Mount Sinai

The Mindich Child Health and Development Institute

Annual Report 2013

The Mindich Child Health and Development Institute (MCHDI) is a translational research enterprise with the mission of advancing knowledge and therapies for diseases affecting infants, children, and adolescents. Led by Bruce D. Gelb, MD, the MCHDI provides an intellectually rich and supportive environment for fostering collaborative scientific investigation and Mount Sinai's "bench to bedside" philosophy, as well as training the next generation of scientific leaders in pediatric medicine.

Physician-scientists and scientists at the MCHDI work in a multidisciplinary manner with researchers and physicians in various departments and institutes at Mount Sinai. Together, we strive toward the objectives of developing robust paradigms for understanding the effects of genetics and environment on the health of infants, children and adolescents, and personalizing pediatric medicine through genetics and genomics.

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Message from the Director

The MCHDI has grown and matured substantially since the concept was first put to paper in 2009. Much effort through late 2012 focused on strategic planning, fundraising, and faculty recruitment needed to get the institute off the ground. Following a generous naming gift from Eric and Stacey Mindich, the doors for the MCHDI's headquarters opened with an official launch in April 2013. I am proud to say that in 2013, we have witnessed the MCHDI move from an abstract idea to a fully-realized collaborative, translational research institute focusing on children's health.

What does the fully-realized enterprise look like? For one, we now reside in a newly constructed space in the Hess Center for Science and Medicine building on Mount Sinai's main campus. We also have continued to recruit an impressive and substantial faculty of both clinical and laboratory experts. Lastly, we have implemented valuable activities and programs – a pilot funding program, an annual retreat for all faculty and trainees, and grant critique programs – that support our roughly 130 faculty and trainees.

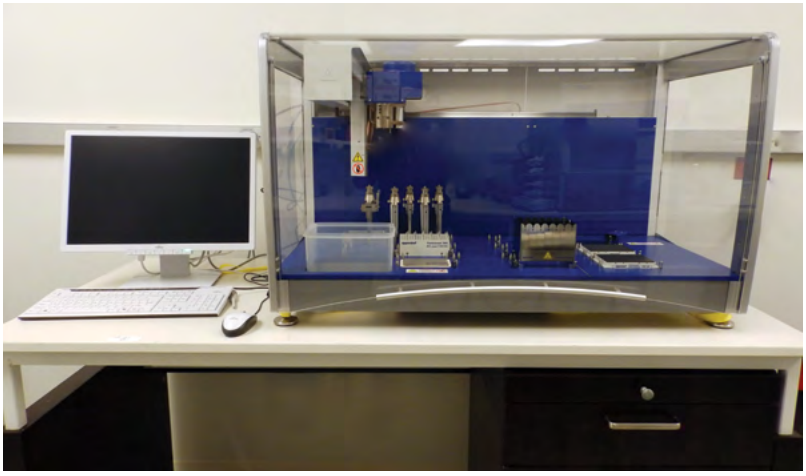
As you will see throughout this 2013 annual report, the MCHDI is making new connections and research projects in child health possible, and affirming its presence as a truly "bench-to-bedside" enterprise.

Bruce D. Gelb, Director

"I am proud to say that in 2013, we have witnessed the MCHDI move from an abstract idea to a fully-realized collaborative, translational research institute focusing on children's health."

Laboratory Headquarters

The MCHDI Headquarters, located in the Hess Center for Science and Medicine Building at Mount Sinai, houses a significant portion of its laboratory and computational research, and the institute's administrative office. The unique layout of the headquarter laboratory space is an open setting, with several laboratory rooms, pieces of equipment, and meeting spaces shared between laboratories. This means research trainees and investigators across departments – from genetics and genomic sciences, pediatrics, developmental biology, and neuroscience – share space and interact without physical barriers. In 2013, the MCHDI headquarters became fully operational with staff and instruments for a variety of applications, from liquid handling robotics to high-throughput sequencing to stem cell culture.



An automated pipetting system (top) and tissue culture hood in the MCHDI headquarters laboratory.

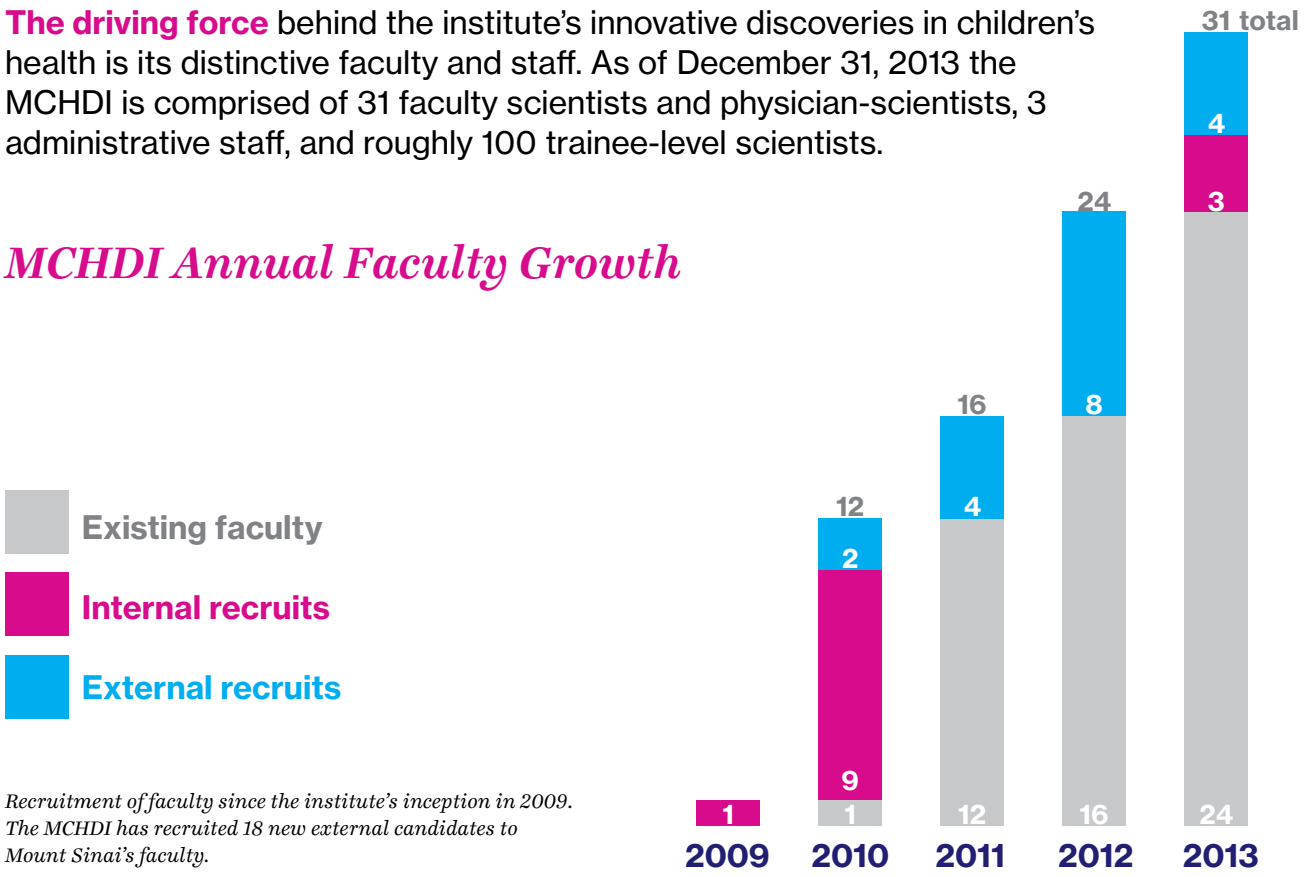
MCHDI faculty in the new headquarters space. Back row (from left to right): Drs. Cecilia Gunarsson (visiting professor), Eyal Shemesh, Bruce Gelb, Jaime Chu, Laura Murillo, Brian Brown, Luca Lambertini. Front row (from left to right): Drs. Ruth Loos, Supinda Bunyavanich, Coro Paisan-Ruiz, Dalila Pinto, Annemarie Stroustrup, Megan Horton, Yong Zhao

Research trainees and investigators across departments – from genetics and genomic sciences, pediatrics, developmental biology, and neuroscience – share space and interact without physical barriers.

Our Team

The driving force behind the institute's innovative discoveries in children's health is its distinctive faculty and staff. As of December 31, 2013 the MCHDI is comprised of 31 faculty scientists and physician-scientists, 3 administrative staff, and roughly 100 trainee-level scientists.

MCHDI Annual Faculty Growth



Recruitment of faculty since the institute's inception in 2009. The MCHDI has recruited 18 new external candidates to Mount Sinai's faculty.

The MCHDI welcomed seven new faculty members and two program staff in 2013.

Faculty

▲ **Harold S. Bernstein, MD** is an Adjunct Professor of Pediatrics. He is currently a Director of Clinical Research at Merck working in early stage therapeutic development. Prior to joining Mount Sinai and Merck, he was a senior faculty member in the UCSF Department of Pediatrics in the Division of Cardiology. While he oversees broad projects in drug development at Merck, his own research has focused on congenital heart disease, cardiomyopathy, Marfan syndrome, and the potential therapeutic application of stem cells for defects in cardiovascular development.

▲ **Jaime Chu, MD** is an Assistant Professor in the Department of Pediatrics in the Division of Hepatology. She recently transitioned to a faculty position after having completed a fellowship in pediatric gastroenterology at Mount Sinai. Dr. Chu attended medical school at NYU Langone. She completed her residency and began her fellowship at Children's Memorial Hospital in Chicago. Currently she works jointly in the MCHDI and the Recanati-Miller Transplantation Institute. Dr. Chu's research is focused on investigating genetic causes for congenital disorders of glycosylation (CDG) using zebrafish models. Children with CDG have debilitating, multi-systemic disease, including liver and gastrointestinal disorders. Her research aims to elucidate metabolic roles of genes in CDG with a goal of identifying new potential therapeutic targets.

▲ **Nicole Dubois, PhD** is an Assistant Professor of Developmental and Regenerative Biology. As an interdisciplinary scientist who has studied genetics, immunology, and developmental biology, she has sought to understand the development of the human cardiovascular system. Dr. Dubois

completed her postdoctoral research at the McEwen Centre for Regenerative Medicine in Toronto, Canada, where she studied human stem cell development in the laboratory of Gordon Keller, a leader in stem cell biology. She received her PhD from the University of Lausanne in Switzerland, where she worked jointly with the Swiss Institute for Experimental Cancer Research, with the support of a prestigious national fellowship. Her work at Mount Sinai and the MCHDI focuses on understanding how human stem cells in the embryo develop into highly specialized cells with cardiovascular function.

▲ **Megan Horton, PhD, MPH** is an Assistant Professor of Preventive Medicine. She joined Icahn School of Medicine at Mount Sinai from Columbia University's Mailman School of Public Health, where she completed her PhD and MPH in environmental health science, and a postdoctoral fellowship in neuroepidemiology at the school's Sergievsky Center. She has received an NIH K99/R00 award to continue her research in neuroepidemiology in the MCHDI. Dr. Horton's research focuses on understanding the mechanisms through which prenatal and early childhood exposure to environmental toxicants adversely affect children's brain development and health.

▲ **Laura Murillo Rodriguez, PhD** is an Assistant Professor in the Department of Genetics and Genomic Sciences. Dr. Murillo was previously a postdoctoral fellow at Columbia University. She completed both her PhD and a postdoctoral fellowship in human genetics at the University of Santiago de Compostela in Spain. She currently works jointly with the research teams of MCHDI Director Bruce Gelb and Inga Peter, Associate Professor of Genetics and Genomic Sciences. Dr. Murillo studies statistical genetics and applies computational methods to identify causes of congenital heart defects.

▲ **Eyal Shemesh, MD** is an Associate Professor of Pediatrics and Psychiatry, and is the Division Chief of Developmental and Behavioral Pediatrics. Dr. Shemesh is trained as both a pediatrician and a psychiatrist. He has published dozens of scientific articles on the emotional impact of chronic illnesses in children and adults, with a special emphasis on distress, posttraumatic stress, depression, and nonadherence to medical treatments. Dr. Shemesh's research currently concentrates on how to measure and improve adherence and posttraumatic stress in medically ill children and adults.

▲ **Annemarie Stroustrup, MD, MPH** is an Assistant Professor of Pediatrics and Preventive Medicine and a member of the Division of Newborn Medicine. Like Dr. Jaime Chu, she recently transitioned from a fellowship at Mount Sinai to a junior faculty position after receiving a prestigious K award from the NIH. Her fellowship was in perinatology and neonatology. She had previously completed her medical degree at Harvard University, and her residency and MPH degree at Mount Sinai. Dr. Stroustrup's research interests span the disciplines of perinatal epidemiology, neonatology, and environmental health. Specifically, she works to better understand modifiable causes of adverse outcomes in neonates born preterm, low birth weight, or otherwise ill. Her current research focuses on elucidating potential environmental contributors to poor neurodevelopmental outcomes in NICU graduates.

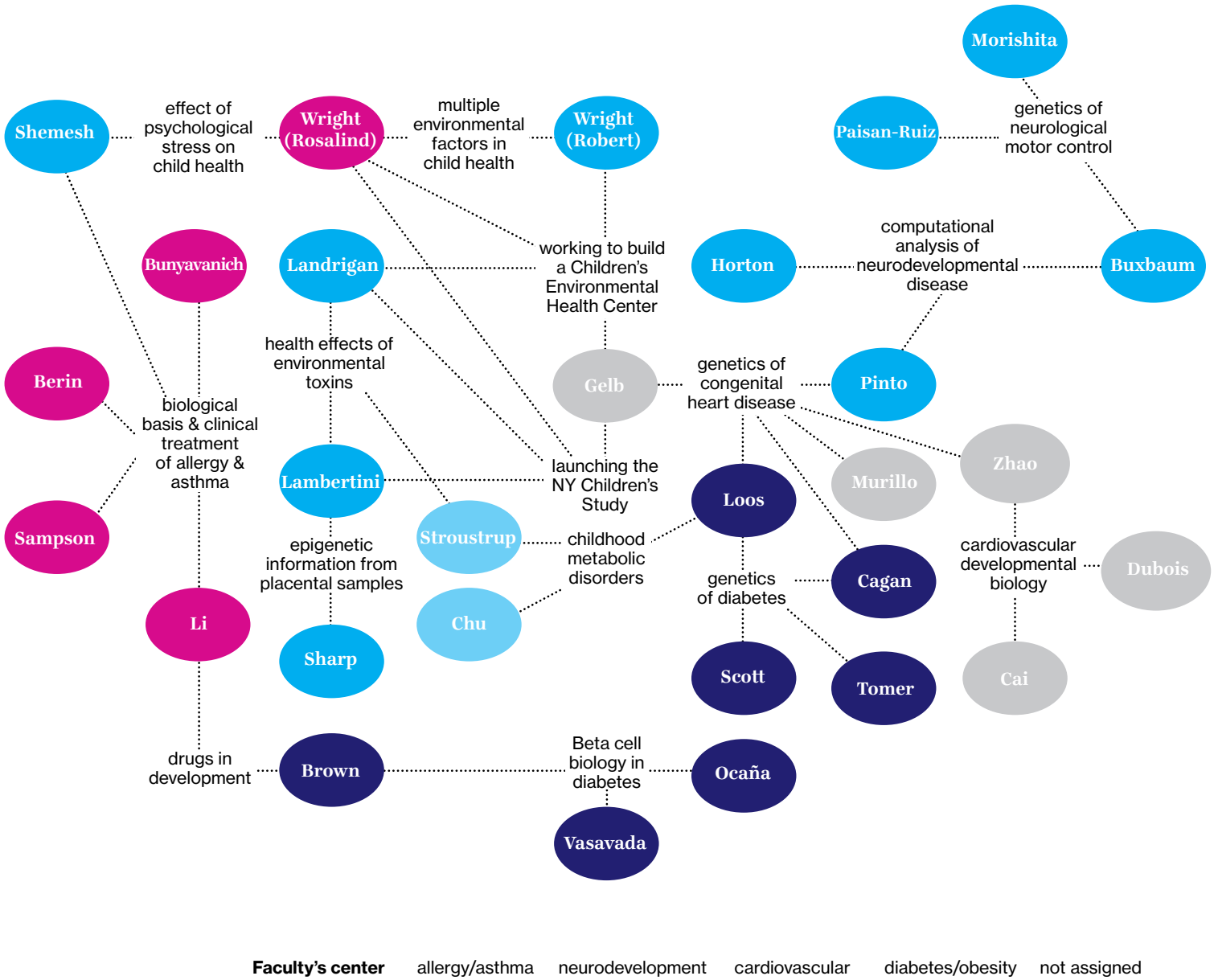
Program Staff

▲ **Brooke Rosenzweig, PhD** is the Program Manager for the MCHDI. She completed her PhD in chemical biology at Yale University and a postdoctoral fellowship in biophysics at the University of Pennsylvania School of Medicine. Her work has been supported by a Fulbright fellowship, a National Science Foundation fellowship, and a Howard Hughes Medical Institute fellowship; her collaborators and advisors have included members of the National Academies of Science and Nobel Laureates. She is an experienced consultant for nonprofit programs in science and social services. For the MCHDI, Dr. Rosenzweig is working in strategic management and establishing programs – such as an annual retreat and the awarding of pilot grants – that support the institute's faculty and trainees.

▲ **Risa Slaughter** is the MCHDI's new administrative coordinator. She comes to Mount Sinai from Columbia University's Mailman School of Public Health, where she assisted in the dean's office. Ms. Slaughter has a BA in accounting from Berkeley College in New York. She is responsible for a variety of administrative duties at the MCHDI.

Faculty Collaboration

The MCHDI was structured to foster group efforts for its investigators to address the most pressing issues in children's health. The diagram below – the faculty "interactome" – illustrates just some of the ways in which the institute faculty collaborate and interact. Originally focusing on four areas – congenital heart defects, diabetes and obesity, neurodevelopment, and asthma and allergy – the research scope of the MCHDI is currently expanding to encompass a broad range of issues affecting child health, through the lens of genetics, genomics, and the environment. For example, in the diagram below, the newest faculty additions of Drs. Chu and Stroustrup work in areas that go beyond the MCHDI's original four research pillars.



Noteworthy Publications

MCHDI researchers continued to make breakthrough discoveries in child health research. Their total publications numbered over 130 for the year 2013. Below is just a sampling of some of the notable publications to come from the institute's investigators in 2013 (click on the title to link directly to the article).

Cecilia Berin, PhD, Associate Professor of Pediatrics
Mucus Enhances Gut Homeostasis and Oral Tolerance by Delivering Immunoregulatory Signals *(Science)*

Brian Brown, PhD, Associate Professor of Genetics and Genomic Sciences
The miR-126-VEGFR2 axis controls the innate response to pathogen-associated nucleic acids *(Nat. Immunol.)*

Ross Cagan, PhD, Professor of Developmental Biology
Transformed Drosophila cells evade diet-mediated insulin resistance through wingless signaling *(Cell)*

Chenleng Cai, PhD, Assistant Professor of Developmental and Regenerative Biology
Tbx20 acts upstream of Wnt signaling to regulate endocardial cushion formation and valve remodeling during mouse cardiogenesis *(Development)*

Jaime Chu, MD, Assistant Professor of Pediatrics
A zebrafish model of congenital disorders of glycosylation with phosphomannose isomerase deficiency reveals an early opportunity for corrective mannose supplementation *(Dis. Model Mech.)*

Bruce Gelb, MD, Professor of Pediatrics and Genetics and Genomic Sciences
De novo mutations in histone-modifying genes in congenital heart disease *(Nature)*

Ruth Loos, PhD, Associate Professor of Preventive Medicine
New loci associated with birth weight identify genetic links between intrauterine growth and adult height and metabolism *(Nat. Genet.)*

Dalila Pinto, PhD, Assistant Professor of Genetics and Genomic Sciences and Joseph Buxbaum, PhD, Professor of Psychiatry and Genetics and Genomic Sciences
Network Topologies and Convergent Aetiologies Arising from Deletions and Duplications Observed in Individuals with Autism *(PLoS Genet.)*

Yaron Tomer, MD, Professor of Medicine
Fine Mapping of Loci Linked to Autoimmune Thyroid Disease Identifies Novel Susceptibility Genes *(J. Clin. Endocrin. Met.)*

Robert Wright, MD, MPH, and Rosalind Wright, MD, MPH,
Professors of Pediatrics and Preventive Medicine
Disrupted Prenatal Maternal Cortisol, Maternal Obesity, and Childhood Wheeze Insights into Prenatal Programming *(Am. J. Respir. Crit. Care Med.)*

Rosalind Wright, MD, MPH, Professor of Pediatrics and Preventive Medicine
Effects of prenatal community violence and ambient air pollution on childhood wheeze in an urban population *(J Allergy Clin. Immunol.)*

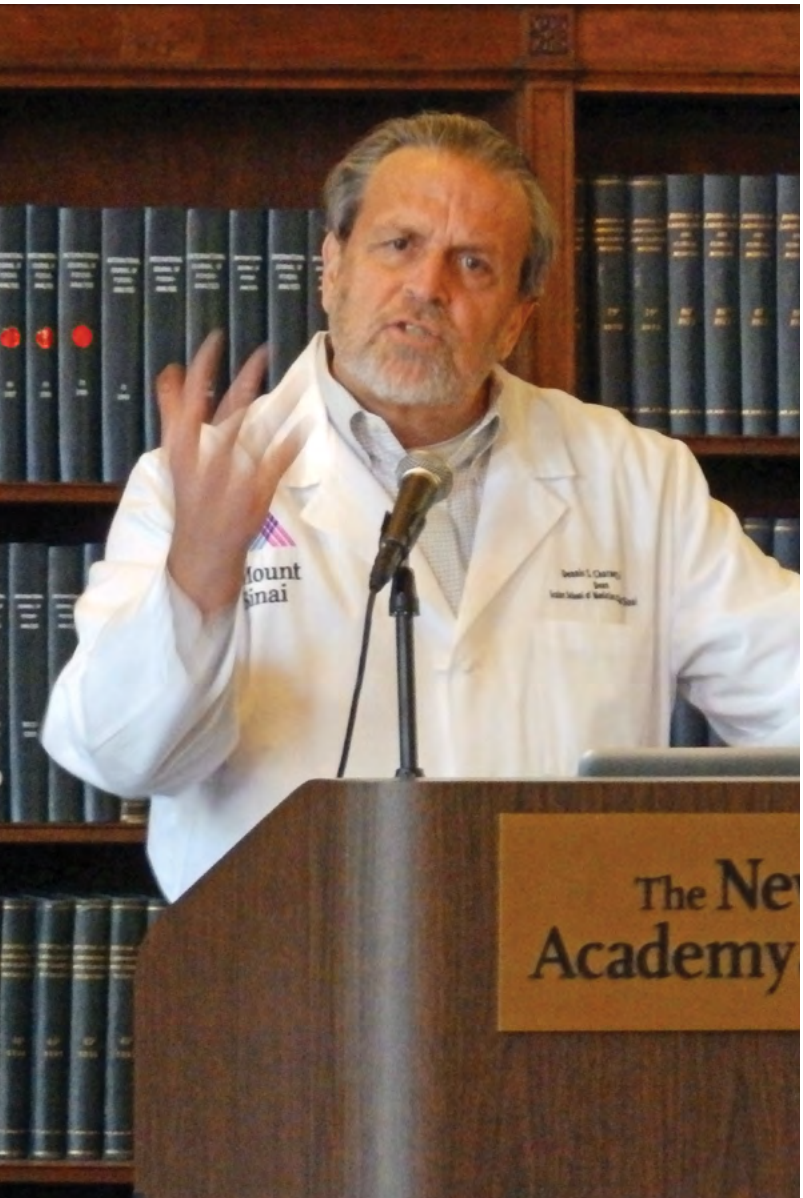
Annual Retreat

The MCHDI's inaugural retreat was held on November 5, 2013 at the New York Academy of Medicine. This was the first opportunity for the institute's investigators and trainees to convene and share their work and findings. Nearly all of the MCHDI's faculty, trainees, and senior research assistants were in attendance. The retreat, which will be an annual event, was designed to educate the attendees about the broad range of research within the MCHDI with the aim of fostering collaborations within the institute. Highlights included a keynote address from Joel Dudley of the Icahn Institute of Genomics and Multiscale Biology and a robust Young Investigator Competition for students and post-doctoral fellows. The day concluded with a moving presentation by a couple whose daughter has a form of autism under study at Mount Sinai.

See the full program for the Annual Retreat on the MCHDI website.

Dennis Charney, MD, Dean of the Icahn School of Medicine at Mount Sinai, welcomes retreat attendees with an address on the importance of child health research (below left).

MCHDI faculty and staff at the retreat poster session (below right).



Pilot Program

In July 2013, three $70k pilot "seed" grants were made available to MCHDI faculty through competitive application. The recipients (listed below*) were announced in October. Projects were selected based on their likelihood to improve children's health, to promote collaboration in the MCHDI, and to leverage additional extramural funding for the principal investigators. Proposals were also encouraged that capitalized on the expertise of others at Mount Sinai to direct their interests onto child health.

▲ "Gene Expression and Epigenetic Modifications in Childhood Food Allergy"
Investigators: **Supinda Bunyavanich, MD, MPH**, MCHDI Investigator and Assistant Professor of Pediatrics; **Hugh Sampson, MD**, MCHDI Investigator and Professor of Pediatrics; Eric Schadt, PhD, Professor of Genetics and Genomic Sciences

▲ "Drug Repositioning for Enhancing Brain Plasticity to Reverse Neurodevelopmental Disorders"
Investigators: **Hirofumi Morishita, MD, PhD**, MCHDI Investigator and Assistant Professor of Psychiatry, Neuroscience, and Opthamology; Joel Dudley, PhD, Assistant Professor of Genetics and Genomic Sciences

▲ "Epigenomics of Neural Tube Defects"
Investigators: **Andrew Sharp, PhD**, MCHDI Investigator and Associate Professor of Genetics and Genomic Sciences; Ethylin Wang Jabs, MD, Professor of Genetics and Genomic Sciences, Pediatrics, and Developmental and Regenerative Biology; Gregory Holmes, PhD, Assistant Professor of Genetics and Genomic Sciences

**Principal investigators in blue are members of the MCHDI.*

Dr. Supinda Bunyavanich monitoring a patient with debilitating food allergy (below left). Her collaborative project with Dr. Hugh Sampson and Dr. Eric Schadt could identify epigenetic causes of allergic reactions to common foods that affect children like the patient pictured here.

The three pilot fund recipients (below right, from left to right) Drs. Andrew Sharp, Supinda Bunyavanich, and Hirofumi Morishita

Grant Support Series

The MCHDI prides itself on a cooperative work environment, and members actively assist one another to apply for the most competitive extramural grants. This year, the institute began offering two formal programs to provide grant support its faculty.

▲ **Incubator series** – in a bimonthly meeting series, MCHDI investigators have the opportunity to share grant proposals with one another. The series provides the investigators an opportunity to receive valuable critiques from a diverse scientific audience prior to submitting applications.

▲ **Mock review** – in November 2013, the MCHDI created a mock study section review program for its faculty who are first-time R01 applicants. The review, held in December 2013, is intended to prepare applicants for submission of proposals to the NIH in February 2014.

By the Numbers

MCHDI Faculty Grants 2013

Agency	Funding from New Grants ($)	Funding from New & Existing Grants ($)
National Heart, Lung, And Blood Institute	1,473,029	4,696,640
National Human Genome Research Institute	1,098,541	1,554,541
National Institute Of Allergy And Infectious Diseases	877,018	6,345,346
National Institute Of Mental Health	817,786	2,375,223
National Institutes Of Health	742,322	742,322
National Institute Of Neurological Disorders And Stroke	678,000	678,000
National Cancer Institute	409,560	1,066,690
National Institute Of Environmental Health Sciences	395,033	2,146,033
DBV Technologies	295,757	295,757
Shire Human Genetics Therapies, Inc.	225,214	225,214
Novartis Pharmaceutical Corporation	208,805	208,805
Nationwide Children's Hospital	203,400	203,400
Children's Hospital, Boston, Mass	200,115	200,115
March Of Dimes	198,855	198,855
Columbia University	197,635	197,635
National Institute Of Diabetes And Digestive And Kidney Diseases	129,020	1,849,413
Washington University	127,126	127,126
Food Allergy Initiative	110,000	842,918
National Institute Of Child Health And Human Development	84,750	463,977
Pitt Hopkins Research Foundation	79,976	79,976
Knights Templar Eye Foundation Inc.	60,000	60,000
Traditional Chinese Medicine World Foundation	56,000	56,000
Immunomic Therapeutics, Inc.	53,277	53,277
UKCRC Centre for Diet and Activity Research (CEDAR)	33,232	33,232
Brain and Behavior Research Foundation	30,000	30,000
University Of Cincinnati	19,494	19,494
Tulane University	18,909	18,909
National Eye Institute	–	423,750
Juvenile Diabetes Foundation International	–	248,581
American Cancer Society, Inc.	–	240,000
Autism Speaks	–	137,173
National Institute Of Arthritis & Musculoskeletal & Skin Diseases	–	130,274
American Diabetes Association	–	112,756
Whitehall Foundation, Inc.	–	75,000
Alzheimer's Association	–	39,657
Fogarty International Center	–	52,410
Columbia University	–	12,845
Total	8,822,854	26,241,344

Mount Sinai

The Mindich Child Health and Development Institute

Program Leadership & Staff

Director Bruce Gelb, MD

Program Manager Brooke Rosenzweig, PhD

Administrative Coordinator Risa Slaughter

Director of Development Monica Sohn

Associate Director of Development Jacqueline Leitzes

Faculty

Cecilia Berin, PhD
Brian Brown, PhD
Supinda Bunyvanaich, MD, MPH
Joseph Buxbaum, PhD
Ross Cagan, PhD
Chenleng Cai, PhD
Jaime Chu, MD
Nicole Dubois, PhD
Bruce Gelb, MD
Megan Horton, PhD, MPH
Luca Lambertini, PhD
Phil Landrigan, MD
Xiu-Min Li, MD
Ruth Loos, PhD
Hirofumi Morishita, MD, PhD
Laura Murillo Rodriguez, PhD
Adolfo García-Ocaña, PhD
Coro Paisán-Ruiz, PhD
Dalila Pinto, PhD
Hugh Sampson, MD
Donald Scott, PhD
Andrew Sharp, PhD
Eyal Shemesh, MD
Annemarie Stroustrup, MD
Yaron Tomer, MD
Rupangi Vasavada, PhD
Robert Wright, MD, MPH
Rosalind Wright, MD, MPH
Yong Zhao, MD, PhD

Leadership Council

Eric and Stacey Mindich
Henry and Vanessa Cornell
Katie Danziger
Sonia E. Gardner
Donald and Georgia Gogel
Michael and Beth Klein
Michael and Andre Koester
The Jack Martin Fund
Eric and Sarah Lane
Glen Nordlinger and Kimara Ahnert
Robert and Ruth Rosania
Ricky and Mara Sandler

For more information on the MCHDI, please visit our website at **www.mssm.edu/mchdi**