prevention, she became interested in ginger's possible cancer-preventing properties. "I'm very keen about wellness and prevention," she said, "and thought it would be wonderful to be able to use something that tasted good to help prevent cancer."

The NCI career award "really kick-started and broadened my research career," said Dr. Zick, a naturopathic physician. "It gave me the ability and time to develop new research skills, to understand the theories behind the research, and to develop grant-writing and manuscript-writing skills—all those things that we're supposed to be able to do to develop into independent scientists," she explained.

Because a diverse set of skills is needed to do rigorous studies of dietary supplements for cancer prevention, Dr. Zick has worked with five research mentors with different areas of expertise. With help from those mentors, she learned skills ranging from how to measure biological markers of disease in human tissue samples to how to carefully design cancer prevention studies. Her primary mentor, also in Michigan's family medicine department, was Mack Ruffin, M.D., M.P.H., whose research interests include cancer chemoprevention. Chemoprevention is the use of drugs, vitamins, or other substances to reduce the risk of cancer or delay its development or recurrence.

Dr. Zick also worked with a mentor who studies the effects of dietary factors on cancer risk and also does laboratory-based research to analyze biological markers of risk. She even spent time watching a senior clinician perform colonoscopies, so she could learn to identify precancerous growths or actual cancers in the colon.

"Right now, there is no treatment that prevents colon cancer in either high-risk or normal individuals," Dr. Zick noted. "We know some things work in epidemiological studies, but that doesn't tell us for sure what will work in a clinical setting."

Dr. Zick is interested in a nutritional approach to cancer prevention, which might involve a combination of diet plus capsules or pills containing dietary supplements shown to prevent cancer. In the case of colon cancer, that might include a capsule containing powdered ginger, Dr. Zick said, or perhaps ginger ale, ginger tea, or ginger candy for individuals those who don't like taking pills. Because it can be hard to convince people to take pills or make dietary changes to prevent a disease they don't have and may never get, Dr. Zick said, "you have to make [this approach] as flexible, appealing, and low toxicity as possible. Giving people options is one way to increase the chance they will actually make these changes."

*GRANT NUMBER: 5K07CA102592-05

Naturopathic Doctor Studies Antioxidant Use in Breast Cancer Patients

CENTER FOR CANCER TRAINING

Many cancer patients take over-the-counter antioxidant dietary supplements while undergoing radiation therapy or chemotherapy. The use of antioxidant supplements is controversial because doctors know little about the short-term or long-term effects. There is a concern that antioxidant supplements may counteract the effects of chemotherapy and radiation therapy, yet antioxidant supplements may also prevent side effects caused by cancer treatments.

"We do not have good data to inform clinical guidelines either way," explained Heather Greenlee, N.D., Ph.D., M.P.H, recipient of a five-year Mentored Patient-Oriented Research Career Development Award* from NCI. Dr. Greenlee, an assistant professor in the epidemiology department at Columbia University's Mailman School of Public Health, is using the NCI grant to help gather data to help resolve the controversy over antioxidant supplement use, in particular during adjuvant therapy for breast cancer. Adjuvant therapy is any treatment given after the primary treatment to reduce the risk that cancer will recur.

As part of this research, Dr. Greenlee will do preliminary clinical studies on the safety and potential benefits of one particular antioxidant, coenzyme Q10 (CoQ10), in women undergoing chemotherapy with doxorubicin, a drug used to treat many types of cancer. "Doxorubicin can cause significant cardiac toxicity—that is, damage to the heart muscle," noted Dr. Greenlee. "For some women with breast cancer, this resolves after treatment is over, but for other women there is permanent damage."

CoQ10 has been shown in laboratory cell cultures and animal studies to prevent cardiac toxicity caused by doxorubicin, but a definitive study has never been done in breast cancer patients, Dr. Greenlee said. An estimated 45% to 80% of breast cancer patients take antioxidant supplements such as CoQ10, either for general health benefits or because they hope the supplements will help treat the cancer or keep it from recurring.

To address the question of the potential benefits of antioxidant supplements from a different angle, Dr. Greenlee will also use data from the Pathways Study, an ongoing observational epidemiology study being funded by NCI. The Pathways Study is gathering detailed information on diet, dietary supplement use, and physical activity from more than 4,000 women diagnosed with breast cancer within the Kaiser Permanente Northern California health system. "We will be able to use the Pathways Study data to see whether or not the use of antioxidants during radiation therapy or during chemotherapy impacts the breast cancer recurrence rate or survival rate," Dr. Greenlee explained.

Dr. Greenlee is one of a handful of naturopathic doctors (N.D.) who are doing cancer research. Prior to going to a naturopathic medical school, "I'd been a research assistant at the Fred Hutchinson Cancer Research Center and I wanted to be able to identify things that women can do proactively to promote their health and prevent cancer," she recalled. "I turned to naturopathic medicine to provide a model of health promotion and wellness, and that turned into me being interested in what cancer survivors can do beyond conventional treatment to improve their quality of life, to improve their recurrence rates, and overall improve their survival."

After her naturopathic training, Dr. Greenlee pursued a Master of Public Health degree in epidemiology at the University of Washington and a Ph.D. degree in epidemiology at Columbia University. Once she completes the additional training, course work, and mentoring provided by the NCI career development award, "my goal is to lead a major research program on the effects of CAM therapies and lifestyle modifications after cancer diagnosis for reducing side effects, reducing recurrence rates, and improving survival—to identify what works and what doesn't work," she commented.

***GRANT NUMBER: 1K23CA141052-01**

NCI Research in Complementary and Alternative Medicine

How much money does NCI spend on CAM research each year? This is one of the questions most frequently posed to OCCAM. Researchers, cancer patient advocates, proponents of CAM, and Congress are interested in the answer, and OCCAM is responsible for gathering the data needed to report the total CAM expenditures budget figure each year.

It is a common misconception that OCCAM manages all of the CAM projects for NCI. The vast majority of CAM projects are managed by other programs and laboratories throughout the Institute. After the close of the fiscal year, NCI's Division of Extramural Activities (DEA) provides OCCAM with a list of funded grants and cooperative agreements coded as containing some component of CAM research. Similarly, NCI's two intramural components, the Center for Cancer Research (CCR) and the Division of Cancer Epidemiology and Genetics (DCEG), provide lists of their potentially relevant projects. Also, a list of contracts identified as potentially containing CAM research is provided. OCCAM staff review each project to confirm they are accurately classified as CAM research. Then aspects of each project are identified allowing their placement into a sub-categories based on the type of research and CAM intervention type.

NCI's total CAM expenditure figure includes money awarded for intramural projects (projects conducted within NIH facilities and labs), extramural grants (projects conducted outside of NIH), cooperative agreements, contracts, and supplements. It is important to note the reported figure for total NCI CAM expenditures for a fiscal year only includes projects for which NCI is the primary funder.

TOTAL ESTIMATED CANCER CAM RESEARCH EXPENDITURE

In FY 2009, NCI invested $114,441,501 for 429 intramural and extramural research projects relevant to CAM. For the purpose of the FY 2009 analysis, the following types of funding are included: intramural projects and extramural grants, cooperative agreements, contracts, and supplements. (See Figure 3.)

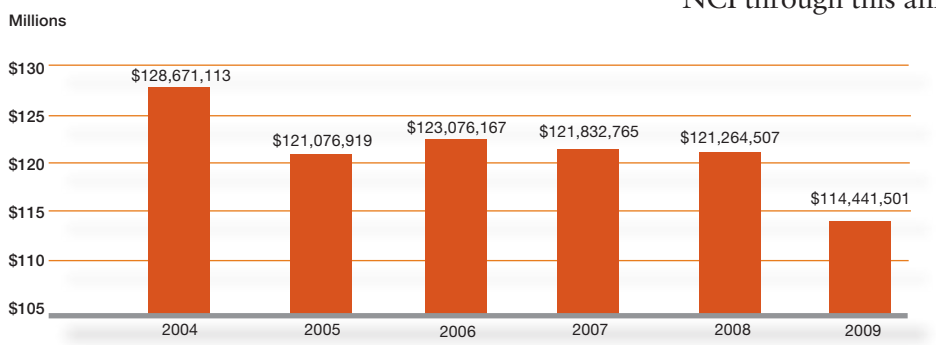
In addition, during FY 2009, NCI used $21,637,877 in funds from the American Recovery and Reinvestment Act (ARRA) to award 104 CAM research grants.

The above numbers do not include CAM training grants (T and F awards), or K (research career) and R25 (cancer education) grants. These numbers are listed separately in Figure 4.

GRANT AWARDS BY FUNDING OPPORTUNITY ANNOUNCEMENT

In FY 2009, there were 73 funding opportunity announcements (FOA) that yielded cancer CAM grants. The program announcement (PA) "Research Project Grants (Parent R01)" (PA-07-070) was the most productive mechanism for attracting new CAM grants to NCI. A total of 65 of the 210 CAM grants awarded through FOAs in FY 2009 came to NCI through this announcement. (See Figure 5.)

FIGURE 3. NCI CAM EXPENDITURES: FY 2004-2009



* Footnote: Includes grants, cooperative agreements, intramural projects, and contracts. Grants and cooperative agreements are only included when NCI is the primary funding agency. Excludes training grants (Ts, Fs, Ks, and R25s). Total projects include all active projects in FY 2009.

FIGURE 4. NCI CAM TRAINING PROJECTS 2009

Training Grant Mechanisms	Number of Grants	Total Funding
F (31, 32)	5	$ 142,346
K (01, 05, 07, 22, 23, 24)	24	$ 2,208,263
R25	3	$ 681,286
T32	1	$ 286,091
TOTAL	**33**	**$3,317,986**

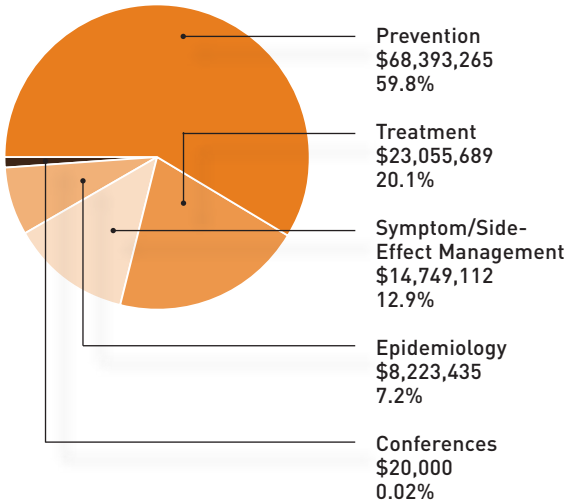
Note: does not include ARRA awards

FIGURE 5. NUMBER OF GRANT AWARDS BY FUNDING OPPORTUNITY ANNOUNCEMENT

*CA05-013	2	PA04-068	1	PA06-314	2	PA07-100	2	PA08-032	1	PAR06-294	4	Total	
*CA05-014	1	PA04-099	2	PA06-315	6	PA07-174	1	PA08-050	1	PAR06-313	21	Solicited	237
*CA07-025	6	PA04-108	1	PA06-351	4	PA07-175	2	PA08-051	1	PAR06-451	1	Total	
*CA08-004	1	PA05-027	1	PA06-400	7	PA07-176	1	PA08-074	1	PAR06-458	1	Unsolicited	150
*CA08-018	1	PA05-040	1	PA06-412	3	PA07-177	1	PA08-121	1	PAR06-505	1	**Total Grants Awarded**	**387**
*ES02-009	1	PA05-059	1	PA06-413	3	PA07-257	2	PA08-149	1	PAR08-020	1	
*HL08-013	1	PA05-125	2	PA06-414	2	PA07-258	1	PA08-209	1	PAR08-055	15	
*OD03-008	1	PA05-141	1	PA06-440	1	PA07-280	1	PAR03-153	1	PAR08-135	2	
PA02-169	1	PA06-042	2	PA06-510	9	PA07-320	1	PAR04-011	1	PAS02-009	1	
PA04-046	1	PA06-283	2	PA07-007	3	PA07-356	1	PAR05-156	5			
PA04-053	3	PA06-303	1	PA07-070	65	PA07-362	5	PAR06-073	2			

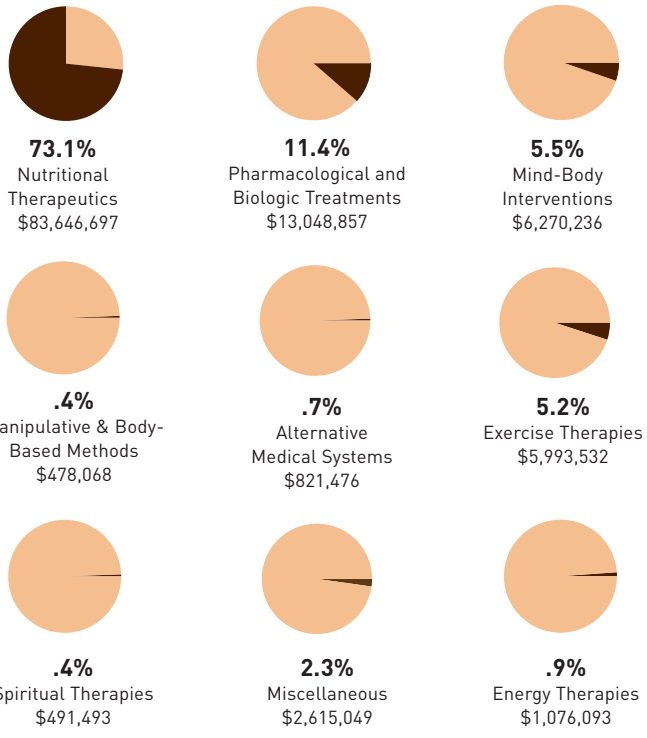
* Request for Applications (RFA).

FIGURE 6. NCI CAM RESEARCH PROJECTS BY RESEARCH TYPE*



* Includes grants, cooperative agreements, intramural projects, and contracts. Grants and cooperative agreements are only included when NCI is the primary funding agency. Excludes training grants (Ts, Fs, Ks, and R25s). Total projects include all active projects in FY 2009.

FIGURE 7. NCI CAM RESEARCH PROJECTS BY CAM CATEGORY*



BREAKDOWN BY RESEARCH TYPE

The accompanying pie-chart (Figure 6) shows the distribution of the projects by prevention, treatment, symptom/side effect management, epidemiology, and conferences. In FY 2009, 59.8% of cancer CAM-related research project funds went to various cancer prevention efforts, while treatment, symptom/side effect management, epidemiology, and conferences received 20.1%, 12.9%, 7.2%, and 0.02%, respectively.

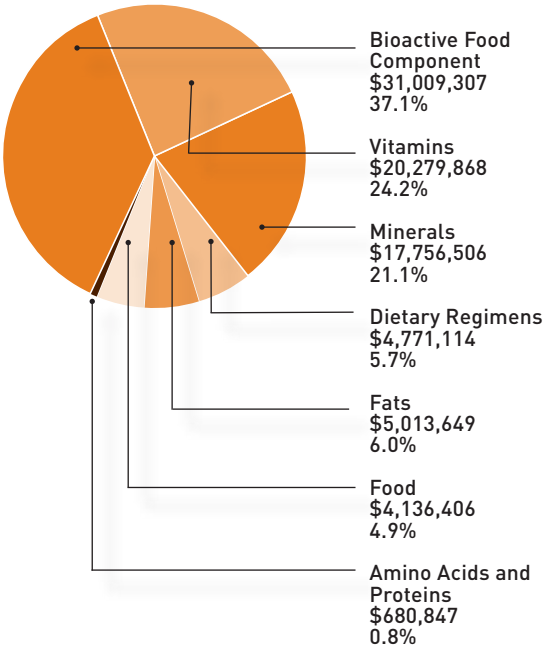
BREAKDOWN BY MAJOR CAM THERAPY CATEGORY

In FY 2009, NCI performed or supported research addressing a variety of CAM therapies (Figure 7). These CAM therapies fall into nine groups: alternative medicine systems, exercise therapies, manipulative and body-based methods, mind-body interventions, nutritional therapeutics, pharmacological and biologic treatments, energy therapies, spiritual therapies, and miscellaneous (See page 4 for definitions of CAM categories.)

The largest percentage (73.1%) of CAM research funding went to projects that investigated nutritional therapeutics, which can be further broken out into subcategories of research on: foods (e.g., broccoli and berries); minerals (e.g., calcium and selenium); vitamins (e.g., vitamins C and D); bioactive food components (e.g., isoflavones and carotenoids); dietary regimens (e.g., caloric restriction and high fruits and vegetables); fats (e.g., linoleic acid and omega-3); and amino acids and proteins (e.g., N-acetyl cysteine and glycine).

Figure 8 shows the distribution of projects by the subcategories of nutritional therapeutics.

FIGURE 8. NCI CAM NUTRITIONAL THERAPEUTICS PROJECTS BY CATEGORY*



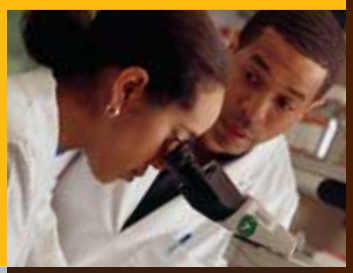
* Includes grants, cooperative agreements, intramural projects, and contracts. Grants and cooperative agreements are only included when NCI is the primary funding agency. Excludes training grants (Ts, Fs, Ks, and R25s). Total projects include all active projects in FY 2009.

FIGURE 9. NCI CAM RESEARCH PROJECTS BY CANCER TYPE*

Bladder	$1,199,673
Brain	$78,271
Breast	$16,507,760
Cervical	$1,139,517
Childhood Cancer	$255,131
Colorectal	$13,328,973
Esophageal	$1,215,134
Gastric	$1,513,176
Head and Neck	$2,734,530
Hematologic	$1,746,274
Kidney	$219,375
Liver	$994,798
Lung	$10,970,632
Multiple Types	$34,929,506
Ovarian	$325,644
Pancreatic	$2,482,683
Prostate	$21,294,607
Skin: Melanoma and Non-Melanoma	$3,460,961
Small Intestines	$44,856
TOTAL:	**$114,441,501**

* Includes grants, cooperative agreements, intramural projects, and contracts. Grants and cooperative agreements are only included when NCI is the primary funding agency. Excludes training grants (Ts, Fs, Ks, and R25s). Total projects include all active projects in FY 2008.

Highlights from NCI's Wide-Ranging CAM Research



The following research highlights are selected from the 429 CAM research projects that NCI supported during FY 2009 at laboratories within the Institute and throughout the United States and the world. These research projects are organized under several categories reflecting NCI's comprehensive research focus on understanding the underlying mechanisms of cancer causation, prevention, treatment, and symptom management and palliation of the disease.

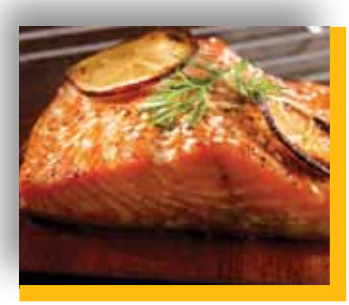
Abstracts for the CAM research projects featured in the report can be found by searching the NIH RePORTer database at http://projectreporter.nih.gov/reporter.cfm.

Understanding the Causes and Mechanisms of Cancer

Cancer is a complex set of diseases that scientists are striving to understand from multiple perspectives. Research that improves our understanding of its causes and the mechanisms that underlie its development – from assessing cancer risk to explaining the process of metastasis – is essential to our ability to develop and apply interventions to preempt cancer initiation and progression.

Pooling Resources to Examine Associations Between Vitamin D and Risk of Rarer Cancers

DIVISION OF CANCER EPIDEMIOLOGY AND GENETICS



Questions about whether vitamin D can increase or reduce the risks of certain cancer types remain vigorously debated in the scientific community. For researchers studying the effect of vitamin D on rarer types of cancer –such as pancreatic and ovarian cancer – the difficulty of teasing out the effects of the vitamin in epidemiologic studies are compounded by the relative scarcity of patients to study.

In 2007, Demetrius Albanes, M.D., senior investigator in the Nutritional Epidemiology Branch of NCI's Division of Cancer Epidemiology and Genetics, joined with a group of scientists from the United States and abroad to launch the NCI Cohort Consortium Vitamin D Pooling Project of Rarer Cancers. The project* was designed to gather data on enough patients with less common cancers to allow the researchers to more accurately estimate the associations between serum vitamin D concentrations and the development of six malignancies: pancreatic, ovarian, upper gastrointestinal (including esophagus and stomach), endometrial, renal, and non-Hodgkin lymphoma.

The project has studied over 5,000 patients diagnosed with one of these rarer cancers and over 5,000 matched control participants without cancer, taken from 10 participating cohort studies. In order to remove the variability sometimes found when blood samples are analyzed in different laboratories and at different times, samples from cancer cases and control participants from all 10 cohorts were analyzed in the same dedicated laboratory with the same equipment over a 3-month period.

In addition, "we matched the cases and controls for the calendar date of when their blood was collected and therefore for the season and approximate sun exposure at the time of collection," explained Dr. Albanes. "We also adjusted for season of collection in our statistical models." This is important, because blood levels of vitamin D are influenced by sun exposure and can vary drastically between seasons and by level of outdoor activity, making the date of blood collection an important factor to control for in such studies.

According to published results** and contrary to the researchers' expectations, "we did not see lower cancer risk in persons with high vitamin D blood concentrations compared to normal concentrations for any of these cancers, nor did we see higher cancer risk for participants with low levels," reported Dr. Albanes.

The researchers did observe an increased risk of pancreatic cancer in patients with the highest blood levels of vitamin D, a finding seen previously by some studies. "This result is a bit troubling, since people tend to believe that taking more vitamin D can only be beneficial," noted Dr. Albanes. "So this needs to be clarified, and it's one thing that we're going to follow up on in future studies."

The Vitamin D Pooling Project has also examined blood samples from their cohorts' patients at the genetic level. In another published report***, the researchers described findings from a genome-wide association study to discover common variations in several genes that are associated with circulating vitamin D levels. One of the genes identified, codes for a binding protein that transports vitamin D within the body and three other genes code for proteins that are involved in vitamin D synthesis and metabolism.

The next step for the investigators will be to look at whether these genetic variations mediate the relationship between circulating vitamin D and cancer risk. "Knowing people's genetic predisposition to higher or lower vitamin D levels should help us refine the relationship between people's actual vitamin D exposures and cancer risk," Dr. Albanes explained. "Some of the inconsistencies we've seen across vitamin D studies to date may be due to such genetic variations."

** Helzlsouer KJ for the VDPP Steering Committee. Overview of the Cohort Consortium Vitamin D Pooling Project of Rarer Cancers. *American Journal of Epidemiology,* 2010;172(1):4–9.

***Ahn J, Yu K, Stolzenberg-Solomon R, Simon KC, McCullough ML, Gallicchio L, Jacobs EJ, Ascherio A, Helzlsouer K, Jacobs KB, Li Q, Weinstein SJ, Purdue M, Virtamo J, Horst R, Wheeler W, Chanock S, Hunter DJ, Hayes RB, Kraft P, Albanes D. Genome-wide association study of circulating vitamin D levels. *Human Molecular Genetics*, 2010;19(13):2739-45.

*** PROJECT NUMBER: Z01 CP010195-04**

Large Populations and Rigorous Methods Needed for Vitamin D Research

DIVISION OF CANCER EPIDEMIOLOGY AND GENETICS

Vitamin D has been thought to potentially affect a person's cancer risk, and in laboratory studies, researchers have shown that it can decrease cancer cell growth, promote cancer cell death, and affect other cellular processes. However, studies examining the relationship between blood levels of vitamin D in humans and the risk of many types of cancer have proved largely inconclusive. "At this stage, we don't really have a clear idea if vitamin D is protective against cancer, and if so against which cancers, or at what stage in a cancer's development," explained D. Michal Freedman, J.D., M.P.H., Ph.D., an epidemiologist in NCI's Division of Cancer Epidemiology and Genetics.

Dr. Freedman and her colleagues from NCI and the Centers for Disease Control and Prevention (CDC) recently analyzed blood samples taken from over 16,000 participants in the Third National Health and Nutrition Examination Survey* (NHANES III) between 1988 and 1994. At the time of the researchers' analysis, the survey participants had been followed through 2000.

During that period, 536 NHANES III participants died of cancer. Although the researchers did not find any association between blood levels of vitamin D and total cancer mortality, they did find a reduced risk of death from colorectal cancer in participants with higher levels of circulating vitamin D. NCI and CDC investigators have continued to follow the NHANES III participants and are using additional data collected on cancer mortality. "With larger numbers, and more cancer deaths, we have opportunities to look at risks by sex, within racial and ethnic groups, and for less common cancer sites," she explained.

Another aspect of Dr. Freedman's work is focusing on how the methods of measuring vitamin D levels may affect the results of epidemiologic studies. In recent research**, she and her colleagues examined whether a delay between blood collection and processing could alter the end results for vitamin D measurement. Fortunately, they found that this was not the case and that variations in the collection process did not affect the measurements.

Currently, they are examining the degree of correlation between levels of vitamin D in blood samples taken during one season with those found in samples collected during other seasons (i.e., winter versus summer)***. "There's an assumption that a single measurement is a good surrogate for usual or long-term circulating levels of vitamin D, and a single measurement is what's been used in most studies," explained Dr. Freedman. "We want to examine this assumption, because our study could shed light on the strength of the evidence provided by the single-sample studies."

**Freedman DM, Looker AC, Chang SC, Graubard BI. Prospective study of serum vitamin D and cancer mortality in the United States. *Journal of the National Cancer Institute,* November 7, 2007;99(21):1594-602.

***Yu CL, Falk RT, Kimlin MG, Rajaraman P, Sigurdson AJ, Horst RL, Cosentino LM, Linet MS, Freedman DM. The impact of delayed blood centrifuging, choice of collection tube, and type of assay on 25-hydroxyvitamin D concentrations. *Cancer Causes and Control,* April 2010;21(4):643-8.

*** PROJECT NUMBER: Z01 CP010132-15**

Targeting Prostate Cancer Cells with Bioflavonoids

DIVISION OF CANCER BIOLOGY

Current treatments for prostate cancer – including surgery, radiation therapy, and hormone therapy – can be effective, and in some cases cure men of their cancer. However, all of these treatments can cause major side effects. Researchers are looking for additional targeted therapies for prostate cancer that will halt the growth of cancer cells while leaving normal cells largely unaffected.

The type II [3H]estradiol binding site plays an important role in regulating cell proliferation in prostate and other cancers. In normal cells, a molecule called methyl p-hydroxyphenyllactate (MeHPLA) is thought to occupy most of the type II [3H]estradiol binding sites, blocking cell-signaling pathways that encourage the cells to divide. Malignant cells, including breast and prostate cancer cells contain higher than normal levels of a type of molecule called esterase that destroys MeHPLA, thereby freeing the type II [3H] estradiol binding sites and triggering DNA synthesis and cancer cell proliferation. Thus, drugs that act like MeHPLA, but are not destroyed by this esterase, are potentially very effective anticancer agents.

Barry Markaverich, Ph.D., associate professor in the Department of Molecular and Cellular Biology at Baylor College of Medicine in Houston, Texas has been studying the type II [3H]estradiol binding sites for over 30 years. Dr. Markaverich and his colleagues discovered that MeHPLA is a metabolite of bioflavonoids – compounds commonly found in plants and thought to have potential medicinal properties, including anti-cancer effects. Bioflavonoids can be obtained in the diet by the consumption of fruits and vegetables.

His laboratory has extended this understanding to a search for natural and synthetic compounds to replace the destroyed MeHPLA in cancer cells, and thus block uncontrolled cell division. Luteolin – a bioflavonoid found in some vegetables, herbs, and other plant products consumed in the diet – is structurally similar to MeHPLA and can successfully bind to the type II [3H]estradiol binding sites.

In a recent set of experiments*, Dr. Markaverich and his colleagues used prostate cancer cell lines to better understand the effects on gene regulation of luteolin and two structurally similar synthetic compounds they designed: BMHPC and ZN-2. The researchers found that luteolin treatment significantly altered 32 important cell regulatory pathways involved in the cell cycle and RNA transcription, which may affect cancer cell growth.

With NCI funding**, Dr. Markaverich is currently examining how luteolin, BMHPC, and ZN-2 affect the epidermal growth factor signaling pathway – a cell-signaling pathway often disregulated in cancer cells. The researchers will focus particularly on an oncogene called c-fos and are planning to test the three compounds in mouse models of prostate cancer.

Since type II [3H]estradiol binding sites are found in all cells, Dr. Markaverich proposes that their compounds could be effective against hormone-dependent prostate cancers (that require the presence of hormones to grow) as well as hormone-independent versions. These types of compounds previously showed anti-tumor activity in all of the cell lines in the Human Tumor Cell Line Screen belonging to NCI's Developmental Therapeutics Program.

NCI Program Director Neeraja Sathyamoorthy Ph.D., commented, "Dr. Markaverich's group is delineating the mechanism by which dietary agents with structures resembling estrogen, inhibit the proliferation of prostate cancer cells. Their group has demonstrated that luteolin regulates gene expression by epigenetic mechanisms. Elucidating the mechanism of action of these agents could lead to the development of type II site binding compounds that inhibit the growth of prostate cancer cells. This could help identify potential strategic sites for targeted therapy."

* Shoulars K, Rodriguez MA, Thompson T, Markaverich BM. Regulation of cell cycle and RNA transcription genes identified by microarray analysis of PC-3 human prostate cancer cells treated with luteolin. *Journal of Steroid Biochemistry and Molecular Biology,* January 2010;118(1-2):41-50.

**GRANT NUMBER: 5R01CA128932-02

Traditional Chinese Mind-Body Practice Studied in Long-Term Cancer Survivors

DIVISION OF CANCER CONTROL AND POPULATION SCIENCES

Researchers are studying the traditional Chinese mind-body practice of qigong (pronounced CHEE-gong) among long-term cancer survivors in China to assess the potential benefits on their quality of life (QOL) and other health outcomes. These efforts seek to establish a strong, evidence-based foundation for the introduction and promotion of qigong to U.S. cancer survivors.

Weimo Zhu, Ph.D., a professor in the Department of Kinesiology and Community Health at the University of Illinois at Urbana-Champaign, has practiced and taught qigong for many years. His interest in the use of qigong in cancer treatment was triggered when he was a graduate student in China in 1982 and was introduced to a woman with stage III stomach cancer. After surgery and chemotherapy, her doctors "thought she had only a few months to live," Dr. Zhu recalled. As a last resort, she learned and began practicing Guo Lin Qi-Gong (GLQG), a special qigong regimen developed by a long-term uterine cancer survivor in the 1950s. He said, "She said after just three qigong practice sessions, she felt like she had more energy."

Years later in 2005, "I organized a research conference supported by the National Institutes of Health on walking for health," Dr. Zhu continued. "I found [the patient in China] not only alive, but she was very healthy and very active. So we brought her to the conference, and she did some demonstrations of qigong. Qigong got a very positive response among the participants."

Dr. Zhu returned to China to learn more about GLQG, which features unique walking (touching heels and toes) and breathing (inhale, inhale and exhale) patterns. Qigong has three general principles: 1) regulate the posture 2) regulate the breathing with a purposive pattern; and 3) regulate the mind with meditation. During the 1970s and 1980s, GLQG became widely popular in China among cancer patients and was credited as an agent in cancer remission in many cases by the Chinese government, Dr. Zhu said. With funding from NCI*, Dr. Zhu conducted a small study among 40 long-term (10 or more years) cancer survivors who had practiced GLQG since shortly after their cancer diagnoses, and he compared them with a control group of 40 long-term survivors who had not practiced qigong.

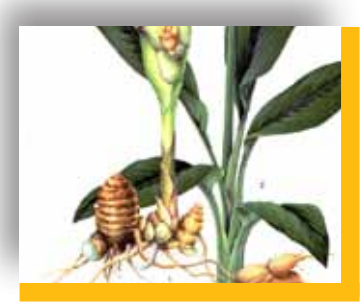
One of preliminary results they found was that "oxygen intake from GLQG practice is really not that high in absolute terms," Dr. Zhu said. "These are really just moderate kinds of physical activity," he added. "Their energy expenditure is moderate intensity, around 3 METs (metabolic equivalent). But the interesting part is, using the unique breathing patterns of qigong, their relative oxygen intake is really high for that level of activity (slow walking at a pace of about 20 meters per minute)." This "slow walking, but moderate-intensity" feature should be very appropriate for cancer patients, considering they may be weak and quick to fatigue during or after conventional treatment. Preliminary data also indicate the GLQG cancer survivors had better health status, lower pain scores, lower recurrence rates, and were less depressed than the control group cancer survivors, Dr. Zhu reported. The GLQG intervention in China is different from using exercise to help offset side effects of cancer and its treatments, as exercise is often used in western societies, Dr. Zhu added. "In China, GLQG is used as a treatment of last resort after conventional medicine and Traditional Chinese Medicine have been tried unsuccessfully."

NCI Program Director Catherine Alfano, Ph.D., commented, "Dr. Zhu's study is part of an important and novel line of research that seeks to identify which kinds of physical activities are most effective for improving health outcomes in cancer survivors suffering from specific long-term effects of cancer treatment that limit their functional ability."

*GRANT NUMBER: 5R03CA126407-02

Traditional Chinese Medicine Oil Studied Against Prostate Cancer

DIVISION OF CANCER TREATMENT AND DIAGNOSIS



Since prostate cancer is the third leading cause of cancer death in U.S. males, an army of researchers is looking for answers. One of these researchers, Yongkui Jing, Ph.D., a biologist at the Mt. Sinai School of Medicine, is doing basic research, focusing on one of the pathways long known to be important to tumor growth in prostate, lung, and other cancers. This pathway is known by the name of one of it major components, the mammalian target of the drug rapamycin or mTOR.

Dr. Jing explained that mTOR seems to act as a switch for the growth and proliferation of tumor cells. The drug rapamycin – also known as sirolimus – was originally discovered from bacteria found in the soil on Easter Island. It seems to have a lot of potential uses in cancer and other conditions and is a staple used to suppress the body's immune system during organ transplants, he added. But rapamycin, like androgen treatments for prostate cancer, can have a lot of side effects, especially in the older patients, who make up the majority of prostate cancer cases, Dr. Jing noted.

Dr. Jing was originally trained in medicine in Beijing, China, and is very familiar with traditional Chinese medicine (TCM). His current NCI-funded work* is focused on a natural product mixture known as the essential oil of Wen Ezhu, which is derived from a tumeric-root tuber plant found throughout Asia called *Curcuma wenyujin*. He and others have found that Ezhu oil targets the mTOR pathway.

"It has been used to combat viruses for a long time," explained Dr. Jing, "and for three or four decades researchers in China and the United States have been finding anti-cancer effects." Though there may be as many as 30 active components in the Ezhu oil used in TCM, his lab is concentrating on the substance curcumol to see whether it is the primary active inhibitor of mTOR. They are testing human prostate cancer cells and mice with prostate cancer for the impact of the Ezhu oil in its natural form, as compared to curcumol. They are also looking at a separate drug designed along the lines of rapamycin, to see whether it adds to the impact on cancer cells when used in combination with the oil or curcumol.

"We really need to figure out if the combination has synergistic or enhanced effects," Dr. Jing said. "Once we are confident we know which signaling pathways are involved, we might be able to use other drugs, less toxic than rapamycin, in combination with Ezhu oil."

NCI Program Director Yali Fu, Ph.D., commented, "This work is a good example of tapping into traditional knowledge on natural medicines in use alone or in combination with modern cancer biology. Active components in Ezhu oil, such as curcumol, used alone or in combination with other mTOR-signaling pathway inhibitors, could potentially reduce toxicity and increase effectiveness of prostate cancer therapy."

*GRANT NUMBER: 1R21CA-144064-01A2

Accelerating Progress in Cancer Prevention

Prevention is our first line of defense against cancer. Efforts to prevent cancer focus on understanding and modifying behaviors that increase risk, mitigating the influence of genetic and environmental risk factors, and interrupting cancer-causing processes through early medical intervention.

West African Plants Studied for Inflammation and Cancer Prevention

DIVISION OF CANCER PREVENTION

Research findings about the harmful effects of chronic inflammation on human health – plus the extensive experience with studying the effects of aspirin and other nonsteroidal anti-inflammatory drugs – have led researchers to suspect a link between chronic inflammation and cancer. In particular, cyclooxygenase (COX) enzymes were found to be turned on by the body in response to long-term inflammation and in the early signs of cancer activity. One class of drugs to reduce pain and inflammation, called COX-2 inhibitors, have shown preliminary signs of success in reducing the development of adenomas that are known to lead to colorectal cancer.

However, problems arose when the most celebrated of these drugs rofecoxib (Vioxx) was pulled off the market in 2004, because it posed an increased risk of heart attack, stroke, and gastrointestinal bleeding. A similar drug celecoxib (Celebrex) is still in use but also carries the same risks. This led Michael Wargovich, Ph.D., F.A.C.N., to wonder "if there might be natural products that would hit these same targets but hopefully without the significant side effects."

Dr. Wargovich, a professor of Cell and Molecular Pharmacology at the Medical University of South Carolina, said his interest in ethnobotany is long-standing and started during a visit to Conakry, capital of the Republic of Guinea in West Africa. An official in the Republic of Guinea's Ministry of Health provided Dr. Wargovich with a catalog of traditional African medicines. He subsequently developed a short-list of plants that practicing native healers use for pain and inflammation. Dr. Wargovich eventually returned to his laboratory with five promising West African plant extracts from the neem and baobab trees, African basil, the kinkrissi bush, and the bark of the Senegal mahogany tree.

With NCI funding*, Dr. Wargovich is studying these natural products in rigorous detail. "There are a number of important steps we need to go through, but eventually, we hope to find the active inhibitors of the pathways leading to inflammation, polyps, and colon cancer," he explained. This entails exposing cancer cells to the isolates and extracts, which Dr. Wargovich and his colleagues develop from the African plants. The researchers also test these plants for specific kinds of anticancer activity, especially COX inhibition, on colon cancer cell lines. Once the active ingredients are isolated and characterized, they hope to learn more about the mechanisms that appear to be working against cancer and test them in animal models.

If successful, the work may eventually progress to human studies, Dr. Wargovich said. "The current COX-drugs are expensive," he commented. "It would be helpful to develop an alternative that was derived from traditional medicine which could be more cheaply available as a preventive in Africa and the developing world."

NCI Division of Cancer Prevention Program Director Vernon Steele, Ph.D., M.P.H., commented, "This is a interesting and potentially very important study on West African medicinal plants to prevent cancer. These plant extracts should present a much lower toxicity profile (necessary for cancer prevention-type drugs) based on generations of use in the African people. There are currently few studies of traditional herbal medicines worldwide to prevent cancer."

*GRANT NUMBER: 7R21CA107138-03

Exercise May Boost the Immune System and Improve Cancer Vaccine Effectiveness

CENTER FOR CANCER RESEARCH

A great deal of epidemiological evidence shows that regular physical activity lowers the risk of developing certain types of cancer, especially cancers of the colon and breast. Scientists have proposed that exercise may protect against cancer by boosting the body's immunity, in particular the immune system's ability to detect cancerous cells and prevent tumor formation. But the immune system is complex; the effects of exercise on this intricate system are not well understood.

John W. Greiner, Ph.D., a staff scientist at NCI's Center for Cancer Research (CCR), is studying this question in collaboration with Connie J. Rogers, Ph.D., M.P.H., an assistant professor at Penn State University. "There's been this knowledge that regular, moderate exercise can enhance the 'innate' immune response, the part of the immune system that immediately reacts to infection," explained Dr. Greiner. "But we looked at whether voluntary exercise can influence the 'adaptive' arm of the immune system" which recognizes and remembers infectious agents such as viruses, enabling the body to quickly eliminate disease-causing organisms when infections recur. This "memory" aspect of the immune system is also responsible for the body's response to vaccines.

Dr. Greiner's research group within CCR's Laboratory of Tumor Immunology and Biology is developing vaccines against prostate and colon cancer. They are interested in ways to increase the effectiveness of anticancer vaccines, and Dr. Rogers was interested in the role voluntary exercise plays in cancer risk.

The researchers did a study* of young, healthy mice that had a propensity for exercising on running wheels. These mice served as an animal model for the effects of moderate, voluntary exercise in humans. Half of the mice in the study had access to running wheels, while the other half did not. After eight weeks, all of the mice were vaccinated with a vaccine that was known to trigger a strong response by the immune system. Dr. Greiner and his colleagues then examined multiple aspects of the immune response in the mice to see if they could build on the response to the vaccine with voluntary exercise.

They found that "in those mice that were running for eight weeks, you get a higher immune response to the vaccine," said Dr. Greiner. The most important finding, he added, "is that we were increasing the immune cells that have memory."

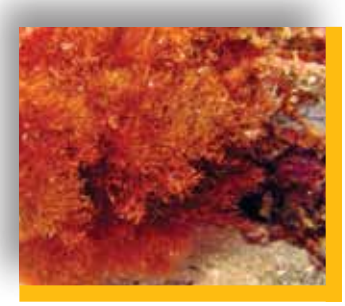
If a similar immune response to exercise occurs in humans, "there are two ways that this could impact prevention of cancer," Dr. Greiner explained. "The first is that just by exercising, you could boost your immune system without a vaccine. The second is that if you have a cancer vaccine, you might be able to increase the effectiveness of that vaccine through exercise," he added.

To investigate these possibilities, Dr. Greiner and Dr. Rogers are collaborating on follow-up studies in both mice and humans. In a strain of mice that is prone to tumors, they are examining whether voluntary exercise can increase the effectiveness of a cancer vaccine that Dr. Greiner's group has developed. He is also establishing collaboration with colleagues in NCI's Cancer Prevention Branch, who are studying whether a 10,000-step daily exercise regimen can help prevent cancer recurrence in women who have had surgery for breast cancer. In an effort to translate his findings to humans, he hopes to ask some women in the study to provide blood and tissue samples that he can analyze to see if the women's immune response has been heightened due to the exercise.

***PROJECT NUMBER: ZIA BC 010967**

Red Algae from the Sea Studied for Colon Cancer Prevention

DIVISION OF CANCER PREVENTION



Calcium is a mineral, the ionic form (Ca2+) of which moves in and out of cells and conveys important signals. It is an essential component of the diet, but calcium's direct relationship with cancer is unclear. Evidence that calcium can prevent cancer is strongest in colorectal cancer compared to other cancers, although some studies have failed to show an impact. In contrast, there is some evidence that high calcium levels might even increase the risk of prostate cancer.

James Varani, Ph.D., professor of Pathology at the University of Michigan, sees these unclear effects of calcium on cancer as an opportunity. Because calcium is instrumental in a wide range of the body's functions, figuring out how it works in different kinds of cancer cells could possibly lead to a number of useful insights, he believes. The calcium-sensing receptor (CaSR) in cells is a major avenue for calcium's ability to regulate cell growth. Some studies have shown little or no expression of CaSR in colon cancer, Dr. Varani noted. "If we could find a way to more effectively deliver calcium by upregulating CaSR, we might be able to stop a lot of the early cellular changes that we know lead to colon cancer."

NCI is funding* Dr. Varani's lab to look at a new and promising way to deliver calcium to these CaSR-deficient cells. Red algae, known as *Lithothamnion calcareum*, extracts calcium from the sea and becomes progressively calcified as it grows. "The fronds accumulate minerals very effectively and eventually become so heavy they are just an organic matrix of minerals," he explained. "Red algae can be harvested from shallow waters. It has been a 'treasure chest' for us, because more than 70 other trace minerals, in addition to calcium, have been identified."

First, "we are trying to confirm that the red algae extract is effective against colon cancer," Dr. Varani said. He and his colleagues are conducting animal studies using a xenograft model, where colon cancer cells are directly grown in mice. The researchers are feeding the mice a high-fat diet for 15 months. Some of the rodents will get either a "plain vanilla" inorganic calcium supplement, while other mice will receive the red algae extract, he explained.

"If the extract is more effective at inhibiting colon cancer and polyps," said Dr. Varani, "it opens up an interesting question: is the high calcium content in the extract getting to the right prevention targets? If so, there must be something else among the many additional trace elements in the algae that is transporting calcium into the cells, compared to the calcium the control mice are getting." Another possibility the researchers need to consider is the direct or synergistic impact of those additional minerals, especially magnesium. The experiments will also provide information about the CaSR receptor's role, if any, in red algae's impact on cancer cells.

*GRANT NUMBER: 5R21CA140760-02

Pomegranate Studied as Preventive Agent Against Prostate Cancer

DIVISION OF CANCER PREVENTION

In recent years, the pomegranate has been on the cancer biologists' research menu because of the Middle Eastern fruit's promise as an antioxidant capable of targeting multiple pathways in the cancer development process. Hasan Mukhtar, Ph.D., director and vice chair of research in Dermatology at the Medical Sciences Center, University of Wisconsin has done some of the earliest studies to isolate the active ingredients in the pomegranate that have been shown to affect a variety of cancer cells in the laboratory.

Earlier work with pomegranate in Dr. Mukhtar's lab identified six distinct anthocyanins that have some activity when exposed to cancer cell lines. Flavonoids like these give the pomegranate its color and are beginning to gain a reputation as a dietary supplement that may have beneficial effects against various diseases. "We tested all six of the compounds, but one of them – delphinidin – had distinctly more impact on these cancer cell lines than the others," he reported. Working as a biological response modifier, delphinidin showed the ability to reduce inflammation, protected healthy cells' DNA, kept blood vessels from growing that might otherwise support tumors, and limited the number of free radicals that are continuously being generated by the body, Dr. Mukhtar noted.

His current work funded by NCI* is focusing on prostate cancer. The active ingredients in pomegranate appear to affect several steps in some of the early stages of the disease. "We're literally slowing this progression of the cancer by interfering at these earlier carcinogenic stages," Dr. Mukhtar said. Prostate cancer "grows very slowly, likely for decades, before symptoms appear, typically in men older than 50, and a diagnosis is finally established," he continued. Because of this long latency period, even a modest delay in disease progression for prostate cancer could have a positive impact at the population level, reducing the number of people who develop clinical disease, he noted.

Dr. Mukhtar and his colleagues are looking at delphinidin's effect on one transcription factor in particular: NFkB. By controlling this cellular "master switch", other genes are turned on and off and can thus affect many of the molecular pathways involved in the survival of cells, he explained. "We are using a very controlled extract to look at delphinidin's impact on NFkB in human prostate cancer cells and also prostate cancer animal models in the lab."

NCI Program Director Marjorie Perloff, Ph.D., commented, "There is a major need for effective and nontoxic agents capable of preventing prostate cancer. Compounds derived from natural substances, such as the pomegranate, hold much promise for potential development as chemopreventive agents. Dr. Mukhtar's work in tissue culture and in animals to define what compounds in the fruit might be most actively involved as cancer preventive agents provides critical information that allows us to determine whether or not these compounds are suitable for further development as chemopreventive agents and specifically whether or not clinical trials should be undertaken."

*GRANT NUMBER: 5R01CA120451-04

Dietary Components May Help Colon Cancer by Targeting Inflammation

DIVISION OF CANCER PREVENTION

Inflammation sits at the intersection of modern cancer research and traditional medicine. Many of the phytochemicals found in plants used in Asian medicines have demonstrated anti-inflammatory, anti-carcinogenic effects in modern laboratories, which suggests why flavonols and certain other common plant compounds recur in the catalogs and pharmacopeias of traditional medicine across cultures and down through time.

Angela Murphy, Ph.D., research assistant professor in the Division of Applied Physiology at the University of South Carolina is trying to look more closely at how inflammation may increase the risk of colorectal cancer (CRC), and how foods or naturally occurring supplements with bioactive components linked to beneficial health effects might reduce that risk.

Dietary flavonols occur in various fruits and vegetables, but one of them quercetin – commonly found in apples, blueberries, grapes, and some vegetables – has only recently begin to draw the attention of researchers, said Dr. Murphy. "Quercetin is an exciting target to study because of its role in inflammation. We have shown some significant anti-inflammatory activity in a mouse model of CRC."

NCI funding* is helping Dr. Murphy and colleagues look deeper into the molecular details of inflammation and CRC. "We and many others have also found significant anti-inflammatory activity with curcumin," another herbal extract from the plant used to make curry in Indian dishes, she added. The researchers will explore whether these two different compounds might have an additive or even synergistic impact on the inflammatory tumor microenvironment found in CRC.

The molecular and chemical process of inflammation at tumor sites is complex, but a central actor is the macrophage, explained Dr. Murphy. Tumor-associated macrophages are mature cells that develop from monocytes, a precursor cell type circulating in the blood. A signal known as monocyte chemoattractant protein recruits these cells to a site in the body where inflammation has or could begin to develop, a process that can cause precancerous polyps to form in the colon, she said. Once there, macrophages fuel inflammation, enhancing the survival, growth and motility of cancer cells.

"We know that macrophage-induced inflammation plays an important role in the initiation and progression of CRC," Dr. Murphy noted, "and it may also be responsible for the fatigue, lack of appetite and body wasting that so compromises the quality of life in these patients. This is a cancer where nutrition and diet play an important role in causing many cases." Their work with curcumin and quercetin is designed to use diet to possibly prevent some of these cancers.

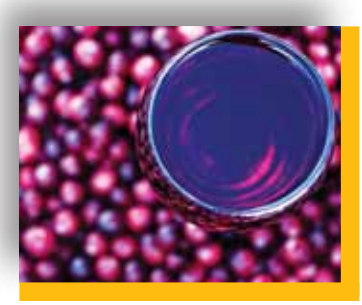
Dr. Murphy said there is already evidence that both curcumin and quercetin work independently against inflammation, however, looking at their impact in dietary combination is a new research approach. "They might be targeting different pathways and stages of the inflammatory process," she said. The researchers will test to see if using the compounds together provides a synergistic effect greater than the sum of the parts. In addition, since the impact of these phytochemicals is dependent on how much of each compound the body actually absorbs, Dr. Murphy and colleagues will also be looking to see if the combination of curcumin and quercetin allows more of either or each ingredient to convert into actively circulating material in genetically-engineered mice.

"This is a great opportunity for us to look more closely at inflammation and cancer at the cellular level," she said, "and possibly add some scientific evidence" to the already significant anecdotal and traditional heritage of two traditional plant-based medicines.

*GRANT NUMBER: 1R21CA135377-01A1

Cranberry Juice Shows Promise for the Prevention of Bladder Cancer

DIVISION OF CANCER PREVENTION



Bladder cancer researchers are interested in certain chemicals in foods or dietary supplements that naturally concentrate in the urine and pass through the bladder that may help protect against bladder tumor formation. Dietary polyphenols are of high interest in recent years because of their promising efficacy with little or no toxicity in several pre-clinical cancer models. One naturally occurring source of these compounds is cranberries.

"Cranberry fruits are rich in dietary polyphenols and it is well known that cranberry juice is helpful in treating and preventing urinary tract infections (UTIs) caused by *E. coli*," noted Jeevan K. Prasain, Ph.D., assistant professor of Pharmacology & Toxicology, University of Alabama at Birmingham. He and his colleagues have conducted previous studies* demonstrating that a commercially available cranberry juice concentrate can prevent urinary bladder cancers in chemically-induced bladder carcinogenesis in rats when compared to the control group of animals that did not receive the juice.

"Although our data suggest that the preventive efficacy of cranberries is due to the inhibition of tumor cell proliferation, at least one report has demonstrated that cranberries can impair angiogenesis (blood vessel growth in tumors) and, therefore prevent tumor growth, suggesting another possible mechanism," he explained.

With funding from NCI **, Dr. Prasain is now seeking to determine the bioavailability (i.e., absorption and retention in an unmetabolized form) of various phytochemicals present in cranberry juice, identify metabolites of these compounds, measure their concentrations in urine in the bladder of rats, and assess their ability to block bladder carcinogenesis.

A major focus is on quercetin and its glycosides, which are the major phytochemicals of cranberry juice concentrate. Their metabolism and bioavailability are complex, he noted. Although final results from the study are not expected until 2011, Dr. Prasain presented some preliminary data at the American Society of Mass Spectrometry annual conference in May 2010.

He and his colleagues are using liquid chromatography tandem mass spectrometry for profiling the constituents of cranberry. They reported that metabolites of quercetin and methyl quercetin were detected in the urine samples collected overnight after oral administration of cranberry powder to rats. "The presence of quercetin glycoside in the urine indicates that the intact glycoside may be absorbed," Dr. Prasain commented. "This report identifying cranberry metabolites in plasma and urine may explain their beneficial effects against bladder cancer."

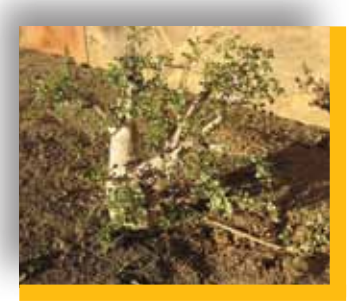
If the final results from the study show further promise, Dr. Prasain will apply for an additional grant "to expand our investigation into the mechanics of activity at the molecular level." Cranberries are "popular as a functional food and the juice is safe to drink," he added. Cranberries are also unique in the sense that they contain a mixture of many types of different natural compounds. "Because of the blending of so many different compounds, cranberries may be more effective than a single purified compound because of synergistic and additive effects," Dr. Prasain said. However, he added, the fruit "has not been very well investigated. For now, the major question is whether it is truly a preventive agent."

* Prasain JK, Jones K, Moore R, Barnes S, Leahy M, Roderick R, Juliana MM, Grubbs CJ. Effect of cranberry juice concentrate on chemically-induced urinary bladder cancers. *Oncology Reports*, June 2008;19:1565-70.

**GRANT NUMBER: 1R21CA137519-01

Ancient Medicine from India Studied to Prevent Prostate Cancer

DIVISION OF CANCER PREVENTION



Prostate cancer is a leading cause of cancer-related deaths among men in the United States. Because the disease is usually diagnosed in the sixth or seventh decades of life, this allows a large window for intervention to prevent disease progression. Clinical development of safe agents that can prevent prostate cancer could have a significant impact on morbidity and mortality for a large segment of the population.

NCI is funding a small study* on Commiphora mukul extract (CME) for prevention of prostate cancer. The Commiphora mukul plant has been used in Ayurvedic medicine practice in India for thousands of years for different ailments, noted Dong Xiao, Ph.D., research assistant professor at the University of Pittsburgh, Pennsylvania. He and his colleagues are using a standardized formulation of CME called Gugulipid GL (GL) (standardized to 3.75% z-guggulsterone, z-Gug). This and two other formulations of CME are already in human use as cholesterol-lowering agents in India.

"For the first time, we have investigated the antitumor activity of GL in human prostate cancer cells and in genetically-engineered (TRAMP) mice which is considered a close animal model for the human disease," Dr. Xiao said. In the lab, GL treatment was found to decrease the viability of human prostate cancer cells LNCaP (androgen-dependent) and its androgen-independent cells by causing apoptosis (cell death) induction at pharmacologically achievable concentrations, he reported. "Interestingly, a normal human prostate epithelial cell line is significantly more resistant to growth inhibition and apoptosis induction by GL, since apoptosis is a highly desirable feature of potential cancer preventive agents," he added.

"Most importantly," Dr. Xiao continued, "our preliminary studies showed that oral administration of GL in TRAMP mice three times per week beginning at five weeks of age for 20 weeks, significantly inhibits prostate cancer incidence and progression without causing weight loss or any other side effects."

He added, "Our next step will be to confirm these findings, using more mice. We also want to identify biomarkers of these responses to GL. These biomarkers will be very useful if GL moves on to human clinical trials."

GL is a promising compound and has significant potential in preventive applications, since it has selective anticancer activity for prostate cancer, Dr. Xiao commented. "If a standardized GL can be developed into a prostate cancer preventive agent, the public health benefit could be tremendous."

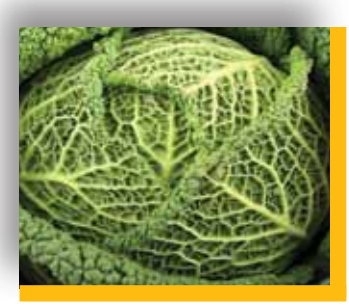
*GRANT NUMBER: 1R21CA143104-01A1

Developing Effective and Efficient Treatments

The development of more efficient and effective cancer treatments – that target cancer cells while leaving surrounding healthy tissue unharmed – is at the heart of NCI's research agenda. We strive to develop well-tolerated, individualized therapies that are tailored to specific features of a patient's cancer.

Vitamin K Studied in Treatment and Prevention of Liver Cancer

DIVISION OF CANCER BIOLOGY



Hepatocellular carcinoma (HCC), the most common type of primary liver tumor, is often found at an advanced stage and available treatments rarely offer a cure once the cancer has spread. There remains an urgent need for agents that can more effectively treat HCC or prevent liver cancer development.

Brian Carr, M.D., Ph.D., professor of medical oncology at Thomas Jefferson University's Kimmel Cancer Center, has been exploring the use of vitamin K1 (simply called vitamin K in the United States) and synthetic derivatives of the compound for the treatment of HCC for over 15 years.

He first became drawn to the potential use of vitamin K in the treatment of HCC after reading the results of studies testing biomarkers to detect liver cancer. Alpha-fetoprotein, commonly used as a biomarker for HCC, is only expressed by 50% of those tumors. In contrast, an immature form of prothrombin (a protein involved in blood coagulation), called DCP, is secreted by about 80% of HCCs.

"A known function of vitamin K in mammals is helping convert the immature protein DCP to mature prothrombin and this mechanism is broken in patients with HCC," explained Dr. Carr.

His laboratory began treating HCC cells with large doses of vitamin K. They observed that these doses restored normal prothrombin production in the cancerous cells and "the natural vitamin K, which corrected this defect, also stopped the cancer cells from growing," Dr. Carr said. He also conducted a phase I/II study* of vitamin K and found no toxicity at doses up to 1,000 mg/day.

With funding from NCI** , Dr. Carr's laboratory collaborated with synthetic chemists to develop and test several derivatives of vitamin K, the most potent of which was called compound 5 (Cpd5). Cpd5 not only stopped cancer cells from growing—a cytostatic effect—it killed them, a cytotoxic effect. This cell-killing effect was caused by over-stimulation of a cell-signaling molecule called extracellular receptor kinase (ERK), which shut down the cell-growth machinery.

Unfortunately, research in animal models showed that the effective dose and the toxic dose of Cpd5 were too close to each other, rendering Cpd5 unsuitable for human clinical trials. However, the recent development of mainstream cytostatic cancer drugs "made me realize that the paradigm we've had for the last 40 years of cancer treatment, of killing cancer cells, may be inadequate," Dr. Carr said. "Instead of looking for more and more potent compounds, which kill normal cells as well as cancer cells, maybe we need to focus on blocking selected signaling pathways in HCC cells."

The Carr laboratory recently turned back to studying natural vitamin K, this time with the cytostatic drug sorafenib (Nexavar®). In preliminary *in vitro* and *in vivo* work, the addition of vitamin K significantly enhanced the effects of sorafenib and reduced the dose required to affect cell growth in both HCC*** and pancreatic cancer****.

*Carr BI. Suppression of DCP/PIVKA-2 and alpha-fetoprotein levels in human hepatocellular carcinoma (HCC) by high doses of vitamin K1 (VK1). *Hepatology* 1996;348A.

***Wei G, Wang M, Hyslop T, Wang Z, Carr BI. Vitamin K enhancement of sorafenib-mediated HCC cell growth inhibition in vitro and in vivo. *International Journal of Cancer,* June 7, 2010;[Epub ahead of print]

****Wei G, Wang M, Carr BI. Sorafenib combined vitamin K induces apoptosis in human pancreatic cancer cell lines through RAF/MEK/ERK and c-Jun NH2-terminal kinase pathways. *Journal of Cell Physiology*,July 2010;224(1):112-9.

**GRANT NUMBER: 5R01CA082723-09

Vitamin D Studied to Treat Advanced Prostate Cancer

DIVISION OF CANCER PREVENTION

Some unanswered questions remain about the link between Vitamin D and cancer risk, which continues to be a priority research topic (see related articles on pages 41 and 42).

People primarily generate vitamin D3 when their skin is exposed to ultraviolet B radiation from the sun, explained Candace S. Johnson, Ph.D., deputy director and the Wallace Family Chair in Translational Research at the Roswell Park Cancer Institute in Buffalo, New York. Dietary vitamin D – found in eggs, fish and fortified dairy and cereal products – is usually inadequate so that people who live further from the equator and those who spend less time outdoors have higher rates of vitamin D deficiency, she added.

Dr. Johnson, and her colleague Roswell Park CEO Donald "Skip" Trump, M.D., have been pioneering ways to explore the vitamin D link to cancer risk, particularly in prostate cancer. In an earlier phase II trial*, more than 30 percent of men had their prostate-specific antigen (PSA) levels reduced by at least half, after taking a synthetic physiologically-active analog of vitamin D (1,25 dihydroxycholecalciferol) known as calcitriol. The vitamin D compound was given along with dexamethosone (one of the synthetic hormones known as glucocorticoids), which appeared to improve the impact of the drug, probably by increasing the amount of vitamin D receptor (VDR) that is expressed on most of the body's cells, including cancer cells.

In her current NCI-funded research**, Dr. Johnson and her colleagues are looking at men with castration-resistant prostate cancer whose disease has usually spread (metastasized) and is growing without restraint. "Many of them have persistent bone pain and are feeling pretty lousy," she noted. Most of these patients were originally treated with radiation or surgery, and now hormone therapy is no longer effective.

"Many of the men in our earlier trial felt better and had less bone pain after treatment with combination of calcitriol and dexamethosone," explained Dr. Johnson. "We need to know more about what is happening at the molecular level, so that we can determine how much calcitriol we can give them safely, and the best way to administer it." It turns out that blood levels of vitamin D do not simply rise when you give higher doses of calcitriol in some people. "I think that the dosing schedule may be a crucial part of the vitamin D puzzle," she said. Early results suggest the best strategy might be to give very large doses for one or a few days, followed by 4 or more days off.

So far, it seems, the more calcitriol, the greater the impact on the cancer and its symptoms, Dr. Johnson added. However, within minutes of calcitriol entering the bloodstream, the cyp24 gene is activated and starts a process that breaks down calcitriol. Dr. Johnson and her colleagues are now looking to add a third drug, ketoconazole, to the combination, with the idea that ketoconazole will turn off induction of cyp24 and thereby increase the amount of calcitriol actually getting to the prostate tumors.

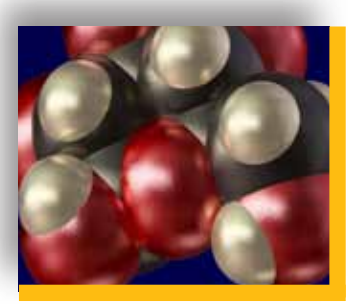
"We're looking at the whole sequence of events from every angle that we can," Dr. Johnson said. If their current phase II trial provides good information about dosing and effectiveness of calcitrol in combination with the two drugs, it may eventually lead to another treatment option in prostate and other solid tumors, she added.

* Trump DL, Potter DM, Muindi J, Brufsky A, Johnson CS. Phase II trial of high-dose, intermittent calcitriol (1,25 dihydroxyvitamin D3) and dexamethasone in androgen-independent prostate cancer. *Cancer*, May 15, 2006;106(10):2136-42.

**GRANT NUMBER: 5R01CA85142-10

Dietary Restrictions Treat Cancer as a Metabolic Disease

DIVISION OF CANCER TREATMENT AND DIAGNOSIS



In an era of targeted cancer treatment strategies, researchers try to exploit the inherent differences between normal and cancer cells. For example, patients often experience significant side effects when cell-killing (cytotoxic) chemotherapy is used because the drugs circulating through the bloodstream affect not only cancer cells but healthy cells as well. Targeted treatments such as Gleevec are designed to interfere primarily with molecules and cells that are actively involved in the cancer process but leave healthy cells alone.

Douglas Robert Spitz, Ph.D., director of the Free Radical Radiation Biology Program at the University of Iowa, thinks he may also be able to direct certain chemotherapies towards cancer cells by changes in the diet. If successful, the new strategy would allow them to deliver larger doses of these drugs more safely.

The body normally converts (metabolizes) food into energy by breaking down the glucose from carbohydrates (glycolysis). However, there is a second way that the body delivers chemical energy – in the form of adenosine triphosphate (ATP) – to its cells. Mitochondria are found in nearly every cell type in the body and because these "cellular power plants" use oxygen to create ATP, the process is known as mitochondrial respiration, Dr. Spitz explained. Researchers have known that cancer cells get their energy by increasing glycolysis, "since their mitochondrial respiration is somewhat compromised," he added. "So we asked: what if you threaten their glucose energy supply? Will they be able to compensate with mitochondrial respiration?"

In work supported by NCI*, Dr. Spitz and his colleagues are treating human cancer cells with 2-deoxyglucose (2DG), an agent that inhibits both glucose metabolism and also the cells' ability to cope with damaging oxidizing compounds known as hydroperoxides. They are finding that these glucose-starved cells are more likely to be found and killed by both radiation and chemotherapy. Compared to cells that were not treated with 2DG, both radiation and the chemotherapy drug cisplatin were more effective against human head and neck cancer cells treated with 2DG. The same was true of pancreatic cancer cells targeted with gemcitabine. The researchers will continue to refine this strategy and try to determine how best to increase the oxidative stress put on the cancer cells.

Before they can test the idea in a human trial, they also need to learn more from testing in mouse models, Dr. Spitz said. To reduce glycolysis in animals – and ultimately humans – you have to develop a diet that will safely force the body to switch its metabolism over to mitochondrial respiration. A ketogenic diet does this by essentially starving the body of carbohydrates, he explained. The dietary formulation they are testing in mice has a 10:1 ratio of fat to protein. Early results with mice on a ketogenic diet show that both radiation and cisplatin are significantly more effective at delaying tumor growth and extending survival when combined with 2DG, which can safely be given to humans as well.

"Radiotherapy and certain kinds of drugs like cisplatin kill cancer cells by increasing oxidative stress," Dr. Spitz added. "When we manipulate these cancer cells closer to the edge of survival, smaller amounts of drugs and radiation appear to have a greater impact."

NCI Program Director Suzanne Forry-Schaudies, Ph.D., commented, "Inhibiting and/or modifying cancer metabolism is an important and timely area of research. What makes Dr. Spitz's work unique is the exploration of diet modification in combination with 2-DG, chemotherapy, or radiation treatment. The rational combination of therapeutic agents is currently an area of emphasis in NCI's Division Treatment and Diagnosis."

*GRANT NUMBER 1R21CA139182-01

Exercise and Antidepressants May Counteract Stress-induced Tumor Growth

DIVISION OF CANCER CONTROL AND POPULATION SCIENCES

Higher levels of physical activity following the diagnosis of cancer have been associated with reduced rates of cancer recurrence. Physical activity has also been demonstrated to have antidepressant effects, benefiting individuals who are chronically stressed, including ovarian cancer patients.

"Because chronic stress contributes to aggressive tumor growth and results in a poor outcome for cancer patients, we predict that changes in behavior that reduce chronic stress may also slow tumor growth," said Rosemarie Schmandt, Ph.D., associate professor, Department of Gynecologic Oncology, University of Texas, M.D. Anderson Cancer Center. "We expect that the same molecular pathways activated by physical activity and antidepressants that reduce stress will also inhibit stress- mediated tumor growth."

With NCI funding*, "we're trying to understand the molecular biology that underlies the beneficial effect of physical activity for cancer patients," Dr. Schmandt explained. "That's what we're looking at now using a mouse model of ovarian cancer." Dr. Schmandt has conducted a series of studies in mice, with the first series comparing the impact of exercise on ovarian tumor growth in stressed and unstressed mice and the second study looking at the effects of the antidepressant fluoxetine on tumors in stressed and unstressed mice. In her experiments, tumors in chronically stressed animals grew to approximately twice the size as those in unstressed animals. Both exercise and the drug held ovarian tumor growth in check in the stressed animals to roughly the same size as the smaller tumors in unstressed mice, she reported.

At a molecular level, she predicts that these effects are modulated by the circuits inside the cells that are affected by brain derived neurotrophic factor (BDNF). This protein is produced in response to either antidepressant drugs or exercise and is required for antidepressant behavioral effects. Dr. Schmandt says, "We know that in cultured ovarian cancer cells, exposure to a 'mature' version of the BDNF protein activates an enzyme called AMPK, which negatively regulates cell growth. It's kind of a tumor suppressor pathway."

"The really interesting thing is that our findings support the concept of 'sound mind, sound body'," Dr. Schmandt noted.

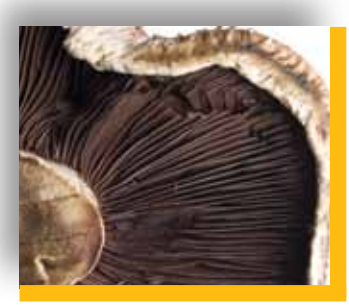
If her findings about the beneficial effects of physical activity and antidepressants in mice and cancer cell lines are eventually confirmed in human studies, it could be helpful for ovarian cancer patients. "Ideally, you'd like people to feel healthy enough after their cancer treatment to go out and begin or resume exercising," Dr. Schmandt said. "However, if a patient doesn't feel up to exercising everyday, like when they're undergoing chemotherapy, having a drug they can use to carry them through until they feel able to exercise again would be a real advantage."

For follow-up, "we're expanding our study to look at obesity which may be contributing to tumor growth in the same way that chronic stress does," she added. "Some of these studies are already underway in our lab. AMPK is known to be activated by exercise as well and by dietary restriction. We're now looking at obesity as a kind of chronic stressor."

* GRANT NUMBER 1R21CA137399-01A1

Enhancing Cancer Immunoprevention and Immunotherapy with Naturally Occurring Beta Glucans

DIVISION OF CANCER PREVENTION



Beta glucans (β-glucans) are polysaccharides – long chains of sugar molecules – found on the surface of microorganisms such as bacteria and yeast, as well as in some plants and edible fungi such as mushrooms. Natural foods containing β-glucans, including Shitake mushrooms, have been used for centuries for treating both infectious diseases and cancer in traditional Asian medicine, but with mixed success.

β-glucans are recognized as foreign by the human immune system, which targets them in a complex pathway involving the complement system, sending leukocytes (white blood cells) to destroy their microbial carriers. Until recently, researchers did not understand the complexity of the immune system reactions involved, explained Jun Yan, M.D., Ph.D., associate professor of medicine in the Tumor Immunobiology Program at the University of Louisville, Kentucky.

As research by Dr. Yan and others has now shown, the ability of β-glucans to increase the activity of leukocytes against cancer cells requires the presence of anti-tumor antibodies that activate the complement system. While the human immune system often does not recognize cancer cells in the bodies as invaders – and therefore does not produce antibodies to fight them – this discovery has important implications for the use of β-glucans as a non-toxic adjuvant for cancer-fighting monoclonal antibody treatments.

Monoclonal antibodies (mAbs) such as cetuximab, bevacizumab, and trastuzumab have improved the survival for many types of cancer. However, even the most effective mAb usually fails to eradicate all of the tumor cells in a patient. Although mAbs take advantage of part of the immune system, they often do not trigger a robust immune response in cancer patients.

By administering β-glucans along with mAbs, Dr. Yan hopes to increase the cancer cell killing effect over what would be achieved with a mAb alone by activating the complement system and triggering an innate immune response by leukocytes. Work performed by his laboratory using animal models of cancer has shown potential efficacy of this approach in several cancer types.*, **

With NCI funding***, Dr. Yan's current research is investigating additional cellular and molecular mechanisms by which yeast-derived β-glucans exert their effect on the immune system. Better knowledge of these mechanisms of action will allow more effective incorporation into immunoprevention and immunotherapy regimens for cancer.

So far, his preliminary data has identified two cellular receptors that play critical roles in the early stages of an immune reaction to β-glucans. "In addition, we've found that β-glucans can also stimulate adaptive immune responses," said Dr. Yan. The adaptive immune response, which 'remembers' previously encountered pathogens and other threats to the body, is what researchers are trying to harness to create anti-tumor vaccines. "And with any vaccine, you need an adjuvant treatment to augment efficacy," he explained.

Dr. Yan and his colleagues are currently planning a clinical trial testing an oral formulation of particulate yeast β-glucans in combination with a dendritic-cell-based tumor vaccine for non-small-cell lung adenocarcinoma.

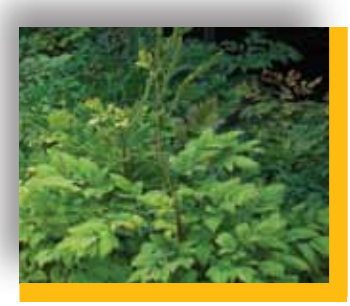
* Driscoll M, Hansen R, Ding C, Cramer DE, Yan J. Therapeutic potential of various beta-glucan sources in conjunction with anti-tumor monoclonal antibody in cancer therapy. *Cancer Biology and Therapy,* February 2009;8(3): 218-25.

** Salvador C, Li B, Hansen R, Cramer DE, Kong M, Yan J. Yeast-derived beta-glucan augments the therapeutic efficacy mediated by anti-vascular endothelial growth factor monoclonal antibody in human carcinoma xenograft models. *Clinical Cancer Research*, February 15, 2008;14(4):1239-47.

*** GRANT NUMBER: 1R01CA150947-01

Botanical Products Examined for Prevention of Endometrial Cancer From Tamoxifen Treatment

DIVISION OF CANCER PREVENTION



Tamoxifen, a drug that blocks the effects of the hormone estrogen in breast tissue, is widely used in the treatment of breast cancer in women whose tumors express the cellular receptors for estrogen. Five years of tamoxifen treatment substantially reduces the risk of breast-cancer recurrence, but the drug has several unwanted side effects, including an increased risk of endometrial cancer.

Birgit Dietz, Ph.D., research assistant professor in the Department of Medicinal Chemistry and Pharmacognosy at the University of Illinois, Chicago (UIC), is searching for natural products that could help prevent endometrial cancer in women taking tamoxifen. Her current work funded by NCI* focuses on two plants – black cohosh (Cimicifuga racemosa) and red clover (Trifolium pratense) – which are available as dietary supplements in the United States. Many women, including breast cancer survivors, use over-the-counter preparations of these herbs for the relief of menopausal symptoms such as hot flashes.

Dr. Dietz and her colleagues first started looking at interactions between black cohosh, red clover, and tamoxifen for safety reasons, since studies had not been done to determine if the herbs interfered with the beneficial effects of tamoxifen in breast tissue. They confirmed that compounds in black cohosh have no estrogen-like activity, making it unlikely that these botanical supplements interfere with the estrogen-blocking effects of tamoxifen.

"Our preliminary data have shown that both black cohosh and red clover contain antioxidative, antiproliferative, anti-inflammatory, and detoxification-enzyme-inducing compounds, which may inhibit carcinogenesis or retard the promotion and progression of precancerous cells," explained Dr. Dietz.

Their studies have since expanded from safety to chemoprevention of endometrial cancer. In collaboration with the NIH Center for Botanical Dietary Supplements Research, Dr. Dietz's laboratory has isolated specific compounds from the two herbs with antiproliferative and detoxification-enzyme-inducing properties, and the researchers are currently measuring which genes and proteins in cell proliferation pathways are affected by these compounds.

In a study presented** at the 2009 Frontiers in Cancer Prevention Research meeting, held by the American Association for Cancer Research, Dr. Dietz and her colleagues showed that black cohosh reduced tamoxifen-induced endometrial cell proliferation in a dose-dependent manner in human cell lines. Future work will use an animal model of tamoxifen-induced endometrial cancer to quantify the effect of the two botanical compounds.

"Interestingly, another research group recently revealed that black cohosh demonstrated synergistic antiproliferative effects in conjunction with tamoxifen in breast cancer cells, and another research group showed that genistein, a compound in red clover, had a similar effect," Dr. Dietz reported. "We are also planning to examine the interactions of black cohosh, red clover, and tamoxifen in breast cancer cells and tissue as part of our future work."

NCI Program Director Maria Agelli, M.D., MS, FACPM, commented, "With a well designed study, moving progressively from cell line to animal model experiments, Dr. Dietz's research will provide experimental evidence critical to assess the ability, and possible role, of black cohosh and red clover in the prevention of endometrial cancer secondary to treatment with tamoxifen."

** Dietz BM, Hagos GK, Yao P, Lantvit DD, Chen SN, Goedecke T, Farnsworth NR, Pauli GF, Bolton JL. Abstract B67: Influence of black cohosh and its isolated triterpenes on tamoxifen-induced endometrial cell proliferation. *Cancer Prevention Research*, January 7, 2010 3:B67; doi:10.1158/1940-6207.PREV-09-B67.

* GRANT NUMBER: 1R21CA135237-01A2

Improving the Quality of Life for Cancer Patients, Survivors, and their Families

Advances in our ability to detect, treat, and support cancer patients have turned this disease into one that is chronic, or readily managed, for many and curable for increasing numbers. While the ultimate goal of eliminating cancer altogether continues to be our long-term commitment, the capacity to dramatically reduce the suffering caused by cancer is within our immediate grasp.

Cranial Stimulation Tried for Managing Side Effects of Chemotherapy in Breast Cancer

DIVISION OF CANCER PREVENTION

Women being treated with chemotherapy for breast cancer often experience multiple side effects including fatigue, mild to moderate levels of anxiety and depressive symptoms, sleep disturbances, and pain. These side effects often occur together. "Conventional medications are not terribly effective for these symptoms," noted Debra Lyon, R.N., Ph.D. "Furthermore, many women with breast cancer don't want to take any extra medication, unless they absolutely have to."

With funding from NCI*, Dr. Lyon, an associate professor and chair of the Department of Family and Community Health Nursing in the School of Nursing at Virginia Commonwealth University is exploring a new, drug-free approach to relieving these symptoms. The approach – known as cranial microcurrent electrical stimulation (CES) – delivers a low-level electrical current to the head using a portable electronic device known as an Alpha-Stim, which is roughly the size of a BlackBerry device. "It was designed to be something that busy people can use in their homes," explained Dr. Lyon. In her study, women can carry the device in a pocket while they are walking around the house, doing chores, relaxing with a book, or watching TV.

Scientists do not yet understand the exact mechanism of how electrical stimulation can affect the brain, Dr. Lyon said, "but there is evidence that CES may initiate a physiological change by inducing changes in brain activity consistent with a relaxed state (as noted by EEG patterns), or by stimulating neurotransmitter or endorphin release. These physiological changes are associated with lower levels of pain and depressive and anxiety symptoms, and may also have positive effects on related symptoms of fatigue and sleep disturbances."

Starting in April 2009, Dr. Lyon and her colleagues are recruiting a total of 166 women, who are receiving chemotherapy for early-stage breast cancer, to participate in the five-year study. Half of the women will be treated with CES for one hour a day. The other half will be given a "sham" device that appears identical to the Alpha-Stim unit but does not deliver any current through the electrodes. Neither the patients nor the researchers will know which device a patient has. The electrical current used in CES is so mild that patients cannot feel it, Dr. Lyon said.

In a previous pilot study, also funded by NCI, Dr. Lyon found that women were not able to tell whether they had the actual or the sham electronic device. "Any standardized, portable, symptom-management therapy that we can use in breast cancer, and potentially in other cancers, to give patients a way to self-manage their common symptoms has potential importance for enhancing their quality of life, and also perhaps leading to their feeling like they can complete their treatment while continuing to manage multiple other daily concerns," said Dr. Lyon.

The cost of an Alpha-Stim device, which is available by prescription in the United States and runs on a 9-volt battery, ranges from $300 to $600. "While the up-front cost may be a little higher than a one-month supply of medication," noted Dr. Lyon, "over time it should be pretty cost-effective."

As part of the current study Dr. Lyon will also investigate whether CES affects the levels of several proteins in the body that play a role in inflammation, and whether there is a link between the levels of these proteins and the symptoms being studied. Dr. Lyon has found that women with breast cancer have high levels of these proteins, and previous findings by others suggest a possible link between depression and elevated levels of inflammatory proteins. "What we're thinking in this study, and in the field called psychoneuroimmunology, is that if individuals are feeling stress relief, that not only can it lead to symptom improvement, but it can also lead to stopping the biological chain reaction that promotes or enhances the level of stress," Dr. Lyon said.

*GRANT NUMBER: 5R01CA127446-02

Exercise Intervention Studied for Heart Failure in Cancer Survivors

DIVISION OF CANCER CONTROL AND POPULATION SCIENCES

One of the more serious and distressing late side effects of cancer treatment is chemotherapy-induced heart failure. Exercise training has been found to be beneficial for non-cancer patients with heart failure, as well as for cancer survivors without heart failure. Researchers are now testing exercise in cancer survivors with chemotherapy-induced heart failure.

Karen Basen-Engquist, M.P.H., Ph.D., professor of behavioral science at the University of Texas M. D. Anderson Cancer Center, is co-principal investigator (co-PI) for the study called Take Heart. "I began planning this study a few years ago with one of the cardiologists at M.D. Anderson," she recalled. The current pilot study, funded by NCI*, is a first-time collaboration between M.D. Anderson's Behavioral Science and Cardiology Departments. Dr. Basen-Engquist works closely with co-PI and cardiologist Elie Mouhayar, M.D., FACC.

Take Heart is a structured exercise intervention for patients with heart failure related to their chemotherapy. Patients in the intervention group exercise under supervision three times a week for 16 weeks, and during the last eight weeks, they also start home-based exercise. "The goal is to get the patients exercising up to 30 minutes at each session," said Dr. Basen-Engquist. "We start from wherever they are. Some come in at first and can only do a couple of minutes, rest, and then do a few more minutes, and that's it. We work on building them up from there."

The pilot study will enroll 80 patients. After baseline testing, the patients will be randomly assigned to receive either the 16-week Take Heart lifestyle intervention or usual care, Dr. Basen-Engquist added. "We'll take patients on the study once they're stabilized on medication for heart failure," she said. "One thing we'd like to learn from this study is whether it is possible to lower their drug dose if their heart failure symptoms are kept more under control with exercise. That's not something we know yet."

If results from the pilot study are promising, "we hope to move on to a larger clinical trial of Take Heart," Dr. Basen-Engquist noted. "There have been cardiac rehabilitation programs for many years. Those of us who are doing exercise research in the cancer field are really looking at the creation of cancer rehabilitation programs. There are multiple benefits from exercise for people with cancer including quality of life. This points toward incorporating more exercise programs into cancer treatment and after-care."

*GRANT NUMBER: 5R21CA135016-02

SCIENTIFIC PUBLICATIONS

This is a selected list of some of the most important peer-reviewed scientific articles about the findings and analyses of NCI-supported CAM research studies published during FY 2009. The articles are classified and grouped according to research type: cancer prevention, cancer treatment, and cancer side effect/symptom management.

Article citations marked with an asterisk (*) are studies which were featured in the *NCI's Annual Report on Complementary and Alternative Medicine: Fiscal Year 2008* which can be read and downloaded at http://www.cancer.gov/cam/attachments/fy2008_CAM_annual_report.pdf.

Abstracts of all the articles are available online through the National Library of Medicine's "PubMed" database at http://www.pubmed.com. A PubMed Identifier (PMID) number is provided for most of the citations.

Prevention

*Carman S, Kamangar F, Freedman ND, Wright ME, Dawsey SM, Dixon LB, Subar A, Schatzkin A, Abnet CC. Vitamin E intake and risk of esophageal and gastric cancers in the NIH-AARP Diet and Health Study. *International Journal of Cancer*, July 1, 2009;125(1):165-70. PMID: 19326432.

Deep G, Raina K, Singh RP, Oberlies NH, Kroll DJ, Agarwal R. Isosilibinin inhibits advanced human prostate cancer growth in athymic nude mice: comparison with silymarin and silibinin. *International Journal of Cancer*, December 15, 2008;123(12):2750-8.

*Dickinson SE, Melton TF, Olson ER, Zhang J, Saboda K, Bowden GT. Inhibition of activator protein-1 by sulforaphane involves interaction with cysteine in the cFos DNA-binding domain: implications for chemoprevention of UVB-induced skin cancer. *Cancer Research,* September 2009;69(17):7103-10. Epub 2009 Aug. 11. PMID: 19671797.

*Islami F, Malekshah AF, Kimiagar M, Pourshams A, Wakefield J, Goglani G, Rakhshani N, Nasrollahzadeh D, Salahi R, Semnani S, Saadatian-Elahi M, Abnet CC, Kamangar F, Dawsey SM, Brennan P, Boffetta P, Malekzadeh R. Patterns of food and nutrient consumption in northern Iran, a high-risk area for esophageal cancer. *Nutrition and Cancer*, 2009;61(4):475-83. PMID: 19838919.

*Lee JI, Nian H, Cooper AJ, Sinha R, Dai J, Bisson WH, Dashwood RH, Pinto JT. Alpha-keto acid metabolites of naturally occurring organoselenium compounds as inhibitors of histone deacetylase in human prostate cancer cells. *Cancer Prevention Research,* July 2009;2(7):683-93. PMID: 19584079.

Leitzmann MF, Koebnick C, Moore SC, Danforth KN, Brinton LA, Hollenbeck AR, Schatzkin A, Lacey JV. Prospective study of physical activity and the risk of ovarian cancer. *Cancer Causes and Control*, July 2009;20(5):765-73. Epub 2008 Dec. 31. PMID: 19116765.

*Mentor-Marcel RA, Bobe G, Barrett KG, Young MR, Albert PS, Bennink MR, Lanza E, Colburn NH. Inflammation-associated serum and colon markers as indicators of dietary attenuation of colon carcinogenesis in ob/ob mice. *Cancer Prevention Research,* January 2009;2(1):60-9. PMID: 19139019.

*Nian H, Bisson WH, Dashwood WM, Pinto JT, Dashwood RH. Alpha-keto acid metabolites of organoselenium compounds inhibit histone deacetylase activity in human colon cancer cells. *Carcinogenesis*, August 2009;30(8):1416-23. Epub 2009 Jun 15. PMID: 19528666.

Peters TM, Schatzkin A, Gierach GL, Moore SC, Lacey JV, Wareham NJ, Ekelund U, Hollenbeck AR, Leitzmann MF. Physical activity and postmenopausal breast cancer risk in the NIH-AARP Diet and Health study. *Cancer Epidemiology, Biomarkers and Prevention*, January 2009;18(1):289-96. PMID: 19124511.

*Qiao YL, Dawsey SM, Kamangar F, Fan JH, Abnet CC, Sun XD, Johnson LL, Gail MH, Dong ZW, Yu B, Mark SD, Taylor PR. Total and cancer mortality after supplementation with vitamins and minerals: follow-up of the Linxian General Population Nutrition Intervention Trial. *Journal of the National Cancer Institute*, April 2009;101(7):507-18. Epub 2009 Mar 24. PMID: 19318634.

*Yaxiong Tang Y, Simoneau AR, Xie J, Shahandeh B, Zi X. Effects of the Kava Chalcone Flavokawain A Differ in Bladder Cancer Cells with Wild-type versus Mutant p53. *Cancer Prevention Research,* November 2008;1(6):439-51. PMID: 19138991.

Treatment

Cohen AN, Veena MS, Srivatsan ES, Wang MB. Suppression of interleukin 6 and 8 production in head and neck cancer cells with curcumin via inhibition of Ikappa beta kinase. *Archives Of Otolaryngology-Head & Neck Surgery*, February 2009;135(2):190-7.

Shabtay A, Sharabani H, Barvish Z, Kafka M, Amichay D, Levy J, Sharoni Y, Uskokovic MR, Studzinski GP, Danilenko M. Synergistic antileukemic activity of carnosic acid-rich rosemary extract and the 19-nor Gemini vitamin D analogue in a mouse model of systemic acute myeloid leukemia. *Oncology*, 2008;75(3-4):203-14. Epub Oct. 14,2008.

Side Effect/Symptom Management

Freeman L, Cohen L, Stewart M, White R, Link J, Palmer JL, Welton D, McBride L, Hild CM. The experience of imagery as a post-treatment intervention in patients with breast cancer: program, process, and patient recommendations. *Oncology Nursing Forum*, November 2008;35(6):E116-21.

Mosher CE, Sloane R, Morey MC, Snyder DC, Cohen HJ, Miller PE, Demark-Wahnefried W. Associations between lifestyle factors and quality of life among older long-term breast, prostate, and colorectal cancer survivors. *Cancer,* September, 1 2009; 115(17):4001-9.

*Schnur JB, David D, Kangas M, Green S, Bovbjerg DH, Montgomery GH. A Randomized trial of a cognitive-behavioral therapy and hypnosis intervention on positive and negative affect during breast cancer radiotherapy. *Journal of Clinical Psychology,* April 2009; 65(4): 443–455.

Quality of Life

Mosher CE, Fuemmeler BF, Sloane R, Kraus WE, Lobach DF, Snyder DC, Demark-Wahnefried W. Change in self-efficacy partially mediates the effects of the FRESH START intervention on cancer survivors' dietary outcomes. *Psychooncology,* October, 2008; 17(10):1014-23.

APPENDIX

An NCI-sponsored clinical trial meets one or more of the following criteria: the protocol (1) has been reviewed and approved by NCI's CTEP Protocol Review Committee or by an approved NCI-designated Cancer Center Protocol Review and Monitoring System and/or (2) receives support through an NCI grant, contract, or cooperative agreement.

PDQ Clinical Trials	Primary ID	Current Status	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Pediatric Trials						
Phase III Randomized Study of Glutamic Acid in Reducing Vincristine-Related Peripheral Neurotoxicity in Young Patients Undergoing Vincristine-Containing Treatment for Wilms' Tumor, Rhabdomyosarcoma, Acute Lymphoblastic Leukemia, or Non-Hodgkin's Lymphoma	HLMCC-0402	Active	Supportive care; Treatment	3 to 20	NCI	Phase III
Phase I Study of Beta-Glucan and Monoclonal Antibody 3F8 in Patients with Metastatic Neuroblastoma	MSKCC-05073	Closed	Treatment; Biomarker/ Laboratory analysis	Any age	NCI	Phase I
Pilot Study of Educational and Promotional Materials Development for Use in Promoting Physical Activity in Community-Based After-School Programs By Multiethnic, Urban Adolescents	MSUHNS-0003669	Active	Prevention; Educational/ Counseling/Training	11 to 14	NCI	No phase specified
Randomized Study of Electroacupuncture for Treatment of Delayed Chemotherapy-Induced Nausea and Vomiting in Patients with Newly Diagnosed Pediatric Sarcoma, Neuroblastoma, Nasopharyngeal Carcinoma, Germ Cell Tumors, or Hodgkin Lymphoma	NCCAM-02-AT-0172	Active	Supportive care	5 to 35	NCCAM; NCI	No phase specified
Adult Trials						
Bladder						
Phase II Randomized Study of Neoadjuvant Polyphenon® E (Defined Green Tea Catechin Extract) in Patients with Nonmetastatic Bladder Cancer	WCCC-UWI06-8-01	Active	Treatment; Biomarker/ Laboratory analysis	18 and over	NCI	Phase II
Brain						
Phase II Randomized Study of Adjuvant Boswellia serrata and Standard Treatment Versus Standard Treatment Alone in Patients with Newly Diagnosed or Recurrent High-Grade Gliomas	CASE-CCF-7348	Active	Treatment	18 and over	NCI	Phase II

PDQ Clinical Trials	Primary ID	Current Status	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Breast						
Phase III Randomized Study of Cranial Microcurrent Electrical Stimulation in Reducing Chemotherapy-Related Symptoms in Women with Stage I-IIIA Breast Cancer Receiving Adjuvant Chemotherapy	MCV-MCC-11995	Active	Supportive care; Biomarker/ Laboratory analysis	Adult	NCI	Phase III
Phase II Randomized Study of Soy Protein in Postmenopausal Women with Breast Disease Taking Tamoxifen and Experiencing Hot Flashes	CALGB-79805	Closed	Supportive care	Postmeno-pausal (20 and over)	NCI	Phase II
Phase II Randomized Study of Three Different Programs of Paced Breathing in Women with Hot Flashes	MAYO-MC06C8	Active	Supportive care	18 and over	NCI	Phase II
Phase II Pilot Study of Magnesium Oxide in Treating Menopausal Hot Flashes in Women with Cancer	MCV-MCC-12062	Active	Supportive care	18 and over	NCI	Phase II
Phase II Randomized Study of Omega-3 Fatty Acids in Women with Newly Diagnosed Ductal Carcinoma In Situ and/or Atypical Ductal Hyperplasia	OHSU-3872	Active	Treatment; Biomarker/ Laboratory analysis	Over 21	NCI	Phase II
Phase II Randomized Study of Broccoli Sprout Extract in Women with Newly Diagnosed Ductal Carcinoma In Situ and/or Atypical Ductal Hyperplasia	OHSU-4702	Active	Treatment; Biomarker/ Laboratory analysis	Over 21	NCI	Phase II
Phase I Study of White Button Mushroom Extract in Preventing the Recurrence of Breast Cancer in Postmenopausal Women Who Are Breast Cancer Survivors	CHNMC-07213	Active	Treatment; Biomarker/ Laboratory analysis	21 and over	NCI	Phase I
Study of Support Groups for African-American Breast Cancer Survivors	CHNMC-07170	Active	Educational/Counseling/ Training; Supportive care	18 and over	NCI	No phase specified

PDQ Clinical Trials	Primary ID	Current Status	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Randomized Pilot Study of Hypnosis in Controlling Hot Flashes in Women Who Are Breast Cancer Survivors	S-WHITE-8165	Active	Supportive care	Over 18	NCI	No phase specified
Pilot Study of Pre-Operative Hypnosis to Reduce Post-Operative Pain and Anesthesia-Related Side-Effects in Women Undergoing Surgery for Breast Cancer	CHNMC-08029	Active	Supportive care	18 and over	NCI	No phase specified
Randomized Pilot Study of the Mindful Movement Program in Older Female Breast Cancer Survivors	CHNMC-08061	Closed	Supportive care	50 and over	NCI	No phase specified
Randomized Study of Hatha Yoga in Improving Physical Activity, Inflammation, Fatigue, and Distress in Female Breast Cancer Survivors	OSU-2007C0004	Active	Supportive care; Biomarker/ Laboratory analysis	21 and over	NCI	No phase specified
Randomized Study of Education with or without Exercise and Counseling in Preventing Lymphedema in Women with Stage I-III Breast Cancer Who Are Undergoing Axillary Lymph Node Dissection	CALGB-70305	Active	Supportive care; Treatment	18 and over	NCI	No phase specified
Cervix						
Phase II Randomized Study of Green Tea Extract (Polyphenon E) for the Prevention of Cervical Cancer in Patients with Human Papillomavirus (HPV) and Low-Grade Cervical Intraepithelial Neoplasia (CIN 1)	UARIZ-UAZ03-1-02	Closed	Prevention	18 and over	NCI	Phase II
Phase II Study of Folic Acid Supplementation in Women Infected with HPV-16 and Diagnosed with Grade 1 or Less Cervical Intraepithelial Neoplasia	UAB-F060511015	Active	Prevention; Biomarker/ Laboratory analysis	19 and over	NCI	Phase II
Phase I Randomized Study of Leucine-Enhanced Essential Amino Acid Supplement and/or Testosterone for Cancer-Related Cachexia in Patients with Advanced or Recurrent Cervical Carcinoma	UTMB-06073	Active	Supportive care; Biomarker/ Laboratory analysis	18 to 59	NCI	Phase I
Randomized Study of Mindfulness-Based Stress Reduction Versus General Health Education in Improving Immune Response to Human Papilloma Virus in Patients with Cervical Dysplasia	FCCC-06851	Active	Behavioral study; Educational/ Counseling/Training; Biomarker/Laboratory analysis	18 and over	NCI	No phase specified
Colon/Rectum						
Phase III Study of the Effect of Vitamin E and/or Selenium on Adenomatous Colorectal Polyps in Men Enrolled on SELECT Trial SWOG-S0000	SWOG-S0000D	Active	Natural history/Epidemiology; Prevention	50 and over	NCI	Phase III
Phase III Randomized Study of Selenium in Patients with Adenomatous Colorectal Polyps	UARIZ-00-0430-01	Active	Prevention	40 to 80	NCI	Phase III

PDQ Clinical Trials	Primary ID	Current Status	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Phase II Randomized Study of Acupuncture in Reducing Postoperative Ileus in Patients Who Have Undergone Segmental or Subtotal Colectomy for Colorectal Cancer	MSKCC-06145	Active	Supportive care	Over 18	NCI	Phase II
Phase I Study of Resveratrol in Patients with Resectable Colorectal Cancer	CCUM-TASK2B	Completed	Treatment; Biomarker/ Laboratory analysis	Over 18	NCI	Phase I
Early Phase I Randomized Study of High ?-Tocopherol Vitamin E Mixture Supplementation in Patients Undergoing Surgery for Colorectal Cancer	CINJ-120901	Active	Treatment; Biomarker/ Laboratory analysis	18 and over	NCI	Phase I
Head/Neck						
Phase II Randomized Study of Fruit and Vegetable Extracts in Patients with Stage I-IVB Head and Neck Cancer	CCCWFU-0112	Closed	Treatment	18 and over	NCI	Phase II
Phase II Randomized Chemoprevention Study of Bowman-Birk Inhibitor Concentrate in Patients with Oral Leukoplakia	UCIRVINE-UCI-98-34	Active	Treatment; Prevention; Biomarker/Laboratory analysis	18 and over	NCI	Phase II
Randomized Pilot Study of Electroacupuncture for Chronic Radiation-Induced Xerostomia in Patients with Head and Neck Cancer	MAYO-MCS285	Active	Supportive care	21 to 89	NCI	No phase specified
Hematologic						
Phase III Randomized Study of American Ginseng Extract to Prevent Respiratory Infection and Reduce Antibiotic Use in Patients with Chronic Lymphocytic Leukemia	CCCWFU-98308	Closed	Supportive care	18 and over	NCI	Phase III
Lung						
Phase III Randomized Chemoprevention Study of Selenium in Participants with Previously Resected Stage I Non-Small Cell Lung Cancer	ECOG-5597	Closed	Prevention	18 and over	NCI	Phase III
Phase II Randomized Study of Green Tea or Polyphenon E in Preventing Lung Cancer in Former Smokers with Chronic Obstructive Pulmonary Disease	UARIZ-HSC-0353	Closed	Prevention; Biomarker/ Laboratory analysis	40 to 80	NCI	Phase II
Phase I Randomized Pilot Study of Dietary Flaxseed Supplementation in Patients with Locally Advanced or Metastatic Non-Small Cell Lung Cancer Undergoing Definitive Chemoradiotherapy	UPCC-03309	Active	Treatment; Biomarker/ Laboratory analysis	18 and over	NCI	Phase I
Phase I Study of Beta-Glucan MM-10-001in Patients with Locally Advanced or Metastatic Non-Small Cell Lung Cancer	CHNMC-07243	Active	Treatment; Biomarker/Laboratory analysis	18 and over	NCI; Pharmaceutical/ Industry	Phase I

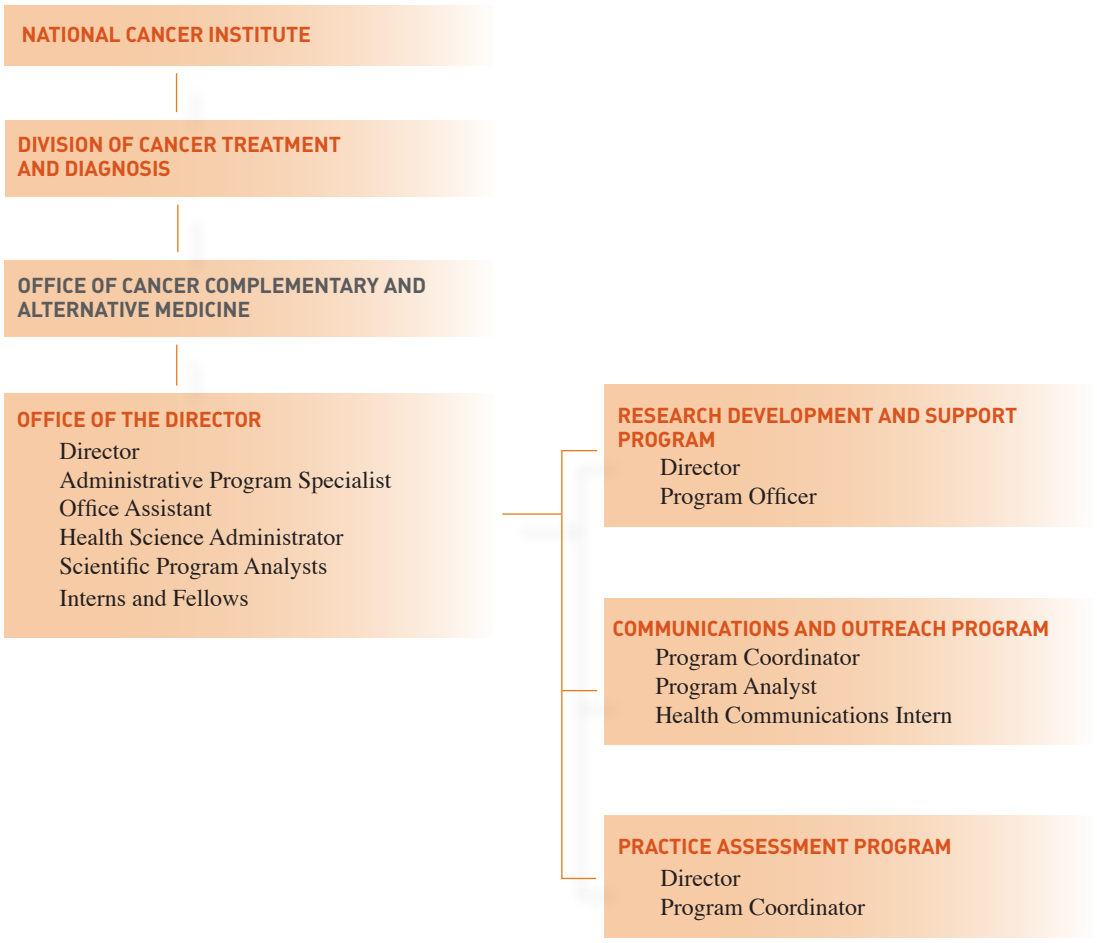
PDQ Clinical Trials	Primary ID	Current Status	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Multiple						
Pilot Randomized Study of Cognitive-Behavioral Therapy Versus Standard Care in Patients with Advanced Gastrointestinal Cancer or Lung Cancer	MGH-2007-P-000368	Active	Educational/Counseling/ Training; Supportive care	Over 18	NCI	No phase specified
Pilot Study of Restorative Yoga for Symptom Management and Stress Reduction in Women with Ovarian or Breast Cancer	CCCWFU-02403	Closed	Supportive care	18 and over	NCI	No phase specified
Non-Cancer/Healthy Volunteers						
Phase III Randomized Study of a Psychoeducation, Paced Respiration, and Relaxation Intervention for Caregivers of Patients Undergoing Bone Marrow Transplantation	UCHSC-080303	Active	Educational/Counseling/ Training; Supportive care; Biomarker/Laboratory analysis	18 and over	NCI	Phase III
Phase III Randomized Study of the Effects of Dietary Soy on Estrogens in Breast Fluid, Serum, and Urine Samples from Healthy Women	UHM-CHS-4116	Closed	Prevention; Biomarker/ Laboratory analysis	30 to 45	NCI	Phase III
Phase II Randomized Study of Defined Green Tea Catechin Extract in Former or Current Heavy Smokers with Abnormal Sputum Score	BCCA-H03-61083	Closed	Prevention; Biomarker/ Laboratory analysis	45 to 74	NCI	Phase II
Phase II Randomized Study of Polyphenon E, A Defined Green Tea Catechin Extract, in Current or Former Smokers with Bronchial Dysplasia	BCCA-H07-02401	Active	Prevention; Biomarker/ Laboratory analysis	45 to 74	NCI	Phase II
Phase II Randomized Study of Inositol for the Prevention of Lung Cancer in Current or Former Smokers with Bronchial Dysplasia	MAYO-MAY06-8-01	Active	Prevention; Biomarker/ Laboratory analysis	45 to 79	NCI	Phase II
Phase I Randomized Study of Nutritional-Grade, Absorption-Enhanced Diindolylmethane (BR-DIM) in Healthy Volunteers	KUMC-HSC-9139-3	Completed	Biomarker/Laboratory analysis; Prevention	18 to 70	NCI	Phase I
Phase I Pilot Chemoprevention Study of IH636 Grape Seed Proanthocyanidin Extract in Healthy Postmenopausal Women at High Risk of Developing Breast Cancer	CHNMC-IRB-03178	Active	Prevention	40 to 75	NCI	Phase I
Phase I Randomized Study of a New Formulation of Bowman-Birk Inhibitor Concentrate in Healthy Male Participants	UPCC-805938	Closed	Prevention; Biomarker/ Laboratory analysis	18 to 65	NCI	Phase I
Randomized Study of a Patient-Directed Lifestyle Change and Health Promotion Program Versus Usual Care in Low-Income, Uninsured Participants in Los Angeles County, California	UCLA-G-060801501A	Active	Behavioral study; Educational/ Counseling/Training; Health services research	18 and over	NCI	No phase specified

PDQ Clinical Trials	Primary ID	Current Status	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Pilot Study of Standardized Freeze-Dried Table Grape Powder on Plasma Estrogen Levels in Postmenopausal Women Participating in the Mayo Mammography Health Study	MAYO-MC0536	Active	Biomarker/Laboratory analysis; Prevention	18 and over	NCI	No phase specified
Pilot Study of Art Therapy Intervention for Caregivers of Pediatric Patients Undergoing Bone Marrow Transplantation for Cancer	CHNMC-08028	Active	Supportive care	18 and over	NCI	No phase specified
Randomized Study of Fish Oil Supplements and Green Tea Extract in Preventing Prostate Cancer in Patients Who Are at Risk for Developing Prostate Cancer	OHSU-CI-CPC-04131-LX	Active	Prevention	18 and over	NCI	No phase specified
Randomized Study of Lycopene in Preventing Prostate Cancer in Healthy Participants	UIC-2004-0217	Active	Prevention; Biomarker/Laboratory analysis	18 and over	NCI	No phase specified
Non-Specified						
Phase III Randomized Study of (Valerian) for Improving Sleep in Patients with Cancer Receiving Adjuvant Therapy	NCCTG-N01C5	Completed	Supportive care	18 and over	NCI	Phase III
Phase III Randomized Study of Levocarnitine (L-carnitine) for the Management of Fatigue in Cancer Patients	ECOG-E4Z02	Completed	Supportive care	18 and over	NCI	Phase III
Phase III Randomized Study of Alpha-Lipoic Acid in Preventing Platinum-Induced Peripheral Neuropathy in Cancer Patients Receiving a Cisplatin- or Oxaliplatin-Containing Chemotherapy Regimen	MDA-CCC-0327	Closed	Supportive care	Not specified	NCI	Phase III
Phase III Randomized Study of Vitamin E in Preventing Chemotherapy-Induced Peripheral Neuropathy in Patients Undergoing Curative Neurotoxic Chemotherapy for Cancer	NCCTG-N05C3	Closed	Supportive care	18 and over	NCI	Phase III
Phase III Randomized Study of American Ginseng (Panax quinquefolius) in Patients with Cancer-Related Fatigue	NCCTG-N07C2	Active	Supportive care	18 and over	NCI	Phase III
Phase II/III Randomized Study of Ginger for Chemotherapy-Related Nausea in Patients with Cancer	URCC-U1902	Closed	Supportive care	18 and over	NCI	Phase II; Phase III
Phase II Randomized Study of a Multimedia Program About Massage Therapy for Cancer Patients and Their Care Partners	COLLINGE-06-200	Closed	Educational/Counseling/Training; Supportive care	21 and over	NCI	Phase II
Phase II Randomized Pilot Study of Massage Therapy in Patients with Cancer Pain	MSKCC-03046A	Closed	Supportive care	18 and over	NCI	Phase II

PDQ Clinical Trials	Primary ID	Current Status	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Phase II Randomized Study of Hatha Yoga for Persistent Sleep Disturbance in Cancer Survivors	URCC-U3905	Closed	Supportive care	21 and over	NCI	Phase II
Pilot Study of Psilocybin in Patients with Clinically Significant Depression or Anxiety Secondary to Cancer	JHOC-J0647	Active	Supportive care; Biomarker/ Laboratory analysis	21 to 70	NCI	Phase II
Phase I Study of High-Selenium Brassica Juncea in Combination with Irinotecan Hydrochloride and Capecitabine in Patients with Advanced Malignancies	CHNMC-05122	Active	Treatment	18 and over	NCI	Phase I
Pilot, Randomized Study of Mindfulness Relaxation Versus Relaxing Music Versus Standard Symptom Management Education in Patients with Newly Diagnosed Solid Tumors Undergoing Chemotherapy	MDA-CCC-0106	Active	Educational/Counseling/Training; Supportive care	18 and over	NCI	No phase specified
Randomized Study of Stress Management Therapy in Patients Undergoing Chemotherapy for Cancer	MCC-0501	Active	Educational/Counseling/Training; Supportive care	18 and over	NCI	No phase specified
Randomized Study of an L-Arginine-Based Nutritional Supplement (Argin-Max®) in Female Cancer Survivors	CCCWFU-05-04-01	Active	Supportive care	Adult	NCI	No phase specified
Randomized Study of the Effect of Animal-Assisted Therapy and Recreational Therapy on Distress in Cancer Patients Undergoing Treatment for Pain	NCI-05-CC-0093	Closed	Supportive care; Biomarker/ Laboratory analysis	18 and over	NCI	No phase specified
Randomized Study of Magnetic Acupressure in Reducing Pain in Cancer Patients Undergoing Bone Marrow Aspiration and Biopsy	JHOC-J07103	Active	Supportive care; Diagnostic	18 and over	NCI	No phase specified
Ovary						
Randomized Study of Restorative Yoga in Patients Undergoing Chemotherapy for Ovarian Cancer	CCCWFU-98408	Completed	Supportive care	18 and over	NCI	No phase specified
Prostate						
Phase III Randomized Study of Selenium for Prostate Cancer Prevention	UARIZ-99-0045-01	Active	Prevention; Biomarker/ Laboratory analysis	Under 80	NCI	Phase III
Phase III Randomized Study of Soy Protein/Isoflavones and Venlafaxine on Vasomotor Symptoms in Patients with Prostate Cancer Undergoing Hormonal Manipulation	CCCWFU-97405	Active	Supportive care	21 and over	NCI	Phase III
Phase III Randomized Study of Pomegranate Extract in Patients with Rising Prostate-Specific Antigen Levels After Surgery or Radiotherapy for Localized Prostate Cancer	ROLL-GUP-0205-1	Active	Treatment	18 and over	NCI; Pharmaceutical/ Industry	Phase III

PDQ Clinical Trials	Primary ID	Current Status	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Phase II/III Randomized Study of Adjuvant Soy Protein Isolate in Preventing Recurrence in Patients Who Have Undergone Radical Prostatectomy for Stage II Prostate Cancer	UIC-2006-0706	Active	Treatment; Biomarker/ Laboratory analysis	40 to 75	NCI	Phase II; Phase III
Phase II Randomized Study of Selenium in Patients with Adenocarcinoma of the Prostate	UARIZ-97-0395	Active	Treatment; Biomarker/ Laboratory analysis	Under 85	NCI	Phase II
Phase II Randomized Study of Neoadjuvant Dietary Supplementation with Soy in Patients Undergoing Radical Prostatectomy for Localized Prostate Cancer	CCCWFU-98203	Closed	Treatment; Biomarker/ Laboratory analysis	Over 18	NCI	Phase II
Phase II Study of Neoadjuvant Oral Microencapsulated Diindolylmethane in Patients with Stage I or II Adenocarcinoma of the Prostate Undergoing Radical Prostatectomy	WSU-2007-128	Active	Treatment; Biomarker/ Laboratory analysis	18 and over	NCI	Phase II
Early Phase I Randomized Study of Vitamin E Supplementation in Patients Who Are at Risk for Prostate Cancer or Have Prostate Cancer	CINJ-120802	Active	Biomarker/Laboratory analysis; Prevention	18 and over	NCI	Phase I
Phase I/II Study of the Effects of Tomato-Soy Juice on Biomarkers of Prostate and Cardiovascular Health in Patients with Prostate Cancer Undergoing Prostatectomy	OSU-2007C0026	Active	Treatment; Biomarker/ Laboratory analysis	Any age	NCI	Phase I; Phase II
Phase I Study of Defined Green Tea Catechin Extract in Patients with Prostate Cancer Scheduled to Undergo Prostatectomy	UARIZ-UAZ05-6-01	Active	Treatment; Biomarker/ Laboratory analysis	18 and over	NCI	Phase I
Phase I Study of White Button Mushroom Extract at Six Different Dose Levels in Patients with Biochemically Recurrent, Hormone-Naive Prostate Cancer After Local Therapy	CHNMC-08012	Active	Treatment; Biomarker/ Laboratory analysis	Not specified	NCI	Phase I

OCCAM ORGANIZATIONAL CHART



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NIH Publication No. 11-7646
Printed February 2011