

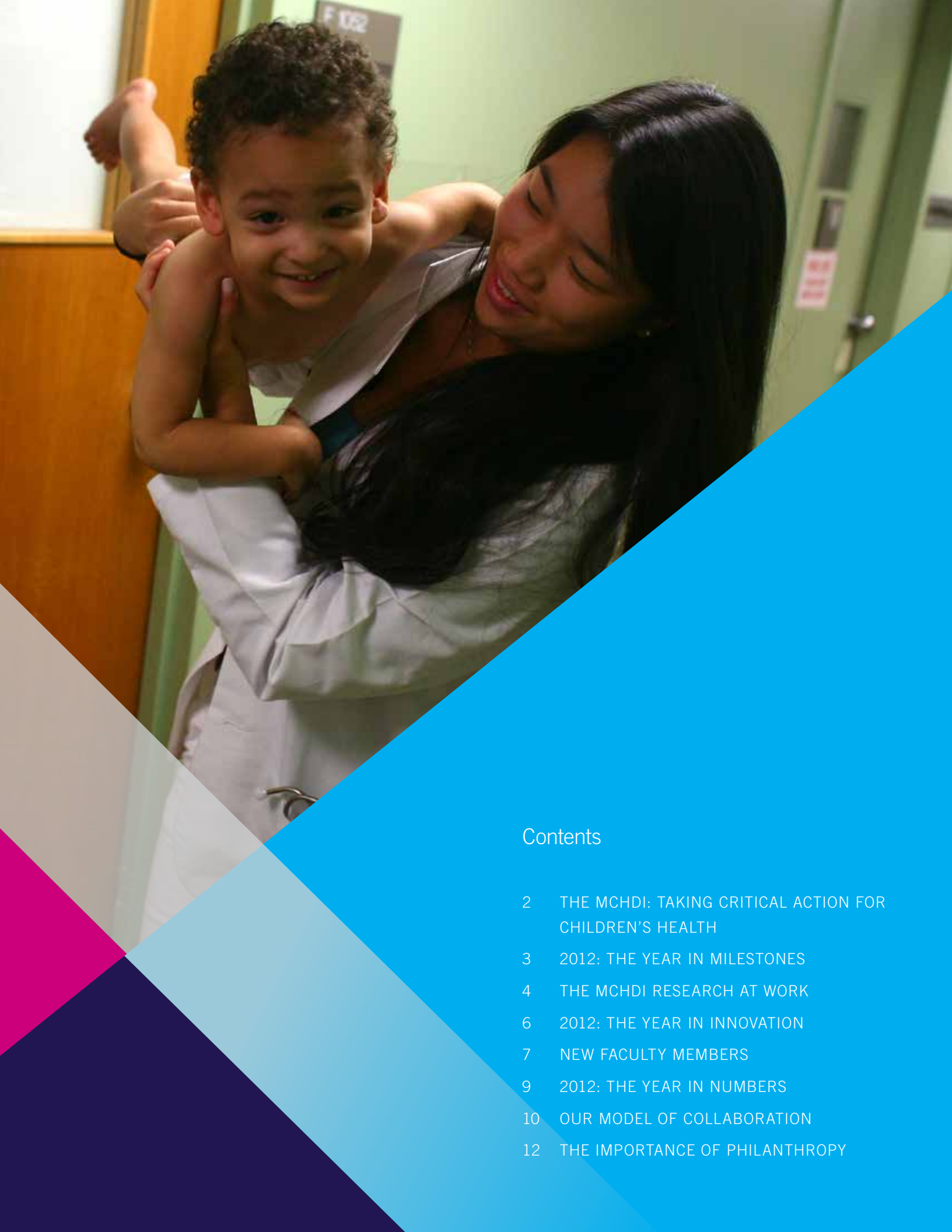


**Mount
Sinai**

The Mindich Child Health
and Development Institute

2012 Annual Report





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Letter from the Director

2012 saw significant growth and activity for The Mindich Child Health and Development Institute, in both the size and the depth of our translational research enterprise, where our sole mission is to change the face of children's health.



We also experienced a tremendous leap forward philanthropically with an exceptional leadership gift from Eric and Stacey Mindich. Recognizing their generosity to substantially advance our mission for children's health research, we have renamed the Child Health and Development Institute in their honor.

As outlined in this report, our Institute continues to be highly successful in attracting outstanding scientists and physician-scientists whose research is focused on improving the health of children. These new investigators come to Mount Sinai from elite academic institutions throughout North America, and range from junior faculty with outstanding promise to highly accomplished, mid-career researchers whose programs are already well-established.

This past year, the MCHDI continued to develop the infrastructure necessary to support the scientific work of its members. Most notably, we established the headquarters for the Institute in Mount Sinai's new Leon and Norma Hess Center for Science and Medicine. In addition to being an administrative hub, our new home brings together several of the Institute's faculty and their research teams. This will further strengthen our commitment to collaborative research within the MCHDI. This strategy has already begun to yield results, both in the ability of our investigators to garner additional funding and through innovative research.

The enterprise of the MCHDI requires commitment from our partners. The Icahn School of Medicine at Mount Sinai, led by Dennis Charney, Anne and Joel Ehrenkranz Dean of the School of Medicine, showed true vision in initially creating our Institute and has been tremendously supportive since our beginning. The MCHDI Leadership Council, led by Don and Georgia Gogel, has been steadfast in its mission of providing the dedication and support that make our work possible. Through the remarkable generosity of the council members and others, more than \$57 million has been committed to the Institute since 2009; their philanthropy has enabled us to grow and expand our research in ways that will have a profound impact on children's health.

On behalf of everyone at the MCHDI, I hope the information contained herein will be a source of great pride for all who have participated in the work of the Institute, and that it will stimulate excitement for those who are considering joining us for the journey ahead.

A handwritten signature in black ink, appearing to read "B. Gelb".

Bruce D. Gelb, Director

MCHDI: Taking Critical Action for Children's Health

The prevalence of complex health disorders that cause lifelong debilitating conditions continues to rise. Unfortunately, our children are the ones at the frontline of an increase in problematic asthma, allergy, diabetes, obesity, neurological disorders, and cardiovascular defects. Without intervention, the number of children who suffer from these disorders will only continue to grow.

At the MCHDI, we continue to bring together outstanding scientists and physician-scientists who interact in innovative ways to address childhood diseases. By focusing on these diseases in their earliest stages—even prior to birth—we can simultaneously understand the cause of these disorders and develop novel strategies to prevent and treat them.



2012: The Year in Milestones

- › **This past spring**, three prominent researchers from the Harvard School of Public Health and the Harvard Medical School committed to joining our enterprise. The addition of physician-scientists Supinda Bunyavanich, MD, MPH, Rosalind J. Wright, MD, MPH, and Robert O. Wright, MD, MPH (see New Faculty Members) has significantly strengthened the MCHDI's commitment to unveiling the environmental and genetic causes of asthma, allergy, and neurodevelopmental disorders.
- › **In July**, the first of what will become thousands of samples were collected for the Pregnancy Biobank, a repository of data and biological samples that the MCHDI leads in partnership with the Children's Environmental Health Center at Mount Sinai. The Biobank will serve as a groundbreaking resource for testing how specific environmental exposures lead to the development of disease. For example, the causes of autism, while still unknown, have been linked to a number of potential environmental chemicals. However, without clear scientific evidence, it has been exceedingly difficult to confirm or rule out these causes. The Biobank will provide the critical biosamples through which this clear evidence can be amassed. By correlating the chemical exposures of thousands of New York City children with their health and development from the womb to adolescence, we expect to advance environmental pediatric medicine significantly.
- › **In September**, the MCHDI conferred its first endowed research chair upon one of our newest physician-scientist recruits, Dr. Rosalind Wright. The Institute's focus on environmental pediatric medicine will be boosted immeasurably with the addition of Dr. Wright's appointment as the Horace W. Goldsmith Professor in Children's Health Research.
- › **In December**, our research faculty began moving into the new MCHDI headquarters in Mount Sinai's recently opened Hess Center for Science and Medicine. The highlight of our new facilities is a dedicated collaborative laboratory space where physical resources, knowledge, and the diverse expertise of our faculty are being pooled to streamline progress in translational medicine. The labs unite MCHDI faculty across our different centers of research through a common focus on the genetic causes of childhood illness. In addition, our new space will serve as a central resource and meeting place for MCHDI faculty members across the Mount Sinai campus.

The MCHDI Research at Work

While this report cannot adequately cover all of the innovations underway at the MCHDI, here is a sampling of some of our most promising recent research.

■ Some of the most revealing discoveries in genetics have less to do with a gene itself, and more to do with what “switches on” that gene, or regulates its activity. **Yong Zhao, MD, PhD** and his research group have found that when a certain kind of RNA, a gene regulator called miR-1, is missing in mice, it causes dilated cardiomyopathy, a common condition resulting in an enlarged and weakened heart. This discovery may reveal an important requirement for healthy heart development in humans. In a related manner, **Chenleng Cai, PhD** recently found that a regulator called Tbx20 plays a crucial role in “switching on” the genes that ensure proper valve development in mammals; when Tbx20 is missing, valve defects occur. The role of Tbx20 could be crucial to understanding and preventing heart valve defects during human embryonic development.

■ **Xiu-Min Li, MD** and her research team made promising progress in treatments for food allergies. The second phase of clinical trials began for FAFH-2, a substance that Dr. Li’s group isolated from Chinese medicinal herbs. These trials are an important step towards making this product an approved medicine for clinical treatment. Dr. Li’s group tested FAFH-2 to learn exactly how it works, and discovered that it seems to alleviate the allergic reaction caused by specific immune cells (T cells and basophils). Her group continues to research this area, and has identified a number of other, similar molecules from traditional Chinese medicine that have the potential to work as well as—or perhaps even better than—FAFH-2.

■ In landmark progress towards optimizing personalized medicine, **Ross L. Cagan, PhD**, Associate Dean of the Graduate School of Biological Sciences, worked towards creating successful models of human disease. Specific individual genes that are responsible for everything from human diabetes to cancer have been placed in fruit flies, allowing several different drugs for these illnesses to be tested in tandem—thus enabling the identification of the most effective drug to administer for that specific gene. Dr. Cagan is considered an authority in his field; last year, his work on a disease fly model was published in the renowned journal *Nature*.

■ **Joseph Buxbaum, PhD** continued to lead progress in understanding the physiological origins of autism, particularly through the discovery of novel autism-related genes. Through Mount Sinai's Seaver Center for Autism, he co-directed the opening of the Autism Sequencing Consortium (ASC), which provides a database, housed on the Mount Sinai campus, of complete genetic information for roughly 28,000 autistic people. Local access to this database will provide an extraordinary resource for MCHDI researchers who focus on the genetics of neurological development. An authority on autism, among other areas, Dr. Buxbaum edited a new textbook, *The Neuroscience of Autism Spectrum Disorders*.

■ **Ruth Loos, PhD** identified several genetic "loci," or specific locations of genes, that vary slightly in their make-up between individuals but can have huge implications for a person's health. She found many novel loci that indicate genetic inclination towards not only obesity, but also physical activity, body mass index, and even where the body deposits fat. This work brings to light very specific factors that can more accurately identify health risks early on.



2012: The Year in Innovation

Technology and knowledge are constantly advancing in science and medicine; in children's health, MCHDI researchers are leading the march. Our faculty not only reached significant translational milestones in 2012 but also broke new ground in exciting and innovative areas of research.

■ **M. Cecilia Berin, PhD** began to examine the role of digestive health and, in particular, the gut microbiota (the population of gastrointestinal bacteria) in food allergy. Her pioneering research has already been productive, as she has identified TLR9, a component in the gut associated with bacterial recognition that is strongly tied to peanut allergy. TLR9 may represent a new target in fighting this life-threatening condition.

■ **Ruth Loos, PhD** began the search for two types of novel genes: “protective” genes that allow individuals with obesity to remain physically healthy, and the genes that prime so many individuals for weight gain. Pinpointing these genes is expected to have a significant impact on understanding both the morbidity and physiology of obesity.

■ **Hirofumi Morishita, MD, PhD**, a recent addition to the MCHDI, established studies to reveal the molecular and circuit mechanisms of brain plasticity. His research aims to discover targets for neurodevelopmental disorders, including one of the most common eye issues for children: amblyopia (“lazy eye”). Dr. Morishita is also researching the molecular mechanisms for cognitive development.

■ **Dalila Pinto, PhD** is at the forefront of using bioinformatics to understand children's neurological development. Recent advances in computational analysis have allowed for more accurate predictions in everything from elections to finance, and the same is true in biomedical science. Dr. Pinto's work focuses on analyzing large amounts of complex biological information to determine the association of particular genes with developmental health. Her work, initiated with the MCHDI last year, shows promise in revealing the genetic and epigenetic underpinnings of autism and epilepsy.

New Faculty Members

In 2012, the MCHDI continued to gain experts and investigators recognized for their potential for innovation:

■ **Supinda Bunyavanich, MD, MPH** is an Assistant Professor of Pediatrics and Genetics and Genomic Sciences. Prior to joining Mount Sinai, she was on faculty at Harvard Medical School and received the Shore Scholars in Medicine Award for her accomplishments and potential as a physician-scientist. Dr. Bunyavanich's research focuses on the environmental and genetic epidemiology of asthma and atopic disorders in children. She has examined environmental and genetic risk factors for allergic rhinitis, food allergy, and early childhood asthma.

■ **Adolfo García-Ocaña, PhD** is a Professor of Medicine recruited to Mount Sinai by the MCHDI and the Diabetes, Obesity and Metabolism Institute from the University of Pittsburgh. Dr. García-Ocaña's current research interests include the identification and characterization of growth factors and intracellular signaling pathways involved in the growth, survival, and function of pancreatic beta cells (the cells that produce insulin). This work has relevance for children with Type 1 diabetes, for whom regeneration of their ability to produce insulin could be curative.

■ **Anne Moon, MD, PhD**, who oversees a cardiovascular research group at Geisinger Health Systems in Pennsylvania, joined the MCHDI and Mount Sinai as an Adjunct Professor in Pediatrics. Her research is devoted to understanding the mechanisms of normal and pathologic cardiac, limb, and lung development, with a focus on the role of fibroblast growth factors. These studies are clarifying the molecular and cellular events that are disrupted in multiple cardiovascular syndromes. Her work in cardiac development has great collaborative potential with cardiovascular geneticists and developmentalists at the MCHDI.

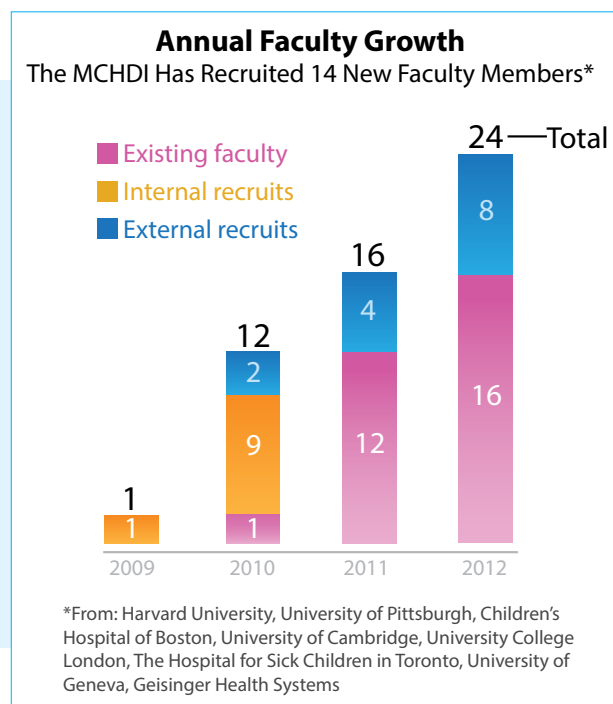
■ **Dalila Pinto, PhD** was recruited by the MCDHI (together with the Seaver Autism Center, The Friedman Brain Institute, and the Icahn Institute for Genomics and Multiscale Biology) based on her outstanding work as a post-doctoral fellow at The Hospital for Sick Children in Toronto. Dr. Pinto's research uses a combination of high-throughput technologies, bioinformatics, and statistical genetics to identify genes and biological pathways involved in neurodevelopmental disorders, including autism, intellectual disability, and epilepsy.

■ **Donald Scott, PhD** was recruited from the University of Pittsburgh and has been appointed Associate Professor of Medicine. His research on diabetes focuses on how nutrients alter the regulation and expression of genes in liver and pancreatic beta cells. This work is relevant for both the cause of diabetes as well as diabetic complications.

■ **Rupangi Chaya Vasavada, PhD**, a Professor of Medicine, was recruited from the University of Pittsburgh. Her current research focuses on the cellular and molecular pathways that enhance pancreatic beta cell survival, growth, and function. Her research goal is to enhance islet survival and function in Types 1 and 2 diabetes and in pancreatic islet transplantation using growth factors or their downstream target molecules.

■ **Robert Wright, MD, MPH** is an interdisciplinary physician-scientist trained in pediatrics (emergency medicine), environmental health, and genetics. He was recruited from the Harvard School of Public Health and has been appointed as a Professor of Preventive Medicine and Pediatrics as well as the Deputy Director of the Children’s Environmental Health Center. Dr. Wright combines the fields of genetics, toxicology, and social sciences—bridging the gaps among these disciplines to conduct sophisticated epidemiologic research on neurodevelopment. His work focuses on the effects of environmental exposures, including heavy metal toxicity, on childhood neurodevelopment and fetal growth. He is establishing the new Laboratory for Environmental Analytical Chemistry at Mount Sinai, which will allow many investigators to detect a wide range of toxic metals and organic compounds at an accelerated pace.

■ **Rosalind Wright, MD, MPH** is a physician-scientist who studies the epidemiology of chronic respiratory disease in both adults and children. Recruited from the Harvard School of Public Health, Dr. Wright has been appointed as a Professor of Pediatrics and Preventive Medicine and is the inaugural holder of the Horace W. Goldsmith Chair in Children’s Health Research, a position conferred upon her by the MCHDI. In addition, Dr. Wright serves as the Vice Chair for Clinical and Translational Research in the Department of Pediatrics. Her work uses multiple longitudinal cohort studies to examine how environmental stressors, including adverse life events, violence, and social deprivation, contribute to asthma rates.



In 2012, the MCDHI:

- raised \$15.6 million in philanthropic funding, increasing its to-date total to more than \$57 million
- recruited seven new tenure-track scientists and physician-scientists, and one adjunct physician-scientist
- secured \$8 million from the initiation of new grants
- published 100 scientific, peer-reviewed articles

2012: The Year in Numbers

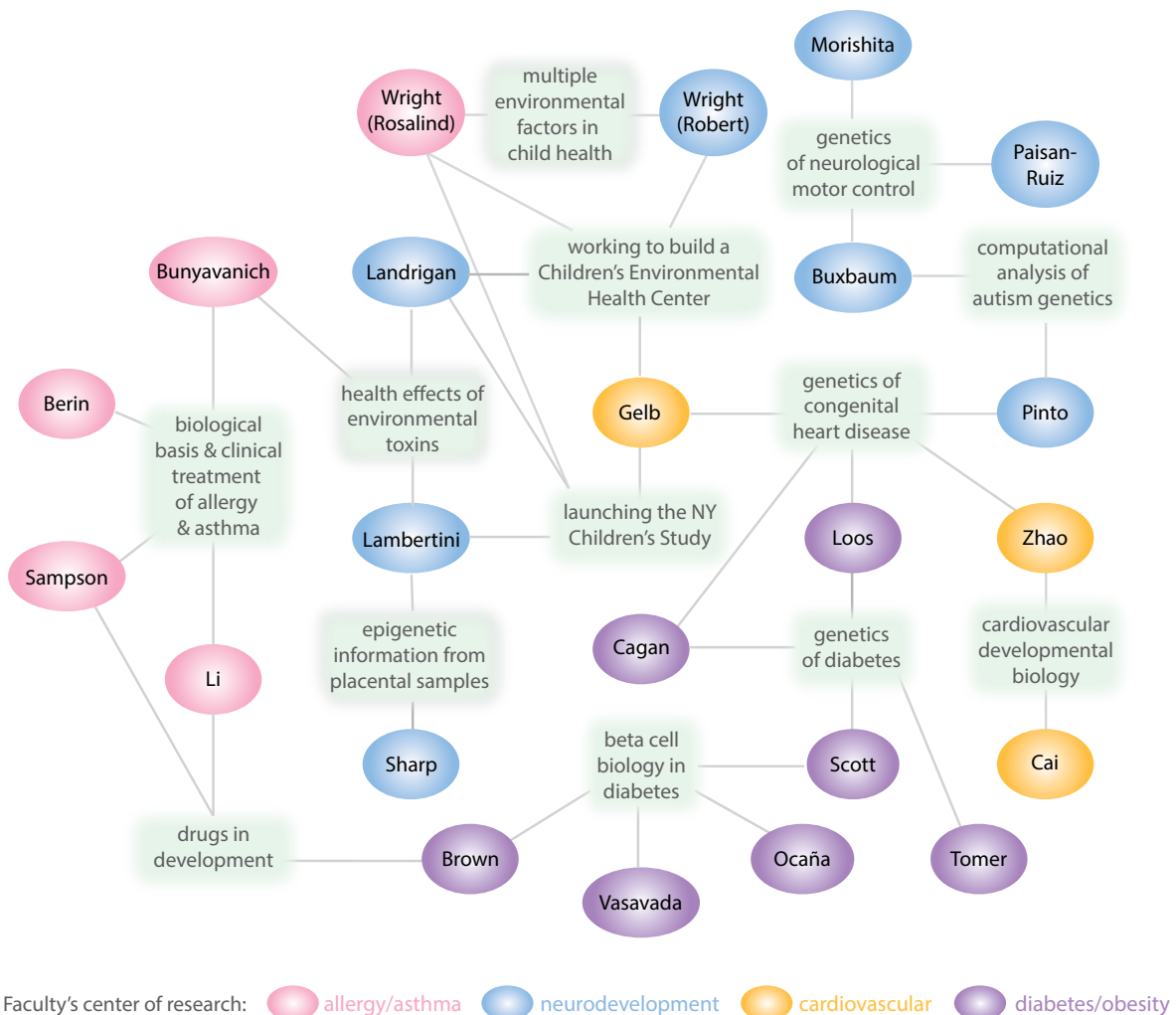
➤ MCHDI Faculty were supported by several grants in 2012, totaling more than \$25 million.

MCHDI Funding from Extramural Grants, 2012		
AGENCY	FUNDING FROM NEW GRANTS (\$)	FUNDING FROM NEW + EXISTING GRANTS (\$)
National Heart, Lung, and Blood Institute	1,385,606	3,698,973
National Institute of Diabetes and Digestive and Kidney Diseases	1,330,267	1,687,913
National Institute of Environmental Health Sciences	1,090,677	1,090,677
National Institute of Mental Health/NIH/DHHS	728,643	1,816,335
National Human Genome Research Institute	673,895	673,895
National Institute of Child Health and Human Development	519,046	8,592,583
National Cancer Institute	423,750	729,167
National Institute Of Allergy and Infectious Diseases	420,419	2,208,918
Sage Bionetworks	412,625	412,625
Juvenile Diabetes Foundation International	248,581	248,581
Hospital for Sick Children Toronto	155,584	155,584
Autism Speaks	136,173	136,173
National Institute of Arthritis and Musculoskeletal and Skin Diseases	127,635	127,635
American Diabetes Association	112,756	112,756
University Of California, San Francisco	85,486	85,486
Whitehall Foundation	75,000	75,000
Knights Templar Foundation	60,000	60,000
Alzheimer's Association	59,013	59,013
Parkinson's Disease Foundation	55,000	55,000
Blacksmith Institute	45,000	45,000
Columbia University	12,846	12,846
The Seaver Center	0	1,250,001
The Food Allergy Initiative	0	979,420
National Eye Institute	0	423,750
New York State Stem Cell Board	0	360,000
American Cancer Society	0	240,000
The Fogarty International Center	0	51,300
Total	8,158,002	25,388,631

2012: Our Model of Collaboration

From our new headquarters, which brings faculty together across different disciplines, to the addition of new recruits, who expand our research enterprise and complement our team’s scientific expertise, the MCHDI is evolving to foster productive collaborations. Historically, collaboration – and the crossover of research in different areas – has led to some of the most significant breakthroughs in science and modern medicine. At the MCHDI, promising connections of this kind are already being established.

MCHDI Faculty Collaborations



Some of the most significant publications by MCHDI researchers in 2012 were the product of faculty members working together:

- **Philip Landrigan, MD, MSc**, Mount Sinai's Dean for Global Health, and **Luca Lambertini, PhD, MPH, MSc** outlined and shared "a research strategy to discover the environmental causes of autism and neurodevelopmental disabilities" in the journal *Environmental Health Perspectives*.
- **Xiu-Min Li, MD** and **Hugh Sampson, MD**, Dean for Translational Biomedical Research, teamed up for two projects: testing FAFH-2, a Chinese herbal medicine-derived therapeutic, as a novel treatment for peanut allergy, and assessing the effects of flavonoids present in anti-asthma medications.
- **Coro Paisan-Ruiz, PhD** identified a novel genetic mutation associated with progressive myoclonus epilepsy in studies she conducted with **Joseph Buxbaum, PhD**.

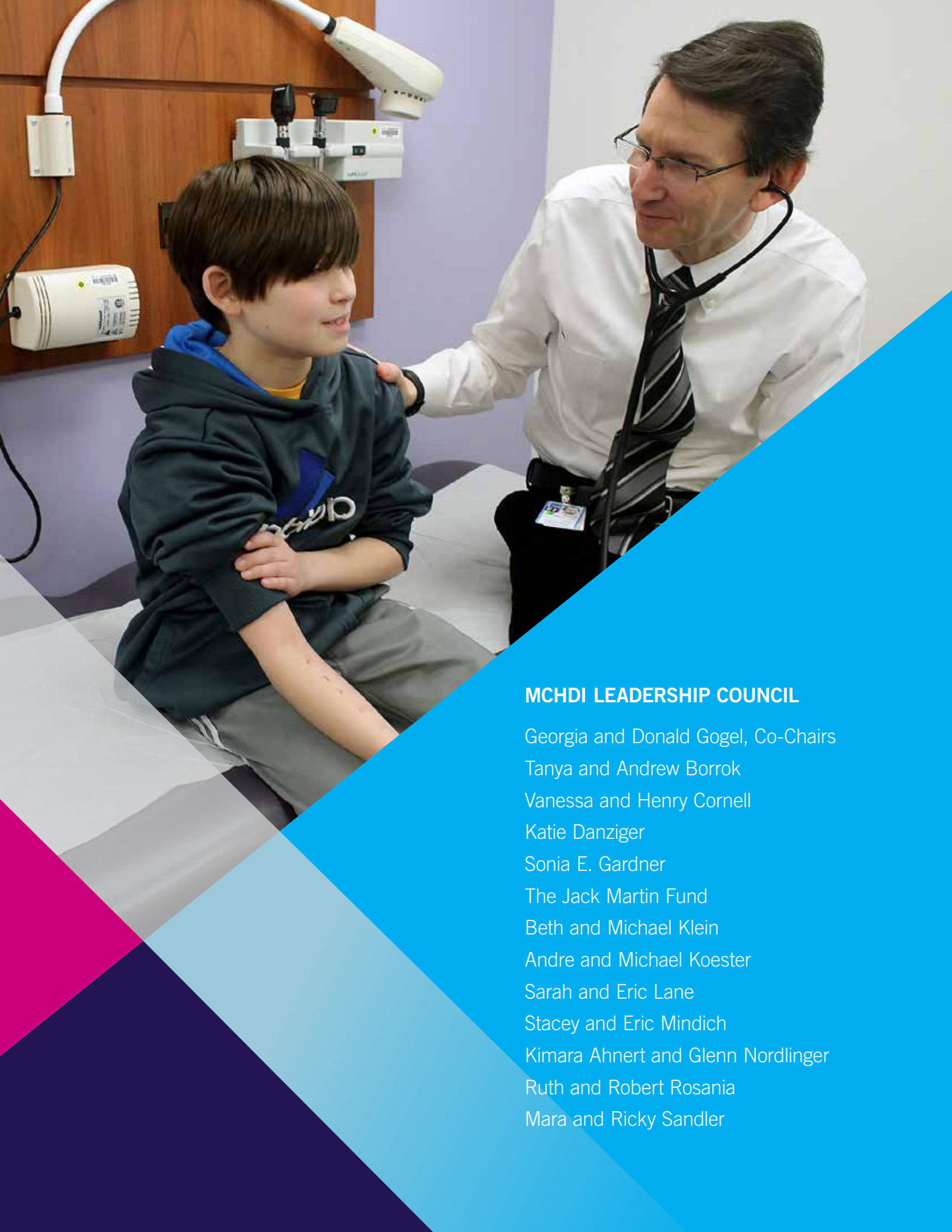


The Importance of Philanthropy

Thanks to the generous support of its philanthropic partners, The Mindich Child Health and Development Institute continues to discover crucial information about—and innovative treatments for—some of the most complex and widespread childhood diseases. Our goal is to translate scientific research findings into standard practices for the prevention, diagnosis, treatment, and ultimately the cure for such diseases.

The support we have received thus far is already making a real difference as treatments for life-threatening allergies are on the horizon, we are understanding the genetic origins of problematic weight gain, and we are securing resources to pinpoint the chemicals in our environment that pose a threat to our children's health.

But more needs to be done. By investing in the MCHDI, our supporters are leaving a matchless legacy: improving the quality of life both for the children who need insights and cures now, and for generations of children to come. We invite you to join us on our journey.



MCHDI LEADERSHIP COUNCIL

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**For more information
about The Mindich Child Health
and Development Institute,**

please contact Monica Sohn,
Director of Development,
at 212-731-7441 or
monica.sohn@mountsinai.org.