Mount Sinai

# Dean's Report

GRADUATE SCHOOL OF BIOMEDICAL SCIENCES

WINTER 2013

## ACCELERATING SCIENCE–ADVANCING MEDICINE

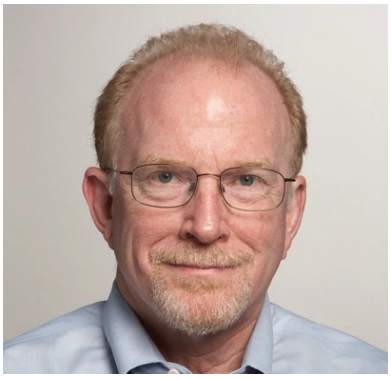
### Integrating Basic Science with Translational Medicine

The quality of any educational program depends on the quality of its faculty. This is particularly true for PhD programs, since the students not only take classes taught by the faculty, but they must pick a thesis adviser who will successfully guide the major component of their PhD education: the thesis project.

The faculty of the Graduate School of Biomedical Sciences at the Icahn School of Medicine at Mount Sinai is superb and highly dedicated to the graduate students and the outstanding Multidisciplinary Training Areas (MTAs) that provide a discipline-based framework for PhD education. These training areas are aligned with our 14 disease-oriented and core technology-focused Institutes, which themselves are aligned to pressing issues and emerging areas in science and medicine today. They are also particularly well funded, as Mount Sinai is third out of 130 medical schools in the nation for National Institutes of Health funding per investigator.

Forty new recruits were added to the Graduate School faculty in the last year, and every one of them is eager to take on PhD students. This represents a faculty increase of nearly 20 percent—in 12 months. In the next two years, we will add at least 60 more positions, resulting in a total increase of 50 percent for the Graduate School of Biomedical Sciences faculty. This degree of growth in the faculty that trains PhD students is very unusual and provides our current and future students with enormous breadth and depth as they make the critically important decision as to who will mentor them as scientists.

Our students also have increasing opportunities to showcase and discuss their work, as Mount Sinai has been organizing and hosting more conferences. In November, our students and faculty came together with prominent speakers from other top academic medical institutions, the biotechnology and pharmaceutical industries, the investment community, and global media for SINA*Innovations*. The three-day conference explored the ways that academic medical centers can accelerate drug discovery and commercialize emerging biotechnologies. To review the program and watch the conference in full, please visit www.mssm.edu/sinainnovations.



John H. Morrison, PhD, Dean of Basic Sciences and the Graduate School of Biomedical Sciences

It is an exciting time to be at Mount Sinai.

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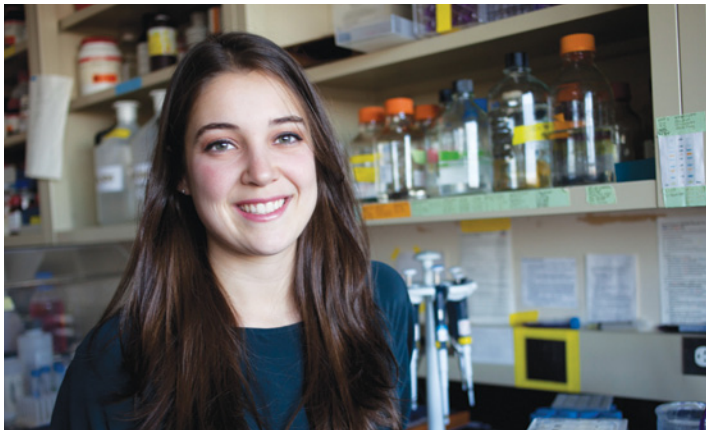
**INNOVATION IN EDUCATION**

### Graduate Student, age 25, Named to *Forbes* List

Jillian Shapiro, a graduate student at the Icahn School of Medicine at Mount Sinai, has been named to the second-annual *Forbes* "30 Under 30" list in "Science and Health." The honorees "reflect the way that the health care landscape is transforming for the better, opening up to revolutionary new ideas and new approaches," according to the editors of *Forbes*.

Ms. Shapiro, 25, discovered a new molecular pathway that can be used to deliver small interfering RNA (siRNA) into cells, with the potential to reprogram molecular activity. Her finding has the potential to sidestep the bottleneck of nuclear export that occurs with the current nuclear-virus technologies. Her work could have significant implications in the development of future therapeutics across disease types.

Ms. Shapiro is a third-year student working in the lab of Benjamin tenOever, PhD, Irene and Arthur Fishberg Professor of Medicine and Professor of Microbiology.



Jillian Shapiro

NEW LEADERSHIP

# Entrepreneurship and Science at Mount Sinai

The need to integrate technology, innovation, and science in education has never been greater than it is today. Big data, digital media, and supercomputing are rapidly changing the way we mine and process biomedical information, giving scientists unprecedented opportunities to conduct entrepreneurial research. With this understanding in mind, Mount Sinai's Graduate School of Biomedical Sciences recently created two new positions aimed at giving students, fellows, and scientists a leading edge in this exciting new environment.

Basil Hanss, PhD

**BASIL HANSS, PHD**, has been named Associate Dean of the Graduate School of Biomedical Sciences at Mount Sinai and founding Director of Mount Sinai's new Science and Medicine Program, which aims to recruit college students from physics, mathematics, computer science, engineering, and other majors that are atypical for medical school.

Building on more than 20 years of experience teaching medical and graduate students, Dr. Hanss has been responsible for oversight and strategic planning for the master's degree programs in the Graduate School of Biomedical Sciences. Considerable effort will be made to create and launch relevant programs while working to strengthen existing ones. The focus of these efforts will be on building new curricula that meet the ever-evolving educational needs of science students to better prepare them for the workplace and position them to make significant contributions to science and medicine.

Dr. Hanss, who is also Associate Professor of Medicine, Medical Education, and Structural and Chemical Biology, has built his career around his passions for research and teaching. His work focuses on discovering the mechanisms by which gene-therapeutic nucleic acids enter the cell. This poorly understood step limits the efficacy of many forms of gene therapy and the knowledge and tools gained from his research will help to overcome this barrier.

Geoffrey W. Smith

**GEOFFREY W. SMITH** has joined the faculty of Mount Sinai's Graduate School of Biomedical Sciences to create and direct the new Center for Technology, Innovation, and Entrepreneurship (C-TIE) and as a Professor in the Department of Health Evidence and Policy. A co-founder and Managing Partner of Ascent Biomedical Ventures, a New York City-based venture capital firm that specializes in investing in seed- and early-stage life science technology companies, Mr. Smith has nearly 20 years of experience evaluating and developing life sciences discoveries in the commercial setting. Five years ago, Mr. Smith founded the Science and Economics Program at The Rockefeller University in New York City to explore the intersection of those fields in order to understand how our choices about resources affect scientific conduct and output, and how scientific advances in turn influence resource choices.

At Mount Sinai, Mr. Smith will teach both faculty and students. C-TIE's educational efforts will be based on the idea that innovation is a discipline that can be taught. The goal of the C-TIE educational program is to have each participant learn a process for reliably producing creative solutions to nearly any challenge. In pursuing this goal, C-TIE will use a variety of teaching methods including simulations, case studies, and peer instruction. Exposure will be provided to a range of perspectives including biology, medicine, engineering, design, and economics.

RESEARCH FRONTIERS

# Anne-Claude Bedard, PhD, Receives 2012 Robin Chemers Neustein Award

Anne-Claude Bedard, PhD, a postdoctoral fellow in the Department of Psychiatry at the Icahn School of Medicine at Mount Sinai, has been awarded the 2012 Robin Chemers Neustein Postdoctoral Fellowship Award.

The $25,000 scholarship will help advance Dr. Bedard's work in the Division of Child and Adolescent Psychiatry under the mentorship of Jeffrey Newcorn, MD, Director of Mount Sinai's Division of Child and Adolescent Psychiatry, and Jeffrey Halperin, MD, Professorial Lecturer in Psychiatry. Dr. Bedard's primary research is the study of impaired cognition in childhood neuropsychiatric disorders, with the ultimate goal of developing effective compensatory strategies or interventions that will improve cognitive performance and influence the trajectory of such disorders.

Dr. Bedard is the third recipient of the Robin Chemers Neustein Postdoctoral Fellowship Award, which is designed to encourage and support female research scientists at Mount Sinai. The award was established in 2010 through a generous gift from Robin Chemers Neustein, a member of Mount Sinai's Board of Trustees. Recipients are senior postdoctoral scientists who intend to complete their training within two years, have demonstrated high-impact accomplishments in the biomedical sciences, and have the potential for a successful independent scientific career.

Anne-Claude Bedard, PhD

## YOUNG PIONEERS

Mount Sinai's Graduate School of Biomedical Sciences is a magnet for visionary scientists, truly compassionate mentors, and the most promising students in basic science. These factors result in significant research success, as demonstrated by this outstanding collection of student-led research papers.

### LAUREN G. FRIEDMAN

Disrupted autophagy leads to dopaminergic axon and dendrite degeneration and promotes presynaptic accumulation of α-synuclein and LRRK2 in the brain.

*Journal of Neuroscience*. May 30, 2012 (vol. 32, issue 22, pp. 7585-7593).

Parkinson's disease (PD) is characterized by dopaminergic (DA) neuron degeneration and has recently been linked to dysfunctional intracellular catabolism. We report that DA neurons with impaired autophagy, an essential degradation pathway, display PD-related neuropathology and protein accumulation. This work suggests that autophagy is one of several systems that may deteriorate with age and contribute to PD pathogenesis. *Mentor: Zhenyu Yue, PhD, Associate Professor of Neurology and Neuroscience*

### AMANDA HUBER

Genetically driven target tissue overexpression of CD40: A novel mechanism in autoimmune disease.

*J Immunol*. September 15, 2012 (vol. 189, issue 6, pp. 3045-53).
doi: 10.4049/jimmunol.1200311.
Epub August 10, 2012.

The CD40 gene, an important immune regulatory gene, is also expressed and functional on nonmyeloid-derived cells, many of which are targets for tissue-specific autoimmune diseases, including thyroid follicular cells in Graves' disease (GD). In this study, we show that target tissue overexpression of CD40 plays a key role in the etiology of autoimmunity. Using a murine model of GD, we demonstrated that thyroidal CD40 overexpression augmented the production of thyroid-specific Abs, resulting in more severe experimental autoimmune GD (EAGD), whereas deletion of thyroidal CD40 suppressed disease. We also showed that in both EAGD mouse thyroids and human primary thyrocytes, CD40 mediates this effect by activating downstream cytokines and chemokines, most notably IL-6. To translate these findings into therapy, we blocked IL-6 during EAGD induction in the setting of thyroidal CD40 overexpression and showed decreased levels of thyroid stimulating hormone receptor-stimulating Abs and frequency of disease. *Mentor: Yaron Tomer, MD, Lillian and Henry M. Stratton Professor of Molecular Medicine Chief, Division of Endocrinology, Diabetes and Bone Disease*

### JENNIFER MILLER

Deciphering the transcriptional network of the dendritic cell lineage.

*Nat Immunol*. July 15, 2012 (vol. 13, issue 9, pp. 888-899).
doi: 10.1038/ni.2370. Epub July 15, 2012.

This work demonstrates that dendritic cells (DC) share a unique genetic signature distinct from their nearest myeloid neighbor—the macrophages. This research further identified the transcriptional regulators likely involved in commitment of myeloid progenitors to the various DC subsets. Finally, a transcriptional program shared by all steady-state migratory cells regardless of tissue resident equivalent was discovered. This may contribute to tolerance to self-antigen. *Mentor: Miriam Merad, MD, PhD, Professor, Oncological Science and Medicine*

### NATALIE PICA

Hemagglutinin stalk antibodies elicited by the 2009 pandemic influenza virus as a mechanism for the extinction of seasonal H1N1 viruses.

*Proc Natl Acad Sci USA*. February 14, 2012 (vol. 109, issue 7, pp. 2573-8).

Following the emergence of the novel pandemic H1N1 influenza virus in the human population, the preceding seasonal virus became "extinct" and disappeared from circulation. We hypothesized that this was due to the induction of antibodies against the stalk of the hemagglutinin molecule, the protein that mediates entry of influenza virus into host cells, following infection with the pandemic strain. Using novel reagents known as chimeric hemagglutinins, our laboratory was able to demonstrate higher levels of virus-neutralizing, stalk-specific antibodies in the sera of individuals infected with the 2009 H1N1 pandemic virus compared to uninfected controls. The identification of these stalk-specific hemagglutinin antibodies provides a mechanistic explanation for the extinction of the seasonal H1N1 viruses in 2009/2010. *Mentor: Peter Palese, PhD, Horace W. Goldsmith Professor and Chair, Department of Microbiology; Professor, Department of Medicine*

### JIE SU

Regulation of embryonic and induced pluripotency by aurora kinase-p53 signaling.

*Cell Stem Cell*. August 3, 2012 (vol. 11, issue 2, pp. 179-94).

Many signals must be integrated to maintain self-renewal and pluripotency in embryonic stem cells (ESCs). However, the exact molecular regulatory mechanisms remain elusive. Through a non-biased shRNA screen of ESC-associated phosphoregulators, we demonstrate that Aurora Kinase-p53 signaling plays an essential role in the regulation of self-renewal, differentiation, and somatic cell reprogramming. This work sheds light on the identities, functions, and overall complexity of signaling networks in ESCs. *Mentor: Ihor R. Lemischka, PhD, Director, The Black Family Stem Cell Institute; Professor, Developmental and Regenerative Biology, Pharmacology and Systems Therapeutics*

### AJAY UMMAT

Structural basis for cisplatin DNA damage tolerance by human polymerase η during cancer chemotherapy.

*Nat Struct Mol Biol*. May 6, 2012 (vol. 19, no. 6, pp. 628-632).

A major clinical problem in the use of cisplatin to treat cancers is tumor resistance. Human DNA polymerase η is a crucial polymerase that allows cancer cells to cope with the cisplatin–DNA lesions that are formed during chemotherapy, hence providing resistance to treatment. Our work provides a structural basis for understanding this resistance and offers a framework for the design of novel inhibitors in cancer therapy. *Mentor: Aneel K. Aggarwal, PhD, Professor, Structural and Chemical Biology, and Oncological Sciences*

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Mount Sinai

## The Icahn School of Medicine at Mount Sinai is home to 14 translational research institutes.

THE BLACK FAMILY STEM CELL INSTITUTE
*Director:* Ihor R. Lemischka, PhD

THE CHARLES BRONFMAN INSTITUTE
FOR PERSONALIZED MEDICINE
*Director:* Erwin P. Bottinger, MD

CHILD HEALTH AND DEVELOPMENT INSTITUTE
*Director:* Bruce D. Gelb, MD

DISEASE PREVENTION AND PUBLIC HEALTH INSTITUTE
*Director:* Paolo Boffetta, MD, MPH

EXPERIMENTAL THERAPEUTICS INSTITUTE
*Director:* Ravi Iyengar, PhD

THE FRIEDMAN BRAIN INSTITUTE
*Director:* Eric J. Nestler, MD, PhD

GLOBAL HEALTH AND EMERGING PATHOGENS INSTITUTE
*Director:* Adolfo García-Sastre, PhD

IMMUNOLOGY INSTITUTE
*Directors:* Lloyd F. Mayer, MD; and Sergio A. Lira, MD, PhD

ICAHN INSTITUTE OF INSTITUTE FOR GENOMICS
AND MULTISCALE BIOLOGY
*Director:* Eric E. Schadt, PhD

METABOLISM INSTITUTE
*Director:* Andrew Stewart, MD

THE RECANATI/MILLER TRANSPLANTATION INSTITUTE
*Director: S*ander S. Florman, MD

THE TISCH CANCER INSTITUTE
*Director:* Steven J. Burakoff, MD

TRANSLATIONAL AND MOLECULAR IMAGING INSTITUTE
*Director:* Zahi A. Fayad, PhD

THE ZENA AND MICHAEL A. WIENER
CARDIOVASCULAR INSTITUTE
*Director:* Valentin Fuster, MD, PhD