SYSTEMS BIOLOGY OF DISEASE AND THERAPEUTICS

SBDT
SYSTEMS BIOLOGY OF DISEASE & THERAPEUTICS

Who we are:
The Graduate School of Biological Sciences offers a PhD in Biomedical Sciences in several training areas, including
Systems Biology of Disease and Therapeutics.
The Graduate School is part of the Mount Sinai Medical Center, which consists of Mount Sinai School of Medicine and Mount Sinai Hospital.

Quantitative reasoning and computational approaches integrated throughout the curriculum
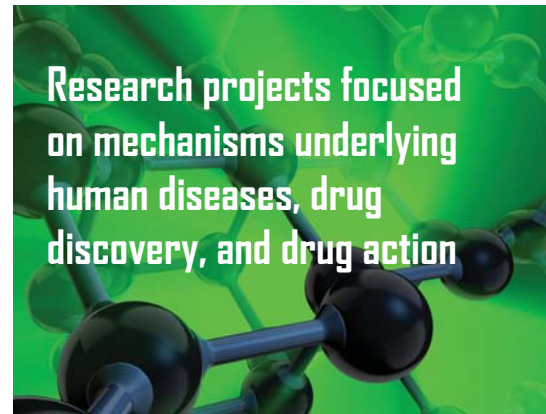
Research projects focused on mechanisms underlying human diseases, drug discovery, and drug action

Integrated training in molecular biology, physiology, pharmacology, and systems biology

PhD candidates at Mount Sinai receive an annual stipend of $32,500

PhD in Biomedical Sciences

MSSM

MOUNT SINAI SCHOOL OF MEDICINE

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CO-DIRECTORS

Jeanne Hirsch, PhD is Associate Professor of Pharmacology and Systems Therapeutics. Her laboratory studies signal transduction pathways that are mediated by heterotrimeric G proteins in the yeast Saccharomyces cerevisiae.

Eric Sobie, PhD is Associate Professor of Pharmacology and Systems Therapeutics, and a member of the Systems Biology Center of New York (SBCNY). His research focuses on gaining quantitative understanding of normal and pathological heart function through the coupling of experimental measurements with mathematical modeling.

OVERVIEW

Systems Biology of Disease and Therapeutics (SBDT) trains graduate students in research that aims to understand the complex interactions underlying human disease, and how drugs can be used to treat these diseases. Knowledge of the healthy and diseased states of a cell, tissue, or organism, requires an understanding of networks of molecular interactions within and between cells.

The Systems Biology of Disease and Therapeutics curriculum emphasizes the integration of concepts from multiple disciplines: genomics, molecular biology and biochemistry, physiology, and pharmacology. Important approaches for this integration are quantitative reasoning and computational biology. This program, set within a tightly knit medical school and hospital environment, provides unique opportunities to study systems from genomes and proteins to cells to animal models to humans at both the bench and the bedside.

Faculty members investigate complex disease processes and drug actions in many cell types, tissues, and organs, with the shared underlying philosophy that systems approaches are required for transformative advances. Many SBDT faculty members employ high-throughput technologies such as proteomics, microarrays or mRNA –Seq to get global pictures of the system being studied. Analysis of these large datasets requires quantitative approaches. Mathematics and statistics provide a common language for understanding biomedical processes across scales of organization, so quantitative reasoning and computational approaches are integrated into the curriculum at all levels and used by many of the faculty in their research programs.

This is an interactive program with a biweekly luncheon-journal club, seminars, works-in-progress and an annual retreat. All of these forums provide extensive opportunities to interact with SBDT faculty. The core courses, journal clubs, lab rotations, and works-in-progress presentations provide our students with an understanding of how to use diverse data sets and computational approaches to delineate biological networks, how to translate this information into new therapeutic and preventive strategies, and how to apply this paradigm to their own research.

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CORE COURSES

Systems Biomedicine

This is a core course for entering PhD, MD/PhD, and Master's students that introduces students to integrated approaches to understanding physiological functions and the underlying biochemical, cell biological and molecular biological mechanisms. Insight from global measurements such as whole genome sequencing, mRNA profiling and proteomics as well as physiological and clinical measurements are integrated with computational models to provide a multiscale understanding of disease initiation and progression and therapeutic action. The course is integrated with a journal club.

Principles of Pharmacology

Graduate and medical courses are integrated to introduce the students to important areas of pharmacology including pharmacokinetics, pharmacodynamics and drug metabolism. Receptors, enzymes, and channels are considered as drug targets. Structural aspects of drug design, computational methods for drug-target docking, current issues in drug discovery and development, and gene therapy strategies are all discussed. Students attend medical pharmacology lectures on drug treatment within the cancer pathophysiology course to get a clinical perspective. The students are introduced to emerging concepts in systems pharmacology and how these may be used for drug discovery and polypharmacology and prediction of complex adverse events based on genomic and epigenomic status.

Cell Signaling Systems

This course uses the primary literature to develop a systems level understanding of the mechanisms underlying both information flow and information processing through cell signaling pathways and networks. Effects of signaling on tissue and organ functions in normal and disease states are considered. Current experimental and theoretical concepts in cellular regulatory and drug action, therapeutic and adverse, are highlighted.

Systems Biology: Biomedical Modeling

This course uses a case-based approach to teach the full range of computational approaches used in systems biology. These include statistical methods for analysis of large data sets, network building and graph theory for network analysis, and mathematical modeling techniques used to develop ordinary differential equation, partial differential equation, and stochastic models. Lectures provide biological background and describe the development of models. This is a computational laboratory class in which the students run their own simulations and perform their own data and network analyses. An emphasis is placed on the analysis of models and networks to generate experimentally-testable predictions.

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RESEARCH PROJECTS

PhD Student Spotlight

An important complication in diabetes is the subsequent loss of kidney function. This complication occurs in some but not all individuals with diabetes. To understand why this is so, Haiying Qi uses experimental systems biology approaches to study the genomic basis of diabetic nephropathy in the laboratory of Dr. Erwin Bottinger in the Institute for Personalized Medicine and the Division of Nephrology. Diabetic nephropathy is characterized by degradation of the kidney's filtration barrier and a loss of a particular cell type, the podocyte, in the kidney. Using high-throughput genomic techniques such as microarray analysis and quantitative trait loci mapping, Haiying is investigating why some strains of mice are susceptible to diabetic nephropathy whereas other strains of mice are resistant. Her analysis has identified xanthine oxidase as a candidate potentially underlying the greater susceptibility of certain mouse strains. This type of research combines systems biology approaches to understand differential disease progression in different individuals, and this knowledge may be exploited to develop personalized therapies.

MD-PhD Student Spotlight

Multiple genes (and gene products) underlie many complex diseases. An important question in developing an integrated understanding of disease mechanisms is the relationship between the genes associated with a disease and the interaction of these gene products with other proteins, including drug targets, within human cells. Seth Berger, working in Ravi Iyengar's laboratory in the Department of Pharmacology and Systems Therapeutics, has been addressing this question by determining the relationships between drug targets and genes associated with the same disease. Using bioinformatics and computational approaches to build and analyze networks Seth found that diseases involving ion channels, such as epilepsy and cardiac arrhythmia syndromes, share substantially overlapping networks, Seth also found that targets of arrhythmia-causing drugs are selectively enriched in subnetworks formed from the genes that cause congenital arrhythmia syndromes. These computational studies provide global pictures of disease origin and drug action and are being used to develop network based classifiers for the prediction of drug –induced adverse events.

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Cancer Therapeutics

Aneel Aggarwal, PhD
Paolo Boffetta, MD
Ross Cagan, PhD
James Gallo, PhD
Andrew Sikora, PhD
Ming-Ming Zhou, PhD
Marc Birtwistle, PhD

Kidney Disease

Erwin Bottinger, MD
Cijiang He, MD, PhD
Michael Ross, MD
Lisa Satlin, MD

Cardiovascular Diseases

Fadi Akar, PhD
Kevin Costa, PhD
Zahi Fayad, PhD
Bruce Gelb, MD
Roger Hajjar, MD
Djamel Lebeche, PhD
Francesco Ramirez, DSc
Eric Sobie, PhD
Sima Tarzami, PhD

Large data sets - Omics Based Approaches

Erwin Bottinger, MD
Lakshmi Devi, PhD
Cijiang He, MD, PhD
Ravi Iyengar, PhD
Ihor Lemischka, PhD
Francesco Ramirez, DSc

Connective Tissue Musculoskeletal Disorders

Evan Flatow, MD
James Iatridis, PhD
Francesco Ramirez, DSc
Nelly Andarawis-Puri, PhD

Neurological Disorders & Drug Addiction

Robert Blitzer, PhD
Lakshmi Devi, PhD
Graham Ellis-Davies, PhD
Samuel Gandy, MD
Ming-Hu Han, PhD
Yasmin Hurd, PhD
Ravi Iyengar, PhD
Susana Neves, PhD
Eric Nestler, MD, PhD
Scott Russo, PhD
Stuart Sealfon, MD
Venetia Zachariou, PhD

Computational Biology

James Gallo, PhD
Ravi Iyengar, PhD
Avi Ma'ayan, PhD
Susana Neves, PhD
Eric Sobie, PhD
Andrew Sikora, MD, PhD
Marc Birtwistle, PhD

Pathophysiological Systems Liver Diseases

Meena Bansal, MD
Arthur Cederbaum, PhD
Scott Friedman, MD

Diabetes & Endocrine Diseases

Terry Davies, MD
Derek LeRoith, MD, PhD
Charles Mobbs, PhD

Stem Cells & Tissue Repair

Kevin Costa, PhD
Ihor Lemischka, PhD
Avi Ma'ayan, PhD

Infectious Diseases

David Bechhofer, PhD
Terry Krulwich, PhD
Viviana Simon, MD, PhD
Adrian Ting, PhD

FACULTY PROFILE

Ming-Hu Han
Assistant Professor, Pharmacology and Systems Therapeutics
Assistant Professor Neuroscience

One of the most fundamental functions of the brain is the capacity to develop adaptive changes in response to environmental stimuli under both physiological and pathophysiological conditions. These neural adaptations can occur at a variety of levels such as at the levels of ion channels, synaptic transmission, and integrative function of neuron and neural network, and they are believed to be responsible for governing behavioral/psychological functioning. Dr. Han's laboratory is specifically interested in identifying the intrinsic plasticity of ion channels and neuronal excitability, and in determining how psychological stress causes adaptive changes in neural networks in the dopamine circuit of the ventral tegmental area, an emotion- and reward-related system. Research in Dr. Han's laboratory focuses on the underlying mechanisms of these neuroadaptations and how they mediate behavioral susceptibility and resilience to stress in laboratory models of depression.

To understand the roles of neuroadaptations in mediating behavioral changes, the laboratory employs both behavioral and electrophysiological approaches. The laboratory uses in vivo and in vitro electrophysiological techniques to identify neuroadaptations and investigate molecular/ionic mechanisms, and employs advanced gene manipulation approaches, including viral-mediated gene delivery, local knockouts of genes of interest, and optogenetic tools, to conduct molecular/ionic manipulation followed by behavioral assays. The combination of these gene manipulation techniques and neurophysiology provides the laboratory with a unique ability to explore the neurophysiological basis of depression.

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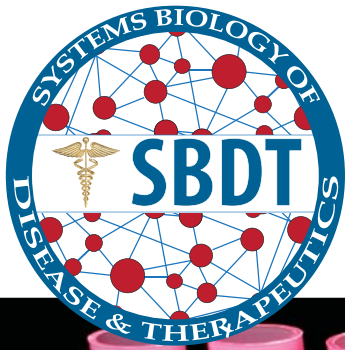
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Facilities and Cores

Students and other researchers have access to a number of cutting edge technology cores in the Experimental Therapeutics Institute, the Genomics Institute, and the Systems Biology Center New York. These include the Integrated High Throughput and High Content Screening Core, the High Throughput Sequencing Facility, the Therapeutic Antibody Center, the Medical Chemistry Core, the Bioinformatics and Network Analysis Core, and the Dynamical Modeling Core.

Financial Support

All students admitted to the PhD programs are provided with an annual stipend of $32,500, full tuition support, health insurance for themselves and their families, and guaranteed housing in a Mount Sinai housing unit. Students who are US citizens or permanent residents are eligible to obtain support from the National Institute of General Medical Sciences funded training grant in Pharmacological Sciences headed by Dr. Terry Krulwich.

Where we are:

The Mount Sinai campus is on the upper East Side of Manhattan between 98 and 102nd streets, adjacent to Central Park, in New York City. Student dorms and housing surround the campus within easy walking distance

Information and Applications

For more information contact by e-mail:
jeanne.hirsch@mssm.edu, eric.sobie@mssm.edu, terry.krulwich@mssm.edu or sherry.jenkins@mssm.edu

To complete application online go to
www.mssm.edu/education/graduate-school/degrees-and-programs/phd-program

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