

Icahn School of Medicine at **Mount** Sinai The Mindich Child Health and Development Institute

# 2020 ANNUAL REPORT

he 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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**Director's Message** 

B DSU

Bruce D. Gelb, MD, Director

"It was the best of times, it was the worst of times, it was the age of wisdom, it was the age of foolishness, it was the epoch of belief, it was the epoch of incredulity, it was the season of Light, it was the season of Darkness, it was the spring of hope, it was the winter of despair..."

This quote from the opening of *A Tale of Two Cities*, written in 1859 by Charles Dickens, captures so much of how 2020 was for us. Notably, Dickens wrote his famous novel during another dreadful pandemic, a seven-year affair caused by cholera, which also featured a major scientific triumph: John Snow's scientific study led to the removal of the handle from the Broad Street water pump in Soho, London in 1854, resulting in a drastic reduction in new cases. This public health achievement gave rise to the field of epidemiology.

In 2020, MCHDI scientists really rose to the occasion, both contributing to efforts related to SARS-CoV-2 and managing to continue their ongoing work under trying circumstances. Most notably among the former, Dusan Bogunovic's group, assisted by several other MCHDI members, performed extensive immunoprofiling of a cohort of Mount Sinai's pediatric patients who presented with the SARS-CoV-2-related

multisystemic inflammatory syndrome in children (MIS-C), a novel disorder first observed this past spring; the resulting peer-reviewed paper appeared in *Cell* in November. Karen Wilson, Rebecca Trachtman and others are now involved in an NIH-funded consortium study to track the longer-term consequences of MIS-C. As of this writing, with the numbers of COVID-19 cases continuing to rise, we anticipate needing to care for more children with MIS-C, which will also provide opportunities to learn more about this serious illness.

The MCHDI's strategic initiatives continued to advance despite the loss of a few months during the research shutdown in the spring. Most notably, the development of the Pediatric Clinical Trials Office (PCTO) was able to resume in the fall. We were delighted to recruit Yair Bitton as our Project Manager. Working closely with Eyal Shemesh and Karen Wilson, the faculty leaders of PCTO, he is now directly managing clinical studies in the PCTO and negotiating with pharmaceutical companies for possible additional ones. Specifically, we, in collaboration with the Department of Cell, Developmental and Regenerative Biology, initiated the Functional Genomics and Disease Model Core, which is being led by Tirtha Das, PhD. This core will generate Drosophila models of Mendelian disorders. Finally, we were delighted to be joined by Ernest Turro, PhD, who intrepidly moved to New York City from Europe this fall. Dr. Turro, who was installed on the Arthur J. and Nellie Z. Cohen Chair at the 2020 Convocation, is a statistical geneticist focusing on child-health relevant traits. We also managed to continue our existing portfolio of MCHDI-sponsored programs, among other things holding our first-ever virtual retreat in late November and awarding our next set of faculty pilot awards.

Finally, 2020 will be remembered for the important renewed focus on diversity, equity and inclusion, starting with the horrifying murder of George Floyd over the summer. This led to important conversations and soul searching at Mount Sinai. During the MCHDI retreat, we gathered helpful information from members at a breakout session, led by Ann-Gel Palermo DrPH, MPH, Associate Dean for Diversity and Inclusion. Using those insights and other input, we look forward to developing new initiatives in the DEI space for 2021 and beyond. Clearly, meaningful change will require a sustained, focused effort, to which the MCHDI is committed.

# FACULTY GROWTH

# MCHDI ANNUAL FACULTY GROWTH 2020



Chart of faculty recruits since our inception in 2009. In 2020, our institute recruited two new external and three internal faculty members.

# MCHDI FACULTY MEMBERS

MCHDI faculty members from left to right: Nicole C. Dubois, PhD; Adolfo García-Ocaña, PhD; Donald K. Scott, PhD; M. Cecilia Berin, PhD; Minji Byun, PhD; David Dunkin, MD; Dalila Pinto, PhD; Andrew J. Sharp, PhD; Dani Dumitriu, MD (no longer at Sinai), PhD; Bruce D. Gelb, MD; Amy R. Kontorovich, MD, PhD; Martin J. Walsh, PhD; Jia Chen, ScD; Rupangi C. Vasavada, PhD (no longer at Sinai)



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# NEW FACULTY

# NEW EXTRAMURAL FACULTY



#### Fernando Ferrer, MD, FACS, FAAP

Fernando Ferrer, MD, FACS, FAAP is a Professor of Pediatric Urology at the Icahn School of Medicine. Dr. Ferrer was most recently Professor of Surgery and Cell Biology at the University of Nebraska, and Surgeon-in-Chief at Omaha Children's Hospital. Previously, he served as Professor of Surgery, Pediatrics and Cell Biology at the University of Connecticut's School of Medicine where he was also Vice-Chairman of the Department of Surgery. In addition, he was the Peter J. Deckers MD, Chair of Surgery and Surgeon-in-Chief of Connecticut Children's Medical Center where he directed the Division of Pediatric Urology.

A native of the northeast, Dr. Ferrer attended Seton Hall University and Georgetown University School of Medicine. He completed his Urologic Surgical training at the University of Connecticut's School of Medicine and his pediatric urology and research fellowship at the Brady Urologic Institute at Johns Hopkins. Dr. Ferrer has published 100 articles and over 25 book chapters. He has given over 35 lectures and visiting professorships. Dr. Ferrer has also been an active investigator funded by the NIH. His research has focused on renal injury and cellular mechanisms of children's cancer. During his career, Dr. Ferrer has served on several national committees, including the Children's Oncology Group and The Pediatric Urologic Oncology Working Group, where he is a Past President. He has been a permanent study section member for the National Cancer Institute, and has reviewed for the National Kidney Foundation, the National Academies and the American Urologic Association. He also serves as a peer reviewer for multiple scientific journals. Dr. Ferrer served as a Diving Medical Officer in the U.S. Navy and participated in operation Desert Storm.



#### **Ernest Turro, PhD**

Ernest Turro, PhD is an Associate Professor in the Department of Genetics and Genomic Sciences and the Arthur J. and Nellie Z. Cohen Chair. He is a biostatistician with 14 years of research experience in genomics and molecular diagnostics.

He has developed Bayesian statistical association methods for identifying the genetic determinants of rare diseases and he has applied them to a wide range of disorders, with an emphasis on hematological disorders and immune deficiencies. His work has implicated several genes in rare diseases for the first time and it has broadened understanding of the etiological roles of several others. Concurrently, Dr. Turro has worked on a diagnostic high-throughput sequencing platform that has been used to test thousands of patients with bleeding and platelet disorders, including patients with hereditary hemorrhagic telangiectasia.

Dr. Turro has also researched the interplay between genetic variation in the mitochondrial and nuclear genomes. This research found evidence that the mitochondrial genome may adapt to the cell nucleus. He has also helped repudiate a recent study questioning the dogma that mitochondrial DNA in humans is exclusively transmitted along the maternal lineage.

Previously, Dr. Turro developed a number of influential statistical methods for modeling gene expression data. He developed the first statistical method for modeling isoform specific expression using microarray data. Later, he developed the first statistical methods for modeling haplotype and isoform specific expression using RNA sequencing data.

Dr. Turro has authored 60 peer-reviewed articles (10 as first author, 11 as last author), including work as a senior author in *Science, Nature, Blood and the American Journal of Human Genetics*, among others.

# **INTRAMURAL FACULTY**



### Tirtha Kamal Das, PhD

Tirtha Kamal Das, PhD is an Assistant Professor in the Department of Cell, Developmental & Regenerative Biology. He obtained his PhD degree at Wesleyan University studying the developmental genetics of fly embryogenesis and later completed his postdoctoral work modeling cancer and therapeutics in flies. He has continued his interest in understanding human disease and his lab uses an 'Integrated Fly-Vertebrate Modeling' approach to study genetic diseases and identify novel therapeutics. They use whole animal fly models, human cell lines, mouse xenografts, and patient data analysis to identify mechanisms of cancer and Mendelian disease progression.

These studies have identified key cellular and molecular mechanisms driving cancer progression, and have shown that: i) oncogenic kinase-gene fusions drive complex signaling through multi-protein hubs, ii) epigenetic components promote programs of cancer cell invasion, and iii) centrosomal components promote metastasis.

The lab combines genetics and drug screening to rationally improve lead compounds and clinical therapeutics. They showed that optimal therapeutic index of cancer drugs is achieved through balanced inhibition of multiple targets – balanced polypharmacology. They further developed drug cocktails to improve therapeutic index of standard of care drugs, by pairing them with low-dose, broad-acting drugs – 'network brakes' – that prevented compensatory activation of cellular networks, which lowered toxicity, and delayed emergence of drug resistance.

This integrated approach has also been applied to study dominant Mendelian-inherited human Rasopathies and identified signaling differences between thirteen variants, and uncovered unique opportunities for therapy. Drugs inhibiting epigenetic components and treatments used for cardiovascular diseases have shown surprising efficacy in these Rasopathy models.



### Yuval Itan, PhD

Yuval Itan, PhD is an Assistant Professor in the Department of Genetics and Genomic Sciences, and a core member of The Charles Bronfman Institute for Personalized Medicine, at the Icahn School of Medicine at Mount Sinai in New York City. He has obtained a BSc in computational biology from Bar-Ilan University, and a PhD in human evolutionary genetics from University College London, followed by postdoctoral research in human disease genomics at the Rockefeller University.

Yuval has been extensively investigating the genetics that underlie human diseases, and has been developing computational methods to predict the functional consequence of human genetic variants in next generation sequencing data of patients. Some examples include: (1) the human gene connectome (HGC) to prioritize disease-causing gene candidates by biological distance in protein-protein interatomic networks; (2) the gene damage index (GDI) to estimate the mutational damage of human genes in the general population; and (3) the mutation significance cutoff (MSC) to provide gene-based deleteri-

ousness scores for accurate predictions. His current work includes: (1) developing a machine learning classifier to differentiate gain-of-function from loss-of-function mutations; (2) developing a deep learning classifier to detect pathogenic mutations based on disease groups; and (3) combining state-of-the-art with cutting edge methods in case-control gene burden association studies to detect novel disease-causing mutations and genes in various patient cohorts such as inflammatory bowel disease, congenital heart disease, COVID-19 and more.

# INTRAMURAL FACULTY-CONTINUED



#### Andrew F. Stewart, MD

Andrew F. Stewart, MD is the Director, Diabetes Obesity and Metabolism Institute and Irene and Dr. Arthur M. Fishberg Professor of Medicine. Dr. Stewart received his BS from Trinity College, and his M.D. from Columbia University. He was a postdoc at Yale, where he rose to tenured Professor. He served as Chief of Endocrinology at the University of Pittsburgh before moving to Mount Sinai in 2012.

His group was the first to induce robust replication of human insulin-producing beta cells. In 2015, they discovered the first drugs able to induce human beta cell replication, findings that have been reproduced around the world in pharma and academia. In 2017 and 2020, they defined the genomic pathways underlying beta cell expansion and insulin over-secretion in human insulinomas: a "wiring diagram" for human beta cell regenerative drug discovery. In 2019 and 2020, they reported that combination treatment with harmine and TGF-beta inhibitors or GLP1 receptor agonists dramatically increases human beta cell proliferation. The work has clear translational implications for Type 1 as well as Type 2 diabetes, both of which result from an absolute or relative deficiency of insulin-producing beta cells.

He has published more than 250 papers in the *NEJM*, *Science, Science Translational Medicine, Cell Metabolism, Nature Medicine, Nature Communications, JCI, PNAS*, and others. He has had continuous NIH grant support for the past 40 years. He served as Councilor and Secretary-Treasurer of the Endocrine Society, and was the 2008 recipient of the Endocrine Society's Gerald Aurbach Award for outstanding scientific achievement. He served as the Chair of the Endocrine Society Meeting in 1998 and American Diabetes Association Annual Meetings for 2010 and 2011.

# ANNUAL RETREAT



Our 8th Annual MCHDI Retreat marked our institute's first ever virtual retreat. As we continue to adapt to our new virtual reality, we were happy to be able to host a webinar to feature faculty and trainee talks on their innovative research. There were close to 100 faculty members, trainees, and guests in attendance this year. The retreat planning committee was comprised of our MCHDI Director, Bruce D. Gelb, MD, Committee Chair, Hala Harony-Nicolas, PhD, MCHDI faculty members, David Dunkin, MD, and Magdalena Janecka, PhD as well as our trainee leadership committee member, Xueying Zhang, PhD. Our keynote speaker, Brian Nosek, PhD (Professor of Psychology, University of Virginia and Co-founder and Executive Director of the Center for Open Science) presented on the topic of "Shifting Incentives From Getting It Published to Getting It Right." We awarded the winner of the Young

Investigators Competition: Louise Malle, MD, PhD candidate (PI: Dusan Bogunovic,

PhD). We also introduced breakout discussion groups moderated by experts with topics including Work/life/family balance, Inclusion and diversity in science, Mentee's mental health and well-being, Gene editing and Bioethics, Single Cell Sequencing, and Translational insights from genetics and genomics for precision medicine in children.

# FACULTY RESEARCH AREAS

PerkinElmer

# ASTHMA AND ALLERGY



M. Cecilia Berin, PhD (Professor, Pediatrics) Research Areas: Immune mechanisms of food allergy and regulation of immune tolerance



Supinda Bunyavanich, MD, MPH (Professor, Pediatrics, and Genetics and Genomic Sciences) Research Areas: Integrative genomics of asthma and allergic diseases



Maria Curotto de Lafaille, PhD (Associate Professor, Pediatrics) Research Areas: Immunology of allergic diseases, B lymphocyte responses



Ke Hao, ScD (Associate Professor, Genetics and Genomic Sciences) Research Areas: Genetic pleiotropy, mendelian randomization, inflammatory bowel disease, placenta biology, ambient air particulate matter exposure



Hugh A. Sampson, MD (Kurt Hirschhorn Professor, Pediatrics) Research Areas: Immunopathogenesis of food allergy and anaphylaxis



Scott H. Sicherer, MD (Director, Jaffe Food Allergy Institute; Division Chief, Pediatric Allergy; Elliot Roslyn Jaffe Professor, Pediatrics) Research Areas: Food allergy epidemiology, treatments, natural course, quality of life



Julie Wang, MD (Professor, Pediatrics) Research Areas: Novel therapeutics for food allergy, epidemiology and management of food allergy and anaphylaxis



#### Karen M. Wilson, MD, MPH (Debra and Leon Black Division Chief, General Pediatrics; Vice-Chair for Clinical and Translational Research, Pediatrics; Professor, Pediatrics) Research Areas: Second hand tobacco smoke, second hand marijuana smoke, inpatient respiratory illness

# CARDIOVASCULAR DISEASE



#### Harold S. Bernstein, MD, PhD

*(Adjunct Professor, Pediatrics)* **Research Areas:** Drug development (target validation through clinical proof of concept), heart failure, metabolic syndrome, diabetes, thrombosis, chronic kidney disease



Nicole C. Dubois, PhD (Associate Professor, Cell, Developmental & Regenerative Biology) Research Areas: Heart development, stem cell differentiation, disease modeling



Bruce D. Gelb, MD

(Gogel Family Professor and Director, Mindich Child Health and Development Institute; Professor, Pediatrics, and Genetics and Genomic Sciences) **Research Areas:** Genetics of cardiovascular diseases, stem cell research



#### Alan Groves, MBChB, MD

(Adjunct Professor, Diagnostic, Molecular and Interventional Radiology) **Research Areas:** Hemodynamics, cardiac function, echocardiography, magnetic resonance imaging



#### Yuval Itan, PhD

(Assistant Professor, Genetics and Genomic Sciences) Research Areas: Human disease genomics, computational biology, and bioinformatics



#### Anne Moon, MD, PhD

(Adjunct Professor, Pediatrics) **Research Areas:** Developmental biology of congenital heart disease and limb defects, functions of Tbx and fibroblast growth factors



Amy R. Kontorovich, MD, PhD (Medical Director, Adult Cardiovascular Genetics; Assistant Professor, Medicine) Research Areas: Myocarditis, genetics of cardiovascular diseases, stem cell research



#### Alison P. Sanders, PhD

(Assistant Professor, Pediatrics, and Environmental Medicine & Public Health) **Research Areas:** Environment, toxic metals, kidney development, hypertension, cardiovascular disease, biomarkers

# NEURODEVELOPMENTAL DISORDERS



#### Michael S. Breen, PhD

(Assistant Professor, Psychiatry and Genetics and Genomic Sciences) **Research Areas:** Functional genomics of neurodevelopmental and neuropsychiatric disorders, transcriptomics, single-cell RNA-sequencing, stem cells, RNA editing and biology



#### Joseph D. Buxbaum, PhD

(Deputy Chair, Department of Psychiatry; Director, Seaver Autism Center for Research and Treatment; Professor, Psychiatry, Neuroscience, and Genetic and Genomic Sciences) **Research Areas:** Autism spectrum disorder, neurodevelopmental disorders, gene discovery, functional genetics, molecular and cellular neuroscience, cell and animal model systems



#### Jia Chen, ScD

(Professor, Pediatrics, Environmental Medicine & Public Health, Medicine, and Oncological Sciences) **Research Areas:** Environmental epigenetics, molecular epidemiology



#### Tirtha K. Das, PhD

(Assistant Professor, Cell, Developmental & Regenerative Biology) **Research Areas:** Integrating fly plus vertebrate disease models, cancer, rare mendelian diseases, therapeutics development



Silvia De Rubeis, PhD (Assistant Professor, Psychiatry) Research Areas: Intellectual disability, autism spectrum disorder, functional genetics, cell and animal model systems, brain development



Lisa Eiland, MD (Associate Professor, Pediatrics) Research Areas: Stress and neurodevelopment



Hala Harony-Nicolas, PhD (Assistant Professor, Psychiatry and Neuroscience) Research Areas: Brain circuits of social behavior, mechanisms of action of the oxytocin hypothalamic system, animal models for autism spectrum disorder



#### Megan K. Horton, PhD, MPH

(Associate Professor, Environmental Medicine & Public Health) Research Areas: Children's environmental health, exposure assessment, pediatric neuroimaging

# NEURODEVELOPMENTAL DISORDERS - CONTINUED



#### Laura Huckins, PhD

(Assistant Professor, Genetics and Genomic Sciences) **Research Areas:** Psychiatric Genetics, specializing in understudied disorders and disorders affecting vulnerable populations. Particular focus on anorexia nervosa, PTSD, sexual assault, OCD. Secondary focus on machine learning algorithms; transcriptomic imputation; multi-omit eQTLbased methodologies.



#### Magdalena U. Janecka, PhD

(Assistant Professor, Department of Psychiatry, Seaver Autism Center) **Research Areas:** Neurodevelopmental disorders; epidemiology; epigenetics; environmental risk factors



#### Alex Kolevzon, MD

(Director, Child and Adolescent Psychiatry; Professor, Psychiatry, and Pediatrics) **Research Areas:** Autism spectrum and other neurodevelopmental disorders



#### Robert S. Krauss, PhD

(Professor, Cell, Developmental & Regenerative Biology, and Oncological Sciences) **Research Areas:** Hedgehog signaling and birth defects, muscle stem cells and regeneration



Paige M. Siper, PhD (Assistant Professor, Psychiatry) Research Areas: Autism, intellectual disability, biomarker discovery, sensory processing



Luca Lambertini, PhD

(Assistant Professor, Obstetrics, Gynecology and Reproductive Science) **Research Areas:** Placental biomarkers of altered fetal and child development



Florence Marlow, PhD (Associate Professor, Cell, Developmental & Regenerative Biology) Research Areas: Genetics of early patterning and germline, neurodevelopment



Marek Mlodzik, PhD (Professor and Chair, Cell, Developmental & Regenerative Biology; Professor, Ophthalmology and Oncological Sciences) Research Areas: Genetics and cell biology of planar cell polarity establishment, cell biology of Wnt-signaling and Notch-signaling

# NEURODEVELOPMENTAL DISORDWERS - CONTINUED



#### Hirofumi Morishita, MD, PhD

(Associate Professor, Psychiatry, Ophthalmology, and Neuroscience) **Research Areas:** Mechanisms of perceptual and cognitive development, drug repurposing for neurodevelopmental disorders



#### Coro Paísan-Ruiz, PhD

(Associate Professor, Neurology, Psychiatry, and Genetics and Genomic Sciences) **Research Areas:** Genetics of neurological and neurodevelopmental diseases, disease modeling in zebrafish



#### Dalila Pinto, PhD

(Assistant Professor, Psychiatry, and Genetics and Genomic Sciences) **Research Areas:** Genetics and genomics of neurodevelopmental disorders (particular focus on autism, epilepsy, schizophrenia, OCD), structural variation, transcriptomics, gene regulation, noncoding RNA



#### Andrew J. Sharp, PhD

(Associate Professor, Genetics and Genomic Sciences) **Research Areas:** Epigenomics, transcriptomics, genome function, structural variation, imprinting, congenital disorders



#### Annemarie Stroustrup, MD, MPH

(Adjunct Professor, Pediatrics and Environmental Medicine & Public Health) **Research Areas:** Neurodevelopment, perinatal environmental exposures, identifying genetic etiologies of congenital disease



#### Shanna H. Swan, PhD

(Professor, Environmental Medicine & Public Health) **Research Areas:** Prenatal exposures, sexually dimorphic development, phthalates, stress, anogenital distance, neurodevelopment, analgesics, glyphosate



Pilar Trelles, MD (Assistant Professor, Psychiatry) Research Areas: Autism spectrum disorder, neurodevelopmental disorders, health disparities

# NEURODEVELOPMENTAL DISORDERS - CONTINUED



#### Bryn D. Webb, MD

(Assistant Professor, Genetics and Genomic Sciences and Pediatrics) **Research Areas:** Identifying genetic etiologies of congenital anomalies, mitochondrial disorders, undiagnosed disease



#### Anusha Yeshokumar, MD (Assistant Professor, Neurology and Pediatrics) Research Areas: Autoimmune encephalitis, outcomes research, inflammatory biomarkers, cognition, behavior

### **OBESITY AND DIABETES**



#### Ross L. Cagan, PhD

(Adjunct Professor, Cell, Developmental & Regenerative Biology) **Research Areas:** Drosophila as a tool to develop therapeutics for cancer, diabetes, and rare mendelian diseases



#### Fernando Ferrer, MD, FACS, FAAP

(Professor, Urology) Research Areas: Cancer, bioactive lipids, renal injury, biomarkers, renal obstruction



Adolfo García-Ocaña, PhD

(Professor, Medicine) Research Areas: Diabetes, pancreatic beta cell biology



#### Allan C. Just, PhD (Assistant Professor, Environmental Medicine & Public Health) Research Areas: Epigenomics, environmental exposures, endocrine disruptors, air pollution, obesity, birth outcomes



#### Ruth J.F. Loos, PhD (Professor, Environmental Medicine & Public Health; Charles Bronfman Professor in Personalized Medicine) Research Areas: Genetics of obesity and related cardiometabolic traits, genetic epidemiology, epidemiology

# **OBESITY AND DIABETES - CONTINUED**



Donald K. Scott, PhD (Professor, Medicine) Research Areas: Obesity and diabetes



Andrew F. Stewart, PhD (Director, Diabetes Obesity and Metabolism Institute, Irene and Dr. Arthur M. Fishberg Professor, Medicine) Research Areas: Type 1 diabetes, Type 2 diabetes, beta cell regeneration, and drug discovery



Susan Teitelbaum, PhD (Professor, Environmental Medicine & Public Health) Research Areas: Environmental chemical exposure assessment, pubertal development, physical growth and development



Ryan W. Walker, PhD (Assistant Professor, Environmental Medicine & Public Health) Research Areas: Clinical microbiome, obesity, nutrition, environmental exposures



#### Martin J. Walsh, PhD

(Professor, Pharmacological Sciences, Genetics and Genomic Sciences, and Pediatrics) **Research Areas:** Chromatin biology, RNA biology and gene transcription in cancer, early development and metabolism

#### **PSYCHIATRIC DISORDERS**



#### Dorothy E. Grice, MD

(Professor, Psychiatry) **Research Areas:** Genetic and epidemiological studies of OCD, Tourette disorder, autism, and related childhood-onset neuropsychiatric disorders, prenatal exposures, including smoking, functional analysis of identified risk genes



#### Avi Reichenberg, PhD

(Professor, Psychiatry, and Environmental Medicine & Public Health) **Research Areas:** Autism, schizophrenia, other psychiatric disorders

# OTHER RESEARCH FOCUSES



James J. Bieker, PhD

(Professor, Cell, Developmental & Regenerative Biology) **Research Areas:** Transcriptional regulation of gene expression in erythroid cells



#### **Dusan Bogunovic, PhD**

(Associate Professor, Microbiology, and Pediatrics) **Research Areas:** Genetics of infectious and inflammatory diseases, Type I Interferons, Pseudo - TORCH syndrome, neurolisteriosis



#### Brian D. Brown, PhD

(Professor, Genetics and Genomic Sciences) **Research Areas:** Immunology and immunotherapy, autoimmune disease, microRNA regulation, and biotechnology



John Bucuvalas, MD (Professor, Pediatrics) Research Areas: Outcomes after liver transplantation, allograft injury in pediatric liver transplant recipients



Minji Byun, PhD (Assistant Professor, Medicine) Research Areas: Genetics of immune disorders, clonal hematopoiesis, immune dysregulation



Jaime Chu, MD (Assistant Professor, Pediatrics) Research Areas: Disorders of glycosylation, cancer metabolism, liver fibrosis



Charlotte Cunningham-Rundles, MD, PhD (David S. Gottesman Professor, Medicine; Professor, Pediatrics) Research Areas: Primary Immune Deficiency, B cells, antibody, B cell memory, hypogammaglobulinemia, immune reconstitution

# OTHER RESEARCH FOCUSES - CONTINUED



David Dunkin, MD (Associate Professor, Pediatrics) Research Areas: Tolerance induction and therapeutics in inflammatory bowel disease, mechanisms of inflammatory diseases of the gastrointestinal tract



Chris Gennings, PhD (Professor, Environmental Medicine & Public Health, and Population Health Science and Policy) Research Areas: Biostatistical methods development for environmental health



Katherine Guttmann, MD, MBE (Assistant Professor, Pediatrics) Research Areas: Palliative care, family-centered care, parent-physician communication, research ethics



Shelley H. Liu, PhD (Assistant Professor, Population Health Science and Policy) Research Areas: Biostatistics, environmental mixtures, public health



Michael Rendl, MD (Professor, Cell, Developmental & Regenerative Biology, and Dermatology) Research Areas: Stem cells, hair regeneration, morphogenesis



Jeffrey M. Saland, MD (Associate Professor, Pediatrics) Research Areas: Kidney disease in children, lipoprotein metabolism in children with CKD, hemolytic uremic syndrome



Lisa M. Satlin, MD (Herbert H. Lehman Professor and System Chair, Pediatrics) Research Areas: Ontogeny and mechanoregulation of epithelial ion channels in secretory epithelia, generation and characterization of functional bioengineered kidneys

# OTHER RESEARCH FOCUSES - CONTINUED



#### Eyal Shemesh, MD

(Professor, Pediatrics, and Psychiatry) **Research Areas:** Remote intervention paradigms, biological correlates of non-adherent behaviors, multi-site and multi-disciplinary clinical trials



#### Rebecca Trachtman, MD (Assistant Professor, Pediatrics) Research Areas: Biomarkers, patient-reported outcomes in juvenile idiopathic arthritis



#### Ernest Turro, PhD

(Associate Professor, Genetics and Genomic Sciences) **Research Areas:** Biostatistics, statistical genetics, functional genomics, Bayesian modeling, rare diseases, inherited blood disorders, primary immunodeficiencies, mitochondrial genetics

# FACULTY RESEARCH INTERACTIONS



# Faculty Highlight: Magdalena Janecka, PhD



Joseph Buxbaum, PhD



**Dorothy Grice, MD** 



**Ernest Turro, PhD** 



**Michael Breen, PhD** 



Avi Reichenberg, PhD

#### Joseph Buxbaum, PhD

- Mentor
- Collaborator on autism epidemiology work
- Collaborator on autism epigenetics project Co-investigator on my R01 "Maternal health in pregnancy and autism risk - genetic and non-genetic mechanisms"

#### Michael Breen, PhD

Collaborator on autism epigenetics project

#### Silvia De Rubeis, PhD

Collaborator on autism epigenetics project

#### Lisa Eiland, MD

Co-PI on Mindich Pilot Award "Gene expres-• sion in endocervix during pregnancy - novel biomarkers of neonatal outcomes"



Silvia De Rubeis, PhD



Andrew J. Sharp, PhD



Lisa Eiland, MD



Shanna Swan, PhD

#### Dorothy Grice, MD

- Collaborator on autism epidemiology work
- Collaborator on autism epigenetics project

#### Avi Reichenberg, PhD

- Mentor
- Collaborator on autism epidemiology work
- Collaborator on autism epigenetics project •
- Co-investigator on my R01 "Maternal health • in pregnancy and autism risk - genetic and non-genetic mechanisms"

#### Andrew Sharp, PhD

Collaborator on autism epigenetics project

#### Shanna Swan, PhD

• Mentor

•

#### Ernest Turro, PhD

Co-PI on Mindich Pilot Award "Gene expression in endocervix during pregnancy - novel biomarkers of neonatal outcomes"





# *Faculty Highlight:* Ruth J.F. Loos, PhD



Bruce D. Gelb, MD



Ke Hao, ScD



Laura Huckins, PhD



Yuval Itan, PhD



Andrew J. Sharp, PhD

Ryan W. Walker, PhD

#### Bruce D. Gelb, MD

• Ruth contributes to the Pediatric Cardiac Genomics Consortium (PCGC)

#### Ke Hao, ScD

• Ruth is a co-investigator on a grant of Ke's currently under review

#### Laura Huckins, PhD

Collaborating on grant of the Klarman Family
Foundation on eating disorders

#### Yuval Itan, PhD

 Collaborating on several papers including paper in Nature Metabolism (in press) entitled "Genome-wide discovery of genetic loci that uncouple excess adiposity from its comorbidities"

#### Andrew J. Sharp, PhD

 Co-Pls on previous MCHDI pilot grant titled "Association studies of multicopy genes in the Mount Sinai BioMe exome sequencing cohort"

#### Ryan W. Walker, PhD

- Ryan is a former postdoctoral fellow in Ruth's lab
- Collaborating on an R01 by NIDDK entitled "Resilience to obesity in carriers of monogenic obesity mutations - a study on the underlying mechanisms"

# AWARDS/HONORS AND PUBLICATIONS

# FACULTY HONORS/AWARDS

**M. Cecilia Berin, PhD,** Icahn School of Medicine at Mount Sinai Convocation 2020, Endowed Chair - Hugh A. Sampson Professor of Food Allergy Research

Supinda Bunyavanich, MD, MPH, Inducted to the American Society for Clinical Investigation (ASCI)

**Robert S. Krauss, PhD,** Icahn School of Medicine at Mount Sinai Convocation 2020, Endowed Chair - Mount Sinai Professor in Cell Biology

Hala Harony-Nicolas, PhD, Federation of European Neuroscience Societies, FENS, July 2020, Chair of Symposium: "Oxytocin and social behavior from animal models to clinical applications: progress and challenges"

Hirofumi Morishita MD, PhD, American College of Neuropsychopharmacology (ACNP), Full Membership

**Dalila Pinto, PhD,** World Conference on Psychiatric Genetics, October 20, 2020, Co-Chair and Speaker of Symposium "PsychENCODE Updates: Discovery of Functional Elements for Psychiatric GWAS Signals"

**Dalila Pinto, PhD,** 23rd Biennial Meeting of the International Society for Developmental Neuroscience, Chair and Speaker of Symposium "Autism Spectrum Disorders"

**Ernest Turro, PhD,** Icahn School of Medicine at Mount Sinai Convocation 2020, Endowed Chair - The Arthur J. and Nellie Z. Cohen Professor of Pediatrics (Genetics)

### TRAINEE HONORS/AWARDS

Xueying Zhang, PhD, National Public Radio, Invited Speaker, "New Study Points To Invisible Killer Of Infants"

# FACULTY PUBLICATIONS

Scurlock AM, Burks AW, **Sicherer SH**, Leung DYM, Kim EH, Henning AK, ... **Berin MC**, ... Consortium for Food Allergy Research (CoFAR). **Epicutaneous immunotherapy for treatment of peanut allergy: Follow-up from the Consortium for Food Allergy Research**. *J Allergy Clin Immunol*. 2020 Dec 5:S0091-6749(20)31701-2.

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# GRANTS

	Funding from	Funding from New &
Agency Name	New Grants (\$)	Existing Grants (\$)
National Institute Of Allergy And Infectious Diseases/NIH/DHHS	\$2,337,766	\$8,977,825
National Institute Of Diabetes And Digestive And Kidney Diseases/NIH/DHHS	\$2,015,714	\$8,721,674
National Institute Of Environmental Health Sciences/NIH/DHHS	\$723,980	\$723,980
National Institute Of Mental Health/NIH/DHHS	\$532,511	\$969,236
National Human Genome Research Institute/NIH/DHHS	\$525,000	\$525,000
National Heart, Lung, And Blood Institute/NIH/DHHS	\$506,627	\$2,395,314
Benaroya Research Institute At Virginia	\$499,013	\$5,062,957
National Institute Of Neurological Disorders And Stroke/NIH/DHHS	\$411,867	\$1,019,396
National Institute Of Arthritis & Musculoskeletal & Skin Diseases/NIH/DHHS	\$395,587	\$895,578
National Institute Of Child Health And Human Development/NIH/DHHS	\$340,000	\$340,000
Albert Einstein College Of Medicine	\$295,175	\$295,175
Johns Hopkins University Medical School	\$254,250	\$1,291,564
Columbia University	\$223,499	\$223,499
National Institute Of General Medical Sciences/NIH/DHHS	\$211,464	\$211,464
National Institute For Occupational Safety & Health/CDC/DHHS	\$166,628	\$166,628
National Eye Institute/NIH/DHHS	\$163,321	\$163,321
National Cancer Institute/NIH/DHHS	\$115,000	\$230,000
Helmsley Foundation	\$100,000	\$100,000
EmoryUniversity	\$99,999	\$99,999
Rutgers	\$90,980	\$90,980
Duke (Doris) Charitable Foundation	\$75,000	\$75,000
University of Copenhagen	\$51,358	\$51,358
Johns Hopkins University	\$43,642	\$121,182
Astellas Pharma US, Inc.	\$40,000	\$40,000
American Academy Of Pediatrics	\$35,000	\$70,000
SimonsFoundation	\$27,544	\$27,544
University Of Michigan	\$16,556	\$16,556
Seaver Foundation	\$12,000	\$12,000
Boston Children's Hospital		\$4,960,904
University Of Pittsburgh		\$3,105,550
New York University, Washington Square		\$2,493,553
Vanderbilt University Medical Center		\$2,202,852
Hirsch/Weil-Caulier Trust		\$1,282,483
University Of North Carolina		\$876,854
Hainwater Charitable Foundation		\$811,085
Stanford University		\$/18,788
University Of Washington		\$421,587
Brain and Behavior Research Foundation		\$394,035
European Commission		\$368,934
Sidra Medical and Research Center		\$342,085
Icahn School of Medicine at Mount Sinai		\$330,000
Albireo AB		\$225,000
National Center for Complementary and Integrative Health/NIH/DHHS		\$200,000
Chan Zuckerberg Initiative		\$197,007
Takeda Pharmaceuticals Of North America, Inc.		\$154,464
Fred Hutchinson Cancer Research Center		\$150,000
AllerGenis		\$116,531
Columbia University		\$114,016
I he Mark Houndation For Cancer Research		\$83,635
President and Fellows of Harvard College		\$83,583
Food Allergy Hesearch & Education		\$70,000
Alkermes, Inc.		\$67,799
American Parkinson Disease Association		\$66,666
Castleman Disease Collaborative Network		\$61,727
US-Israel Binational Science Foundation		\$39,999
Massachusetts General Hospital		\$31,744
Harry Frank Guggenneim Foundation		\$9,600
	\$10,309,481	\$52,897,711

# MATERIAL TRANSFER AGREEMENTS/LICENSES

Research Focus	Outgoing Material Transfer Agreements (#)	Technology Licenses (#)
Neurodevelopmental disorders	7	7
Cardiovascular disease	0	5
Diabetes and Obesity	10	4
Allergy and Asthma	1	6
Others	2	1
Total	20	23

Licenses	Total Number
Antigens/Antibodies	7
Reagents/Methods/Cell Lines	8
Genes/Adapters/Vectors/Oligonucleotides	6
Gene Testing/Therapeutics	2
Total	23

# PILOT PROJECTS FUNDED FOR 2020-2021

new

## TRAINEE PILOT AWARDS

Two new trainee awardees were selected for the trainee pilot program in the amount of \$10K over a one year period. The purpose of the program is to support postdoctoral/clinical fellows or PhD/MD-PhD students in pursuing an independently funded research project that is separate from their ongoing projects under their current Principal Investigator/mentor. Successful applications were required to a) demonstrate that they can achieve independence and will generate preliminary data that could lead to career development or other grants and b) be relevant to children's health.



Sharon Baumel-Alterzon, PhD Postdoctoral Fellow, Diabetes, Obesity and Metabolism Institute

**Investigator:** Sharon Baumel-Alterzon, Postdoctoral fellow, Diabetes, Obesity and Metabolism Institute

**Project Title:** The Role of Nrf2 in Expanding Neonatal Pancreatic  $\beta$ -Cell Mass

**Primary Mentor:** Donald K. Scott, PhD, Professor of Medicine, Diabetes, Obesity and Metabolism Institute, Mindich Child Health and Development Institute

Secondary Mentor: Adolfo García-Ocaña, PhD, Professor of Medicine, Diabetes, Obesity and Metabolism Institute, Mindich Child Health and Development Institute



Daniel Lozano-Ojalvo, PhD Postdoctoral Fellow, Precision Immunology Institute

Investigator: Daniel Lozano-Ojalvo, PhD, Postdoctoral fellow, Precision Immunology Institute

**Project Title:** The Distinct Role of Allergen-Specific T Follicular Helper Cells in IgE-Mediated and Non-IgE-Mediated Cow's Milk Allergy

Primary Mentor: M. Cecilia Berin, PhD, Professor, Department of Pediatrics

Secondary Mentors: Maria Lafaille, PhD, Associate Professor, Department of Pediatrics and David Dunkin, MD, Assistant Professor, Department of Pediatrics

# FACULTY PILOT AWARDS

Three pilot projects were selected for \$70K in institutional funding for a one year period starting February 1, 2021. The purpose of the pilot program is to provide MCHDI faculty with funding for initial stages of research projects, with the goal of generating sufficient data to apply for larger, external grants. Projects are encouraged that are likely to: a) improve children's health, b) promote collaboration within the MCHDI, and c) leverage additional extramural funding for the Principal Investigators (PIs).

#### **Project Title:**

Brain activity landscape with cellular mapping: Probing circuitry mechanism in a mouse model of intellectual disability

Principal Investigators: Silvia De Rubeis, PhD (communicating PI) and Zhuhao Wu, PhD (co-PI)



Silvia De Rubeis, PhD (communicating PI)

Assistant Professor, Department of Psychiatry Seaver Autism Center for Research and Treatment Mindich Institute for Child Health and Development Friedman Brain Institute



Zhuhao Wu, PhD (co-Pl)

Assistant Professor, Department of Cell, Developmental & Regenerative Biology & Department of Neuroscience Friedman Brain Institute

#### **Project Title:**

Gene expression in endocervix during pregnancy - novel biomarkers of neonatal outcomes

Principal Investigators: Magdalena Janecka, PhD (communicating PI), Lisa Eiland, MD, FAAP (co-PI) and Ernest Turro, PhD (co-PI)



#### Magdalena Janecka, PhD (communicating PI)

Assistant Professor, Department of Psychiatry Mindich Child Health and Development Institute Seaver Autism Center for Research and Treatment



#### Lisa Eiland, MD, FAAP (co-Pl)

Associate Clinical Professor, Department of Pediatrics Mindich Child Health and Development Institute Division of Newborn Medicine



#### Ernest Turro, PhD (co-Pl)

Associate Professor, Department of Genetics and Genomic Sciences Mindich Child Health and Development Institute

# FACULTY PILOT AWARDS - CONTINUED

#### **Project Title:**

A Family-Mediated Intervention to Improve Outcomes in Minority Children with Autism Spectrum Disorder affected by the COVID-19 Pandemic

Principal Investigators: M. Pilar Trelles, MD (communicating PI) and Jennifer Foss-Feig, PhD (co-PI)



M. Pilar Trelles, MD (communicating PI) Assistant Professor,

Department of Psychiatry Seaver Autism Center for Research and Treatment Mindich Child Health and Development Institute



#### Jennifer Foss-Feig, PhD (co-PI)

Assistant Professor, Department of Psychiatry Seaver Autism Center for Research and Treatment

# COMMUNICATIONS

MCHDI delivers the latest updates on research advancements, events and news, both internally and externally, via various communications channels. Below is information about the MCHDI website, newsletter and social media platforms:

#### Website

Our website includes detailed information about our signature programs, shared resources, trainee education, and employment opportunities. You can also find our complete list of faculty and links to their research websites as well as the latest press releases featuring our faculty. Our annual reports and MCHDI newsletters are also accessible via our website. Please visit our website at www.mountsinai.org/mchdi

#### Newsletter

*The MCHDI Developmental Outcomes* is a bi-annual newsletter distributed internally to faculty, trainees, and other Institute affiliates to highlight important research breakthroughs, publications, awards, and events within MCHDI. View our latest newsletters featured on http://icahn.mssm.edu/research/mindich/about/newsletters

#### Facebook

Our official MCHDI Facebook page was launched in 2014 and currently has 500+ likes and followers. Our team posts almost daily to share updates on faculty research, seminars, and events, and other information relevant to children's health. Please like and follow our page at www.facebook.com/mindichchdi

#### **Twitter**

Our tweets are streaming on our website in real time. Follow or tweet to us @MindichCHDI or on our website at www.mountsinai.org/mchdi

# SHARED RESOURCES

# **GRANT FORWARD**

Grant Forward is a pre-award funding database with a comprehensive list of federal, foundation, and other funding sources. It offers a user-friendly search interface, automated e-mails alert, and tailored grant recommendations. Grant Forward subscriptions for MCHDI faculty and trainees are covered by our Institute.

To sign up please visit: https://www.grantforward.com

### **BIOME BIOBANK**

The BioMe Biobank contains the largest collection of DNA and plasma samples at Mount Sinai, enabling high-throughput disease genotyping and phenotyping while maintaining patient confidentiality through the Epic electronic medical record (EMR). The goal is to integrate patient clinical care information and research data. Observational epidemiologic studies of children have expanded in the past decade in response to the rising prevalence of childhood diseases including obesity, autism, and asthma and of environmental risk factors such as lead and pesticides, and the ability to genotype DNA has enabled further inquiry into the genetic basis of childhood diseases. MCHDI, in collaboration with the Charles R. Bronfman Institute for Personalized Medicine, is funding the collection of DNA samples from pediatric patients with allergies, and since February 2012 the Jaffe Food Allergy Institute has recruited >1000 enrollees. The pediatric cohort is comprised of samples from diverse racial and ethnic groups.

#### For more information please visit:

www.icahn.mssm.edu/research/institutes/institute-for-personalized-medicine/innovation-and-technology/bi-ome-platform

# BIOREPOSITORY CORE SHARED RESOURCE FACILITY

The biorepository CORE facility provides basic histology services such as processing and embedding section fixed and frozen tissues from animal or human sources. In addition, services include DNA/RNA/miRNA extractions, preparing and analyzing tissue microarrays, and supporting functions for tissue procurement, both from consented and anonymized collections.

For a full list of their services visit their website at:

http://icahn.mssm.edu/research/resources/shared-resource-facilities/histology

# STRATEGIC PLAN IMPLEMENTATION

# PEDIATRIC CLINICAL TRIALS OFFICE

Clinical Trials are the final step that is required to prove that a therapeutic method can work in humans. Most such trials are done in adults, but the results of trials in adults are not necessarily entirely applicable to children. Pediatric clinical trials are therefore required to evaluate the efficacy of therapeutic or diagnostic strategies in pediatric populations, and the conduct of such trials has long been recognized as a priority by regulatory and funding agencies.

However, conducting clinical trials in children necessitates specific approaches to study design and conduct that require special expertise. For example: the approach to consent is different (consent is required from the parents, and an assent, which is not a full consent, is required of children – depending on the age and cognitive ability), study design and processes may be quite different in different developmental stages, medication doses are calculated per patient/patient characteristics (e.g., body mass index) rather than kept as a constant, and so on. It is further-more recognized that patient recruitment to pediatric trials could be more complicated and that because pediatric diseases are generally less common, trials are likely to involve multisite designs.

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Our vision is to enhance and expand current efforts, allow the development of future ideas and initiatives, and reduce the startup costs and time-to-implementation of novel therapeutics, while promoting a collaborative multidisciplinary research enterprise in order to improve the health and quality of life of children.

For those reasons, MCHDI leadership created a pediatric clinical trials office (PCTO) that serves the needs of researchers within the Mount Sinai health system who wish to conduct pediatric clinical trials. The office offers expertise in regulatory, budgeting, and operations of trials that involve children and families. We have partnered with the Clinical Trials Office (CTO) in Internal Medicine to provide this unique service to existing and "in development" trials, whether they involve investigator-initiated, industry-funded, or federally funded efforts.

With the support and supervision of the PCTO Director, Dr. Eyal Shemesh, CTO Director, Michele Cohen, MCHDI leadership, and a dedicated group of pediatric investigators who are already successfully engaged in clinical trials research, Yair Bitton, the program manager, is creating an operational team that provides knowledgeable, efficient and convenient support to our diverse initiatives (which have been run in separate silos up until now). Currently, the PCTO is in various stages of involvement (from negotiation to implementation) in 7 trials.

Our vision is to enhance and expand current efforts, allow the development of future ideas and initiatives, and reduce the startup costs and time-to-implementation of novel therapeutics, while promoting a collaborative multidisciplinary research enterprise in order to improve the health and quality of life of children.

# CENTER FOR INBORN ERRORS OF IMMUNITY

The Center for Inborn Errors of Immunity (CIEI) seeks to illuminate the elusive pathogenesis behind genetic disorders of the immune system. We strive to lay the foundation for a paradigm-shifting approach to the design of both preventative therapies (such as prophylactic drugs, vaccines, and genetic counseling) and novel treatments.

Our research is being done in the following areas:

#### **Genetics of Immune Disorders**

Primary immunodeficiencies (PIDs) are a varied group of inborn genetic errors that result in susceptibility to infections, predisposition to malignancy, or disorders of immune overactivation. Currently more than 400 genetic defects have been described. The CIEI seeks to diagnose individuals with known disease and discover new genetic etiologies of disease by using the latest sequencing and analysis technologies. Many of our member labs are working to identify and study these genetic defects. Additionally, CIEI is a part of The Mindich Child Health and Development Institute's Undiagnosed Disease Program, which is investigating the genetic underpinning of many childhood diseases, including those pertaining to the immune system. Finally, Mount Sinai's BioMe Biobank collaboration with the Regeneron Genetics Center will allow us and others to identify those individuals who might have silent or late onset conditions.

The average patient with a primary immunodeficiency (PID) waits more than 9 years from symptom onset to diagnosis. The Percha Lab, a CIEI member lab, is committed to helping such patients achieve earlier diagnosis and relief from symptoms. Our investigators use machine learning and natural language processing of electronic medical records to identify patients with high risk of PID in order to pave the way to prompt diagnosis.

#### **Detailed Pathophysiology**

Understanding the underlying mechanisms of a disease is key to developing successful treatment. To achieve this understanding, each genetic variant must be studied in isolation in order to glean key mechanistic insights. Our CIEI labs use genomics, genetics, molecular biology, cellular biology, immunology, and clinical tools to dissect these phenotypes and develop therapeutics.

#### Novel Therapeutics, Technologies, and Clinical Trials

The Inborn Errors of Immunity program uses the latest technologies to investigate pathophysiology, but also to unveil existing FDA approved therapies, such as JAK inhibitor therapy. We are also facilitating the development of novel therapies such as transient gene therapy: Modified mRNA, which is an attractive and novel in vivo gene delivery method that allows high gene expression in a variety of organs, including those involved in the immune system. Expression is seen within 20 minutes following delivery and can last from several days to a week. The strength of modified mRNA as a gene delivery therapy is in its safety, transience, and high expressivity, as recently evidenced by the success of modRNA based SARS-CoV-2 vaccines by two different companies. At the CIEI, we are developing modRNA tools to successfully modify immune state and cure disease.

#### **Immune Monitoring**

A key component to understanding inborn errors of immunity is the detailed mapping and functional assessment of the immune system. The Inborn Errors of Immunity program is thus working closely with the Human Immune Monitoring Center, which leverages cutting-edge technologies and deep immunological and technical expertise to provide comprehensive immune monitoring for clinical and translational studies.

# PEDIATRIC PRECISION MEDICINE

Precision medicine (PM) uses individualized patient data to accurately and rapidly diagnose disease, better predict the outcomes of medical issues, and treat illnesses more precisely and effectively. Currently, medical problems with strong genetic underpinnings such as birth defects, neurodevelopmental delays, and inborn errors of immunity are ones that typically manifest during infancy, childhood, and/or adolescence, and where a PM approach can be transformative. Moreover, these types of conditions can lead to diagnostic odysseys, during which young patients are subjected to extensive medical testing for months or years, families wait anxiously for definitive answers, and effective therapies, when available, are delayed.

The MCHDI is focusing on pediatric PM as one of its main strategic initiatives, for which there has been significant progress over this past year. The Undiagnosed Diseases Program (UDP), led by Bryn Webb, MD, has continued to recruit infants, children and adolescents with unsolved diseases that seem likely to have a genetic underpinning and then use new generation DNA sequencing, primarily of exomes, in order to pinpoint the causal genetic variation. This approach remains successful and has resulted in the discovery of novel disease genes, including two associated with neurodevelopmental delays, described in peer-reviewed publications this year. A third discovery for an immunological trait resulted in PhD thesis work by Conor Gruber, an MD/PhD candidate in Dusan Bogunovic's laboratory, which was also published this year.

A major challenge for PM generally is determining whether novel variants, particularly ones in putatively new disease genes, are truly biologically damaging. While informatics tools are quite helpful, functional studies are often required in order to more definitively assign causality. To facilitate such functional assessments, the MCHDI partnered with the Cell, Developmental and Regenerative Biology Department to initiate the Functional Genomics and Disease Model Core, which is being led by Tirtha Das, PhD. Building on a platform first devised by Dr. Ross Cagan, this Core will model genetic variants in Drosophila using state-of-the-art approaches such as transgenesis, CRIS-PR-mediated gene editing and CRIMIC. As the Core becomes established, the intent is to provide a resource for the UDP, various pediatric PM studies (such as GEMINI and NYCKidSeq) as well as individual investigators to nominate putative disease-causing variants for modeling studies.

Finally, more robust statistical analytic approaches are needed when seeking ultra-rare genetic variants of relatively large effect size that underlie Mendelian disorders. This is particularly important now that large population-based and disease-based cohorts are having their exomes or even genomes sequenced. To that end, a major new member of the MCHDI is Ernest Turro, PhD, a statistical geneticist who was recruited from the University of Cambridge in England. Dr. Turro's statistical genetics work focuses on such child health-relevant traits. Dr. Turro, who arrived this fall, was installed on the Arthur J. and Nellie Z. Cohen Chair at Convocation this year. We are excited to have him join the MCHDI!



Icahn School of Medicine at **Mount** Sinai

The Mindich Child Health and Development Institute

# LEADERSHIP AND STAFF

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



The Mindich Child Health and Development Institute