Sample Projects 2018

Susan Ackerman, PhD

Summer Lab Size: 15

Local Summer Program: http://grad.ucsd.edu/degrees/summer-researches/stars/schedule.html
Program Dates: June 25-August 18, 2017 (Note:10 weeks will be required)

University of California - San Diego

Genetics, Neuroscience

Identification of Novel Mutations That Cause Neurodegeneration

Many of our lab's projects involve a phenotype-driven approach to identifying genes involved in cerebellar function. This approach allows the identification of pathways without a priori assumptions. We have identified a new mouse mutant with late-onset degeneration of specific cerebellar neurons that results in a loss of motor coordination or ataxia. We have genetically mapped this gene to a small region of chromosome 3. This project will focus on the identification of the underlying mutation in this mutant strain by molecular analysis of genes residing within the genetic interval. In addition, the student will perform additional pathological analysis of mutant brains. The student will have an opportunity to learn bioinformatic approaches to prioritize candidate genes, isolation of RNA, RT-PCR, Northern blot, and sequence analysis techniques. In addition, students will learn histological and immunohistological techniques and neuroanatomical analysis.

Paul Ahlquist, PhD

Summer Lab Size: 15

Local Summer Program: http://biology.wisc.edu/Undergraduates-GettingInvolvedBeyondtheClassroom-UndergraduateResearch-IntergratedBiologicalSciencesSummerResearchProgram.htm

Program Dates: May 30-August 5, 2017 (Note:10 weeks will be required)

University of Wisconsin-Madison

Microbiology, Molecular Biology

Viral RNA Replication Complex Structure and Molecular Genetics

Most viruses store and replicate their genomes as RNA, not DNA. To understand and control such RNA replication and the responsible viruses, we are using molecular genetics, biochemistry and structural biology. Our nanoscale imaging of an advanced model system by cryo-electron microscopy (Ertel et al. 2017 eLife 6:e25940) shows that RNA replication occurs in virus-induced, membrane-bounded mini-organelles that protect the viral dsRNA templates and organize replication steps. Viral replication proteins, including the RNA-dependent RNA polymerase and other essential factors, are organized in a striking 12-fold symmetric multimer crowning the cytoplasmic gate of the vesicular RNA replication compartment. Our ongoing studies are revealing the viral protein-protein, protein-RNA and protein-membrane interactions that direct assembly, structure and function of these remarkable RNA replication complexes, the unexpected roles of many host proteins, and other results with dramatic implications for viral function, evolution, and control.

David Anderson, PhD

Summer Lab Size:

Local Summer Program: http://www.surf.caltech.edu/
Program Dates: June 14-August 16, 2017 (Note:10 weeks will be required)

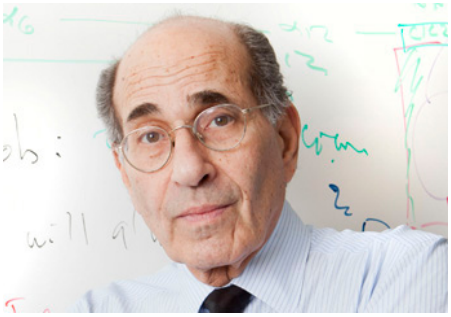
California Institute of Technology

Genetics, Neuroscience

Understanding the Neurobiology of Emotion

Research in the Anderson laboratory is aimed at understanding the neurobiology of emotion. We seek to elucidate how fundamental properties common to emotional states, such as arousal, are encoded in the circuitry and chemistry of the brain and how these internal states combine with sensory stimuli to elicit specific emotional behaviors, such as fear and anxiety or aggression. Our work employs molecular genetic tools to mark, map, and manipulate specific circuits to determine how identifiable populations of neurons contribute in a causal manner to behavior. These studies are complemented by the use of electrophysiology and functional imaging to measure activity in neural circuits. We use mice and the fruit fly Drosophila melanogaster as model organisms, with roughly equal emphasis on each.

Richard Axel, MD



Summer Lab Size: 34

Local Summer Program: http://www.spurs.columbia.edu/index.html
Program Dates: June 19-August 18, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Columbia University

Neuroscience

Representations of Olfactory Information in the Brain

Richard Axel's laboratory is interested in the representation of olfactory information in the brain and the neural mechanisms that translate these representations into appropriate innate and learned behavioral responses. A randomly distributed population of sensory neurons in the olfactory epithelium is consolidated into a discrete stereotyped map of neural activity in the olfactory bulb. Stereotyped projections from the olfactory bulb to the cortical amygdala mediate innate aversive and appetitive behavioral responses to odors. Distributed, unstructured projections to the piriform cortex implicate this cortical structure as a mediator of learned olfactory behavior. Random input to pyramidal neurons of the cortex allows the organism to contextualize a rich diversity of novel sensory experiences, a feature consistent with the role of this brain center in mediating learned olfactory associations and behavior. We are interested in how valence is imposed on these representations in cortex to elicit appropriate behavioral responses.

Michel Bagnat, PhD

Summer Lab Size: 8

Local Summer Program: http://gradschool.duke.edu/student-life/diversity/diversity-programs-and-events/duke-summer-research-opportunity-program

Program Dates: May 29-August 4, 2018 (Note:10 weeks will be required)

Duke University

Developmental Biology, Cell Biology

Organism-wide nutrient sensing by a specialized population of enterocytes

This project investigate the role of a conserved and specialized population of intestinal cells we call Lysosome Rich Enterocytes (LREs) in organism-wide nutrient sensing. We found that LREs are critical for protein uptake and utilization in early intestine and obtained evidence supporting a role for these cells in nutrient sensing. Using zebrafish as a main model system and state-of-the-art live imaging and genetics we will investigate how nutrient sensing in LREs regulates whole body energy and nutritional homeostasis. We will then extend some our findings to mouse models.

David Baker, PhD

University of Washington

Biochemistry, Computational Biology

Summer Lab Size: 24

Local Summer Program: http://www.washington.edu/research/urp/amgen/

Program Dates: June 19-August 18, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

De Novo Design of Inhibitors of Protein-Protein Interactions

Protein-protein interactions play critical roles in biology both inside and outside cells. However it is currently difficult to probe the importance of specific intracellular protein-protein interactions at a particular developmental stage and location, or in a particular cell type. Few protein-protein interfaces can be disrupted with small molecules, and even where available, it is very difficult to deliver small molecules to specific tissues. Extracellular protein-protein interactions can be probed using antibodies that disrupt the interface by competition, but it is difficult to deliver antibodies inside cells. Whole proteins can be eliminated by gene knockouts, but this does not allow interrogation of the importance of individual interactions made by one domain in a modular multidomain protein. This project will use the Rosetta protein design methodology to arrive at de novo designed protein inhibitors of protein-protein interactions.

Emily Balskus, PhD

Summer Lab Size: 25
Local Summer Program: No URL available
Program Dates: June 5-August 11, 2017 (Dates for 2018 should be similar**;** Note:10 weeks will be required)

Harvard University
Chemical Biology, Microbiology

Understanding xenobiotic metabolism by the human gut microbiota

The human gut microbiota plays an important role in processing ingested small molecules, including dietary components, drugs, and industrial chemicals. Chemical transformations carried out by these organisms can alter the bioavailability, bioactivity, and toxicity of these compounds. However, we do not yet understand the details of this microbial chemistry. This project will seek to discover and characterize genes and enzymes used by human gut bacteria to metabolize important drugs and dietary nutrients. The techniques used will include bioinformatics, anaerobic microbial cultivation, molecular biology, protein expression, and in vitro biochemical assays.

James Bardwell, PhD

Summer Lab Size:

Local Summer Program: http://www.rackham.umich.edu/current-students/programming/srop
Program Dates: May 31-July 28, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

University of Michigan
Biochemistry, Genetics

Chaperone Discovery 1

Human diseases that involve defects in protein folding include Alzheimer's disease, cystic fibrosis, and type 2 diabetes. Chaperones constitute the major cellular defense against protein-folding stress, thus they play important roles in the development and progress of these diseases. We have devised a genetic selection that enables chaperone discovery by giving bacteria the stark choice between death and stabilizing poorly folded proteins. The bacteria respond to this selection by enhancing the expression of several distinct proteins. The expression of these folding helper proteins enables the bacteria to substantially increase the level of the unstable proteins and therefore live. This project will involve the genetic and biochemical characterization of these helper proteins. Many when purified turn out to be effective in vitro as molecular chaperones, which help prevent the aggregation of proteins and aid in protein refolding. Optimizing protein folding in the cell will thus lead to the uncovering of several previously uncharacterized chaperones.

Chaperone Discovery 2

Surprisingly little information is available about how chaperones and substrates interact or what exactly it is that chaperones do to affect the folding of their substrate proteins. This project will continue our fruitful investigation of the function and mechanism of a newly discovered chaperone called Spy, in part because its biophysical properties have proven it to be uniquely suited for examining the basic principles of chaperone action. These studies will enable us to understand how Spy binds proteins and how it facilitates protein refolding in unprecedented detail. These studies will significantly enhance our understanding of protein chaperone function and protein-folding mechanisms.

Bonnie Bartel, PhD

Summer Lab Size: 1 postdoc, 5 grad students, 7 undergrads

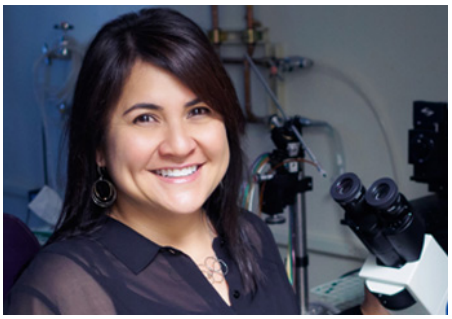
Local Summer Program: http://www.bcm.edu/smart/
Program Dates: May 29-July 27, 2018 (Note:10 weeks will be required)

Rice University
Cell Biology, Plant Biology

Characterization of Arabidopsis Peroxisomes: Biogenesis, Function, and Dynamics

Peroxisomes are single membrane-bound organelles that compartmentalize certain metabolic reactions critical to human and plant development. All proteins functioning in the peroxisome must be synthesized in the cytosol and imported post-translationally. We are studying peroxisomal processes in the reference plant Arabidopsis thaliana, including the import of matrix proteins from the cytosol into the organelle matrix and the degradation of proteins that become damaged or obsolete after arrival in the peroxisome. Peroxisomal import depends on more than a dozen peroxin proteins that bring proteins bearing peroxisome-targeting sequences into the organelle. We use forward, reverse, and chemical genetic approaches to probe functions of various peroxins, and we are using these tools to elucidate the mechanisms and importance of peroxisome biogenesis and function during plant development. The student will characterize Arabidopsis peroxin mutants isolated through forward and reverse genetic screens in physiological (measuring growth responses) and biochemical (Western blotting) assays. The interactions between mutant and wild-type peroxin derivatives will be characterized using yeast two-hybrid assays, overexpression studies, and double-mutant analyses. In humans, deficiencies in peroxins underlie the peroxisomal biogenesis disorders, which are frequently lethal in early infancy. Successful completion of these experiments will advance our understanding of peroxisome biogenesis and metabolism in a genetically distinct model system, enabling the continued refinement of our understanding of these essential organelles.

Diana Bautista, PhD



Summer Lab Size:
Local Summer Program: No URL Available
Program Dates: May 30-July 28, 2018

University of California, Berkeley

Physiology, Neuroscience

Dissecting the molecular and cellular mechanisms underlying itch and pain

My lab at UC Berkeley studies the molecular and cellular mechanisms underlying the sensations of itch, touch and pain. I am also a co-director for the Neurobiology Summer Course at the Marine Biology Lab in Woods Hole, MA. This is an intensive and comprehensive laboratory-oriented course in cellular and molecular neurobiology. The goal of this course is to emphasize the strengths of a multidisciplinary approach for studying the function of the nervous system at the cellular and molecular levels, and consists of daily lectures as well as hands on training in diverse techniques. (http://www.mbl.edu/education/courses/neurobiology/). An EXROP summer student will join me, and several members of my lab, at the MBL, May 30-July 28. In addition to participating in many aspects of the course (daily lectures, seminars, technical workshops, etc.) our summer student will also work on a team project aimed at understanding the molecular changes that occur in the nervous system under disease conditions. This will involve learning to perform neuronal cultures, quantitative live-cell imaging, genomics and bioinformatics.

Stephen P. Bell, PhD

Summer Lab Size: 13
Local Summer Program: https://biology.mit.edu/outreach_initiatives/UG_summer_internship
Program Dates: June 4-August 12, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Massachusetts Institute of Technology
Biochemistry, Molecular Biology

Identification and Characterization of Nanobodies that Inhibit DNA Replication

The events of eukaryotic DNA replication involve the carefully choreographed assembly of dozens of proteins into a pair of DNA replication machines at each origin of replication. We are interested in the molecular interactions that lead to the appropriate assembly of these machines and how they are regulated during the cell division cycle. This project will involve isolating nanobodies (~17 kd single chain antibodies derived from Alpaca) that recognize specific DNA replication proteins and identify the subset of these nanobodies that inhibit DNA replication using genetic screens. These nanobodies will then be characterized to determine the step in DNA replication that they inhibit using in vitro DNA replication assays that recapitulate the events of DNA replication using only purified proteins.

Hugo Bellen, DVM, PhD

Summer Lab Size: 32

Local Summer Program: http://www.bcm.edu/smart/
Program Dates: May 29-July 27, 2018 (Note:10 weeks will be required)

Baylor College of Medicine

Genetics, Neuroscience

The Life and Death of a Neuron

How neurons acquire their identity, how they communicate with each other, and ultimately, how they die are the key research areas in my lab. We designed genetic screens to identify novel genes that affect these processes in fruit flies. Hence, our research allows us to increase the understanding of human neurodegenerative diseases such as ALS, Parkinson's disease, Friedreich's ataxia, Leigh syndrome, and many others. A recent screen of the X chromosome (Yamamoto et al., 2014, Cell; Haelterman et al., 2014, Genome Research) allowed us to isolate components that affect neuronal development and function, as well as neuronal survival. We have mapped more than 165 new genes and are studying the phenotypes associated with the loss of many of these genes in much more detail, using electrophysiology, transmission electron microscopy, immunohistochemistry, cell biology techniques, and sophisticated genetic manipulations. For examples see Sandoval et al., 2014, PloS Biology; Liu et al., 2015, Cell; Jaiswal et al., 2015, PloS Biology. The challenge is to unravel the molecular and cellular mechanisms by which the phenotypes arise and how they affect neurodegeneration. Applicants are welcome to work on any aspect of this research, which includes the characterization of cell biology phenotypes associated with the loss of a gene, the tagging of genes, assessing the expression of gene/proteins, generating antibodies against the proteins, integrating human cDNAs in the flies to rescue the mutant fly homologs, etc.

Sue Biggins, PhD

Summer Lab Size:

Local Summer Program: http://www.fhcrc.org/en/education-training/undergraduate-students.html
Program Dates: June 11-August 10, 2018 (Note:10 weeks will be required)

Fred Hutchinson Cancer Research Center

Cell Biology, Biochemistry

The effects of cancer mutations on kinetochore function

Duplication and equal segregation of genetic material is essential for the development and survival of all organisms. In eukaryotes, including yeast and humans, cell division relies on multiple regulatory mechanisms to ensure high-fidelity transmission of chromosomes. The first step during the mitotic process is to form a physical linkage between spindle microtubules and chromosomes. The kinetochore serves both as this connection and as a catalytic signaling platform that prevents mitotic exit until every single kinetochore is appropriately attached to microtubules. Errors in mitosis and thus chromosome segregation have profound effects on human disease, particularly in cancers. The loss or gain of whole chromosomes contributes to the initiation and evolution of cancer cells, thus tumors often contain mutations in kinetochore proteins. Genetic mutations observed in cancer are detected within the linear structure of DNA; however, the proteins encoded by DNA are folded into complex three-dimensional structures. Thus mutations occurring at distant regions of DNA sequence can actually affect the same structural region within a protein. We propose a summer project combining public databases of cancer mutations with high-resolution structural data. Mapping documented mutations in three-dimensional space will allow us to identify important functional regions within kinetochore proteins. Moreover, advances in computational protein folding algorithms allow us to model these same mutations into both yeast and human proteins. In this way we can utilize both human and yeast systems to better understand how cancer alters chromosome segregation. This project will include aspects of bioinformatics and computational biology that can be validated using biochemistry and cell biology according to a student's interests.

Günter Blobel, MD, PhD

Summer Lab Size: 14-15

Local Summer Program: http://www.rockefeller.edu/surf/
Program Dates: June 4-August 10, 2018 (Note:10 weeks will be required)

The Rockefeller University
Cell Biology, Structural Biology

Assembly and Structure of the Nuclear Pore Complex

The nuclear pore complex (NPC) is a massive (120 megadaltons [MDa] in vertebrates) supramolecular assembly composed of ~30 different proteins (nucleoporins or nups) that are organized into several subcomplexes. Because of its high symmetry, the NPC contains multiple copies of each subcomplex, thus accounting for ~1,000 protein molecules in the vertebrate NPC. As the sole mediator of macromolecular transport across the nuclear envelope, the NPC plays a pivotal role in cellular physiology, which becomes evident in many oncogenic and developmental defects caused by nut mutations. Although the basics of NPC architecture have been known for decades, its detailed structure has largely remained elusive, primarily as a result of heterogeneity of isolated, purified NPCs. Therefore, our research group has embarked on an alternative approach, which ultimately aims to build up the NPC from single components to arrive at a well-defined state. Because the assembly of the entire NPC is a formidable task, we have thus far focused on the structural and functional characterization of various subcomplexes, including the yeast heptameric Nup84 complex, which is a key building block of the NPC. Our crystallographic studies suggest that multiple copies of this subcomplex cluster in a specific way, forming a coat for the nuclear pore membrane. We are also working on the central channel subclomplex composed of the three nucleoporins, p62, Nup54, and Nup58. Our structural and biophysical data have elucidated a novel stoichiometry for this subcomplex nups and led us to postulate the “ring cycle” hypothesis where sliding of alpha helical segments of these nups allows for large diameter changes in the central channel coupled to karyopherin occupancy of their FG-repeat domains. We expect our data to provide profound insights into the principles of NPC assembly, structure, and function and hence contribute to a better understanding of NPC-related diseases. Students will be exposed to various stages of the pipeline from gene to a 3D protein structure, including recombinant protein expression in bacteria, protein purification, biochemical analysis, cryo-electron microscopy, crystallization, and structure determination.

Jesse Bloom, PhD

Summer Lab Size: 14

Local Summer Program: http://www.fhcrc.org/en/education-training/undergraduate-students.html
Program Dates: June 11-August 10, 2018 (Note:10 weeks will be required)

Fred Hutchinson Cancer Research Center

Evolutionary Biology, Virology

Mapping evolutionary pathways of viral antibody escape

This project will use a combination of experimental and computational approaches to map mutations that enable influenza virus to escape from antibody-based immunity. We encourage applicants with interest or training in either computational or experimental work. The experimental work would focus on using deep-sequencing to map all mutations that affect virus-antibody interactions, and experimental virology to validate the effects of the mutations. The computational work would involve writing computer programs to visualize the experimental results and relate them to virus evolution in nature.

Dan Bolnick, PhD

Summer Lab Size: 10

Local Summer Program: http://ugs.utexas.edu/our/find/srsp
Program Dates: May 31-August 4, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

University of Texas at Austin

Cell Biology, Microbiology, Immunology

Genetic Basis of Adaptation to Divergent Parasite Communities

Natural populations harbor diverse sets of macroparasites such as helminths. When parasite communities differ between host populations (e.g., between different lakes containing stickleback fish), the host populations may evolve divergent immunological responses to their different parasites. We can take advantage of that evolutionary response to understand the genetic basis of adaptation to parasites. The EXROP student will participate in both field and laboratory work. The main goal is to experimentally evaluate how immune response and parasite load depend on the interaction between genes and environment. The work can entail either field research collecting specimens from natural populations, including canoeing and possibly snorkeling in lakes in British Columbia, as well as laboratory work, or laboratory work alone at the University of Texas at Austin. The laboratory work includes DNA and RNA extraction, genotyping, and flow cytometry as well as experimental infection assays. Participants may also work with computational analysis of next generation sequence data or flow cytometry data. For computational work, prior experience with UNIX, PERL, PYTHON, or R is required. For field research and molecular genetics or immunological work, training in essential skills can be provided, though prior experience is helpful.

Squire Booker, PhD

Summer Lab Size: 13 (two undergraduates included)

Local Summer Program: TBD
Program Dates: May 24-August 3, 2018 (Note:10 weeks will be required)

Pennsylvania State University
Biochemistry, Chemical Biology

Functional annotation and characterization of enzymes within the radical S-adenosylmethionine superfamily

Enzymes within the radical S-adenosylmethionine (SAM) superfamily catalyze a dazzling array of chemical transformations that proceed via free radical intermediates. Common to these enzymes is a potent 5'-deoxyadenosyl 5'-radical that is generated via a reductive cleavage of SAM using a required iron-sulfur (Fe/S) cluster cofactor. Radical SAM (RS) enzymes use this radical to initiate catalysis by abstracting hydrogen atoms from their respective substrates. To date, ~114,000 individual sequences of RS enzymes have been identified using bioinformatics methods, but the functions of greater than 50% of them are unknown. Moreover, with advances in sequencing of microbial genomes, the number of sequences is growing at a fast pace. This project will focus on developing methods to annotate the functions of RS enzymes catalyzing unknown reactions. Students will learn how to generate sequence similarity and genome neighborhood networks to provide insight into function via bioinformatics methods. They will also learn molecular biological techniques, such as cloning and site-directed mutagenesis and gene expression. Lastly, they will be learn how to purify and manipulate these oxygen-sensitive proteins under anaerobic conditions and characterize them spectroscopically, using UV-vis, electron paramagnetic resonance (EPR), and M_ssbauer spectroscopies; biochemically, using mass spectrometry based enzymes assays; and structurally by X-ray crystallography.

Michael Brainard, PhD

Summer Lab Size:

Local Summer Program: http://graduate.ucsf.edu/srtp
Program Dates: May 30-August 2, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

University of California - San Francisco

Neuroscience

Genetic Contributions to Individual Differences in Vocal Learning

While our prior work has described general features and mechanisms that characterize song learning, we have noted that there is striking variation across individuals in the quality of learning. Such behavioral differences provide a powerful starting point for investigating why the capacities for learning, and other complex phenotypes, differ across individuals and across the lifespan. This has motivated design of experiments that are intended to address how individual differences arise in the capacity for learning, and in the developmental regulation of learning.

Our approach is to precisely quantify phenotypic differences across individuals in song structure and song learning and to correlate these with underlying genetic differences. To accentuate phenotypic variation, we have generated a hybrid population by cross-breeding distinct species of finches. This population exhibits significant heritable variation in song phenotypes, as well as other complex traits (such as plumage). To understand the underlying basis of this variation we use high-throughput sequencing to generate genetic markers for parental strains to map genetic determinants of different phenotypes. The project will involve quantitative behavioral analysis to characterize differences in quality of song and song learning and other phenotypes across individuals, high throughput sequencing, and computational analysis to determine heritability of traits as well as potential linkage of genetic loci to traits of interest.

Axel Brunger, PhD

Stanford University
Neuroscience, Structural Biology

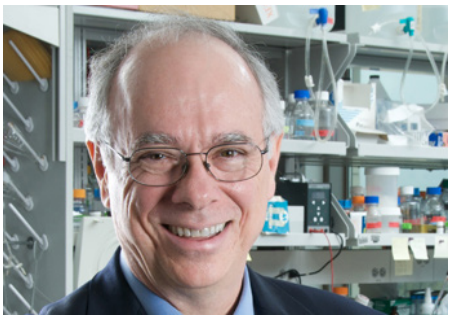
Summer Lab Size:

Local Summer Program: http://ssrp.stanford.edu/
Program Dates: June 23-August 25, 2018 (Note:10 weeks will be required)

Studies of the molecular mechanism of neurotransmitter release

My laboratory conducts studies of the molecular mechanisms of neurotransmitter release using structural and biophysical tools in reconstituted systems. There are opportunities to collaborate with postdocs and graduate students in my laboratory on a variety of projects. Prior experience with biochemistry and/or molecular biology would be desirable.

Kevin Campbell, PhD



Summer Lab Size:

Local Summer Program: No URL available
Program Dates: TBD (Note:10 weeks will be required)

University of Iowa

Biochemistry, Medicine and Translational Research

Gene transfer studies to treat muscular dystrophy in mice

No project description available. Please visit Dr. Campbell's HHMI scientist page for more information about current research.

Thomas Cech, PhD

Summer Lab Size: 19

Local Summer Program: http://www.colorado.edu/GraduateSchool/DiversityInitiative/undergrads/smart/index.html
Program Dates: June 5-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

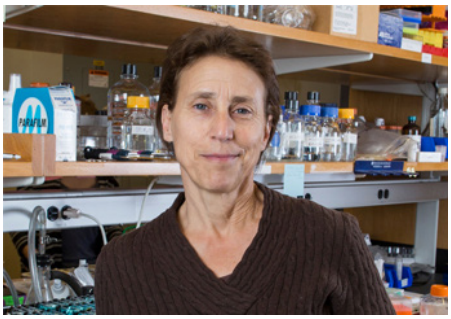
University of Colorado Boulder

Biochemistry, Structural Biology

Studies on Telomerase and Other Noncoding RNPs

Telomerase is an enzyme responsible for the replication of telomeric DNA repeats that protect and stabilize the ends of human chromosomes by preventing degradation, end-to-end chromosomal fusions, and chromosomal rearrangements. It is a ribonucleoprotein (RNP), composed of essential protein (TERT) and noncoding RNA (TR) subunits. Telomerase activation occurs in approximately 90 percent of cancer cells, while telomerase insufficiency has been associated with several diseases, including aplastic anemia. The Cech Lab is using biochemistry, cell biology, and CRISPR-Cas9 genome editing to study the activation and function of telomerase in human cancer cells. The lab is also using similar techniques to study other long noncoding RNAs and their protein partners. A key system is Polycomb Repressive Complex 2, a histone methyltransferase that modifies histone H3 protein, leading to epigenetic gene silencing.

Connie Cepko, PhD



Summer Lab Size: 20

Local Summer Program: No URL Available
Program Dates: June 5-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Harvard Medical School
Developmental Biology, Neuroscience

Cell Fate Determination in the Vertebrate Retina

We are interested in the mechanisms that direct development and degeneration of the central nervous system (CNS) of vertebrates. We are focusing our studies on the vertebrate retina, a relatively simple and well-characterized area of the CNS. We have used genomics approaches to characterize genes with dynamic temporal patterns to better determine which genes are candidates for playing a role in cell fate determination. We are now trying to determine how the retina uses this large repertoire of genes to form this complex tissue of >60 neuronal cell types. We are particularly interested in the diversification of the different types of interneurons becausethese cells form critical elements in retinal circuitry. In addition, we are interested in the mechanisms that direct formation of the photoreceptor cells becausethey are crucial for vision and are the target of many genetic diseases that lead to blindness. To study these processes, we perform gain- and loss-of-function studies using the genes that we have identified. In addition, we carry out lineage studies wherein we mark individual progenitor cells in vivo and analyze the types of neurons produced. Of interest is whether progenitor cells produce cells that are connected in various types of retinal circuits. We are also using them to learn more about retinal circuitry. Finally, we use an additional approach to study the regulatory elements in the genome that direct specific expression of particular genes to probe the genetic networks that produce the different types of retinal neurons.

Transsynaptic Viral Tracers

The connections among neurons within the central nervous system are so numerous, and complex, that it has been difficult to map and quantify them. We have been developing viral tools to allow one to map connections in vivo. The tools are based on vesicular stomatitis virus, which is a rapidly replicating virus similar to rabies virus. It can replicate and spread transsynaptically in mice and in a broad range of other organisms, including fish and birds. We have several projects aimed at further characterizing the activity of these tracers as well as expanding their capabilities.

Molecular Mechanism of Cone Photoreceptor Death in Diseases of the Retina

Humans rely on cones for vision in daylight and on rods in very dim light. Many forms of blindness are due to mutations in genes that are expressed only in the rod photoreceptors. To look at models for these disorders, we have acquired several strains of mice suffering from loss of vision caused by a mutant gene expressed only in rods. However, these mice exhibit both rod and cone degeneration. In some models, the rods die very quickly, within 1 week, but much more slowly (as long as 6 months) in others. In each case, cones die after most of the rods have died. We have used microarrays to find genes that are up- or down-regulated relative to age-matched controls. We are particularly interested in those genes that change their level of expression during the onset of cone death in all of the models. The genes discovered to change to date are involved in retinal metabolism. This findingled to an examination of whether manipulating signaling through the mTOR pathway might alter the rate of cone death. We found that the rate of cone death can be changed through signaling via the insulin receptor. We are now continuing to study whether metabolic dysregulation might drive the cone death. In addition, as cones are in a hyperoxic environment after rods die, and show signs of oxidation, we have developed AAV gene therapy vectors to deliver genes that fight oxidation as a way to preserve cone activity and survival.

Vivian Cheung, MD

Summer Lab Size: 15

Local Summer Program: http://www.rackham.umich.edu/current-students/programming/srop
Program Dates: May 31-July 28, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

University of Michigan
Computational Biology, Genetics

RNA Processing in Health and Human Diseases

Dr. Vivian Cheung is a pediatric neurologist who studies RNA biology. Our project focuses on basic mechanisms of RNA processing. We use biochemical, genetics, and computational methods to study the sequences, expression, and structures of nucleic acids. Our work spans from yeast to human cells, including those from patients that Dr. Cheung sees in the neurogenetics clinic.

Gene expression levels are regulated at multiple levels to allow cells to respond to environmental stimuli and stresses, as well as to perform cellular functions. We are particularly interested in ways that cells make different gene transcripts and protein isoforms from the same DNA sequences. These are achieved in RNA processing steps such as differential splicing and RNA editing. Splicing and editing allow cells to make transcripts and alter their expression levels quickly to adapt to different needs. We study how these steps are regulated in normal human cells and how dysregulations lead to diseases. We are particularly interested in the abnormal RNA processing in neurodegenerative diseases such as amyotrophic lateral sclerosis and other types of neuromuscular diseases.

Our EXROP students will study the basic biology of gene regulation from yeast to humans using genome-wide approaches such as nascent RNA sequencing to mass spectrometry, and learn to use informatics approaches to turn “big data” into biological questions and answers.

Daniel Colón-Ramos, PhD

Summer Lab Size: 13

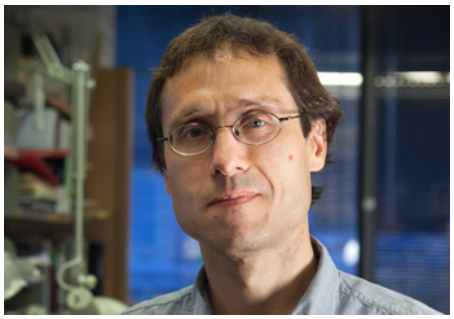
Local Summer Program: http://medicine.yale.edu/biomedsurf/
Program Dates: June 5-August 2, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Yale University
Neuroscience, Developmental Biology

The cell biology of metabolism at synapses

Synapses do not consume energy at a consistent rate, but rather have extended periods of low activity punctuated by periods of intense activity. How are changing energy demands at synaptic sites dynamically met? We recently discovered a metabolic compartment that forms in vivo and ad hoc near synapses to meet local energy demands and support synaptic function (Jang et al, 2016). Our discoveries provide unique opportunities to examine the cell biology of metabolism at the synapse, both under normal physiological conditions and in disease. The project will examine how membrane-less metabolic subcompartments form through liquid-phase transition, and the physiological implications of their localization to subcellular regions in neurons. We will use high-end microscopy imaging and custom-built microfluidic devices to examine these questions in neurons of living animals through FRAP and FLIM methods. For candidates, an interest in quantitative biophysics and cell biology a plus.

Jason Cyster, PhD



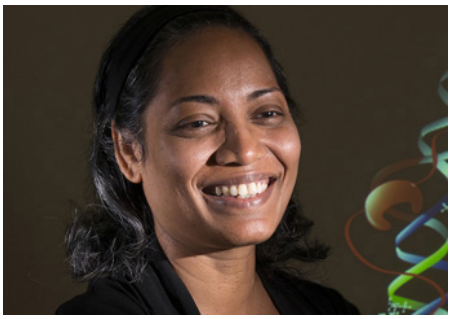
Summer Lab Size:
Local Summer Program: http://graduate.ucsf.edu/srtp
Program Dates: May 30-August 2, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

University of California, San Francisco
Cell Biology, Immunology

Molecular and Cellular Analysis of Lymphocyte Egress-Regulating CD69-S1PR1 Complex

Lymphocyte egress from lymphoid organs is essential for immune surveillance and for effector cells to travel to sites of infection or autoimmune inflammation. The G protein-coupled sphingosine-1-phosphate receptor-1 (S1PR1) plays a critical role transmitting an egress-promoting signal in response to lymph and plasma S1P. In the early phases of an immune response, innate stimuli cause a “shutdown” in lymphocyte egress from responding lymphoid organs, a change in flux that increases local cell numbers and facilitates responses. Shutdown occurs as a result of type I interferon upregulating CD69, a type II transmembrane protein that physically associates with S1PR1 and inhibits its egress-promoting function. In past work we have used mutagenesis, domain swapping, and cell transduction approaches to identify regions of CD69 and S1PR1 involved in the interaction.This project has three goals. The first is to further define the molecular requirements for the CD69-S1PR1 interaction. As well as inhibiting S1PR1â€™s promigratory signaling, CD69 promotes internalization of the receptor. The second is to use cell biological approaches to discern requirements for receptor internalization. The third is to determine whether analogous interactions occur between other G protein-couple receptors and type II transmembrane proteins as part of a more general mechanism for regulation of this large class of signaling receptors. The project would be performed in the context of ongoing in vivo studies in the lab that aim to elucidate additional requirements for cell emigration from tissue and to fully define egress-regulatory mechanisms. FTY720, a drug that inhibits S1PR1 and lymphocyte egress, was approved in 2010 as a treatment for the autoimmune disease multiple sclerosis. Further defining the physiological mechanisms of egress regulation may suggest new approaches for treating immunological diseases.

Victoria D’Souza, PhD



Summer Lab Size: 9

Local Summer Program: No URL available
Program Dates: June 5-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Harvard University

Structural Biology, Microbiology

Understanding transcriptional transactivation in human immunodeficiency virus-1

Complete synthesis of the HIV mRNA transcript requires overcoming stalled transcriptional elongation — a process in which the virus hijacks a positive elongation factor from host cells and recruits it to the stalled viral transcript. The project involves comparing the RNA-protein complexes present in the HIV virus (Tat-TAR) and the host cell (7SK-HEXIM) to understand how the viral complex is able to co-opt the cellular counterpart for productive transcription. This will be done by examining atomic level details of both complexes, hypothesizing on the mechanism, and testing the same in biophysical and cellular assays. The fellow will collaborate with scientists working on viral, NMR, cryo-EM, and crystallographic studies to understand viral RNA-driven processes.

Yang Dan, PhD

Summer Lab Size:

Local Summer Program: http://amgenscholars.berkeley.edu/
Program Dates: May 30-August 4, 2018 (Note:10 weeks will be required)

University of California - Berkeley

Neuroscience, Physiology

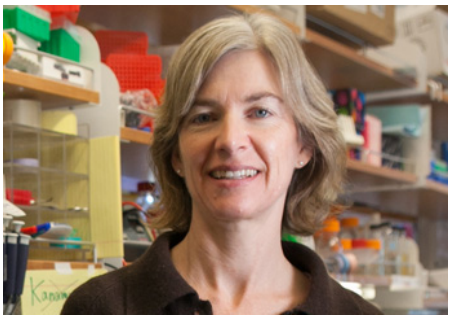
Neural circuits controlling sleep

No project description available. Please visit Dr. Dan's HHMI scientist page for more information about current research.

Prefrontal cortical circuit for behavioral control

No project description available. Please visit Dr. Dan's HHMI scientist page for more information about current research.

Jennifer Doudna, PhD



Summer Lab Size: 15

Local Summer Program: http://amgenscholars.berkeley.edu/
Program Dates: May 30-August 4, 2018 (Note:10 weeks will be required)

University of California - Berkeley

Biochemistry, Structural Biology

Dissecting Dicer: How Regulatory RNAs Are Made and Used

Two RNA-binding proteins, TRBP and PACT, have been shown to influence human Dicer activity in vivo, but their roles in RNA-silencing pathways remain poorly defined. Quantitative biochemical experiments are proposed to determine effects of TRBP and PACT on human Dicer catalysis, substrate specificity, and target cleavage. We will test the hypothesis that TRBP and PACT affect binding and processing of distinct classes of RNA substrates. These experiments will provide important insights into the behavior and mechanism of Dicer in the context of its natural binding partners.

Understanding and Engineering Viral Immunity in Bacteria

The hallmarks of prokaryotic adaptive immunity are genomic clustered regularly interspaced short palindromic repeats (CRISPRs), containing an ~550 base pair leader sequence followed by a short (24 - 48 nt) repeat sequence adjacent to a similarly sized “unique” spacer sequence. The spacers, which often match segments from phage and plasmids, confer resistance to propagation of phage or plasmids bearing those sequences. In S. thermophilus, CRISPR-associated (Cas) proteins encoded by open reading frames adjacent to the CRISPR element were found to be required for CRISPR-mediated phage resistance. Experiments in E. coli showed that a large macromolecular complex called Cascade (CRISPR-associated complex for antiviral defense), formed from multiple Cas proteins, recognizes long transcripts from CRISPR arrays and generates short crRNAs consisting of a repeat-spacer unit. These small CRISPR-derived RNAs serve as homing oligos for the targeted interference of DNA-based foreign genetic elements. However, the mechanisms responsible for this novel regulatory system remain undetermined. The overall goal of this project is to provide a comprehensive understanding of microbial adaptive immunity. We will address (1) how foreign DNA is selectively targeted, (2) how genetic silencing is achieved, and (3) how adaptive immunity has evolved across microbial populations. The long-term objective of this work is to enable engineering of adaptive immunity to control gene expression in environmentally important microbes.Specific projects (1) test the requirements for DNA recognition by Cascade and related complexes from organisms with active CRISPR systems, using a combination of biochemical reconstitution and structure determination; (2) determine the fate of DNA molecules targeted by crRNAs within Cascade and related complexes, and (3) map the coevolution of CRISPR repeat sequences with the associated Cas genes, using sequence- and structure-based computational analysis.

Catherine Drennan, PhD

Summer Lab Size: 13

Local Summer Program: https://biology.mit.edu/outreach_initiatives/UG_summer_internship
Program Dates: June 4-August 12, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Massachusetts Institute of Technology

Biophysics, Structural Biology

Structural Biology of Metalloproteins

EXROP students will learn protein crystallization techniques (e.g., vapor diffusion: hanging drop or sitting drop). If quality crystals are obtained, students will learn cryocrystallography and data collection procedures using our in-house x-ray equipment. EXROP students may also learn about protein purification, enzyme assays, and molecular biology as well as carry out experiments that use biophysical techniques such as calorimetry, electron microscopy, and analytical ultracentrifugation. No previous experience with crystallography, protein biochemistry, or biophysics is required. Students will be trained in all procedures.

Catherine Dulac, PhD

Harvard University

Genetics, Neuroscience

Summer Lab Size: 18

Local Summer Program: No URL Available
Program Dates: June 5-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Molecular Biology of Pheromone Communication in Mice

Animals use chemical cues called pheromones, which provide information about the social and sexual status of individuals within a group, to communicate with other animals. Our laboratory is using molecular and genetic tools to identify molecules and neuronal circuits involved in pheromone-induced behaviors in the mouse. Available projects include the identification of receptors to specific pheromones, the behavioral study of animals in which pheromone communication has been genetically impaired, and the development of new genetic tools to uncover neuronal circuits in the brain underlying specific innate behaviors.

Maitreya Dunham, PhD

University of Washington
Genetics, Evolutionary Biology

Summer Lab Size: 14

Local Summer Program: http://www.washington.edu/undergradre-search/
Program Dates: June 19-August 18, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

High throughput analysis of genetic variation in pharmacogenes

Personalized medicine is already becoming a reality in the field of pharmacogenomics, where patient genotypes inform drug dosing decisions to improve therapeutic response and avoid adverse events. As more human genomes are sequenced, potentially important rare alleles of these genes continue to be discovered. These so-called Variants of Unknown Significance (VUSs) present a particular challenge, since most have insufficient data to guide clinical practice. We are using yeast coupled with saturation mutagenesis and an activity dependent cellular assay as a platform to measure the functional consequences of all possible mutations in a set of Cytochrome P450 enzymes, an important family of pharmacogenes. The student will work closely with a senior postdoc and graduate student on this project, and will gain experience with yeast genetics and sequence analysis.

Michael Elowitz, PhD

Summer Lab Size: 17

Local Summer Program: https://www.sfp.caltech.edu/programs/wavefellows
Program Dates: June 19-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

California Institute of Technology
Bioengineering, Systems Biology

Synthetic protease circuits that compute

Post-translational regulatory circuits hold great promise for synthetic biology and bio-engineering, especially in mammalian cells. Synthetic biology, with its prokaryotic roots, has predominantly relied on transcriptional interactions to implement new designed functions in cells. While powerful, this approach is limited in mammalian cells by the laborious process of introducing and screening multiple parts, and sensitivity to genomic integration site and chromatin context. By contrast, protein based circuits could offer many advantages: They should interface better with endogenous signaling inputs, afford faster signal processing, and enable parallel computing in subcellular compartments. Because all components can be delivered on a single transcript eliminating the need to insulate genes from one another within a circuit and between a circuit and its surrounding genomic regions expediting the design-build-test cycle. This project will involve design, construction, and analysis of new protein-based circuits in mammalian cells to implement a variety of novel computational functions.

MEMOIR: recording past molecular events in the genomes of individual mammalian cells.

During their journey from zygote to multicellular animal, cells transition from one state to another. Although fundamental to our understanding of development, the trajectories of single cells during these transitions have been elusive, since conventional approaches based on population averages smear out distinct cellular states. To track the molecular trajectories of individual cells in developmental contexts, new approaches are needed. Recently, we published a CRISPR/Cas9-based method, called MEMOIR, which involves “writing” of structured mutations at defined sites in the genome, where they can be read out using multiplexed in situ hybridization (K. Frieda et al, Nature 2017). Approaches analogous to phylogenetic inference can then be used to reconstruct lineage and event histories based on the mutation patterns. In this project, we will improve the recording system and/or apply it in embryos to study dynamics of cell state transitions. This work will eventually provide the tools and theoretical basis for reconstructing lineage trees and annotating them with dynamic gene expression information.

Mammalian-cell population control with synthetic paradoxical signaling

Animal growth faces a difficult challenge: A single cell must replicate into a population of trillions of cells, while preventing any single cell from developing an unrestricted growth pattern and becoming cancerous. Several mechanisms have been discovered in mammalian systems to regulate cell population size by utilizing a variety of circuit designs including mechanical signal sensing, creating special niches and negative feedback cytokines. A major challenge of building such systems is that in most simple circuit designs, ‘escape’ mutants can quickly overtake the cell population. Here, as a proof of principle for control circuits in engineered cells and tissues, we will use synthetic biology approaches to design and build a control circuit that is predicted to be robust to such effects, and determine whether it can stably control population sizes.

Elizabeth Engle, MD

Summer Lab Size: 16

Local Summer Program: No URL Available
Program Dates: June 5-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Boston Children's Hospital

Genetics, Neuroscience

Identification and Function of Genes Critical to Cranial Motor Neuron Development

(1) Identification of Human Neurodevelopmental Disease Genes. We study congenital disorders of eye and face movement by first defining their genetic etiologies. Discovering the genetic cause of an orphan disorder can provide a starting point to uncover the underlying molecular pathogenesis and may lead to new therapeutic approaches. The student will learn how to interpret next-generation exome and whole-genome sequence data to identify new human disease genes and/or to design functional studies to prove pathogenicity and mechanistic studies to understand pathophysiology. (2) Characterization of Normal and Abnormal Cranial Nerve Development. The human brain is highly organized and contains a myriad of axon tracts that follow precise pathways and make predictable connections. The lab focuses in particular on ocular and facial cranial nerves that innervate cranial muscles in highly stereotypical and tractable patterns. Working primarily in mouse and zebrafish, we define these developmental processes through a combination of approaches, including gene expression, imaging, and knockout studies. The student will learn how we strive to understand these normal developmental pathways at an anatomical, cellular, and/or molecular level.

Irving Epstein, PhD

Summer Lab Size: 8
Local Summer Program: http://www.brandeis.edu/mrsec/education/reu-overview.html
Program Dates: May 30-August 4, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Brandeis University

Biophysics, Neuroscience, Physical Science

Pulse-Coupled Chemical Oscillators as a Model for Neural Networks

We are studying the behavior of systems consisting of the Belousov-Zhabotinsky oscillating chemical reaction in flow reactors coupled via pulses of chemicals injected into the “postsynaptic” reactor when the electrochemical potential of the “presynaptic” reactor crosses a threshold. The system resembles a set of synaptically coupled neurons. We can control the strength of the coupling, whether it is excitatory or inhibitory, the delay between the “action potential” and the delivery of “neurotransmitter,” and the topology of the coupling. Initial experiments are aimed at modeling the behavior of the pyloric network in the crustacean stomatogastric ganglion. The project involves learning about chemical oscillators; performing experiments; and, if the student has strong computational skills, carrying out numerical simulations.

Stanley Fields, PhD

University of Washington

Genetics, Molecular Biology

Summer Lab Size: 12

Local Summer Program: http://www.washington.edu/research/urp/am-gen/
Program Dates: June 19-August 18, 2017 (Dates for 2018 should be similar; Note: 10 weeks will be required)

Generation of a biosensor for a herbicide

Biosensors are macromolecules that transmit the binding of a ligand into an observable output. Our lab has collaborated on a general strategy to build biosensors that relies on the principle of ligand-dependent stabilization. In this strategy, a protein domain that can bind a ligand is linked to the transcriptional machinery. We then identify amino acid mutations that destabilize the ligand-binding domain, such that in the absence of ligand, the biosensor is rapidly degraded, but in the presence of the ligand, the biosensor binds the ligand and becomes stabilized. Because the biosensor leads to the expression of a reporter gene, a more stable biosensor results in higher levels of expression. Using this ligand-dependent stabilization strategy, the summer undergraduate will build a biosensor for the herbicide atrazine. Atrazine is the most commonly detected groundwater contaminant in the United States, which is a problem because it is a suspected endocrine disruptor. The student will mutagenize an atrazine-binding domain and identify potential biosensors that are stabilized by atrazine. The biosensors could be used to rapidly quantify atrazine levels in natural ground water and soil samples. Additionally, we would be able to link these biosensors to an atrazine degradation pathway in order to develop novel atrazine bioremediation technology.

Erol Fikrig, MD

Yale University

Immunology, Microbiology

Summer Lab Size: 22

Local Summer Program: http://medicine.yale.edu/biomedsurf/
Program Dates: June 5-August 2, 2017 (Dates for 2018 should be similar; Note: 10 weeks will be required)

New Strategies to Prevent Arthropod-Borne Diseases

Our laboratory primarily focuses on understanding the pathogenesis of, and immunity against, arthropod-borne infectious diseases. Ongoing research projects encompass illnesses transmitted by ticks or mosquitoes, including Lyme disease, human anaplasmosis, West Nile encephalitis, dengue fever, and malaria. We are defining the triangular relationships that occur when vector, pathogen, and host products interact during the feeding process. Approaches to interfere with these associations may lead to new vaccines and therapies for many of these diseases.Lyme disease: We are investigating how Borrelia burgdorferi gene expression differs in diverse tissues, and the immunopathogenesis of Lyme arthritis.Human granulocytic anaplasmosis: We are studying how this unusual obligate intracellular pathogen persists in both ticks and mammalian neutrophils.Flaviviral infections: We are elucidating the factors essential for the survival of West Nile virus and dengue virus in mosquitoes and the vertebrate host. Our group also examines the innate immune responses that contribute to the genesis of West Nile encephalitis.Translational projects in the laboratory focus on defining how innate immune responses change as we get older, or are given immunosuppressive agents, and how this influences susceptibility to infection and the ability to respond to vaccines.

Robert Froemke, PhD

Summer Lab Size: 25

Local Summer Program: https://med.nyu.edu/research/sackler-institute-graduate-biomedical-sciences/summer-undergraduate-research-program
Program Dates: June 5-August 4, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

New York University School of Medicine

Neuroscience

Large-Scale System for Studying the Neural Basis of Social Behavior

We are building an integrated large-scale system for studying naturally-occurring social interactions in mice. We are focusing on maternal care and cross-fostering by co-parents of mouse pups, using a combination of videography, audio recordings, neural recordings, and perturbation experiments, to continually monitor social behavior over a period of weeks or longer. This project involves behavioral analysis and possibly anatomical studies and/or programming. No experience required.

David Ginsburg, MD

Summer Lab Size: 15

Local Summer Program: http://www.rackham.umich.edu/current-students/programming/srop
Program Dates: May 31-July 28, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

University of Michigan
Genetics, Medicine and Translational Research

Analysis of ENU-Induced Mutations in Mice Affecting Blood Clotting

Our lab is focused on studying the genetics of blood coagulation. One particular blood-clotting disease, called venous thromboemboembolism, affects ~300,000 individuals/year in the United States. A polymorphism in the coagulation factor V gene, called Factor V Leiden (FVL), is the most common genetic risk factor for venous thrombosis, although it displays only 10% penetrance. We previously demonstrated synthetic lethality between homozygosity for FVL (FVQ/Q) and heterozygous tissue factor pathway inhibitor deficiency (TFPI+/ -) in mice. To identify novel thrombosis modifier genes, we recently performed a mouse whole-genome ENU mutagenesis screen. By screening through ~8,000 mice, we identified >120 putative thrombosis modifiers. We are now performing whole-exome sequencing in these mice in an effort to identify those genes carrying suppressing mutations. Candidate genes will be validated by gene targetting experiments and crosses into mice with the otherwise lethal gene combination. The identification of these suppressor mutations should provide novel insights into hemostatic regulation and will provide a starting point for future experiments aimed at determining the precise role of these genes in venous thrombosis and other hemostatic disorders. During this project, the student will participate in interpreting the whole exome sequence data and validating the candidate modifier genes using mouse models.

Using CRISPR Technology to Modify COPII Genes in Human Cell Lines

About 30% of the human genome encodes proteins that rely on the proper function of the secretory pathway. Endoplasmic reticulum-to-Golgi transport represents the entry point of the secretory pathway and is mediated by the evolutionarily conserved coatamer complex II (COPII). Mutations in several COPII genes lead to distinct genetic diseases in human patients, with often markedly different findings in genetically engineered mice deficient in the orthologous protein. This project will aim to use a new genome-editing technology using CRISPR to specifically tailor individual COPII genes in relevant cell types of human origin.

Antonio Giraldez, PhD

Summer Lab Size: 10

Local Summer Program: http://medicine.yale.edu/biomedsurf/
Program Dates: June 5-August 2, 2017 (Dates for 2018 should be similar; Note: 10 weeks will be required)

Yale University

Molecular Biology, Developmental Biology

Deciphering the regulatory code shaping mRNA stability and translation during embryogenesis

While previous efforts have uncovered individual mechanisms regulating mRNA stability, there are major gaps in our understanding of how translation is regulated, and how different regulatory inputs are integrated to explain the dynamics of mRNA decay and translation across the transcriptome. This project will combine i) a novel high throughput parallel reporter assay to identify regulatory elements controlling mRNA stability and translation during development, and ii) integrate the inputs of mRNA decay, translation and endogenous gene expression, with intrinsic and extrinsic features such as codon identity, tRNA availability, RNP and microRNA target sites using machine learning techniques, to understand the overall combinatorial effect of these inputs on mRNA stability and translation regulation. The ultimate goal is to develop a global model of gene regulation in vertebrates. Together, these approaches will provide deeper understanding of the individual effect of the regulatory elements, their interactions as well as how they are orchestrated in the cell in order to control protein output and shape embryogenesis.

Joseph Gleeson, MD

Summer Lab Size: 20

Local Summer Program: http://grad.ucsd.edu/degrees/summer-researches/stars/schedule.html
Program Dates: June 24-August 17, 2018 (Note:10 weeks will be required)

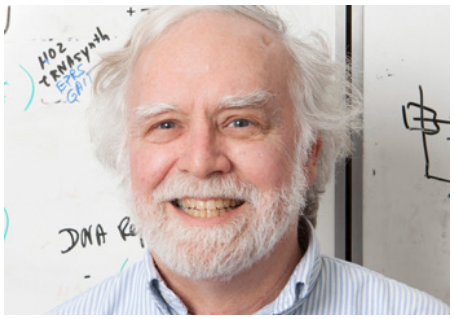
University of California - San Diego

Genetics, Neuroscience

Genetic basis of pediatric brain disease: Whole genome sequencing and stem cells

This project examines a group of patients with autism and epilepsy on whom whole genome sequencing and induced pluripotent stem cells are generated, in order to discover new causes of disease. We are interested in identifying new genes and new mechanisms of disease leading to pediatric brain disease. Project can be personalized based upon individual research background and interests, but includes generation of mini-brains (cortical organoids), genetic profiling, and analysis of whole genome sequencing files and bioinformatic analysis. Previous background in cell culture, RNAseq or computer programming (R, Python, SQL) are recommended.

Stephen Goff, PhD



Summer Lab Size: 6
Local Summer Program: http://www.spurs.columbia.edu/index.html
Program Dates: June 5-August 4, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Columbia University
Molecular Biology, Virology

Assays for self vs. non-self discrimination in primary cultured hemocytes and disseminated neoplasia cells of molluscs

We are studying a leukemia-like disease of molluscs that we have learned is spreading in the wild by horizontal transmission of a clonal cell line from animal to animal. This transmission is typically restricted to the species of origin but the basis of that restriction is not known. We will be devising tests for mixed lymphocyte responses of cultured cells, hoping to define the molecules and pathways involved in cell-cell recognition. Because so little is known about the primitive immune system of these animals, the student will need to be exceptionally creative, independent, and resourceful.

Host factors involved in retrovirus replication: Studying the mechanism of action of gene products involved in protein trafficking, RNA trafficking, and DNA damage repair that affect retroviral replication.

The student would work with a postdoctoral fellow analyzing the role of one of a set of host factors that we have identified in large-scale screens as impacting retroviral replication. The project would involve generating cell lines overexpressing the factor, or deficient in the factor by shRNA-mediated knockdown or CRISPR-mediated mutagenesis, and then determining the consequences for infection by retroviruses or retroviral-based reporter genomes. The analyses could include characterization of the step in the viral life cycle affected by the factor, identification of the viral protein affected by selection for viral escape mutants, and mapping the domains of the protein essential for activity. The work would heavily depend on cell culture and basic molecular biology methods.

Susan Golden, PhD

Summer Lab Size:

Local Summer Program: http://grad.ucsd.edu/degrees/summer-researches/stars/schedule.html
Program Dates: June 24-August 17, 2018 (Note:10 weeks will be required)

University of California - San Diego

Microbiology

Mechanisms and consequences of circadian timing in a prokaryotic model organism

Cells of diverse organisms, from cyanobacteria to humans, execute temporal physiological programs that are driven by circadian oscillators. The circadian clock of the cyanobacterium Synechococcus elongatus regulates global patterns of gene expression, the timing of cell division, and metabolism. We use *S. elongatus* as a model to understand how a cell keeps track of time, executes activities according to a temporal program, and synchronizes the internal clock with the external solar cycle. Projects in the lab use microbial genetics, genomics, bioinformatics, biochemistry, cell biology, and metabolomics to understand the mechanisms and consequences of circadian timing. Cyanobacteria are also being developed as biotechnology production platforms, to harness photosynthesis to make useful chemicals as petroleum replacements. Some projects in the lab facilitate the biotechnological development of *S. elongatus* through building improved genetic tools and determining how cells switch between biofilm and planktonic growth.

Eric Gouaux, PhD

Summer Lab Size:

Local Summer Program: http://www.ohsu.edu/xd/about/vision/center-for-diversity-inclusion/academic-resources/internships/summer-equity-internship.cfm
Program Dates: June 18-August 10, 2018 (Note:10 weeks will be required)

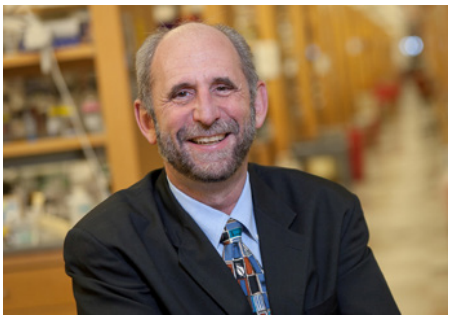
Oregon Health and Science University

Neuroscience, Structural Biology

Mechanism of Ion Selectivity and Block in Acid-Sensing Ion Channels

This project involves x-ray crystallographic studies of acid-sensing ion channel 1a in complex with ion channel blockers and anomalously scattering monovalent ions.

Michael Green, MD, PhD



Summer Lab Size: ~15

Local Summer Program: https://www.umassmed.edu/summer/
Program Dates: May 27-August 1, 2018 (Note:10 weeks will be required)

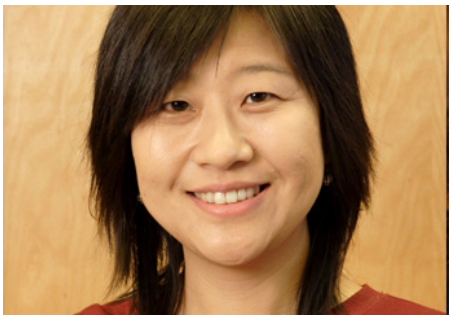
University of Massachusetts Medical School

Cancer Biology, Cell Biology

Genome-Wide RNA Interference Screens to Identify Factors Involved in Cancer Initiation and Progression

Our lab has a broad interest in understanding the mechanisms that regulate gene expression in eukaryotes and the role of gene expression in various human disease states. We are particularly interested in how transcriptional regulation plays a role in cancer initiation and progression. For example, some oncogenes and tumor-suppressor genes are themselves transcription factors; inactivation of genes critical for cancer development often occurs by epigenetic silencing; some genes involved in cellular growth control and apoptosis (programmed cell death) are selectively transcribed in cancer or normal cells; and some apoptotic pathways are transcriptionally regulated.We are using a variety of molecular biological, genetic, and biochemical approaches to (1) study these transcription-based processes, (2) delineate the relevant regulatory pathways, and (3) identify the components in these pathways. Currently, we are performing a series of genome-wide RNA interference (RNAi) screens to identify factors involved in oncogene-induced epigenetic silencing, oncogene-induced senescence, transcriptional regulation of tumor-suppressor genes, and the induction of apoptosis by chemotherapeutic agents. We are also using genome-wide RNAi screens to identify new tumor-suppressor genes and genes that regulate metastasis. The EXROP student will learn the principles of designing an effective RNAi-screening procedure and gain experience in a variety of biochemical and molecular biology techniques (e.g., recombinant DNA cloning, DNA sequencing, qualitative and quantitative PCR and RT-PCR, RNAi, immunoblotting, and chromatin immunoprecipitation) and/or cell biology protocols (e.g., mammalian tissue culture, apoptosis assays, cell proliferation assays, in vitro metastasis assays).

Chenghua Gu, PhD



Harvard Medical School

Neuroscience

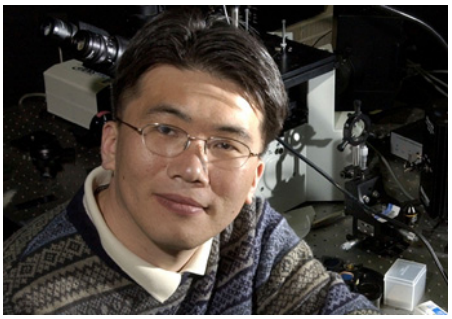
Summer Lab Size:

Local Summer Program: No URL Available
Program Dates: June 5-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Molecular mechanisms underlying the function and regulation of the blood-brain barrier

Using molecular, genetic, and imaging techniques to identify and characterize key regulators that are specifically expressed in CNS endothelial cells for the blood-brain barrier function.

Taekjip Ha, PhD



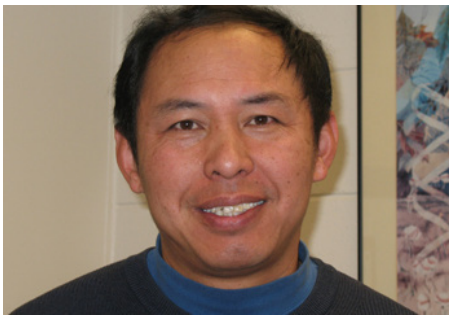
Summer Lab Size: 20
Local Summer Program: https://www.hopkinsmedicine.org/education/graduate-programs/student-life/diversity/sip.html
Program Dates: May 28-August 5, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Johns Hopkins University
Biophysics, Structural Biology

Mechanobiology of stem cells and cancer cells at the single molecule level

It is now widely appreciated that cancer cells and stem cells can change their cell fate (differentiation, metastasis, etc.) depending on their mechanical environment. Mechanical sensing is likely to be initiated by individual membrane receptor proteins that are in direct contact with the mechanical environment. In a sense, cells perform many single molecule mechanical measurements in parallel and process the information before making a critical cell fate decision. In order to understand how molecular level mechanical events trigger a cellular response, we need to examine the forces applied across individual cellular proteins during mechanical signaling. This project involves the development and use of DNA-based single molecular sensors to study mechanobiology mediated by membrane receptors such as integrins and Notch.

Min Han, PhD



Summer Lab Size: 12

Local Summer Program: http://www.colorado.edu/GraduateSchool/DiversityInitiative/undergrads/smart/index.html
Program Dates: June 5-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

University of Colorado at Boulder

Molecular Biology

Investigation of the mechanisms by which nutrient availability impacts development and behaviors in worms and mice

No project description available. Please visit Dr. Han's HHMI scientist page for more information about current research.

Stephen Harrison, PhD

Summer Lab Size: 20

Local Summer Program: No URL Available
Program Dates: June 5-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Harvard Medical School
Biochemistry, Structural Biology

Antibody Affinity Maturation

Antibodies are the main line of defense against many viral pathogens. Initial exposure to a virus or to a vaccine induces proliferation of B cells that recognize viral antigens, but the first response generates relatively weakly binding antibodies. Continued proliferation in the presence of antigen, together with a process of somatic hypermutation that randomly alters the variable regions of the encoded antibody molecule, leads to selection of B cells that secrete more tightly binding antibodies.Recently developed technologies allow one to obtain the sequences of the variable regions of antibody heavy and light chains from many individual B cells in a donor sample. In suitable cases, such as influenza vaccination, it is possible to reconstruct the “evolutionary tree” of a set of such antibodies, deducing the amino acid sequences of the progenitor antibody (i.e., the antibody produced by the initially stimulated B cell) and of various intermediates between the progenitor and the mature antibodies present at the time a blood sample is obtained. Structural, biochemical, and computational analysis of these lineages give us a picture of protein evolution over a short period of time, in response to a defined selective pressure. This information may be useful for new modes of vaccine design. A student who participates will be carrying out biochemical and molecular-biological experiments to express and purify suitable antibodies for structural and physicochemical studies.

Virus Structure and Cell Entry

From the perspective of structure and entry mechanisms, viruses that infect humans or other vertebrates fall into two broad classes: those with lipid-bilayer membranes of their own (e.g., influenza virus, HIV), called “enveloped” viruses, and those without lipid membranes, called “nonenveloped” viruses. Enveloped viruses enter cells by a process in which the viral membrane fuses with a cellular membrane, depositing the internal contents of the virus, including its genome, into the cytoplasm of the new host cell.Projects for the summer will involve studies of the molecular mechanism of membrane fusion as facilitated by viral “fusion proteins” (such as the hemagglutinin of influenza virus or the envelope protein of HIV). The viruses we are studying include influenza virus, dengue virus, and HIV. A student who participates will be carrying out biochemical, molecular-biological, and physicochemical experiments, probably involving one of these viruses in noninfectious form (e.g., virus-like particles). The student will learn about mechanistic approaches to problems in cell biology and about basic virology and virus-cell interactions.

Elizabeth Haswell, PhD

Summer Lab Size: 10

Local Summer Program: http://dbbs.wustl.edu/divprograms/Summer-ResearchforUndergrads/Pages/BiomedRAP.aspx
Program Dates: May 29-August 4, 2018 (Note:10 weeks will be required)

Washington University in St. Louis

Plant Biology, Biophysics

Mechanosensitive Ion Channels as Translators of the Cell

We are interested in how mechanosensitive ion channels translate the language of physics (force) into a language of biology (a biochemical signal). This project aims to understand the functional relationship between several kinds of mechanosensitive ion channels by studying their expression patterns, subcellular localization, and protein-protein interactions. The lab is friendly and eager to mentor new people. No previous experience is necessary, though familiarity with molecular biology and microscopy would be a plus.

Sheng Yang He, PhD

Summer Lab Size:

Local Summer Program: TBD
Program Dates: TBD (Note:10 weeks will be required)

Michigan State University
Microbiology, Plant Biology

Bacterial Disease Susceptibility in Arabidopsis

No project description available. Please visit Dr. He's HHMI scientist page for more information about current research.

Ekaterina (Katya) Heldwein, PhD

Summer Lab Size:
Local Summer Program: No URL Available
Program Dates: TBD (Note:10 weeks will be required)

Tufts University School of Medicine

Virology, Structural Biology

Structural biology of herpesviruses

Herpesviruses are ubiquitous pathogens that infect most of the world's population for life and can cause a panoply of diseases. The Heldwein lab studies the mechanisms by which herpesviruses enter and exit their host cells using the tools of structural biology, biochemistry, biophysics, and cell biology. We are especially interested in how herpesviruses manipulate host membranes and cytoplasmic traffic. EXROP students will contribute to the ongoing work in the lab aimed at determining the mechanistic underpinnings of interesting functional phenotypes. Students will learn how to express and purify viral proteins and complexes and characterize their properties and activities using biophysical techniques, such as circular dichroism and electron microscopy, and functional assays. EXROP students may alternatively choose to characterize viral phenotypes in tissue culture using cell biological and virological assays.

Helen Hobbs, MD

Summer Lab Size: 12

Local Summer Program: http://www.utsouthwestern.edu/education/graduate-school/programs/non-degree-programs/surf.html
Program Dates: June 4-August 10, 2018 (Note:10 weeks will be required)

University of Texas Southwestern Medical Center

Genetics, Medicine and Translational Research

Role of angiopoeitin like proteins in energy metabolism

No project description available. Please visit Dr. Hobbs' HHMI scientist page for more information about current research.

Gene defects in fatty liver disease

No project description available. Please visit Dr. Hobbs' HHMI scientist page for more information about current research.

Structure/function relationships of a cholesterol transporter: ABCG5/ABCG8

No project description available. Please visit Dr. Hobbs' HHMI scientist page for more information about current research.

Oliver Hobert, PhD

Summer Lab Size: 5

Local Summer Program: http://www.spurs.columbia.edu/index.html
Program Dates: June 5-August 4, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Columbia University
Genetics, Neuroscience

Identifying Genes Required for Brain Development

The nematode Caenorhabditis elegans is a simple invertebrate model system that allows us to study nervous system development. We have generated a number of transgenic C. elegans strains in which specific subsets of neurons are labeled with a green fluorescent protein (GFP) marker. One key advantage of C. elegans is its amenability to mutant screens. In such screens, one mutagenizes animals and identifies mutant worms that are unable to correctly express the GFP-tagged neuronal fate marker - suggesting that one has “hit” a gene required for neuronal development.In this summer project, up to two undergraduate students will work with one or two postdoctoral fellows to conduct such “mutant hunts.” This project will provide insights into how brain development is programmed into our genes. We will also hunt for genes that may be involved in neurodegeneration - that is, we seek mutants in which neurons degenerate during adult life, thereby modeling neurodegenerative diseases, such as motor neuron diseases. Identifying such genes in worms may not only reveal potential disease gene candidates but also provide the opportunity to understand exactly how they work. Participation in the project does not require much previous experience, just a keen, observant, and curious mind. The student will learn how to “think genetically”; how to use some basic molecular techniques; how to look at the nervous system of a live, behaving animal; and how to work in a research team. See our lab page for more details.

Hopi Hoekstra, PhD

Harvard University

Evolutionary Biology, Genetics

Summer Lab Size:

Local Summer Program: No URL Available
Program Dates: June 5-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

The Genetic Basis of Behavior in Mice

We are looking for a student who is interested in studying the genetics and neurobiology of differences in natural behaviors of wild mice. Students could be involved in designing and running behavioral assays; genetic or genomic analyses; and molecular or neurobiological lab-based experiments.

André Hoelz, PhD

Summer Lab Size: 20
Local Summer Program: https://www.sfp.caltech.edu/programs/wavefellows
Program Dates: June 19-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

California Institute of Technology

Structural Biology, Biochemistry

Structure-function analysis of proteinaceous mega assemblies

Our main goal is the structural, biochemical, and in vivo characterization of the nuclear pore complex (NPC), an ~120 million Dalton (MDa) assembly that is the sole mediator of bi-directional nucleocytoplasmic transport in all eukaryotes. Each NPC is composed of ~34 different proteins called nucleoporins that occur in multiple copies, yielding a ~1,000 protein assembly. When we began our work, an atomic level understanding of the NPC was lacking, primarily due to its sheer size and flexibility. Our effort has since resulted in the structural characterization of about half of the NPC's structured mass and we have determined a near-atomic composite structure of its ~60 MDa symmetric core. The project focuses on the biochemical reconstitution of complexes between nucleoporins and components of the transcription and mRNA export machineries, virulence factors and transport factors, their structural characterization by X-ray crystallography or single particle cryo-electron microscopy, and their functional analysis in yeast or mammalian cells. A particular focus are nucleoporins associated with various human diseases, including aggressive cancers, viral infections, neurodegenerative diseases, and specialized nucleocytoplasmic transport events.

Neil Hunter, PhD

Summer Lab Size: 10

Local Summer Program: No URL Available
Program Dates: TBD (Note:10 weeks will be required)

University of California - Davis

Cell Biology, Genetics

Delineation and Analysis of the SUMO-Modified Proteome During Meiosis

Meiosis produces haploid gametes through an interdependent sequence of chromosomal events, including pairing, synapsis, and recombination. Defects in these processes are a leading cause of infertility, pregnancy loss and congenital disease in humans. Recent studies indicate central roles for the SUMO-conjugation and ubiquitin-proteasome systems in orchestrating the events of meiotic prophase. In particular, SUMO promotes the crossover outcome of homologous recombination, which is required for accurate chromosome segregation at the first division of meiosis. A major hurdle to understanding how SUMO regulates meiosis is identifying target proteins and mapping the sites of SUMO conjugation. The long-term objectives of this proposal are to delineate the SUMO-modified proteome during meiosis and understand how SUMO regulates meiotic recombination. To this end, we have developed an efficient regimen to map SUMO-conjugation sites by mass spectrometry during meiosis in budding yeast. The resulting datasets provides unprecedented insights into the landscape and dynamics of SUMO modification during meiosis.
This project will extend these breakthroughs to achieve two broad aims. Aim 1 will define meiotic specific substrates of the four known SUMO E3 ligases in budding yeast, Zip3, Siz1, Siz2 and Mms21. Of special interest are targets of Zip3, a meiosis-specific E3 ligase. Both Zip3 and its human ortholog, RNF212, accumulate at designated crossover sites where they act to promote crossing over. Notably, common alleles of human Rnf212 are responsible for heritable variation in crossover rate. Aim 2 we will exploit our unique proteomics dataset to understand how SUMO orchestrates meiosis, with a special focus on the regulation of recombination. An efficient pipeline has been developed to simultaneously mutate the multiple SUMO-conjugation sites found in a typical target protein. The resulting SUMO-defective mutants will be analyzed using the comprehensive battery of molecular, genetic, biochemical and cytological assays uniquely available in budding yeast to monitor the events of meiotic prophase. The findings of this proposal will be germane to understanding pathologies associated with human meiosis, and are expected to define paradigms that are broadly relevant for understanding the biology of SUMO.

RNF212B - a Novel SUMO E3-Ligase With Roles in Meiosis

Meiosis is the specialized cell division that produces gametes (sperm and eggs) containing a single copy of each chromosome. Errors in meiosis are the leading cause of miscarriage and congenital diseases, including Down, Klinefelter, Edwards, Patau and Triple X syndromes. These diseases result when a fetus inherits the wrong number of chromosomes, termed aneuploidy. Fetal aneuploidy most often derives from a defective egg that was unable to correctly segregate its chromosomes. Successful chromosome segregation requires that pairs of matching chromosomes become connected through a process called crossing over. For unknown reasons, crossing over is inefficient in human females leading to defective segregation. Thus, to understand and ameliorate human aneuploidy, we need to elucidate the processes that regulate crossing over. This project will study the function of RNF212B, a newly identified factor that facilitates crossing over. RNF212B belongs to a class of regulatory proteins that modify the activities of other proteins. Specifically, RNF212B catalyzes protein modification by the ubiquitin-family protein, SUMO. The function of RNF212B will be elucidated using cytological and genetic approaches in mouse models, and biochemical approaches using the human SUMO and recombination mchinery. The goals are to characterize how RNF212 promotes crossing over, identify its target proteins and understand how their activities are regulated, and relate these findings to the inefficient crossing over that occurs in human females.

Effects of Atrazine on the Developing Ovary

Effects of Atrazine on the Developing Ovary breaks. A few breaks are assigned a crossover rate in such a way that each pair of chromosomes obtains at least one crossover, as required for accurate segregation. We have obtained evidence

that this crossover control process involves the differential stabilization of key recombination factors, which in turn stabilize DNA recombination intermediates. A role for ubiquitin-dependent protein turnover is invoked by these data. This project will address the role of the proteasome in the turnover of specific recombination factors. We will also take an unbiased approach to identify meiotic proteins that undergo ubiquitin-dependent turnover during meiotic prophase. The project will utilize genetic, cytological, biochemical, and mass spectrometry approaches.

Darrell Irvine, PhD

Summer Lab Size:

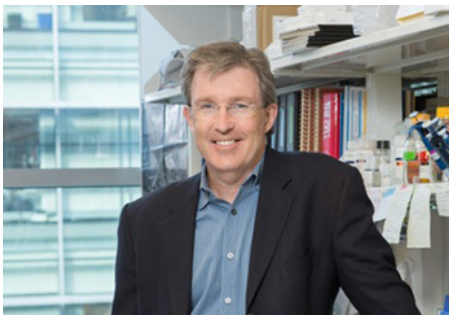
Local Summer Program: https://biology.mit.edu/outreach_initiatives/UG_summer_internship
Program Dates: June 4-August 12, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Massachusetts Institute of Technology
Bioengineering, Immunology

Immune System Bioengineering

Our laboratory has had a longstanding interest in developing novel materials as delivery agents and adjuvants for vaccines. For example, we recently developed a novel class of lipid vesicles, interbilayer-crosslinked multilamellar vesicles (Moon et al., Nat. Materials, 2012; Li et al., Sci. Transl. Med., 2013), which elicit long-lived, high-titer, and high-avidity antibody responses relevant to the present vaccination studies and which can be administered by parenteral or noninvasive (e.g., pulmonary) routes. Using this system, we showed that nanoparticle vaccines adjuvant the humoral responses by multiple mechanisms, prolonging antigen delivery to lymph nodes, enhancing germinal center formation, and promoting differentiation of antigen-specific follicular helper T cells (Moon et al. PNAS, 2012). In other recent work, we developed novel lymph node targeting amphiphile vaccines, based on lipid-polymer conjugate compounds (Liu et al., Nature, 2014). This new approach offers a strategy to enhance both the potency and safety of subunit vaccines, but our efforts to date have all been in small animals. In this project, we continue to develop and seek to understand the underlying mechanisms of lymph node-targeted vaccines.

Tyler Jacks, PhD



Summer Lab Size: 40

Local Summer Program: https://biology.mit.edu/outreach_initiatives/UG_summer_internship
Program Dates: June 4-August 12, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Massachusetts Institute of Technology

Cancer Biology, Molecular Biology

Cancer Genetics and Development

Tyler Jacks is interested in many aspects of cancer development, such as cancer genetics, metastasis, immunology, tumor microenvironment, and chemotherapy resistance. Through advanced genetic engineering and genome editing methods, the Jacks laboratory has generated a series of genetically-engineered mouse strains that serve as animal models of tumor development and as a means to study the functions of cancer-associated genes and test new methods for cancer therapy.

William Jacobs, PhD

Summer Lab Size: 30

Local Summer Program: http://www.einstein.yu.edu/education/phd/the-summer-undergrad-research-program.aspx
Program Dates: June 5-July 27, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Albert Einstein College of Medicine

Genetics, Microbiology

Fighting Fire with Fire: Harnessing ADCC immunity elicited by HSV-2 Δ*gD* to protect against pandemic diseases

"Herpes Simplex Viruses 1 and 2 (HSV-1 and HSV-2) cause significant global morbidity and mortality. An estimated two thirds of the world's population is infected with HSV-1 and one sixth is infected with HSV-2. Communicable diseases on the whole account for approximately one third of global deaths, highlighting the dire need for novel therapeutics and vaccines. That's where we come in. The Jacobs laboratory specializes in creating genetically recombinant bacteria and viruses that serve as tools for studying immunity against infectious disease. Recently, in collaboration with the laboratory of Dr. Betsy Herold, we engineered a broadly protective vaccine against herpes simplex virus (HSV) subtypes 1 and 2. This vaccine consists of a recombinant HSV-2 virus lacking the glycoprotein D locus (HSV-2 Δ*gD*), which codes a protein required for viral entry. To our surprise, mice given two doses of this vaccine were completely protected against morbidity, mortality, and establishment of latency following challenge with a range of HSV-1 and HSV-2 clinical isolates. We now know that the vaccine initiates an incredibly broad antibody response which induces antibody dependent cell-mediated phagocytosis and cytotoxicity (ADCP and ADCC).

The virus must be in complementing VD60 cells that produce endogenous gD. When the virus infects non-complementing cells, it produces virions that cannot enter additional cells (since they lack gD). Thus, HSV-2 Δ*gD* virions undergo exactly one round of replication in their host before they are inactivated. This attenuation allows us to use HSV-2 Δ*gD* as the genetic backbone for creating a number of biological and therapeutic tools.
The ability of HSV-2 Δ*gD* to generate a potent ADCC response is unique for an immunogen. As a result, the mechanisms by which immunogens generate ADCC immunity in general are not well understood. At the same time, ADCC and ADCP are being increasingly recognized for their ability to protect against infectious diseases and cancers. A growing body of literature points to ADCC as the main immune correlate for vaccine-mediated protection against influenza and HIV. We propose that vaccines against these pathogens must induce the creation of ADCC antibodies to be fully effective. To test this hypothesis, we have been recombining influenza A (IAV), HIV, and tuberculosis antigens into HSV-2 Δ*gD* and measuring immune correlates of protection. Further studies with these and other recombinant HSV-2 Δ*gD* viruses will help us determine the mechanism of generating ADCC immunity as well as the potential of HSV-2 Δ*gD* as a vaccine vector specializing in ADCC."

Christine Jacobs-Wagner, PhD

Yale University

Cell Biology, Microbiology

Summer Lab Size: 13

Local Summer Program: http://medicine.yale.edu/biomedsurf/
Program Dates: June 5-August 2, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Bacterial Cell-Cycle Control

Specific projects will be determined on the basis of the student's interest in genetics, biochemistry, fluorescence microscopy, quantitative analysis, and/or modeling. Potential projects range from identifying new genes involved in cell-cycle events or cell-size regulation to characterizing known regulators genetically or biochemically, quantifying their behavior at the single-cell level using microscopy, and modeling the processes of interest. The model bacterium will be Escherichia coli or Caulobacter crescentus.

Yuh-Nung Jan, PhD

Summer Lab Size: 20

Local Summer Program: http://graduate.ucsf.edu/srtp
Program Dates: May 30-August 2, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

University of California - San Francisco
Biophysics, Neuroscience

How Do Different Types of Neurons Acquire Their Distinctive Dendritic Morphology?

Since dendrites are the antennas for neurons to receive information, it is important to know how neurons acquire their distinctive dendritic morphology. Our approach is to use Drosophila (fruit fly) genetics to identify the essential molecular components. The Drosophila dendritic arborization (da) neurons are sensory neurons with a fairly elaborate dendritic branching pattern. They can be subdivided into four classes, each with distinctive dendritic morphology. We are using forward genetics of Drosophila to identify genes that control the development of the dendritic morphology of those da neurons. These studies have begun to provide us with molecular insights into how neurons acquire their class-specific dendritic morphology. We have also been working on the influence of dendritic morphology on neuronal function.Students will participate in one or more of the following research areas: (1) Genetic screening of mutants affecting dendrite development. This will involve fly genetics and confocal microscopy work. (2) Phenotypic characterization of Drosophila mutants. This will involve learning Drosophila anatomy, immunocytochemistry, molecular genetics, and possibly electrophysiology. (3) Since many molecular mechanisms controlling various biological processes are well conserved during evolution, we presume the control of dendrite development is no exception. We have begun to extend our findings from Drosophila to the vertebrates. This will involve finding vertebrate homologs of the genes we identified from Drosophila (by bioinformatics or by cloning) and testing their role in controlling dendrite development by studying the effect of transfecting those genes into cultured vertebrate neurons.

Vivek Jayaraman, PhD

Summer Lab Size:

Local Summer Program: http://www.janelia.org/student-programs/undergraduate-program
Program Dates: June 6-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Janelia Research Campus

Neuroscience

Reconstructing Neural Circuitry Underlying Navigation

The neural basis of spatial navigation has largely been studied in mammals, with notable discoveries of neurons that respond selectively to an animal's heading and place in its environment, for example head directions cells, place cells, and grid cells. However, it has been challenging to understand how such abstract neural representations arise in the mammalian brain, due partly to the sheer numerical complexity of the distributed circuits involved. Our lab aims to understand the mechanistic basis of navigational neural dynamics by using a more tractable experimental system. We use Drosophila melanogaster, a model organism with a small brain, and powerful genetic tools that enable us to perturb and record the activity of specific subsets of neurons. In recent years, Janelia labs have shown both that Drosophila perform visual place learning (Ofstad et al., Nature, 2011), and that circuits in their brain capture their orientation with dynamics that share similarities with mammalian head direction cells (Seelig & Jayaraman, Nature, 2015).

In our effort to understand how such activity patterns are generated, we would like to reconstruct the underlying neural circuits. You would work in collaboration with groups at Janelia that are performing electron microscopy (EM) of large volumes of the fly central brain, including the brain region (the "central complex") that we believe to be specialized for navigation in insects. Our goal would be to trace entire neural networks involved in navigation, making clear the structural basis for the interesting neural activity we observe. Such connectomic reconstruction of complete circuits, which will help us draw broadly relevant conclusions about how navigational circuits work, is, at the moment, impossible to perform in larger brains. The ideal candidate would be attentive and patient, have an eye for detail and care about accuracy, all while being genuinely interested in understanding how the structure of neural circuits enable behavior.

As part of your experience in the intellectually stimulating, collegial, and highly collaborative Janelia Research Campus, you would also be actively involved in journal clubs and lab meetings.

Joseph Jez, PhD

Summer Lab Size:

Local Summer Program: http://dbbs.wustl.edu/divprograms/Summer-ResearchforUndergrads/Pages/BiomedRAP.aspx
Program Dates: May 29-August 4, 2018 (Note:10 weeks will be required)

Washington University in St. Louis

Biochemistry, Structural Biology

Exploring Biochemical Regulatory Networks in Plants and Microbes

EXROP students can fit into any of the three major projects in the lab, all of which use a combination of biochemical and structural biology approaches. Specific projects can be tailored to fit the background and expertise of a student but typically include molecular cloning, protein expression and purification, biochemical assays, and protein crystallization. Some projects also include plant genetics using Arabidopsis thaliana as a model organism.

1. Metabolic Regulatory Networks and Environmental Responses A fundamental challenge for biologists is to understand how organisms respond to their environment to maintain growth, development, and propagation.Environmental changes lead to multiple adjustments across metabolic, signaling, and gene expression pathways.A major goal of this research is to develop a molecular view of how key regulatory proteins function in the context of metabolic networks and cellular localization using structural biology and biochemical approaches.

2. Enzymatic Control of Plant Hormone ResponsesPlant development, growth, and fitness are all determined by the complex integration of multiple signaling pathways and hormone responses; however, perception by receptors is only one piece of this biological puzzle. As part of the system that regulates plant hormone effects, GH3 proteins control levels of major plant hormones, including jasmonates and auxins, and modulate pathways for plant growth and development, seed development, light signaling, drought response, and pathogen resistance. Structural and mechanistic investigations are required to understand how these proteins catalyze hormone modifications and to decipher the determinants of both acyl acid and amino acid substrate specificity that allow GH3 proteins to modulate a wide range of plant hormone action.

3. Lessons from Plant Metabolism: Antiparasitic Targets The worldwide impact of parasites on human, animal, and plant life is profound.As drug-resistant strains of parasites emerge, there is an urgent need to identify new biochemical targets for developing antiparasitic compounds. Our studies suggest that Caenorhabditis elegans and other nematodes, unlike other animals, use a plant-like pathway as the major biosynthetic route to phosphatidylcholine. In this pathway, a pair of phosphoethanolamine methyltransferases (PMTs) catalyze the sequential methylation of phosphoethanolamine to phosphocholine, which can be incorporated into phosphatidylcholine.Because the PMTs are highly conserved across nematode parasites of humans, livestock, and plants, as well as in protozoan parasites, understanding how these enzymes function and the identification of inhibitors will aid in the development of new antiparasitic compounds of potential medical, veterinary, and agricultural value. This project aims to explore and characterize the PMTs for the development of antiparasitic compounds.

Simon John, PhD

Summer Lab Size: 12

Local Summer Program: http://education.jax.org/summerstudent/index.html

Program Dates: June 4-August 10, 2018 (Note:10 weeks will be required)

Jackson Laboratory
Genetics, Neuroscience

Alleviating the Neuronal Energy Crisis in Glaucoma Using Gene Therapy

Retinal ganglion cell axons in the optic nerve head are insulted early in animal models of glaucoma. Recent analysis suggests a neuronal energy crisis in retinal ganglion cells that may contribute to or drive cell death, optic nerve degeneration, and vision loss. The John lab will be using cutting-edge gene therapy in DBA/2J mice (model of age-related ocular hypertensive glaucoma) to test our energy crisis related hypotheses.

Identifying Genes Controlling Aqueous Humor Outflow Using Cutting Edge Techniques

Elevated intraocular pressure (IOP) is a key causal risk factor for the blinding disease glaucoma, which will afflict 80 million people by 2020. Elevated IOP arises from increased resistance to drainage of the aqueous humor (AQH). The AQH drains through two routes. The conventional pathway is through the trabecular meshwork (TM) followed by Schlemm's Canal (SC) - both located in the wall of the iridocorneal angle at the limbus. The conventional pathway drains the majority of the AQH and the amount of drainage through it is pressure dependent. In normal individuals, IOP is maintained within a narrow range, indicating a high degree of regulation. The mechanisms controlling AQH outflow and hence IOP are unclear. We are actively engaged in determining the molecular basis of the mechanisms controlling AQH outflow and IOP. To complete this study effectively we need to develop modern tools to conditionally knock out genes using Cre-LoxP technology. Towards this effort, one project that we are focusing on is to identify genes that are exclusively expressed in either the SC or TM using immunofluorescence, in situ hybridization, and mouse strains expressing fluorescent proteins in the SC or TM. The goal, after gene identification, is to express Cre-recombinase under control of the promoter of genes identified. Another project will involve screening chemical compounds for their effect on AQH outflow, which will be measured using a device that we have developed in our lab. In the Simon John lab you will have the opportunity to learn a wide array of techniques including mouse genetics, physiological measurements of IOP and AQH outflow, high-resolution light microscopy and electron microscopy, and next generation sequencing. You will work in a scientific environment that is both intense and exciting.

Tracy Johnson, PhD

Summer Lab Size:

Local Summer Program: http://www.ugeducation.ucla.edu/urc-care/summerprog.htm
Program Dates: June 25-August 31, 2018 (Note:10 weeks will be required)

University of California - Los Angeles

Biochemistry, Cell Biology

Understanding mechanisms of co-transcriptional splicing

RNA splicing, the removal of noncoding intron sequences from messenger RNA, is carried out by a large, dynamic macromolecular machine called the spliceosome. Elegant biochemical studies over the last several decades have revealed the “parts list” of the spliceosome, which is made up of 5 small nuclear RNAs and over 100 proteins! Recent 3-D structures have even given us a glimpse of how these parts come together. However, the recognition that assembly of the spliceosome onto RNA occurs while the RNA is still being synthesized (i.e. co-transcriptionally) has raised profound questions about whether spliceosome assembly is influenced by transcription or even the environment in which transcription occurs. For example, we have shown that chromatin modifications such as histone acetylation can affect intron recognition and removal. This project involves using yeast as a model system with its powerful genetic, biochemical, and molecular tools to understand the interactions between chromatin and the splicing machinery and assess how this affects regulation of the splicing reaction.

Eric Kandel, MD

Summer Lab Size: 30

Local Summer Program: http://www.spurs.columbia.edu/index.html
Program Dates: June 5-August 4, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Columbia University
Molecular Biology, Neuroscience

Molecular Basis of Drug Abuse and Posttraumatic Stress Disorder

The lab works on two interrelated projects concerning the molecular basis of drug abuse, the molecular basis of posttraumatic stress disorder (PTSD), and the factors leading to comorbidity of drug abuse and PTSD. The Gateway Hypothesis describes the sequence of steps whereby use of one class of drug, for example, cigarettes (nicotine), precedes the use of other drugs, such as cocaine. We test the molecular basis of this model in mice and rats. Our approach is further based on the evidence that addiction shares molecular steps and molecular logic with long-term memory. We have also identified a mouse model of PTSD where loss of a particular gene leads to a sex-specific increase in stress response. The student will be performing basic biochemistry and molecular biology to further elucidate the role that the molecules involved in memory play in addiction and PTSD.

Molecular Mechanisms of Synaptic Plasticity, Learning, and Memory

Neurons communicate with one another via physical connections known as synapses, and it is widely believed that stable changes in synaptic strength underlie our ability to learn and to establish long-term memories. These enduring changes in synaptic efficacy are brought about by both transcriptional and translational processes, which together regulate the composition of proteins in the neuron.Multiple projects in the lab aim to gain a better understanding of the molecular underpinnings of these processes. Foremost is our discovery that the molecules involved in the persistence of memory storage seem to act as functional prions. We also examine how these processes break down with age, leading to age-related memory loss, and how deficits lead to psychiatric disorders such as schizophrenia.Students will gain experience with a variety of molecular and biochemical techniques, including recombinant protein purification, quantitative PCR, Western blotting, immunoprecipitation, and fluorescence in situ hybridization. Opportunities may also exist for learning confocal microscopy and neuronal cell culture.

Katrin Karbstein, PhD

Summer Lab Size: 7

Local Summer Program: No URL Available
Program Dates: TBD (Note:10 weeks will be required)

The Scripps Research Institute

Biochemistry, Molecular Biology

Testing the role of the ribosomal protein Rps10 in sequence-specific mRNA recruitment

We are interested in better understanding how haploinsufficiency of ribosomal proteins such as Rps10 leads to both growth defects and cancer development, and why deficiency of different ribosomal produces both similar and different biological outcomes. To address these questions, this project uses a combination of luciferase reporter assays, ribosome purifications and yeast analyses to test the role of the ribosomal protein Rps10 in sequence-specific mRNA recruitment to ribosomes. Prior experience in the lab is not necessary but high motivation is essential.

Nicole King, PhD

Summer Lab Size: 10

Local Summer Program: http://amgenscholars.berkeley.edu/
Program Dates: May 30-August 4, 2018 (Note:10 weeks will be required)

University of California - Berkeley

Developmental Biology, Evolutionary Biology

Choanoflagellates and the Evolution of Animal Gene Regulation

In the King lab, we seek fundamental insights into animal biology through a reconstruction of animal origins. The evolution of animals from their single-celled ancestors likely involved both the cooption of ancient genes and evolution of new molecular mechanisms to guide cell proliferation and differentiation. As the closest living relatives of animals, choanoflagellates can provide insights into the evolution of animal development. Join us in investigating how choanoflagellates regulate genes to control the development of a simple multicellular form called a rosette. We will study changes in choanoflagellate gene expression using a battery of tools from genetics, biochemistry, and bioinformatics.

Prior experience with cell culture, biochemistry or bioinformatics would be helpful, but is not essential.

John Kuriyan, PhD

Summer Lab Size:

Local Summer Program: http://amgenscholars.berkeley.edu/
Program Dates: May 30-August 4, 2018 (Note:10 weeks will be required)

University of California - Berkeley
Biophysics, Structural Biology

Molecular mechanism for the regulation of activation in calcium/calmodulin-dependent protein kinase II (CaMKII)

Calcium/calmodulin-dependent kinase II (CaMKII) is a Ser/Thr kinase, which plays a critical role in neuronal and cardiac signaling. Unregulated / perturbed activation of CaMKII leads to several pathological conditions, like severe impairment in learning and memory, cardiac arrhythmias and heart failure. Owing to the physiological importance of the activated state of CaMKII, it is obvious that the activation of CaMKII is tightly regulated in cells.

The proposed project aims at understanding the molecular basis of this regulation using two approaches:

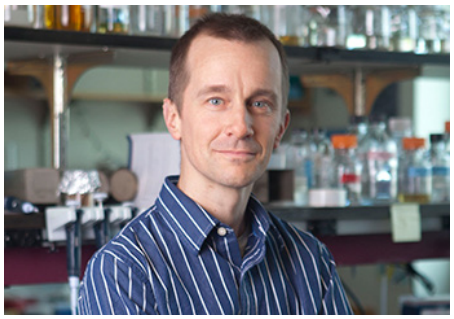
(1) design of a photoactivatable CaMKII using a dimeric protein, pdDronpa, that dissociates in cyan light (500 nm) and re-associates in violet light (400 nm). Following a successful design, we aim to use this optically controlled CaMKII to study the regulation of activation, specifically in terms of the frequency of the activation stimulus, in cells.

(2) reconstitute the regulatory circuit of CaMKII, including its membrane-associated interaction partners, such as the NMDA receptor, the dopaminergic D3 receptor and the phosphatases, on a supported membrane bilayer. Using this simplistic model, we will study the effect of various signal inputs to this circuit to examine the regulatory constraints on CaMKII at the synapse.

Molecular Dynamics Simulation in Structure-Function Studies of T Cell Signaling

When a T cell receptor is activated by contact with a peptide:MHC complex, it sets off a cascade of signals that ultimately result in activation of the T-lymphocyte. The primary step of this signaling pathway is the assembly of the T cell receptor (TCR) complex, whose formation is mediated by a series of phosphorylation reactions carried out by kinases, such as those of the Src family, and dephosphorylation reactions. We will be using several theoretical methods ranging from molecular dynamics simulations to more complex multistate dynamics methods, to complement experiments carried out by our group and understand how the cellular environment and surrounding, interacting proteins affect the structure and function of the members of the TCR complex.

Michael Laub, PhD



Summer Lab Size:

Local Summer Program: https://biology.mit.edu/outreach_initiatives/UG_summer_internship
Program Dates: June 4-August 12, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Massachusetts Institute of Technology

Microbiology, Genetics

Mechanisms of signal integration impacting cell-cycle progression

Organisms need to respond efficiently to environmental changes to survive. Sophisticated networks of regulatory proteins have evolved in all cells to transducing external signals into cells, but how such signals ultimately affect growth and proliferation remain poorly understood. An EXROP student will study how carbon starvation signals are integrated by the bacterium Caulobacter crescentus to control the cell cycle and cell differentiation program of this organism. Genetics and biochemistry will be combined with live-cell and fluorescence microscopy using microfluidic devices to dissect the regulatory strategies used.

Stephen Liberles, PhD

Summer Lab Size:
Local Summer Program: No URL Available
Program Dates: June 5-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Harvard Medical School

Neuroscience, Molecular Biology

Neural sensing within internal organs

Autonomic physiology is precisely controlled by the nervous system. Vital functions such as breathing, heart rate, and metabolism are under dynamic regulation by sensory inputs that signal the physiological status of internal organs. The vagus nerve is a key component of the communication axis between body and brain, with different sensory neurons detecting nutrients, changes in blood pressure, toxins, and mechanical stretch of the stomach, airways, and heart. Despite medical importance, vagus nerve sensory biology remains poorly charted at a mechanistic level. My lab uses molecular and genetic approaches to understand how the vagus nerve detects internal organ cues. Genetic approaches are used to map, image, ablate, and control subsets of vagal sensory neurons, while molecular approaches are used to characterize sensory transduction mechanisms.

Christopher Lima, PhD

Summer Lab Size:

Local Summer Program: http://www.sloankettering.edu/gerstner/html/54513.cfm
Program Dates: June 5-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Memorial Sloan Kettering Cancer Center

Biochemistry, Structural Biology

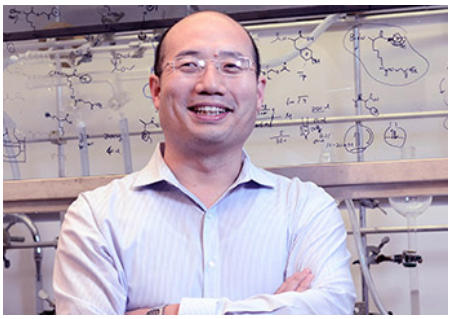
RNA processing and decay

The eukaryotic RNA exosome is an essential multi-subunit complex that processes or degrades nearly every class of RNA in the nucleus and cytoplasm. The RNA exosome interacts with several key co-factors to recruit or prepare the RNA substrates for degradation or processing. Our focus is to understand how the RNA exosome targets particular substrates for modification, degradation or processing. Projects will employ biochemical reconstitution of human and yeast RNA exosomes, their co-factors and substrates, analysis of their activities through biophysical and biochemical approaches, and structural approaches to delineate interactions important for these activities.

Ubiquitin-like protein conjugation pathways

Post-translational modification of protein substrates by ubiquitin (Ub) and ubiquitin-like (Ubl) proteins such as SUMO regulate nearly every facet of eukaryotic cell biology. SUMO and ubiquitin are essential proteins that share structural similarity and their attachment to substrates occurs through a sequential cascade of activities catalyzed by evolutionarily related E1 activating enzymes, E2 conjugating enzymes and E3 ligases. Projects in this area of research will employ biochemical and structural approaches to delineate mechanisms for substrate recognition by the Ub/Ubl conjugation machinery. Interests are also focused on Ub/Ubl-mediated signal transduction through receptors that specifically interact with Ub/Ubl-modified substrates.

Hening Lin, PhD



Summer Lab Size:

Local Summer Program: No URL Available
Program Dates: TBD (Note:10 weeks will be required)

Cornell University
Biochemistry, Chemical Biology

The role of sirtuins and novel protein post-translational modifications in cancer

Sirtuins are a class of enzymes with NAD+-dependent protein lysine deacetylase activities. They regulate numerous biological processes, including transcription and metabolism. Among the seven mammalian sirtuins, four of them (SIRT4, SIRT5, SIRT6, and SIRT7) do not have efficient deacetylase activity. Our lab discovered novel activities for some of these sirtuins. For example, we found SIRT5 can efficiently remove succinyl and malonyl groups from protein lysine residues and SIRT6 can efficiently remove long chain fatty acyl groups. We found that several sirtuins, by removing these novel protein post-translational modifications, regulate the transformed phenotype of cancer cells. We are interested in understanding the detailed molecule mechanisms and developing small molecule inhibitors to target these sirtuins for cancer treatment.

Dan Littman, MD, PhD

New York University
Immunology, Microbiology

Summer Lab Size:

Local Summer Program: https://med.nyu.edu/research/sackler-institute-graduate-biomedical-sciences/summer-undergraduate-research-program
Program Dates: June 5-August 4, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Characterization of Human Dendritic Cell Subsets Susceptible to Infection with HIV-1

Dendritic cells (DCs) are resistant to productive infection with HIV-1, but instead deliver nonreplicating viral particles to CD4+ T cells, facilitating their infection. DCs have intrinsic resistance to infection with HIV-1, and viral replication is arrested prior to reverse transcription of the incoming viral RNA. The resistance can be overcome when Vpx is provided to DCs by the related simian immunodeficiency virus (SIV). Vpx delivered by SIV particles targets a host cell restriction factor (that is not yet identified) and permits productive infection with HIV-1. When this occurs, there is completed reverse transcription and integration of the proviral DNA into host chromosomes. Expression of the viral genes then results in production of infectious viral particles. We found that when monocyte-derived DCs (MDDCs) are thus infected, there is strong activation of the innate immune response, with production of type I interferon and up-regulation of molecules that help activate HIV-specific T lymphocytes. This DC-specific response requires production of viral capsid (CA) protein and its interaction with a host molecule, cyclophilin A (CypA). This sets in motion a signaling cascade that results in transcription of the Î²-interferon gene and subsequent activation of an antiviral program. We would like to learn how to harness such a response to prevent and treat HIV infection. While all MDDCs can be infected with HIV-1 in this manner, infection of primary blood DCs levels out at 30 percent of cells, suggesting that there are at least two different subsets of circulating DCs that are differentially susceptible to infection. The project will be to separate these populations based on their differential infectivity and characterize their properties by gene expression profiling, using both gene chip and deep sequencing technologies. The results may then be applied to identify candidate genes that contribute to resistance or susceptibility of DCs to infection with HIV-1.

Identify Effector Functions of Th17-Inducing Segmented Filamentous Bacteria

Segmented filamentous bacteria (SFB) are unusual bacteria that adhere tightly to the epithelium of the small intestine, initiating signals that result in the differentiation of T cells that secrete the cytokines IL-17 and IL-22 (Th17 cells). Th17 cells protect the host by limiting the growth of a variety of potentially pathogenic bacteria, but they also mediate inflammatory autoimmune diseases. It is therefore important to determine how commensal bacteria such as SFB contribute to establishing a balanced level of Th17 cells in the intestine. Our goal is to determine how the host “senses” the presence of SFB adhering to the epithelial cells. We are currently sequencing the genome of SFB, and we aim to express a series of recombinant SFB proteins that can be tested in cultures of epithelial cells, dendritic cells, and T cells for their ability to induce IL-17.

Stavros Lomvardas, PhD

Summer Lab Size: 17

Local Summer Program: http://www.spurs.columbia.edu/index.html
Program Dates: June 5-August 4, 2017 (Dates for 2018 should be similar; Note: 10 weeks will be required)

Columbia University
Neuroscience, Molecular Biology

Deciphering how nuclear architecture governs monogenic and monoallelic olfactory receptor gene regulation

This project explores the interplay between genomic organization and singular olfactory receptor (OR) gene expression. Our studies revealed that the ~1000 olfactory receptor genes form interchromosomal nuclear compartments during the differentiation of mouse olfactory neurons, which culminates in the tight repression of most OR genes and the strong transcriptional activation of a single OR allele that is surrounded by a large number of enhancer elements. We seek to characterize the stepwise process of genomic folding that culminates in the formation of these unique nuclear compartments during differentiation, using a combination of genomic and imaging methodologies. Students interested in this project will be working with mice or mouse tissue and will benefit by a strong computational background.

Loren Looger, PhD

Summer Lab Size: 7

Local Summer Program: http://www.janelia.org/student-programs/undergraduate-program
Program Dates: June 6-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be reuquired)

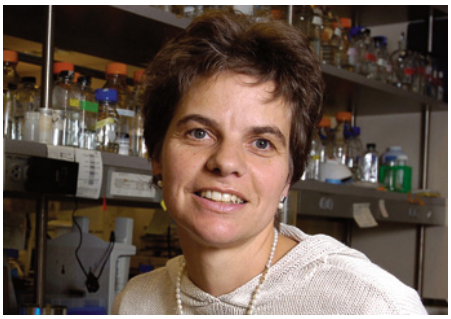
Janelia Research Campus

Molecular Biology, Structural Biology

Engineering for neuroscience applications

Our lab works on many different things, with a primary focus on engineering & optimizing tools for neuroscience. We test variants as proteins and then in cells, and work with a number of great collaborators to help us test promising constructs in animals. A number of specific project goals are possible, and will be decided collectively with applicants. Prior experience with molecular biology would be nice but is not essential. Similarly, programming skills would be handy but again are not essential.

Karolin Luger, PhD



Summer Lab Size:

Local Summer Program: http://www.colorado.edu/GraduateSchool/DiversityInitiative/undergrads/smart/index.html
Program Dates: June 5-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

University of Colorado Boulder

Molecular Biology, Structural Biology

Decoding the centromere

The centromere is a specialized region on each chromosome to which the kinetochore and ultimately the mitotic spindle attaches. We study the interaction of proteins with centromeric nucleosomes, using biophysical approaches and cryo-electron microscopy. The project involves protein purification, complex preparation and characterization, as well as introduction to cryo-EM.

Irresistible force meets immovable object: transcription through the nucleosome

Nucleosomes present formidable barriers to the transcription machinery, requiring remodeling factors and histone chaperones in addition to RNA polymerase. We are using single molecule fluorescence in a completely reconstituted system to study the mechanism by which nucleosomes are navigated by the transcription machinery. The project involves protein purification, bulk transcription assays, and introduction to single molecule FRET assays.

David Lynn, PhD

Summer Lab Size:

Local Summer Program: No URL Available
Program Dates: May 31-August 3, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Emory University
Chemical Biology

Alternative Chemistries of Life

Click on the following link for background information on the project: http://alternativechemistries.emory.edu.

Infectious Proteins in Alzheimer's Disease

Prion-like conformational replication events appear to underlie the progressive spread of Alzheimer's Disease, and we are interested in unraveling the mechanism.

John MacMicking, PhD

Yale University

Immunology, Microbiology

Summer Lab Size: 15

Local Summer Program: http://medicine.yale.edu/biomedsurf/
Program Dates: June 5-August 2, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Characterizing new human immune proteins that control infection

This project will test the importance of new human host proteins identified through genome-wide Cas9-CRISPR screens to help protect human cells against infection. Specifically, the work will entail generating clean chromosomal deletions of selected human genes in different cell types for infection by globally important pathogens causing HIV, malaria, typhoid fever and Zika. There is an opportunity to look at the involvement of these host proteins interacting with intracellular pathogens inside human cells using live super-resolution imaging within a dedicated infection suite. Experience with mammalian cell tissue culture, molecular genetics, microbiology and fluorescence microscopy would be advantageous.

Harmit Malik, PhD

Summer Lab Size: 12

Local Summer Program: http://www.fhcrc.org/en/education-training/undergraduate-students.html
Program Dates: June 11-August 10, 2018 (Note: 10 weeks will be required)

Fred Hutchinson Cancer Research Center

Experimental Evolutionary Biology, Genetics

Investigations of Genetic Conflicts

No project description available. Please visit Dr. Malik's HHMI scientist page for more information about current research.

Joshua Mendell, MD, PhD

Summer Lab Size: 20
Local Summer Program: http://www.utsouthwestern.edu/education/graduate-school/programs/non-degree-programs/surf.html
Program Dates: June 4-August 10, 2018 (Note:10 weeks will be required)

University of Texas Southwestern Medical Center

Molecular Biology, Cancer Biology

The regulation and function of mammalian noncoding RNAs

The Mendell laboratory is interested in mechanisms of post-transcriptional gene regulation and the roles of these pathways in normal mammalian physiology and diseases such as cancer. A major aspect of our work focuses on how noncoding RNAs, including microRNAs and long noncoding RNAs, interface with these regulatory mechanisms. Potential summer projects include the analysis of noncoding RNA functions in cellular and animal models and the dissection of the mechanisms underlying these activities. These experiments typically employ both high throughput approaches (for example RNA-seq, CLIP-seq, CRISPR-Cas9 screening) and biochemical and molecular biological approaches (for example analysis of RNA-protein interactions, genome editing to modulate noncoding RNA function).

Elliot Meyerowitz, PhD

Summer Lab Size:

Local Summer Program: https://www.sfp.caltech.edu/programs/wavefellows
Program Dates: June 19-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

California Institute of Technology

Developmental Biology, Plant Biology

Cell-Cell Communication in Arabidopsis Shoot Apical Meristems

We have a number of different studies for which an applicant will be considered, all concerning chemical signaling via peptides, auxin, or cytokinins, and mechanical signaling, between cells in the shoot stem cell niche of plants.

Danesh Moazed, PhD

Harvard Medical school

Biochemistry, Cell Biology

Summer Lab Size:

Local Summer Program: No URL Available
Program Dates: June 5-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Search for factors that mediate epigenetic inheritance

The project involves using an inducible system to search for and study factors that mediate the decay or epigenetic memory of heterochromatin in fission yeast. Heterochromatin in this yeast shares many conserved features, including histone H3 lysine 9 methylation and association with HP1 proteins, with mammalian heterochromatin. The system developed in our lab allows the establishment and epigenetic inheritance components of heterochromatin to be analyzed separately. Working with a graduate student or postdoc, you will participate in isolation and biochemical characterization of mutations that affect epigenetic inheritance.

Mala Murthy, PhD

Summer Lab Size:

Local Summer Program: No URL Available
Program Dates: TBD (Note:10 weeks will be required)

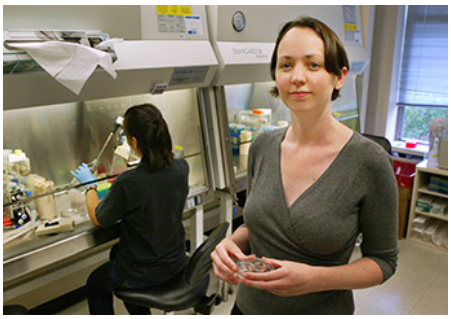
Princeton University

Neuroscience, Computational Biology

Neural Mechanisms of Acoustic Communication in Drosophila

This project examines how a subset of neurons in the female Drosophila brain control the response to male courtship song. Experiments will include optogenetic activation and silencing of these neurons and assaying flies using highly quantitative behavioral readouts, computational modeling of behavioral data, and in vivo calcium imaging of these neurons in behaving females. Prior experience with computer programming or data analysis would be helpful but is not required.

Celeste Nelson, PhD



Summer Lab Size: 15

Local Summer Program: No URL Available
Program Dates: TBD (Note:10 weeks will be required)

Princeton University

Bioengineering, Developmental Biology

Quantitative imaging analysis of tissue differentiation and lung development

The tree-like geometry of the airways of the lung builds itself at the same time as the embryonic airway epithelium begins to differentiate into a variety of cell types. We previously found that physical forces from fluid pressure increase the rate of development and maturation of the lung. Here, the student will quantify morphology of the epithelium and pattern of expression of differentiation markers under different levels of pressure. The results of these studies will help to infer whether physical forces favor differentiation into specific epithelial cell types.

Jennifer Nemhauser, PhD

University of Washington

Plant Biology, Synthetic Biology

Summer Lab Size: 12

Local Summer Program: http://www.washington.edu/undergradre-search/

Program Dates: June 19-August 18, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Building tools to track and manipulate cell fate in plants

Normal development hinges on a group of progenitor cells coordinately adopting distinct expression profiles that will define the fate of their descendants. One striking feature of plant development is the post-embryonic addition of entirely new organs such as lateral roots. My lab is working to understand how events separated in time and space, yet triggered by the same hormone, reprogram cells to begin the process of creating a new root. This project will use molecular biology and imaging techniques to test a new in vivo tagging approach to mark, track and isolate root cells undergoing a switch in fate.

Dianne Newman, PhD

Summer Lab Size: 16

Local Summer Program: https://www.sfp.caltech.edu/programs/wavefellows
Program Dates: June 19-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

California Institute of Technology

Genetics, Microbiology

Exploring the role of pathogen physiology in infectious disease

In the Newman lab, we study how bacterial pathogens alter their physiology to survive inside human hosts. We examine how pathogens form biofilms, shift from aerobic to anaerobic metabolism, and enter into quiescent states, all of which can increase pathogen resistance to antibiotics. We also characterize the environments that pathogens encounter in the body, quantifying what nutrients are available to pathogens and visualizing how pathogens physically interact with host cells. We use this information to explore new ways of treating infectious diseases. Our research employs a variety of approaches and tools, including genetics, microscopy, analytical chemistry, and bioinformatics. The Newman lab's diversity of projects and techniques will introduce an EXROP student to a breadth of exciting and important scientific questions, and provide tools to support his/her growth as a scientist.

Jacquin Niles, PhD

Summer Lab Size: 12

Local Summer Program: https://biology.mit.edu/outreach_initiatives/UG_summer_internship
Program Dates: June 4-August 12, 2017 (Dates for 2018 should be similar;Note:10 weeks will be required)

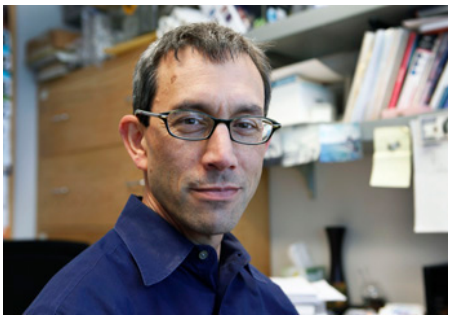
Massachusetts Institute of Technology

Bioengineering, Parasitology

Synthetic Devices for Studying Transcriptional Control in Malaria Parasites

Malaria is a major global human health challenge. Plasmodium falciparum is the parasitic organism that causes the majority of malaria-related deaths. Though it is a highly successful pathogen, we lack fundamental understanding of many facets of its biology. For example, detailed knowledge of transcriptional regulation in these eukaryotic parasites–beginning with the minimal information required to drive robust transcription–is unknown. In this project, we will use synthetic biology approaches to define critical sequence-level information required for controlling both the timing and level of gene expression in these parasites. This will involve using bioinformatics tools to design transcriptional regulatory regions that will be physically assembled into reporter contexts for quantitative analyses of gene expression in transgenic parasites. This studies will provide both basic insight into how transcription is regulated, as well as the opportunity to design functional, synthetic transcriptional units de novo for applications aimed at understanding the roles different genes play in parasite survival and pathogenesis.

Krishna Niyogi, PhD



Summer Lab Size:

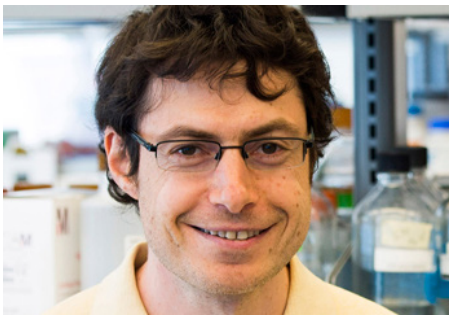
Local Summer Program: http://amgenscholars.berkeley.edu/
Program Dates: May 30-August 4, 2018 (Note:10 weeks will be required)

University of California, Berkeley
Biochemistry, Plant Biology

Biogenesis and Assembly of Photosynthetic Membrane Complexes

Photosynthesis is the biological process that converts solar energy and carbon dioxide into biomass, from which we derive food and fuel. Photosystem II (PSII) is the pigment-protein complex in photosynthetic membranes that uses light energy to oxidize water and produce high-energy electrons. Although high-resolution structures are now available for PSII, a thorough understanding of how the pigments, protein subunits, and cofactors are assembled into functional complexes is lacking. To identify novel factors that are necessary for PSII assembly, we are characterizing mutants of the model photosynthetic eukaryote, Chlamydomonas reinhardtii, that lack PSII. Genetic analysis of the mutants will involve crosses to determine the underlying genetic basis for the phenotype and identification of the defective gene by PCR-based approaches and DNA sequencing. Membrane protein composition will be investigated by SDS-PAGE, blue-native PAGE, and immunoblotting, and the architecture of the photosynthetic membrane will be imaged by electron microscopy and atomic force microscopy.

Evgeny Nudler, PhD



New York University
Biochemistry, Molecular Biology

Summer Lab Size: 20

Local Summer Program: https://med.nyu.edu/research/sackler-institute-graduate-biomedical-sciences/summer-undergraduate-research-program
Program Dates: June 5-August 4, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Turning an antibiotic from bacteriostatic to bactericidal

Some of the most commonly used antibiotics for treating infections inhibit growth reversibly without killing of the pathogen. This leaves the door open for pathogens to resuscitate once the concentration of antibiotics drops below a certain threshold at the site of infection. This project will test the hypothesis that bacterial stress responses actively prevent such antibiotics from killing bacteria. The project includes antibiotic killing assays in E.coli, bacterial genetics methodologies, transposon mutagenesis, next generation sequencing, coding in python and data analysis.

Benjamin Ohlstein, MD, PhD

Summer Lab Size:

Local Summer Program: http://www.spurs.columbia.edu/index.html
Program Dates: June 5-August 4, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Columbia University Medical Center

Developmental Biology, Cell Biology

Novel Mechanisms Regulating Intestinal Stem Cell Number

Studies of intestinal homeostasis have focused largely on replacement of differentiated cells that are lost due to digestive function and exposure to ingested bacteria and chemical damage. However, mechanisms of ISC replacement have been largely unexplored. To this end, we developed a physiologically relevant starvation assay to induce rapid loss of stem cells. Within two days of starvation, loss of approximately half of the intestinal stem cell population in the posterior midgut is observed. Upon re-feeding of starved animals, ISC number returns to that of controls. Our analysis demonstrates that generation of new stem cells appears to proceed through a spindle-independent ploidy reduction of cells in the enterocyte lineage through a process known as amitosis, a poorly understood process implicated in cancer initiation. To gain insight into the exact mechanism of polyploidy dedifferentiation we are using real-time imaging to determine the cellular mechanism of EC dedifferentiation. We are also carrying out large scale genetic screens in Drosophila to identify genes required for initiation, progression, and resolution of amitosis.

Baldomero Olivera, PhD

Summer Lab Size: 12
Local Summer Program: https://our.utah.edu/spur/information/
Program Dates: May 23-August 3, 2018 (Note:10 weeks will be required)

University of Utah

Biochemistry, Chemical Biology, Neuroscience

Discovery of Natural Products That Affect Catecholamine Transporters

There is considerable pharmacological interest in compounds that affect the transport of catecholamines, since many drugs for disorders of the nervous system are based on increasing or decreasing the concentration of dopamine, norepinephrine, or serotonin. Only one compound has been isolated from the venoms of cone snails so far; this compound affects the norepinephrine transporter. This has proved to be an analgesic and is being developed by a biotech company as a therapeutic to alleviate pain. The fact that cone snails have a peptide that affects the norepinephrine transporter suggests that a broader survey of cone snail venoms may define novel families of peptides that target catecholamine transporters. The EXROP student will carry out assays on novel venoms and, after identifying the venom that has activity that affects transporter function, will work with a graduate student or advanced undergraduate researcher to purify the compound of interest and, ultimately, to validate the assignment of function through peptide synthesis.

Aydogan Ozcan, PhD

Summer Lab Size:

Local Summer Program: http://www.ugeducation.ucla.edu/urc-care/summerprog.htm
Program Dates: June 25-August 31, 2018 (Note:10 weeks will be required)

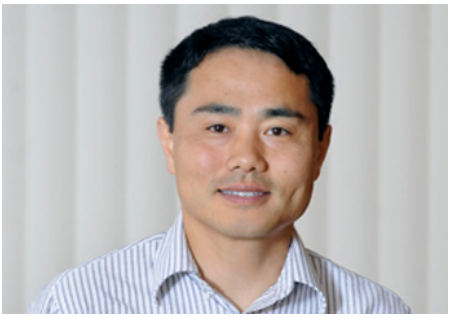
University of California - Los Angeles
Engineering, Global Health

Mobile Imaging, Sensing and Diagnostics for m-Health, Telemedicine and Global Health Applications

My research focuses on the use of computation/algorithms to create new optical microscopy, sensing, and diagnostic techniques, significantly improving existing tools for probing micro- and nano-objects while also simplifying the designs of these analysis tools. For example, in our lab we created a set of computational microscopes which use lens-free on-chip imaging to replace traditional lenses with holographic reconstruction algorithms. Basically, 3D images of specimens are reconstructed from their “shadows” providing considerably improved field-of-view (FOV) and depth-of-field, thus enabling large sample volumes to be rapidly imaged, even at nanoscale. These new computational microscopes routinely generate >1_2 billion pixels (giga-pixels), where even single viruses can be detected with a FOV that is >100 fold wider than other techniques. At the heart of this leapfrog performance lie self-assembled liquid nano-lenses that are computationally imaged on a chip. These self-assembled nano-lenses are stable for >1 hour at room temperature, and are composed of a biocompatible buffer that prevents nano-particle aggregation while also acting as a spatial “phase mask.” The field-of-view of these computational microscopes is equal to the active-area of the sensor-array, easily reaching, for example, >20 mm2 or >10 cm2 by employing state-of-the-art CMOS or CCD imaging chips, respectively.

In addition to this remarkable increase in throughput, another major benefit of this technology is that it lends itself to field-portable and cost-effective designs which easily integrate with smartphones to conduct giga-pixel tele-pathology and microscopy even in resource-poor and remote settings where traditional techniques are difficult to implement and sustain, thus opening the door to various telemedicine applications in global health. Some other examples of these smartphone-based biomedical tools include imaging flow cytometers, immunochromatographic diagnostic test readers, bacteria/pathogen sensors, blood analyzers for complete blood count, and allergen detectors. Through the development of similar computational imagers, we also reported the discovery of new 3D swimming patterns observed in human and animal sperm. One of this newly discovered and extremely rare motion is in the form of “chiral ribbons” where the planar swings of the sperm head occur on an osculating plane creating in some cases a helical ribbon and in some others a twisted ribbon. Shedding light onto the statistics and biophysics of various micro-swimmers’ 3D motion, these results provide an important example of how biomedical imaging significantly benefits from emerging computational algorithms/theories, revolutionizing existing tools for observing various micro- and nano-scale phenomena in innovative, high-throughput, and yet cost-effective ways.

Duojia Pan, PhD



Summer Lab Size:

Local Summer Program: http://www.utsouthwestern.edu/education/graduate-school/programs/non-degree-programs/surf.html
Program Dates: June 4-August 10, 2018 (Note:10 weeks will be required)

University of Texas Southwestern Medical Center

Developmental Biology, Genetics

Characterization of Genes Controlling Organ Size

My lab uses the fruit fly Drosophila as a model to discover novel genes and pathways that regulate organ size in development. Our research has led to the discovery of signaling pathways that play conserved roles in the growth of mammalian organs. In this project, students will conduct genetic screens to isolate growth control genes in Drosophila, and carry out functional studies of these genes using a variety of experimental models. Students will gain experience with genetics, biochemistry, and molecular biology. These positions offer exciting opportunities to join a research team working in the areas of developmental biology, cell signaling, and cancer biology.

Roy Parker, PhD

Summer Lab Size: 15

Local Summer Program: http://www.colorado.edu/GraduateSchool/DiversityInitiative/undergrads/smart/index.html
Program Dates: June 5-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

University of Colorado Boulder

Biochemistry, Cell Biology

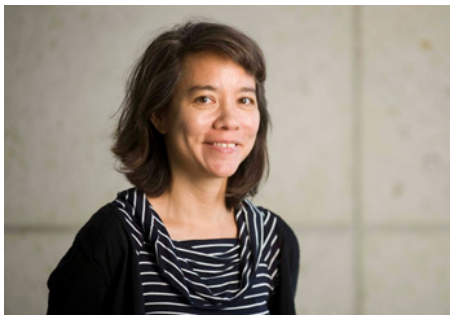
Analysis of Normal and Aberrant RNP Granules in Degenerative Diseases

Assemblies of RNA and protein form in a number of normal and aberrant conditions. For example, a variety of degenerative diseases (e.g. ALS) include the formation of aberrant inclusions that contain both RNA and protein. Using genetic and biochemical approaches, we study how these assemblies form and their functions in both normal and disease conditions.

Analysis of viral populations

We have developed methods to identify virsues present in a variety of samples. We will use those methods to interogate unanalyzed samples for new potential viruses.

Tanya Paull, PhD



Summer Lab Size: 15-17

Local Summer Program: http://ugs.utexas.edu/our/find/srsp
Program Dates: May 31-August 4, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

University of Texas at Austin
Biochemistry, Molecular Biology

Roles of the MRN Complex in the DNA Damage Response

The repair of double-strand breaks (DSBs) in chromosomal DNA occurs through recombination, either through nonhomologous mechanisms (NHEJ) or through homologous mechanisms that require replication from an intact template. Correct repair of DSBs in cells is essential for the maintenance of genomic stability, and errors in these pathways predispose mammalian organisms to cancer.The Mre11/Rad50/Nbs1(Xrs2) [MRN(X)] complex is one of the first enzyme complexes to recognize and localize to a DSB in eukaryotic cells. MRN(X)-deficient cells exhibit reduced levels of DSB processing in vivo and are completely unable to process DSBs during meiosis when chromosomal breaks are made by the Spo11 protein. Genetic experiments have also identified other cellular factors that act in cooperation with MRN(X) to process DSBs in eukaryotic cells, including the Sae2 (CtIP/Ctp1) endonuclease, the Exo1 exonuclease, and the Sgs1 helicase. Our studies investigate the biochemical basis of the involvement of MRN(X) and Sae2/CtIP in the processing of 5' strands at DSBs using purified proteins in vitro, and characterize how posttranslational modifications of these factors affect their activities. We also investigate the functional effects of mutations in DSB repair factors in vivo in budding yeast and in human cells, examining how catalytic mutations and inhibition of posttranslational modifications affect cell cycle progression, DNA repair, and DNA damage signaling. The summer project will likely involve analysis of MRN(X) and Sae2/CtIP catalytic functions.

The ATM Protein Kinase and Regulation of Redox Homeostasis

The ataxia-telangiectasia mutated (ATM) kinase initiates a rapid cascade of protein phosphorylation in response to double-strand breaks in chromosomal DNA and also in response to oxidative stress. Loss of ATM function in humans causes the debilitating neurodegenerative disorder Ataxia-Telangiectasia (A-T), and the oxidative stress response of ATM is implicated in the neuronal function of ATM. Current projects in the lab focus on the role of ATM In maintenance of protein homeostasis and redox control, which we are investigating using methods that interrogate global patterns of protein aggregation and chaperone function.

Norbert Perrimon, PhD

Summer Lab Size: 30

Local Summer Program: No URL Available
Program Dates: June 5-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Harvard Medical School
Developmental Biology, Genetics

Genetic Dissection of Pathways Involved in Stem Cell Biology

We have recently identified novel stem cell populations residing in the Drosophila gastrointestinal tract that provide a unique system to apply the powerful genetic tools available in this organism to identify new factors and pathways that regulate the number of stem cells and their differentiation. The Drosophila gut is an ideal system to study stem cell biology because, while it is simpler than that in mammals, it is highly similar at cellular and molecular levels. Both systems rely on multipotent stem cells to replenish the loss of two broad classes of cell types, absorptive and secretory cells, that regularly undergo apoptosis and delamination into the gut lumen. Moreover, the molecular basis driving the differentiation of stem cell daughters into either absorptive or secretory cells appears to be conserved; in both mammals and Drosophila, high levels of signaling by the Notch pathway promote differentiation to the absorptive cell fate by inhibiting development of the secretory fate (which requires only low levels of Notch signaling). Thus, the overall biology of Drosophila gut stem cells appears to recapitulate the major features of mammalian gut stem cell biology. We have recently developed a powerful luciferase-based assay that enables us to carry out screens for genes and bioactive chemicals that affect stem cell growth in the adult Drosophila gut. The EXROP student will participate in our ongoing project to develop models of human stem cell colon cancer using the Drosophila gut as a model system and will apply our luciferase technology to carry out pilot screens for genes and small molecules that can have therapeutic effects

Hormonal regulation of physiology

Drosophila has emerged in recent years as a prime model to dissect the intricate interactions between organs and the role hormones play in coordinating the state of one organ/tissue with others. For many years most hormonal studies focused on Insulin signaling, regulated by Dilps, and to some extent on AKH/Glucagon. However, in recent years a number of additional hormonal systems have been uncovered. In particular, our lab identified Upd2 as theDrosophila Leptin ortholog and characterized the mechanism by which Upd2 senses fat in adipose tissues. In addition, we showed that Drosophila muscles, depending on their physiological states, produce a number of systemic factors, such as ImpL2/IGFBP, Myostatin/GDF11, and Activin-beta that affect the physiology of other tissues. We also showed that ImpL2, which is produced from gut tumors, triggers systemic organ wasting reminiscent to cachexia by downregulating systemic Insulin levels. We are currently exploiting this “cachexia” model to characterize the underlying molecular mechanisms of muscle wasting, focusing on the roles of the ubiquitin-proteasome system (UPS) and the autophagic-lysosome pathway in muscle atrophy. In addition, we are interested in identifying additional factors derived from gut tumors important for organ wasting. The EXROP student will participate in genetic screens to characterize factors involved in the communication between organs.

Samuel Pfaff, PhD

Summer Lab Size:

Local Summer Program: http://grad.ucsd.edu/degrees/summer-researches/stars/index.html
Program Dates: June 24-August 17, 2018 (Note:10 weeks will be required)

The Salk Institute for Biological Studies

Developmental Biology, Neuroscience

Molecular characterization of peripheral neuropathies and spinal cord disease

Our laboratory studies the spinal cord to understand disease pathways that affect movement. We use molecular biology and mouse genetics to investigate the pathways that affect neuronal function and survival, and characterize the affects of disease-causing mutations using a variety of methods ranging from next generation sequencing and bioinformatics to high resolution cellular imaging.

Michael Rape, PhD

Summer Lab Size:

Local Summer Program: http://amgenscholars.berkeley.edu/
Program Dates: May 30-August 4, 2018 (Note:10 weeks will be required)

University of California - Berkeley

Biochemistry, Cell Biology

Molecular pathways of cell fate determination

Using different stem cell models, we are investigating molecular pathways of cell fate differentiation during development of the peripheral nervous system as well as during myogenesis. As an entry point, we are using high-throughput genetic screens to identify ubiquitylation enzymes that are essential for certain differentiation reactions. Building off of subsequent proteomic approach tailored to isolate the critical ubiquitylation substrates, we then dissect the molecular mechanisms underlying essential developmental reactions. A typical EXROP project could address each of these steps, i.e. genetic discovery, proteomic analyses, or dissecting the role of ubiquitylation in specific differentiation reactions using more biochemical approaches.

Tom Rapoport, PhD

Summer Lab Size: 20

Local Summer Program: No URL Available
Program Dates: June 5-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Harvard Medical School

Cell Biology, Structural Biology

Studies of Bacterial Protein Translocation In vitro using a Reconstituted System

While all bacterial proteins are synthesized in the cytosol, a large number must be exported from the cell in order to function properly. These proteins are trafficked through the bacterial translocation channel SecY either during, or immediately after, synthesis at the ribosome. In order to be targeted to the translocation machinery, secreted proteins encode signal sequences N-terminal to their mature domains. These signal sequences are approximately 20-30 amino acids in length and comprise a basic patch, followed by a hydrophobic stretch, and a cleavage site for the signal peptidase, which removes the signal sequence from the secreted protein after translocation. While the roles of the latter two domains are well understood, the purpose of the N-terminal basic residues remains unclear. In this project, the EXROP student will use an in vitro reconstitution of bacterial protein translocation to investigate the efficiency of translocation with a variety of signal sequence mutants involving these amino acids. The goal would be to understand the tolerance of targeting and translocation to perturbations at these positions in the substrate.

Michael Reiser, PhD

Summer Lab Size: 5-6
Local Summer Program: http://www.janelia.org/student-programs/undergraduate-program
Program Dates: TBD (10 weeks required)

Janelia Research Campus

Neuroscience

Visual place learning in flies using optogenetics

No project description available. Please visit Dr. Reiser's HHMI scientist page for more information about current research.

A comparative investigatoin of color and motion vision in drosophila

No project description available. Please visit Dr. Reiser's HHMI scientist page for more information about current research.

Rebecca Richards-Kortum, PhD

Summer Lab Size: 20

Local Summer Program: http://www.bcm.edu/smart/
Program Dates: May 29-July 27, 2018 (Note:10 weeks will be required)

Rice University

Bioengineering, Medicine and Translational Research

Low-Cost, High-Performance Global Health Technologies

Guided by the belief that all of the world's people deserve access to health innovation, Rebecca Richards-Kortum's research and teaching focus on developing and disseminating low-cost, high-performance global health technologies. Specifically, we are working to develop cost-effective optical imaging and spectroscopy tools to reduce the incidence and mortality of cancer, as well as infectious disease through early detection at the point of care.In collaboration with the University of Texas MD Anderson Cancer Center, we have developed novel cellular and molecular imaging technologies to recognize signatures of early neoplastic disease. At the same time, we have developed optically active, targeted nanoparticles and fluorescent dyes to directly image the molecular hallmarks of cancer. Through clinical trials at MD Anderson, Mount Sinai Medical Center, and diverse partners in Latin America, we have optimized these agents and imaging systems, demonstrating that they can detect precancerous lesions and early cancers in the cervix, oral cavity, and the esophagus with high sensitivity and specificity.More recently, we have initiated a multidisciplinary effort to develop molecular-specific contrast agents and optical microfluidic chips for point-of-care detection of infectious disease through collaborations at Baylor College of Medicine.

Michael Rosbash, PhD

Brandeis University
Molecular Biology, Neuroscience

Summer Lab Size: 14

Local Summer Program: http://www.bio.brandeis.edu/undergrad/summerResearch/index.html
Program Dates: May 29-August 3, 2018 (Note:10 weeks will be required)

Neuron-Specific Gene Expression and Circadian Locomotor Activity and Sleep

The circadian network in Drosophila consists of ~75 pairs of neurons in the central brain. Rhythmic circadian locomotor activity of flies and many other insects has two activity peaks per day: One is centered on dawn and the other on dusk. The markedly reduced activity between these two peaks constitutes a siesta, which is a third behavioral feature in the middle of the day. We have shown that these 3 daytime activity features derive from the neuronal activity of 3 groups of circadian neurons: morning cells, evening cells and DN1-sleep cells. Each of these three groups contains 5-10 adjacent neurons. We are interested in how they differ and how they communicate, with each other, with other circadian neurons and with other neurons elsewhere in the fly brain. Part of this project involves activating or recording from these discrete neuron groups, either in dissected brains or in wake-behaving flies, with optogenetic and calcium tracing techniques respectively. In the case of dissected brains, we can assay for downstream neuronal connections; in the case of wake-behaving flies, we can assay the direct behavioral consequences of activation or track the temporal calcium profiles of specific neurons. We are also profiling differential gene expression by RNA-Seq, both spatially and temporally. Spatial profiling is a comparison of the 3 different neuron subtypes, whereas temporal profiling assays time points across the 24 hour day for each of the subtypes.

Sleep and Aging

Although there is no consensus on why we sleep, that is, its function(s), work on Drosophila sleep over the past decade has improved our understanding of its regulation. Indeed, much progress has been made in the identification of genes, anatomical regions, and neurochemicals with strong effects on fly sleep. Among the most important wake-promoting chemicals is dopamine, and a couple of chemicals strongly promote sleep. The circadian system is also important for the normal timing of sleep and wake, that is, the daily regulation of sleepiness and alertness. What is more poorly understood is homeostatic regulation, or whatever keeps track of sleep need. For example, sleep deprivation leads to increased sleep or “sleep rebound” in flies as well as humans (and an increased depth of sleep in mammals), and this regulation is supposed to be largely independent of circadian time. However, our recent results in flies indicate a close connection between the circadian system and sleep regulation. Aging also influences sleep regulation similarly in humans and flies. For example, the strongest effect of aging is on sleep fragmentation, which is roughly speaking an increase in the number of awakenings per night; in contrast, total sleep time is only modestly affected by aging. We also found that sleep rebound is very compromised in old flies, suggesting a relationship between aging and homeostatic sleep regulation. We plan to use biochemical methods to look for molecular signatures of sleep deprivation and sleep rebound in flies, focusing on brain neurons and circuits important for sleep regulation, including the DN1-sleep cells mentioned above. We also plan to explore the function of these regions in sleep rebound, including looking for mutants that enhance or suppress sleep rebound in old versus young flies. Screening directly in older flies and subscreening in young flies might reveal interesting aspects of sleep regulation that contribute to some of these old vs young differences. This strategy is designed to reveal vulnerabilities or idiosyncrasies of the aging nervous system, which might in turn reveal an interesting aspect of homeostatic sleep regulation, aging, or their interface.

The function of the timeless protein and the regulation of circadian gene expression

It is generally acknowledged that the period protein (PER) is the major circadian repressor of CLK:CYC mediated transcription. CLK:CYC is the fly ortholog of mammalian CLK:BMAL1 and activates transcription of period and timeless. In contrast to PER, the function of the timeless protein (TIM) in gene expression regulation has been more elusive. This is despite the fact that TIM and PER are tightly associated for much of the circadian cycle. There is also rather little known about the circadian regulation of chromatin in the fly system. To address these missing features of circadian transcriptional regulation, we have been using ATAC-seq to map open chromatin “around the clock” in the fly system. We are paying particular attention to the regulatory regions of key clock genes like period and timeless. We have also used CRISPR to delete specific sequences from the timeless regulatory region. These deletions not unexpectedly reduce timeless expression. More interestingly, they also have specific effects on chromatin and transcriptional regulation, both within the timeless gene as well as on other circadian genes. The deletions also have strong effects on behavior. The project uses state-of-the art methods and has a broad reach, to understand mechanistic aspects of gene expression and chromatin regulation as well as their impact on behavior.

Michael Rosenfeld, MD

Summer Lab Size:

Local Summer Program: http://grad.ucsd.edu/degrees/summer-researches/stars/index.html
Program Dates: June 24-August 17, 2018 (Note:10 weeks will be required)

University of California, San Diego School of Medicine
Cancer Biology, Molecular Biology

Mechanisms of Regulated Gene Transcription in Development, Health and Disease

Lab Composition and Activities: Four graduate students from several programs, a talented group of enthusiastic (and helpful) postdoctoral fellows and a full-time laboratory manager. We have one full laboratory meeting, one graduate student-only meeting, and one individual meeting each week. We also have joint lab meetings with another lab weekly.
Research Interests: Our central laboratory focus this year is to understand the molecular mechanisms of the transcriptional and chromosomal architectural programs that underlie development, regulation and disease, focusing on enhancer networks in neurons, astroglia, and microglia, in accord with our new grant to investigate this as an age-related causative mechanism underlying Alzheimer's disease, and interest in mechanisms of learning and memory . We have focused on these programs utilizing global genomic approaches to uncover and investigate the "enhancer code" controlled by new, previously unappreciated pathways that integrate the genome-wide response to permit proper homeostasis and that also function in aging/senescence, and in disorders of the CNS, including neurodegeneration. Our broader biological focus is on molecular mechanisms of the "enhancer code" regulating learning and memory; aggressive prostate and breast cancer, and underlying events of senescence/aging. Epigenomic events studied include non-histone methylation events and non-coding RNAs. The emerging importance of non-coding RNAs and regulation of nuclear architecture is rapidly altering our concepts of neuronal function, homeostasis and disease. Our laboratory is "Seq-ing" (RIP-seq, ChIP-seq, RNA-seq, GRO-seq, CLIP-seq, ChIRP-seq, Drug-seq), and employing "FISH-seq," for open-ended discovery of long-distance genome interactions to uncover new "rules" of regulated gene transcriptional programs and new roles for lncRNAs in biology of normal, cancer, neuro-affective disorders and aging cells, with particular interest in the rapidly-emerging ideas about phase transition and subnuclar architectural structures in regulation of neuronal transcriptional programs. Coupling this with chemical library screens, we hope to introduce new types of therapies based on targeting specific gene enhancers, histone protein readers and writers, and lncRNAs. Recent surprising findings include the connection between DNA damage repair and gene transcription, the unexpected roles of enhancer RNAs, initial evidence that enhancer activation requires relocation to specific subnuclear architectural structures, and the discovery of unexpected roles of Condensins and of DNA binding factor complexes assembled in trans ("MegaTrans") at enhancers for activation of regulated transcriptional programs. Our focus is on creating single cell real time imaging approaches to dissect the principles of regulated alterations in the chromosomal enhancer and subnuclear structure interactions in activated neurons, and in defining the roles of eRNA-dependent enhancer phase separation evenrts in enhancer functions/interactions.
Current projects for potential rotations include:
• Roles of cell type-specific enhancers in determining chromosomal architecture and the idea of "first tier" interactions dictating transcriptional programs.
• Roles and mechanisms of enhancer actions in learning and memory and in specific cancers.
• GWAS guides to functional enhancers in neuropsychiatric disorders.
• Testing a new hypothesis regarding the origin and birth of enhancers, effects of aging.
• 4D nucleome and mechanisms of long non-coding RNAs dictating chromosomal boundaries.
• Mechanisms of neuronal latency of Herpes viral infections- viral/host genome interactions, roles of lncRNAs.
• Understanding roles of subnuclear structures in transcriptional regulatory programs: Roles of phase separation events in relocation of transcription units between subnuclear architectural structures in regulated gene expression.
• Mechanisms of negative regulation of enhancer programs by nuclear receptors, and effects on behavior.
• Chemical library screens to gene signature as an approach toward new cancer and behavioral therapeutic reagents.
• Roles of epigenomic regulators and enhancers in cellular senescence.

10 Representative Publications (2013-2017):

Li W, Notani D, Ma Q, Tanasa B, Nunez E, Chen AY, Merkurjev D, Zhang J, Ohgi K, Song X, Oh S, Kim HS, Glass CK, Rosenfeld MG. Functional roles of enhancer RNAs for oestrogen-dependent transcriptional activation. Nature. 2013 Jun 27;498(7455):516-20. PMID:23728302.

Fullgrabe, J., et al. The histone H4 lysine 16 acetyltransferase hMOF regulates the outcome of autophagy. Nature 500, 468-471. 2013

Yang, L., Lin C, Jin C, Yang JC, Tanasa B, Li W, Merkurjev D, Ohgi KA, Meng D, Zhang J, Evans CP, Rosenfeld MG. lncRNA-dependent mechanisms of androgen-receptor-regulated gene activation programs. Nature 500, 598-602. 2013. PMID:23945587.

Liu W, Ma Q, Wong K, Li W, Ohgi K, Zhang J, Aggarwal AK, Rosenfeld MG. Brd4 and JMJD6-associated anti-pause enhancers in regulation of transcriptional pause release. Cell. 2013 Dec 19;155(7):1581-95. PMID:24360279.
Skowronska-Krawczyk, D., et al Required Interactions of Enhancers with Matrin-3 Nuclear Architecture for Transcriptional Activation by Homeodomain Factor. Nature 2014;514(7521):257-61. PMID:25119036.
Basnet H, Su XB, Tan Y, Meisenhelder J, Merkurjev D, Ohgi KA, Hunter T, Pillus L, Rosenfeld MG. Tyrosine phosphorylation of histone H2A by CK2 regulates transcriptional elongation. Nature. 2014 Dec 11;516(7530):267-71. PMID:25252977.
Liu Z, Merkurjev D, Yang F, Li W, Oh S, Friedman MJ, Song X, Zhang F, Ma Q, Ohgi KA, Krones A, Rosenfeld MG. Cell. 2014 Oct 9;159(2):358-73. Enhancer activation requires trans-recruitment of a mega transcription factor complex. PMID:25303530.

Puc J, Kozbial P, Li W, Tan Y, Liu Z, Suter T, Ohgi KA, Zhang J, Aggarwal AK, Rosenfeld MG. Ligand-dependent enhancer activation regulated by topoisomerase-I activity. Cell. 2015 Jan 29;160(3):367-80. PMID:25619691.
Li W, Hu Y, Oh S, Ma Q, Merkurjev D, Song X, Zhou X, Liu Z, Tanasa B, He X, Chen AY, Ohgi K, Zhang J, Liu W, Rosenfeld MG. Condensin I and II Complexes License Full Estrogen Receptor α-Dependent Enhancer Activation. Mol Cell. 2015 Jul 16;59(2):188-202. PMID:26166704.
Telese F, Ma Q, Perez PM, Notani D, Oh S, Li W, Comoletti D, Ohgi KA, Taylor H, Rosenfeld MG. LRP8-Reelin-Regulated Neuronal Enhancer Signature Underlying Learning and Memory Formation. Neuron. 2015 May 6;86(3):696-710. PMID:2589230.
Yang,F, Ma,Q, Li,W, Tan, L, Jin,C,Ma,W,Hu,Y, Shen,J, Ohgi, KA, Tlese,F, Liu,w, Rosenfeld, MG. Glucocorticoid receptor: MegaTrnas Switching Mef=diates the Repression of an ERα-Regullated transcriptional Program. Mol Cell. 2017 May4;66(3):321-331

Carla Rothlin, PhD

Yale University
Immunology

Summer Lab Size: 12

Local Summer Program: http://medicine.yale.edu/biomedsurf/
Program Dates: June 5-August 2, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

What happens after cells die?

Turnover of cells occurs through apoptosis during development, tissue homeostasis and after tissue damage. During many instances of developmental apoptosis, such as digit formation, there is simply a need to cull. Conversely, in the case of apoptosis following tissue damage or injury, there is a fundamental need to replace the dying cells; disposal must be linked to regenerative signals. In this project, we will focus on how macrophages recognize and respond to the engulfment of dead cells generated in different physiological and pathological contexts. Our ultimate goal is to understand the code by which the context of cell death is translated into the most appropriate biological response.

Jared Rutter, PhD

University of Utah

Biochemistry, Genetics

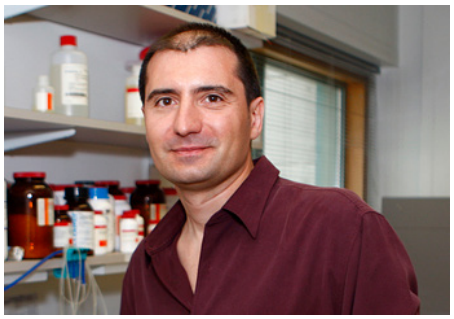
Summer Lab Size:

Local Summer Program: http://www.bioscience.utah.edu/affiliated-research-programs/summer-undergraduate.php
Program Dates: May 23-August 3, 2018 (Note:10 weeks will be required)

Discovering new roles for mitochondria in cancer, diabetes and neurodegenerative disease.

No project description available. Please visit Dr. Rutter's HHMI scientist page for more information about current research.

Bernardo Sabatini, MD, PhD



Harvard Medical School

Biophysics, Neuroscience

Summer Lab Size:

Local Summer Program: No URL Available
Program Dates: June 5-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

The circuitry behind action selection in the mouse

Each animals need to consider its goals, past experience, current environment and internal state in order to select what to do next. This process is called “action selection” and is governed, at least in part, by an evolutionarily old part of the brain called the basal ganglia. Dysfunction of the basal ganglia cause profound diseases in humans, including Parkinson’s, Huntington’s, and drug addiction. We study the basal ganglia in mice to understand the process of action selection and how it is mediated by neural circuitry. A project in our lab would involve working with mice and could include components of behavioral analysis, tissue processing, fluorescence imaging and quantitative analytical methods. The laboratory has members with diverse skills and backgrounds and is an exciting environment in which to learn more about the mammalian brain and get experience with some basic laboratory techniques.

Pardis Sabeti, MD, DPhil

Summer Lab Size: 35
Local Summer Program: No URL Available
Program Dates: June 5-August 4, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Harvard University

Computational Biology, Genetics

Characterization of Host RNA Editing Enzymes Acting on Ebola Virus RNA

Several hundreds of Ebola virus (EBOV) genomes were sequenced from human clinical samples during the West African epidemic. A fraction of these genomes exhibit a striking pattern of A>G / T>C hypermutation, a signature of cellular adenosine deaminases acting on double-stranded RNA (ADARs). This pattern has even been observed in non-human primates treated with antibody cocktails, suggesting that host RNA editing may constitute one route of Ebola virus escape from selective pressure. While the interferon-inducible ADAR1 has been repeatedly implicated, no molecular work has definitely identified the specific enzyme responsible for this hypermutation; moreover, it remains unclear whether this factor is pro- or anti-viral (or both!). Our aim is to determine whether ADAR1 is the key enzyme responsible for A>G / T>C hypermutation, to identify potential hypermutation hotspots on the viral genome, and to further show that hypermutation can provide virus with increased mutation rate and therefore faster evolution.

Validation of functional CTCF deletions from large scale non-coding CRISPR screen

We have been developing the first genome-wide, non-coding CRISPR screens. Projects like ENCODE have created cell-type specific maps of millions of regulatory elements identified by their associations with biochemicals marks and proteins that are associated with function. While these elements are associated with marks of regulatory activity, very few of these million sites have been characterized for function. We're interested in understanding how non-coding variation plays a role is disease and evolution, but that requires understanding the function of these elements. We're endeavouring to build these types of new tools to characterize regulatory functions, in a high throughput manner, genome wide.

Robert Sah, MD, ScD

Summer Lab Size: 20

Local Summer Program: http://grad.ucsd.edu/degrees/summer-researches/stars/schedule.html
Program Dates: June 24-August 17, 2018 (Note:10 weeks will be required)

University of California - San Diego
Biophysics

Bioengineering Joints
The diarthrodial joint is the most common type of joint in the body. Such a joint consists of a synovium-lined cavity containing synovial fluid that separates articulating cartilage-covered bones. Often, such joints are functional for a lifetime, with the synovial fluid-bathed articular cartilage providing surfaces that are low-friction, wear-resistant, and load-bearing. In adults, damaged articular cartilage does not heal effectively after injury, and a common aging-associated malady is osteoarthritis with progressive cartilage deterioration. Successful therapies for large defects utilize grafts with mechanically mature and appropriately contoured articular cartilage and subchondral bone. However, the supply of such grafts is limited. Bioengineering methods offer the possibility of fabricating such biological tissues. The long-term objectives are to assemble, grow, and maintain joint fragments and whole joints that can be used for “Biological Joint Replacement” surgery. We recently developed a variety of technologies that facilitate joint-scale bioengineering. These include the rapid assembly of cartilaginous tissue, the rapid attachment of soft and hard tissues, the shaping of immature tissue, and evaluation of large osteochondral grafts in animal models. Such fabricated living biomaterials will facilitate the future arthroplasty treatment of a number of orthopedic maladies. “Biological Joint Replacement” thereby represent a paradigm shift from the non-living materials and biomaterials used traditionally and the current generation of engineered tissues.

Joint Lubrication and Osteoarthritis
Bathed in synovial fluid, articular cartilage bears load and slides relative to an apposing tissue surface with remarkable low-friction and low-wear properties. However, in aging and osteoarthritis, the articular surface becomes roughened and eroded. Such deterioration may result in part from a biomechanical deficiency in synovial fluid lubricants after acute injury and during aging and osteoarthritis. This project seeks to contribute to the understanding of the biological and biochemical basis for this, as well as to develop therapeutic strategies. The results may ultimately facilitate diagnostic analysis and therapeutic manipulation of deficient fluid in susceptible joints.

Skeletal Development, Growth, and Maturation
Our skeleton represents one of the most complex, yet highly controlled, structures of the body. The formation of each bone and joint involves the orchestrated activities of cells synthesizing, depositing, and degrading matrix and mineral. The availability ofthree-dimensional imaging technologies at multiple scale levels, and of ever-increasing data storage and computational speed, allows for the development of detailed skeletal atlases and growth maps. Such spatiotemporal information provides the foundation for understanding the integrated biological activities that comprise normal skeletal development, growth, and maturation to the adult form, as well as inherited and acquired abnormalities, that lead to deformity and dysfunction.

Mark Schnitzer, PhD

Stanford University
Bioengineering, Neuroscience

Summer Lab Size:

Local Summer Program: http://ssrp.stanford.edu/
Program Dates: June 23-August 25, 2018 (Note: 10 weeks will be required)

In vivo imaging of striatal ensemble neural dynamics in a parkinsonian mouse model reveals the effects of dopamine depletion on motor coding

We have developed means of tracking the dynamics of hundreds of individual neurons in freely behaving mice, and we are now applying this new technology to examine how the encoding of motor activity is altered in the basal ganglia of parkinsonian mice.

Stuart Schreiber, PhD

Summer Lab Size: 18

Local Summer Program: No URL Available
Program Dates: June 5-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Harvard College

Chemical Biology, Medicine and Translational Research

Next-Generation Chemistry in Therapeutics Discovery

This project combines two modern principles driving the science of therapeutics. The first applies modern methods of asymmetric synthesis to yield novel compounds having special properties that greatly facilitate small-molecule probe and drug discovery, including bar coding using DNA oligonucleotides. The second annotates the compounds by making thousands of multiplexed measurements of the actions of the compounds on cells. This “biological spectrum” enables the discovery of compounds having novel mechanisms of action. These two activities are developed in the context of therapeutic discovery efforts that begin with insights from human biology.

Chemical biology-based approach to understanding and overcoming cancer therapy resistance

This project the biological basis of and medical potential for our discovery of a novel cancer cell state induced by cancer therapeutics. This cell state fails to undergo apoptotic cell death, yet we also discovered that it has an unusual vulnerability that can be targeted with small molecules. We are finding this cell state is more pervasive than previously imagined and believe it may be the key to achieving cancer cures in the future.

Mike Shadlen, MD, PhD

Columbia University
Neuroscience, Physiology

Summer Lab Size: 10

Local Summer Program: http://www.spurs.columbia.edu/index.html
Program Dates: June 5-August 4, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Examination of Speed and Accuracy of Visual Perception

This project examines a simple kind of decision making that occurs when we form categorical judgments based on imperfect evidence. We are interested in how the brain makes decisions about visual stimuli. By measuring both the accuracy of perception and the time needed, we gain insight into the computations that the brain uses to reach a decision. The project involves measurement of eye movements in human subjects, computer programming, and data analysis using MATLAB software. There are opportunities to collaborate with scientists conducting related studies in nonhuman primates and mice. Prior experience with computer programming is essential.

Jay Shendure, MD, PhD

University of Washington
Genetics

Summer Lab Size: 35

Local Summer Program: http://www.washington.edu/research/urp/amgen/
Program Dates: June 19-August 18, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Technology development for global views of development at single cell resolution

We are actively developing and implementing experimental and computational methods for globally capturing the developmental history of model organisms, including single cell profiling of the lineage history, the transcriptome, and the epigenome. Both wet-lab and dry-lab projects are potentially available.

Nelson Spruston, PhD

Janelia Research Campus

Neuroscience

Summer Lab Size:

Local Summer Program: http://www.janelia.org/student-programs/undergraduate-program
Program Dates: June 6-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Cell-type-specific silencing of hippocampal projection cells during behavior

No project description available. Please visit Dr. Spruston's HHMI scientist page for more information about current research.

Tim Stearns, PhD

Stanford University
Cell Biology, Genetics

Summer Lab Size: 10

Local Summer Program: http://ssrp.stanford.edu/
Program Dates: June 23-August 25, 2018 (Note: 10 weeks will be required)

Understanding Human Genetic Variation

The goal of the summer project will be to use our yeast assay system to study genetic variation in one or more human genes. We will choose genes for which there is a yeast ortholog of the human gene, then replace the yeast gene with the human gene, creating a “humanized” strain specific for that gene. The known sequence variants will then be expressed in yeast, derived either from the single-nucleotide polymorphism (SNP) database or from recently sequenced cancer genomes. The panel of strains will then be assessed for parameters of growth and physiology, which we have found to be sensitive indicators of gene function.

Joan Steitz, PhD

Yale University
Biochemistry, Molecular Biology

Summer Lab Size: 22

Local Summer Program: http://medicine.yale.edu/biomedsurf/
Program Dates: June 5-August 2, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Mystery of Noncoding RNAs in Mammalian Cells

MicroRNAs (miRNAs) are a class of noncoding RNAs (22 nucleotides long) that regulate translation by interacting with messenger RNAs. We are studying their biogenesis, which is disrupted in many disease states, and their decay, which regulates miRNA populations and therefore their functioning inside cells. Another set of RNAs under study in the lab are made when viruses infect cells to either replicate or transform, causing tumors. We are studying noncoding RNAs (including miRNAs) from Epstein-Barr virus, which causes infectious mononucleosis as well as several tumors. Likewise, Kaposi's sarcoma virus makes a mysterious large nuclear RNA, whose function we are trying to pin down. Herpesvirus saimiri, a monkey virus, makes noncoding RNAs that bind host miRNAs to manipulate their decay. Finally we are studying lengthy extensions (often kilobases long) on mRNAs that appear under stress conditions and remain in the nucleus. We hypothesize that they may serve to protect nuclear structure during the period of stress. Projects are available studying all the different noncoding RNAs listed above.

David Stern, PhD

Summer Lab Size:

Local Summer Program: http://www.janelia.org/student-programs/undergraduate-program
Program Dates: June 6-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

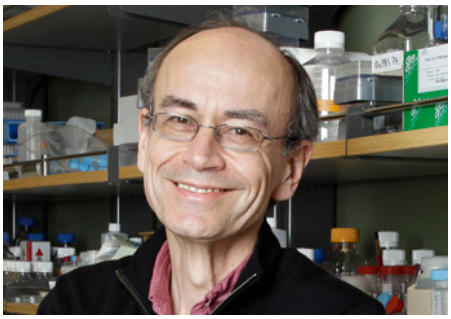
Janelia Research Campus

Experimental Evolutionary Biology, Genetics

The causes and consequences of female courtship song in Drosophila teissieri

This is project to study the ethological mechanisms underlying a novel courtship behavior. We have discovered that during D. teissieri courtship, the female vibrates her wings and produces a “song” composed of short pulses when touched by the male. The female song of D. teissieri is very similar to one type of song produced by males. This behavior seems to be unique to D. teissieri and has not been observed in closely-related species. This behavior therefore may provide a unique system to study how novel, complicated behavior evolves within a short evolutionary time. Towards this goal, we require a good characterization of the behavior. This summer project will include experiments testing (1) how the mating status of male and females affect the behavior; (2) the sensory stimuli that trigger the behavior (chemosensory vs mechanosensory); and (3) the biological roles of the behavior (rejection vs courtship).

Thomas Südhof, MD



Summer Lab Size: 20

Local Summer Program: http://ssrp.stanford.edu/
Program Dates: June 23-August 25, 2018 (Note:10 weeks will be required)

Stanford University

Neuroscience

Exploring mechanisms of autism pathogenesis

No project description available. Please visit Dr. Sudhof's HHMI scientist page for more information about current research.

Michael Summers, PhD

Summer Lab Size: 30

Local Summer Program: http://summerbiomed.umbc.edu/
Program Dates: June 5-August 11, 2017 (Dates for 2018 should be similar)

University of Maryland, Baltimore County
Biochemistry, Structural Biology

RNA Genome Recognition and Packaging by Retroviruses

Students may participate in one of several related projects that focus on determining the molecular mechanisms by which retroviruses assemble and package their genetic material. Most studies focus on genome packaging by the human immunodeficiency virus (HIV) and evolutionarily related lentiviruses. Students will use modern molecular biology methods to prepare and purify protein and RNA samples for in vitro structural and assembly studies. The primary tool used in our laboratory is NMR spectroscopy, and students have access to 600, 800, and 950 MHz NMR instruments. Students assist in the collection and analysis of multidimensional NMR data obtained for isotopically labeled RNAs (prepared by in vitro transcription), and use the data for three-dimensional structure calculations and molecular dynamics simulations. Other techniques commonly used by students in the laboratory include gel-shift electrophoresis, isothermal titration calorimetry, and advanced computational methods. Our most recent work in this area is highlighted in two articles that included 18 undergraduate coauthors (Lu, K., et al. 2011. Science, 334:242-245; Keane et al. 2015. Science 348:917-921). Information on the research environment and structure of my lab can be found in Summers, M. F. 2011. Protein Science, 20:1796-1801.

The HIV-1 Gag Protein and the Development of Novel Antiviral Inhibitors of Capsid Assembly

Subsequent to budding, non-infectious HIV particles undergo a maturation process, triggered by proteolytic cleavage of the Gag polyprotein, in which the liberated capsid proteins assemble to form the polyprotein shell of the central capsid particle. Viral infectivity is critically dependent on capsid formation and stability, making the capsid a potentially attractive antiviral target. Students use modern molecular biology methods to prepare and purify protein samples for in vitro assembly studies; design and evaluate compounds that inhibit assembly; and participate in a multi-laboratory effort to develop “assembly inhibitors” as a new class of antiviral agents for the treatment of AIDS. Information on the research environment and structure of my lab can be found in Summers, M. F. 2011. Protein Science, 20(11):1796 - 1801.

Joseph Takahashi, PhD

Summer Lab Size: 20

Local Summer Program: http://www.utsouthwestern.edu/education/graduate-school/programs/non-degree-programs/surf.html
Program Dates: June 4-August 10, 2018 (Note:10 weeks will be required)

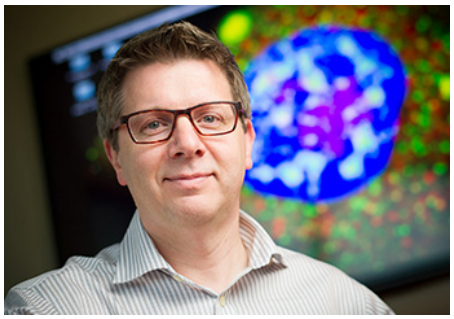
University of Texas Southwestern Medical Center

Genetics, Neuroscience

Genome-Wide Analysis of Circadian Gene Expression in the Mouse

Circadian control of gene expression is pervasive approximately 10-20 percent of transcripts expressed in cells and tissues are under circadian regulation. Students will be involved in bioinformatic analysis of genome-wide circadian expression in the mouse. Projects involve RNA profiling using RNA-seq, analysis of RNA processing, global circadian transcription factor analysis, and chromatin remodeling.

J. Paul Taylor, MD, PhD



Summer Lab Size:

Local Summer Program: No URL Available
Program Dates: May 30-August 4, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

St. Jude Children's Research Hospital

Molecular Biology, Neuroscience

The Role of RNA Granule Dynamics in ALS and Related Diseases

Upon synthesis, messengers RNAs (mRNAs) associate with proteins to form complex structures called ribonucleoprotein particles (mRNPs). The composition of mRNPs, which changes throughout the lifetime of an individual mRNA, determines how the mRNA is used (e.g., whether it is transported, translated, or degraded). A conserved feature of mRNPs is that they assemble into higher-order structures. Once those structures are large enough to be visible via light microscopy, they are considered RNA granules. We have discovered that many forms of amyotrophic lateral sclerosis (ALS) and related diseases are caused by a disturbance in the normal assembly of RNA granules. The successful applicant will join a team that is elucidating the molecular and genetic details of how RNA granules normally assemble and how disturbance of this process causes neurological disease.

Robert Tjian, PhD

Summer Lab Size: 18
Local Summer Program: http://amgenscholars.berkeley.edu/
Program Dates: May 30-August 4, 2018 (Note:10 weeks will be required)

University of California, Berkeley
Biochemistry, Molecular Biology

Tracking the dynamic behavior of transcription factors my single molecule live cell imaging and in vitro biochemistry

Using a combination of in vitro biochemistry, genomics and super resolution single cell single molecule imaging modalities to study the dynamic behavior of transcription factors (TFs) in ESCs and differentiated cell-types. We strive to decipher the molecular mechanisms governing protein:protein and protein: DNA transactions that regulate gene expression during mammalian development and differentiation. Students will work with experienced graduate students and postdocs to learn a plethora of techniques and approaches to dissect gene regulatory pathways and mechanisms in vitro and in vivo.

Russell Vance, PhD

Summer Lab Size:

Local Summer Program: http://amgenscholars.berkeley.edu/
Program Dates: May 30-August 4, 2018 (Note:10 weeks will be required)

University of California - Berkeley

Immunology, Microbiology

Detection of Bacterial Pathogens by NAIP Innate Immune Sensors

The goal of this project is to determine one mechanism for how the innate immune system detects bacterial pathogens. We study a class of sensor proteins called NAIPs that detect specific bacterial proteins, for example, flagellin, rod, or needle proteins. These sensor proteins trigger immune responses that protect against infection. However, the motifs within these proteins that are recognized by NAIPs are poorly characterized. The project will be to introduce point mutations into flagellin, rod, and needle proteins to determine how these mutations affect recognition by the NAIP sensor proteins. Our hypothesis is that a highly conserved motif within these bacterial proteins should be detected by NAIPs and that we should be able to identify this motif.

Matthew Vander Heiden, MD, PhD

Summer Lab Size:

Local Summer Program: https://biology.mit.edu/outreach_initiatives/UG_summer_internship
Program Dates: June 4-August 12, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Massachusetts Institute of Technology

Cancer Biology, Biochemistry

Understanding metabolic interactions in cancer

To proliferate, cancer cells must acquire the materials necessary to duplicate cell mass. The interaction between cancer cells and host tissue can help fulfill these metabolic requirements, but the ways in which nutrients are shared and how this supports tumor growth are not well understood. A project in the Vander Heiden lab is to understand how cancer cells interact with host tissue to support tumor growth.

Gia Voeltz, PhD

Summer Lab Size: 10

Local Summer Program: http://www.colorado.edu/GraduateSchool/DiversityInitiative/undergrads/smart/index.html
Program Dates: June 5-August 11, 2017 (Dates for 2018 should be simila; Note:10 weeks will be required)

University of Colorado Boulder

Cell Biology, Structural Biology

Reconstitution of mitochondrial division in vitro.

We have shown that Endoplasmic Reticulum (ER) tubules wrap around mitochondria and define the position where mitochondria undergo division. We will try to reconstitute mitochondrial division in vitro by purifying mitochondria from Xenopus egg extract. In parallel, we will purify ER vesicles from Xenopus egg extracts, allow vesicles to fuse to generate ER tubules (by GTP addition), and upon mixing with mitochondria, ask whether we can reconstitute mitochondrial tethering, constriction, and division, in vitro. This system will allow us to probe the effect of addition or depletion on ER-associated mitochondrial division in a reconstituted system.

Matthew Waldor, MD, PhD

Summer Lab Size: 17

Local Summer Program: No URL Available
Program Dates: June 5-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Brigham and Women's Hospital

Cell Biology, Microbiology

Cell Biology and Virulence of Enteric Pathogens

The chief goal of our work is to enhance understanding of pathogen-host interactions, particularly in the context of animal models relevant to human infection. We mainly focus on the pathogenicity and cell biology of three human enteric pathogens: Vibrio cholerae (the cause of cholera), Vibrio parahaemolyticus (the cause of seafood-borne enteritis) and Shiga toxin-producing Escherichia coli (aka EHEC, which causes diarrhea and renal failure and is associated with consumption of undercooked meat). Ongoing projects include the following:I. Use of infant rabbit models of diarrheal disease to study host-pathogen interactions. Studies of the biology of enteric pathogens during infection have been hampered by the lack of non-surgical small animal models of diarrheal disease. We found that infant rabbits orally inoculated with EHEC, V. cholerae, or V. parahaemolyticus develop diarrheal diseases that mimic the respective human infections. We are taking advantage of these models to gain insights into bacterial physiology during growth in the host as well as host-pathogen interactions.II. Development and implementation of new approaches to comprehensively identify pathogen and host factors critical for virulence using high throughput transposon- and CRISPR-based screens.III. We developed an approach (STAMP) that utilizes high-throughput sequencing data to characterize pathogen population dynamics within an infected host. Such analyses reveal the extent and sites of host barriers to infection, as well as pathways by which pathogens disseminate within hosts. We are using STAMP to investigate V. cholerae transmission and to define the factors that control V. cholerae population dynamics. STAMP analyses are particularly interesting for pathogens that disseminate to secondary sites of infection through uncharacterized bottlenecks; e.g., we are using STAMP to investigate passage of Listeria monocytogenes from the GI tract to secondary infection sites. These studies will also identify pathogen and host factors that modulate dissemination routes and founding population sizes.IV. D-amino acids in bacterial and host physiology. We found that diverse bacteria release a variety of D-amino acids both in culture and in the intestine. We are studying the mechanisms by which released D-amino acids control cell wall metabolism and cell shape as well as modulate host defense against pathogens and the composition of the intestinal microbiota.

Bruce D. Walker, MD

Summer Lab Size: 16

Local Summer Program: No URL Available
Program Dates: June 5-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Massachusetts General Hospital
Immunology, Medicine and Translational Research

Anitviral Function of HIV-Specific CD8 T Cells

HIV-specific CD8 T cells are generated early after acute HIV infection in humans, and appear coincident with the rapid decline in plasma virus levels. This suggests that these cells play an important role as an antiviral host defense. However, when the generally accepted methods of CD8 T cell quantitation are used to define the magnitude of these responses directed against HIV, there is no difference between persons who control the virus to very low levels without anti-HIV drugs and those who maintain high viral loads with rapid disease progression. These data suggest differences in the antiviral activity of these cells. We have determined the viral peptides targeted by these responses and the HLA alleles that present them to the immune system and have developed a method for precise quantitation of the relative antiviral effect of these cells in an in vitro assay. The project will define the relative antiviral efficacy of immune responses targeting different epitopes in the context of different alleles. In particular, we will assess the role of specific T cell receptor usage by these antigen-specific cells in mediating viral control. These assays are functional, and the project can progress rapidly over the course of the summer.

Spontaneous Control of HIV as a Guide to Immunogen Design

Approximately 1 person in 300 who become infected with HIV is able to control HIV replication without the need for medication, but the reasons for this remain unclear. Using samples from a longitudinal cohort of persons who control viremia and then lose control over time, the student will assess the changes in immune function that account for loss of control. We have developed new techniques that allow one to measure the actual antiviral activity mediated by HIV-specific CD4 and CD8 T cells from such persons, termed “elite controllers,” and have found that many of the immune responses generated in infected persons have little or no antiviral activity, as if HIV is causing the immune system to generate strong responses that are irrelevant, as if the virus were providing a decoy to the immune system. HIV-specific CD4 T cells appear to be critical for maintenance of virus-specific CD8 T cell responses, yet are thought to be lost in HIV infection. The student will use multicolor flow cytometric techniques as well as in vitro assays that assess viral replication in the presence or absence of added immune cells, in order to determine the properties of those cells that are the most potent. To define the functional properties of these cells, we will use quantitative PCR, class I and II tetramers, multicolor flow cytometry, and RNA-seq analyses in a unique cohort of persons we have assembled who are able to control HIV infection without medication, in those who fail to achieve immune control, and in those in who have received candidate HIV vaccines. CRISPR/Cas9 mediated gene knock-in and knock-out experiments using HIV-specific CD8 T cell clones will be used to define specific effector functions. These assays are functional, and the project can progress rapidly over the course of the summer.

Effects of HIV Infection on Antigen Processing

HIV infection elicits a strong and multispecific cytotoxic T lymphocyte response in infected persons, yet, despite induction of this adaptive immune response, most persons progress to develop AIDS. Because peptides must be processed prior to class I presentation, we hypothesize that immunodominance is influenced by these processes. The general MHC-I-restricted antigen-processing pathway is a multistep pathway that includes the degradation of proteins by the 26S proteasome, the trimming of peptides by cytosolic aminopeptidases and in a few documented cases the tripeptidylpeptidase, and their translocation in the endoplasmic reticulum, where aminopeptidases can shorten N-extended peptides. This project will focus on defined HIV epitopes and determine the relationship between antigen processing and immune recognition, with an emphasis on determining the role of antigen processing in shaping an immunodominant response. These assays are functional, and the project can progress rapidly over the course of the summer.

Christopher Walsh, MD, PhD

Summer Lab Size:

Local Summer Program: No URL Available
Program Dates: June 5-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Boston Children's Hospital

Genetics, Neuroscience

Massively Parallel in vitro Analysis of Noncoding Human Accelerated Region Mutations in Autism Spectrum Disorder

Mutations in human accelerated regions are thought to underlie differences in social and cognitive functions in individuals with ASD. To demonstrate such effects, massively parallel in vitro assays combining multiplex reporter pools and targeted high coverage RNA-sequencing are performed using the wild-type and mutant alleles we identified from targeted deep sequencing. Such assays allow for the systematic and simultaneous screening of hundreds to thousands of such alleles in order to quickly identify those having the greatest effect on regulatory activity.

David Walt, PhD

Summer Lab Size: 20

Local Summer Program: No URL Available
Program Dates: June 5-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Brigham and Women's-Harvard Medical School

Chemical Biology

Early Detection of Disease Using Single Molecule Arrays

The goal of this project is to use single molecule detection of proteins to develop a fingerprint for early detection of diseases including breast cancer, Parkinson's Disease and Tuberculosis. The ultrasensitivity of our previously established single molecule array (Simoa) detection platform allows for extremely low concentrations of proteins to be detected in bodily fluids, such as blood. This digital detection platform facilitates the development of a simple, minimally invasive sampling method that could provide biological information about a disease at its early stages that is not detectable by current methods, such as imaging. Eventually, Simoas could be used to not only detect, but also help to monitor therapeutic efficacy as well as recurrence of disease.

Single Cell Analysis for High Resolution Diagnosis of Cancer

There is a need to perform high-resolution single cell analysis including phenotypic, genetic, and proteomic molecular level analysis of a large number of single tumor cells. This analysis is critical to gain a population-level understanding of the diversity of a tumor, the presence of rare and potentially dangerously aggressive cells, the presence of drug-resistant cells, the presence of cancer stem cells, and the presence of specific stromal cells that contribute to the malignant tumor phenotype. Presently, tumors are analyzed by staining cells for histological examination or by homogenizing a sample and analyzing the entire lysate for proteins, metabolites, or genetic composition. This approach provides the average composition of the population and results in an ensemble measurement. The large number of other cells in the population swamps rare cells such that rare variants cannot be observed. Only by looking with resolution at the single cell level would it be possible to observe rare cells. Our lab is developing methods to analyze the protein and microRNA content of individual cells to detect rare cells in a population that may be more aggressive and predictive of patient outcome.

Johannes Walter, PhD

Harvard Medical School

Biochemistry, Biophysics

Summer Lab Size: 15

Local Summer Program: No URL Available
Program Dates: June 5-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Exploring the mechanism of DNA interstrand cross-link repair

No project description available. Please visit Dr. Walters' HHMI scientist page for more information about current research.

Peter Walter, PhD

Summer Lab Size: 22

Local Summer Program: http://graduate.ucsf.edu/srtp
Program Dates: May 30-August 2, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

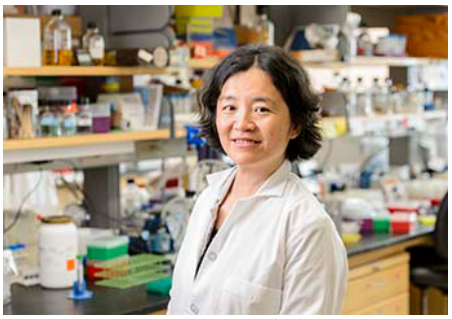
University of California - San Francisco

Biochemistry, Cell Biology

The Biogenesis and Function of Intracellular Organelles

Differentiated cells all have different internal structures that allow them to carry out their specialized tasks in our bodies. How are these structures built? How do proteins know where to go so that they end up in the correct compartment? How does a living cell adjust the amount of organelles according to need? For the most part, the answers to these questions are unknown. Recently, we have made great progress in deciphering intracellular signaling pathways that allow organelles to affect the gene expression programs in the cell nucleus. The pathways studied have revealed fascinating new ways of propagating signals. One example is the pathway by which the abundance of the endoplasmic reticulum is regulated by the “unfolded protein response” (UPR), which utilizes an mRNA-splicing step that bypasses all of the machinery commonly involved in mRNA splicing. A student will explore mechanistic and physiological aspects of these signaling pathways. The goal is to learn how individual proteins function as molecular switches and how these switches are connected to one another in signaling networks that regulate organelle function and abundance. A combination of genetic, molecular engineering, microscopic, and biochemical techniques will be applied in both mammalian and yeast systems, with increasing emphasis on cancer biology. In particular, we are exploring whether pharmacological UPR modulation can be of therapeutic value in multiple myeloma, a cancer of cells of the immune system. Results obtained in evolutionarily distant cells will be compared to distinguish fundamental aspects of regulation common to all eukaryotic cells from species-specific variations. See our lab page for more details.

Jue Jade Wang, PhD



Summer Lab Size:

Local Summer Program: http://biology.wisc.edu/Undergraduates-GettingInvolvedBeyondtheClassroom-UndergraduateResearch-IntergratedBiologicalSciencesSummerResearchProgram.htm
Program Dates: May 30-August 5, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

University of Wisconsin-Madison

Microbiology, Genetics

Building an Atlas of the metabolome-proteome response to stress

Antibiotic resistant bacteria are threatening human health globally. The current interest of my laboratory is to understand the fundamental processes required for bacteria to survive antibiotic treatment. We have unraveled a global alteration of the bacterial metabolome which underlies stress survival and antibiotic tolerance. The student will perform high throughput biochemical assays to screen for and characterize direct interactions between stress-altered metabolites and the proteome of a pathogen. There are also opportunities to collaborate with scientists using microfluidics approaches to examine antibiotic tolerance in single cells. Prior experience with computer programming is a plus.

Meng Wang, PhD

Summer Lab Size: 17
Local Summer Program: http://www.bcm.edu/smart/
Program Dates: May 29-July 27, 2018 (Note:10 weeks will be required)

Baylor College of Medicine

Genetics, Developmental Biology

Genetic screens of longevity regulators

In this project, the students will conduct genetic screens searching for the regulators of organism longevity in Caenorhabditis elegans. Through proteomic studies, a group of genes have been linked with a newly characterized lysosome-to-nucleus longevity signaling pathway. Further functional characterization of these genes will demonstrate their importance in regulating cellular homeostasis and longevity. The students will be trained in genetics/genomics, fluorescence microscopy imaging, and aging biology.

Isiah Warner, PhD

Summer Lab Size: 20

Local Summer Program: No URL Available
Program Dates: TBD (Note:10 weeks will be required)

Louisiana State University

Physical Science

Biomedical Applications of Ionic Liquids and Solid Phase Analogues

My research group has been exploring the development of novel materials using room-temperature ionic liquids (RTILs) for several years. Recently, we have extended the range of these materials to include similar solid phase materials, i.e. organic salts with melting points of frozen ionic liquids (25 0C to 100 0C) up to melting points of 250 0C. To contrast these new materials from RTILs, we have created the acronym, GUMBOS (Group of Uniform Materials Based on Organic Salts). These GUMBOS have similar tunable properties to RTILs, including solubility, melting point, viscosity, thermal stability, and functionality. Thus, these materials have a myriad of applications in biology, chemistry, engineering, and physics. Current projects include research in the areas of bioanalytical and materials chemistry (biosensors, environmental sensors, thin films for optoelectronics and OLEDS applications, molecular spectroscopy, drug development for cancer and infectious diseases, and nanotechnology).

Development of Nanomaterials for Selective Cancer Therapy and Imaging

This research is designed to address key questions regarding the overall utility of novel nanomaterials for biomedical imaging and cancer therapy. The overall hypothesis of this new research is that it is possible to develop nanoparticles from GUMBOS well suited for biomedical imaging and selective cancer therapy." This research is divided into three distinct areas: 1) development of methodology and chemistry which contributes to production of nanoparticles from GUMBOS for biomedical imaging and therapy; 2) characterization of nanoGUMBOS and use of computational methods to better understand them at a fundamental level; and 3) evaluation and understanding of the properties, including cytotoxicity, of nanoGUMBOS, that contribute to biomedical imaging and selective therapy. Our nanoGUMBOS have some distinct advantages for biomedical applications. For example, recent research from our laboratory has demonstrated that nanoGUMBOS can be tuned to achieve selective cancer therapy, i.e. toxic to cancer cells and non-toxic to normal cells. These properties have been demonstrated for in vitro and in vivo applications and mechanisms of action are currently being studied. Thus, many advantages accrue from our approach and are quite applicable for summer undergraduate research.

Muhammad Zaman, PhD

Boston University
Bioengineering, Global Health

Summer Lab Size: 7 graduate students, 4 undergraduates, 3 post-docs.

Local Summer Program: http://www.bu.edu/surf/
Program Dates: June 6-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be reqruied)

Understanding the Role of Substandard Antibiotics in Developing Anti-microbial Resistance

Among the grand challenges in health facing people all around the world, rapid resistance to antibiotics ranks among the very top. While the problem is truly global, it has much more profound implications for populations in the developing world. In the developing countries, it is estimated that 30-50% of all drugs, in particular antibiotics, may be substandard or counterfeit, thereby rapidly accelerating long-term drug resistance. The goal of this project is to use tools rooted in fundamental molecular biology, cell biology, imaging, fluidics and biomedical engineering to study the effect of poor-quality antibiotics on drug resistance. The project will be twofold. The first part will involve using field samples of poor-quality drugs to study resistance, and the second part will involve developing molecular probes to quickly assess the quality of available drugs. The project will be with a team of researchers that include pharmacists, pharmacological experts, molecular biologists, biomedical engineers, and public health professionals.

Our hope is that students engaged in this project will not only appreciate the scientific rigor and learn novel experimental tools but will also understand the societal context and the global health significance of this work.

Richard Zare, PhD

Summer Lab Size: 15-20

Local Summer Program: http://ssrp.stanford.edu/
Program Dates: June 23-August 25, 2018 (Note:10 weeks will be required)

Stanford University
Biophysics, Physical Science

Ambient Ionization Mass Spectrometry as a New Diagnostic Tool

Mass spectrometry is being significantly advanced by ambient ionization techniques in which ions are generated in air at room temperature and atmospheric pressure and transported to the inlet of a mass spectrometer for chemical identification. We are exploring a number of different ways to accomplish this task for the purpose of analyte identification and analyte imaging. If you are interested, some recommended readings are: http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1002108 Jae Kyoo Lee, Erik Jansson, Hong Gil Nam, and Richard N. Zare, "High-Resolution Live-Cell Imaging and Analysis by Laser Desorption/Ionization Droplet Delivery Mass Spectrometry," Anal. Chem. 88, 5453_5461 (2016). Zhenpeng Zhou, Jae Kyoo Lee, Samuel C. Kim, and Richard N. Zare, "Nanotip Ambient Ionization Mass Spectrometry," Anal. Chem. 88, 5542-5548 (2016). Maria T. Dulay, Livia S. Eberlin, and Richard N. Zare, "Protein Analysis by Ambient Ionization Mass Spectrometry using Trypsin-Immobilized Organosiloxane Polymer Surfaces," Anal. Chem. 87, 12324-12330 (2015). M. T. Dulay and R. N. Zare, " Polymer Spray Mass Spectrometric Detection and Quantitation of Hydrophilic Compounds and Some Narcotics," Rapid Communications in Mass Spectrometry 31, 1651-1658 (2017).

Marta Zlatic, PhD

Summer Lab Size: 6

Local Summer Program: http://www.janelia.org/student-programs/undergraduate-program
Program Dates: June 6-August 11, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Janelia Research Campus
Neuroscience

Neural circuit mechanisms of memory-based decision-making

Animals are born with innate representations of valences of many sensory cues, acquired through evolution. Some odors are innately attractive and others are innately repulsive. However, to behave adaptively in an ever-changing environment, animals are also able to learn new valances for sensory cues. Furthermore, the new, learnt valances can be in conflict with the innate ones. For example, repeated association of an innately attractive food odor with negative consequences (eg. pain, or illness) allows a switch from innate attraction to learnt aversion of the same odor. The representations of innate and learnt valences are thought to be stored in separate brain areas in both vertebrates and invertebrates. However, the way in which these representations are integrated to produce a coherent behavioral choice is unknown. How can the learnt valences override conflicting innate valences? What are the circuit mechanisms that enable a switch from innate attraction to learnt avoidance? The aim of this project is to address these open questions using the tractable genetic model system, the Drosophila larva. Insects, especially their larval stages, have smaller and more compact brains, readily amenable to large-scale electron microscopy circuit mapping, but are also capable of associative learning. In Drosophila larva, we can therefore combine large scale electron microscopy reconstruction with targeted manipulation of uniquely identified neuron types and calcium imaging and electrophysiological recordings in identified neurons to uncover the circuit mechanisms of behavioural choice1,2,3,4,5.

The project will involve a number of cutting edge techniques: high-throughput automated behavioural experiments (training animals to associate rewards or punishments with specific odors), calcium imaging of neural activity, patch-clamp recordings and optogenetic manipulation of identified neurons.

References

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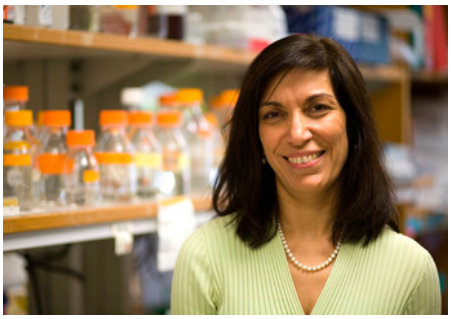
2. Ohyama T., Schneider-Mizell, C., Fetter, R. D., Valdez-Aleman J., Francoville R., Rivera Alba M., Mensh, B., Simpson, J. H., Branson, K., Truman, J. W., Cardona, A. and Zlatic M. (2015): Multilevel multimodal integration enhances action selection. Nature 520: 633-639.
3. Jovanic T.f , Schneider-Mizell, C.f , Shao M., Masson J.-B., Denisov G., Fetter R. D., Truman J. W., Cardona, A.c and Zlatic M.c. (2016) Competitive disinhibition in early sensory processing mediates behavioral choice and sequences in Drosophila. Cell, 167: 1-13.
4 Eichler K., Li F., Kumar A. L., Andrade I., Schneider-Mizell C., Saumweber T., Huser A., Gerber, B., Fetter R. D., Truman J.W., Abbott L. F., Thum A., Zlatic, M. and Cardona A.. The complete connectome of a learning and memory center in an insect brain (2017). Nature 548, 175–182. doi:10.1038/nature23455
5. How to map the circuits that define us (2017). Nature 548, 150–152. doi:10.1038/548150a

Huda Zoghbi, MD



Summer Lab Size: 23

Local Summer Program: http://www.bcm.edu/smart/
Program Dates: May 29-July 27, 2018 (Note:10 weeks will be required)

Baylor College of Medicine

Genetics, Neuroscience

Characterization of Pathways Mediating Neurological Phenotypes

Neurodegenerative diseases, such as Alzheimer's disease, Parkinson's, and inherited ataxias, are diseases where misfolded proteins accumulate and cause neuronal dysfunction and degeneration. Mouse genetic studies showed that decreasing the level of the culprit protein will suppress the symptoms of the disease and will rescue neuronal function. Our lab has an ongoing project designed to identify new gene targets that, when inhibited, the levels of mutant Ataxin-1 will decrease. Mutant Ataxin-1 is the protein that causes the inherited neurodegenerative disease spinocerebellar ataxia type 1. The screen to identify these targets relies on a genome-wide RNAi screen. We have completed the screen successfully and we have expanded it to another protein, tau, that causes dementia. The student will participate in following up on some of the promising candidates identified through the screen to study their effects on Ataxin-1 and tau and to establish how they might reduce the levels of the protein. The work will involve cell culture work, RNAi, and Western analysis. For the animal studies, the student will participate (with the help of postdocs or graduate students) in studying the behavioral features of certain mouse models of autism spectrum disorders such as Rett syndrome and contribute to molecular studies in this disorder.

Leonard Zon, MD

Summer Lab Size: 40

Local Summer Program: No URL Available
Program Dates: June 5-August 11, 2017 (Dates for 2018 should be similar)

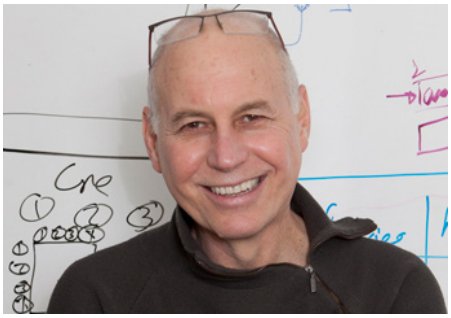
Boston Children's Hospital

Developmental Biology, Genetics

Zebrafish as a Model System for Understanding Vertebrate Blood Development

The zebrafish is an excellent model for understanding blood development. The embryos are transparent, and blood can be seen circulating throughout the body at 24 hours postfertilization. In addition, the zebrafish is an excellent genetics system, and we have collected 26 complementation groups of mutants that affect hematopoiesis. The project will use in situ hybridization to characterize cDNAs from hematopoietic-specific libraries. This will establish where the gene is expressed in the embryo. By studying a number of cDNAs, we will establish a panel of markers that are specifically expressed in hemangioblasts. These cells are bipotential for their ability to make blood cells and vascular cells. Some of these genes will then be injected into zebrafish embryos to determine if over expression of the gene leads to an expansion or a deficit of blood formation. The project will involve molecular biology and an introduction to developmental biology.

Charles Zuker, PhD



Summer Lab Size: 20

Local Summer Program: http://www.spurs.columbia.edu/index.html
Program Dates: June 5-August 4, 2017 (Dates for 2018 should be similar; Note:10 weeks will be required)

Columbia University
Neuroscience, Physiology

The Biology of Mammalian Taste

We use the taste system as a model for our studies of brain function, because it provides a powerful platform to dissect the processing of sensory information, from detection at the periphery to perception in the brain. In addition, the sense of taste is exquisitely modulated by the internal state of the organism (e.g., hunger, satiety, expectation, emotion), thus it serves as a rich model to explore multisensory integration. Our research of the past few years has focused on identifying the receptors and cells for sweet, umami, bitter, sour, salty, and carbonation and, in the process, defining the logic of taste coding at the periphery. Currently, we are continuing our work on the periphery, but we also study how taste is represented in the brain and how the information is used to guide actions and behaviors.