



Icahn School
of Medicine at
Mount
Sinai

*The Mindich
Child Health and
Development Institute*

MCHDI Developmental Outcomes

SPRING 2022

Promotion of Bruce D. Gelb, MD, to Dean for Child Health Research

Dr. Gelb is the Gogel Family Professor of the Mindich Child Health and Development Institute and founding Director of the Institute. He also holds professorships in Pediatrics, and Genetics and Genomic Sciences. He is an internationally recognized expert on the genetics and genomics of cardiovascular diseases, particularly those affecting children. Dr. Gelb's promotion represents an expansion of his responsibilities to address child health research opportunities and needs for our School as the Mount Sinai Health System further develops its offerings in children's health. He will advise on and guide resource allocation and faculty recruitment in child health-relevant research, including strengthening research enterprises in departments and institutes that already have substantial portfolios and developing them in others where there are untapped opportunities.

"I am honored to be selected for this new position at our School and excited to facilitate an even bigger and better research enterprise focused on improving the health of children."

In this position, he will lead strategic planning, resource allocation, and integration of child health research across Icahn Mount Sinai departments and institutes with a focus on further expansion of our effects in pediatric genomic medicine and clinical trials. He will also work to develop childhood-relevant efforts in health systems research and applications of artificial intelligence and machine learning.

In 1991, Dr. Gelb joined the Mount Sinai faculty as an Assistant Professor, following training in pediatrics at Columbia and in pediatric cardiology and molecular genetics at Texas Children's Hospital/Baylor College of Medicine. Over more than three decades, he has established a renowned research program in the genetics of cardiovascular disease, particularly for congenital heart defects. The Gelb group has identified disease genes for numerous

Congratulations

Bruce D. Gelb, MD

We are proud to announce the promotion of Bruce D. Gelb, MD, to Dean for Child Health Research at the Icahn School of Medicine at Mount Sinai.



Mendelian genetic traits, most notably the ones for Noonan syndrome and the related RASopathies.

Through his work with the Pediatric Cardiac Genomics Consortium, Dr. Gelb has applied state-of-the-art genomic approaches to understand congenital heart disease as a complex genetic trait. He is also a leader in pediatric genomic medicine through several National Institutes of Health-funded studies that are exploring the implementation of next-generation DNA sequencing in clinical care for pediatric patients. He has led our National Heart, Lung, and Blood Institute-funded T32 program in molecular and cellular cardiology for more than 18 years. Dr. Gelb remains active clinically, co-directing our Cardiovascular Genetics Program.

Dr. Gelb has been active nationally and internationally with several academic organizations. He has served as President of the American Pediatric Society and the International Pediatric Research Foundation and as Chair of the Pediatric Academic Societies. He recently completed his term as Treasurer of the American Society of Human Genetics and currently chairs that organization's Investment Committee. Dr. Gelb has been elected to the American Society for Clinical Investigation and the National Academy of Medicine. He is the recipient of the E. Mead Johnson Award from the Society for Pediatric Research and the Normal J. Siegel Award from the American Pediatric Society.

SARS-CoV-2 and Immune Deficiency

One of the main topics of conversation in these past months has been how patients with immune defects will fare if they contract the SARS-CoV-2 virus. While the production of protective antibodies is one the mainstays of public health, immune defects are common, leaving many patients unprotected. As a major referral center for pediatric and adult patients with immune defects, we have been challenged with numerous questions in the past two years, starting with how much risk there is for our immune deficient patients, what treatments to use if they became ill, and are vaccinations are useful in any way.

Mount Sinai Immune Deficiency program follows 900-1,000 patients, including infants referred for newborn screening for SCID, patients with agammaglobulinemia, and many others with hypogammaglobulinemia, complement, T cell or neutrophil defects. But who is most at risk for serious infection? In the first 6 months of this pandemic, 15 patients became infected; 8 had hypogammaglobulinemia, 3 had XLA, 1 each had IgA-IgG2 deficiency or X-linked hyper IgM; this suggested that loss of antibody function might be a particular risk. As Dr Hsi-en Ho published, 13 of these patients were hospitalized, and 4, all with antibody defects died (1, 2). We very quickly benefited from the plasma infusion program, being able to treat the XLA males and others with protective antibody (3, 4). With the passage of time, by May 2022, 120 of our patients have become infected with COVID known mutations leading to this immune defect, 12 have XLA, and others have a scattering of other immune defects.

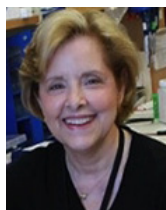
A few early publications suggested that immune globulin products contained cross reactive antibody to previous coronaviruses might provide some measure of protection to our patients. But we assessed this early in the pandemic (Spring 2020) with Dr. Florian Krammer, analyzing 21 different batches of Ig products; none contained antibody to the SARS-CoV-2 receptor binding domain or spike protein (2). Now two years later, Dr. Kimberly Cousins has repeated this study with Dr. Kaori Sano and Dr. Krammer, testing 125 unique lots of 11 different products. Significantly increased antibody is found in products with later collection dates, as compared to Ig products collected earlier. For example, 60 and 85 percent of immune globulin products with expiration dates of

2023 and 2024 are positive for antibody to SARS-CoV-2 proteins respectively (5).

To better understand COVID-19 infection in other patients, those receiving biologic and immunomodulatory therapies, we also evaluated COVID-19 cases and outcomes at Mount Sinai in the Therapeutic Infusion service. During the height of the pandemic, March to May 2020, Dr. Kaoru Harada with Dr. Ho evaluated 2,074 patients who receive these treatments (6). Only 1.64% developed a COVID-19 infection. Of these, an antibody defect was again the most common diagnosis -- for 11 patients (CVID, XLA, IgA-IgG2 deficiency). The second most common diagnoses were inflammatory bowel disease (in 7, on infliximab or vedolizumab) or multiple sclerosis (in 7, on natalizumab or ocrelizumab). Most of these patients had mild cases, and the only deaths were those noted in the 4 patients with primary immune defects noted in our first study.

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6. Harada K, Ho HE, Cunningham-Rundles C. [COVID-19 prevalence and outcomes in patients receiving biologic therapies at an infusion center in New York City.](#) *Clin Immunol.* 2021;230:108803.



Charlotte Cunningham-Rundles, MD, PhD
Professor, Medicine
Professor, Pediatrics

Unlocking the Potential of *In Vitro* Cardiomyocytes as a Metabolic Omnivore

Imagine research without ex vivo tissue culture models. Cell culture models have improved extensively ever since 1951, when cells from Henrietta Lacks enabled the generation of a cell line that could be kept alive and propagated outside of the human body. Cancer cell lines, immortalized cell lines of different origin and phenotype and numerous primary cells have since contributed to understanding many important biological problems. Most recently, induced pluripotent stem cells (iPSCs) have revolutionized the field due to their potential to generate any cell type of the human body, from any individual.

The first decade of iPSC research has focused on adopting concepts of developmental biology to reliably generate specific cell types *in vitro*. With many such strategies in hand, the current challenges lie in building complex tissues, or organoids, and to mature iPSC-derived cells beyond the embryonic state that they are currently stuck in. Achieving progress in these areas will be critical for iPSC model to be relevant for disease modeling, drug discovery and regenerative therapy.

Strategies to enhance maturation of iPSC-derived cardiomyocytes (iPSC-CMs) have focused primarily on long-term cultures, tissue engineering and manipulation of various signaling pathways. However, the heart undergoes extensive changes in its metabolic activity, both pre- and postnatally. In a highly collaborative study involving broad expertise at Mount Sinai (Dubois, Costa, Houten, Ma'ayan, Akbarian, Sobie, Chipuk, Iyengar, Sebra and Beaumont labs), Dubois and colleagues hypothesized that such metabolic changes will broadly contribute to cardiac maturation, and should thus be recapitulated *in vitro*. Wickramasinghe et al first demonstrated that changes in substrate (glucose versus fatty acids) alone is not sufficient to induce the metabolic switch from glycolysis to fatty acid oxidation (FAO) observed during development. In search of an up-stream regulator of the FAO program they systematically interrogated the role of the Peroxisome-Proliferator-Associated-Receptor (PPAR) pathway, a well-known metabolic regulator in adult hearts, during cardiac maturation. Of the three isoforms (PPARA, PPARD, PPARG), PPARA was the only one required for iPSC-CM viability. However PPARA activation was not able to enhance FAO. In

contrast, and unexpectedly, PPARD activation efficiently induced the transcriptional program for FAO and led to enhanced overall metabolic activity, increased FAO and a corresponding increase in mitochondrial content and mitochondrial structural maturation. As hypothesized by the team, this PPARD-induced metabolic switch further led to enhanced cardiac maturation as evidenced by improved sarcomere organization, changes in electrophysiological parameters and contractility in engineered tissue (Figure 1, Wickramasinghe et al., Cell Stem Cell 2022).

These results demonstrate that the metabolic switch that occurs in the embryo can indeed be recapitulated *in vitro*, in iPSC-CMs. In the future it will be intriguing to learn if similar metabolic activities can enhance maturation of other iPSC-derived cell types and lineages, potentially outside of the heart, and if the PPARD-induced iPSC-CMs represent a more relevant model for disease modeling, drug discovery and potentially cardiac regenerative strategies.

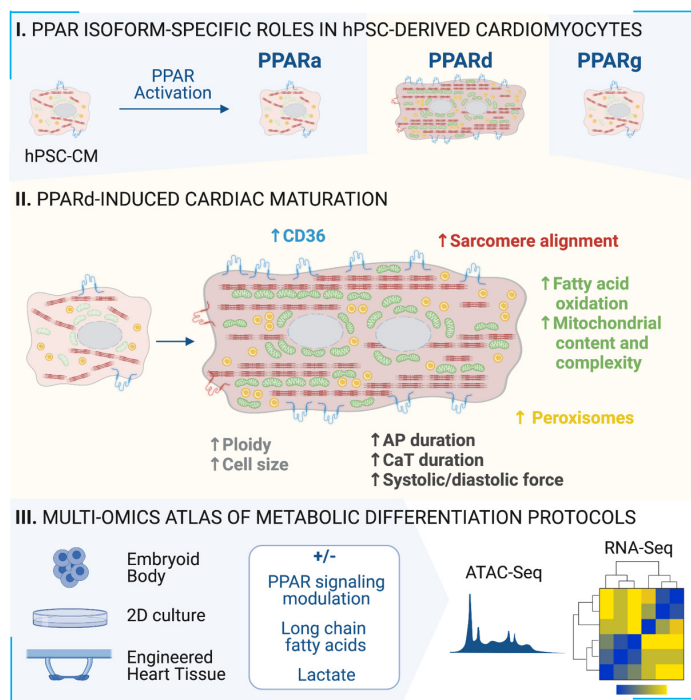


Figure 1: I. Isoform-specific interrogation of PPARs illustrates the unique ability for PPARD to enhance cardiac maturation. II. Specific parameters of cardiac maturation enhanced by PPARD activation. III. Generation of a multi-omics atlas of the mechanisms of PPAR regulation during cardiac maturation.



Nicole C. Dubois, PhD

Associate Professor, Cell, Developmental & Regenerative Biology

Pilot Project: 2022 Awardees

Project Title: Genotype-Phenotype Correlations in Cardiac and Skeletal Muscle of Fatty Acid Oxidation Deficiencies

Principal Investigators: Nicole C. Dubois, PhD (Communicating PI), Sander Houten, PhD (Co-PI), George Diaz, MD, PhD (Co-I), Nenad Bursac, PhD (Co-I), Justin Cross, PhD (Co-I)

Abstract: Fatty acid oxidation disorders (FAODs) are inborn errors of metabolism that are due to defects in either mitochondrial β -oxidation or transport of fatty acids. FAODs present with a broad spectrum of clinical phenotypes, ranging from neonatal onset with severe cardiomyopathy to presentation during adolescence with hypoglycemia and rhabdomyolysis. Mutations associated with FAODs have been identified in the majority of genes of the FAO machinery, and clinical phenotypes have suggested a genotype-phenotype correlation potentially explaining the disease severity spectrum. Treatment of FAOD patients is currently limited to dietary restrictions and substrate supplements and the morbidity and mortality are high. There remains an unmet need to understand the underlying adaptive mechanisms of FAODs in order to define better treatments that extend the life span and improve quality of life

of FAOD patients. We have recently established a new protocol to generate metabolically mature human pluripotent stem cell-derived cardiomyocytes (hPSC-CMs) by activation of PPAR signaling. We have further established one of the first model system to generate and characterize human PSC-derived skeletal muscle (hPSC-SKM) from healthy and diseased hPSCs. We show that the same PPARD-induced metabolic switch found in hPSC-CMs can be induced in hPSC-SKM. The overall goal of the current proposal is to capitalize on the new metabolic maturation approach to determine the mechanisms underlying FAO deficiencies in a mutation- and cell type-specific manner. In Aim1 we will investigate genotype-phenotype correlations in VLCADD with respect to metabolic mechanisms in cardiac and skeletal muscle, two prominently affected cell types in

VLCADD. In Aim 2 we will determine correlations between different severities in metabolic deficiency and their cell autonomous physiological consequences. Characterizing the mechanisms FAOD, in a patient- and cell type specific manner, promises to uncover new disease mechanisms that may lead to targeted and more efficient therapies.



Nicole C. Dubois, PhD (Communicating PI)
Associate Professor, Cell, Developmental & Regenerative Biology
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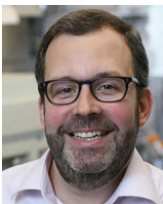
Sander Houten, PhD (Co-PI)
Associate Professor, Genetics and Genomic Sciences



George Diaz, MD, PhD (Co-I)
Professor, Genetics and Genomic Sciences and Pediatrics



Nenad Bursac, PhD (Co-I)
Professor, Biomedical Engineering and Cell Biology
Duke Cancer Institute
Director of Duke Regeneration Center
Duke University, Durham



Justin Cross, PhD (Co-I)
Director, Donald B. and Catherine C. Marron Cancer Metabolism Center
Memorial Sloan Kettering Cancer Center, New York

Pilot Project: 2022 Awardees-Continued

Project Title: Immunophenotypic Comparison of Systemic Juvenile Idiopathic Arthritis and Multisystem Inflammatory Syndrome in Children

Principal Investigators: Rebecca Trachtman, MD (Communicating PI) and Dusan Bogunovic, PhD (Co-PI)

Abstract: Multisystem Inflammatory Syndrome in Children (MIS-C) is a newly recognized hyperinflammatory syndrome with similarities to some established autoinflammatory diseases in children, especially systemic juvenile idiopathic arthritis (sJIA). Although the immunologic mechanism of sJIA has been explored, there is still much that is not understood. Our prior research has evaluated the complex immunologic features



Rebecca Trachtman, MD (Communicating PI)

Assistant Professor, Pediatrics
Mindich Child Health and Development Institute

of a cohort of nine children with MIS-C. In this proposal, we test the hypothesis that children with sJIA have similar immunophenotype to children with MIS-C.

The aim of this study is to assess the clinical and immunologic characteristics of children with sJIA, and compare these to features of children with MIS-C, in order to understand both populations better.

In order to achieve this aim, we will utilize serum samples from two existing studies. We will perform extensive immunophenotyping and statistical comparisons to evaluate the similarities and differences between these two groups.

Dusan Bogunovic, PhD (Co-PI)

Professor, Pediatrics, Microbiology, and
Oncological Sciences
Mindich Child Health and Development Institute
Director, Center for Inborn Errors of Immunity
Precision Immunology Institute



Project Title: Whole-Genome Sequencing of Neonatal Fatalities

Principal Investigators: Ernest Turro, PhD (Communicating PI), Felix Richter, MD PhD (Co-I), Katherine Guttman, MD, MBE (Co-PI), Mafalda Barbosa, MD, PhD (Co-PI)

Abstract: Each year, approximately 4,000 children born after 28 weeks of gestation die in a neonatal intensive care unit (NICU) in the United States. From an evolutionary perspective, and on the basis of observations in stillbirths and live infants with rare diseases, a large proportion of such deaths are likely to be attributable to highly penetrant rare pathogenic alleles. Large-scale genetic studies on this population of patients have the potential to reveal the genetic architecture of this class of fatalities in the NICU and uncover novel etiologies of disease and biological mechanisms. Nevertheless, such studies are almost entirely absent from the scientific literature.

Our project will develop a collaboration among regional NICUs in New York State to obtain DNA samples from deceased "28+ weekers" and their parents. Our target is to enroll 50% of eligible patients in 50% of regional NICUs, providing



Ernest Turro, PhD (Communicating PI)

Associate Professor, Genetics and Genomic Sciences
Mindich Child Health and Development Institute
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access to approximately 50 patients over the course of 12 months. We will extract DNA from patients and their parents in a Clinical Laboratory Improvement Amendments (CLIA)-certified laboratory and perform research-standard whole-genome sequencing on the patients. We will develop web applications to collect phenotype data securely and encode them in a standardized manner. We will screen the patient genomes for pathogenic variants following American College of Medical Genetics and Genomics guidelines. Subject to parental consent, we will validate any findings in a CLIA-certified laboratory and return the results to the parents to assist with planning future pregnancies.

This pilot project is intended to seed a future R01 grant encompassing NICUs across the entire country. Having put in place the processes required to enroll patients across NICUs in New York, our team will be well placed to obtain funding to enroll on the order of 1,000 patients per year. A cohort of this scale would be amenable to genetic association analysis. Our interdisciplinary team has the requisite expertise to fulfill this ambition.

Felix Richter, MD, PhD (Co-I)

Pediatrics Resident Physician
Mindich Child Health and Development Institute



Katherine Guttman, MD, MBE (Co-PI)

Assistant Professor, Pediatrics
Mindich Child Health and Development Institute



Mafalda Barbosa, MD, PhD (Co-PI)

Assistant Professor, Genetics and Genomic Sciences
Mindich Child Health and Development Institute



New Intramural Faculty

Mafalda Barbosa, MD

Mafalda Barbosa, MD, PhD, is an Assistant Professor of Genetics and Genomic Sciences at the Icahn School of Medicine at Mount Sinai. Dr. Barbosa received her MD from the University of Porto and completed her first Medical Genetics residency in Portugal. She then moved to the United States for her PhD studies at Mount Sinai where she specialized in novel molecular diagnostics of Neurodevelopmental Disorders. During her graduate studies she became proficient in the analysis of microarrays, exome sequencing and methylation profiles/epimutations. Because she wanted to be able to provide patient care, after graduating from her PhD, she completed a combined Pediatrics/Genetics residency at Mount Sinai.

In the summer of 2021, Dr. Barbosa enthusiastically joined Sinai's faculty with an appointment that entails mostly clinical work with some protected time for research, supported by The Mindich Child Health & Development Institute. Her research focus will continue to be on children with genetic conditions, including



Mafalda Barbosa, MD, PhD

Assistant Professor, Genetics and Genomic Sciences

spearheading the well-known Undiagnosed Diseases Program. Dr. Barbosa dedicated the last 15 years of her life to Medical Genetics, aiming to help children (and their families) with genetic disorders as both clinician and researcher. She is committed to continuing to serve this population as a physician-scientist while contributing to advances in Science and Medicine.

Key Publications:

Fu JM, Satterstrom FK, Peng M, Brand H, Collins RL, Dong S, Klei L, Stevens C, Cusick C, Babadi M, Banks E, Collins B, Dodge S, Gabriel SB, Gauthier L, Lee SK, Liang L, Ljungdahl A, Mahjani B, Sloofman L, Smirnov A, **Barbosa M**, et al. Rare coding variation illuminates the allelic architecture, risk genes, cellular expression patterns, and phenotypic context of autism. *Nat Genet*. 2022. [In press]

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Sharon Baumel-Alterzon, PhD

Sharon Baumel-Alterzon, PhD is an instructor in the Diabetes, Obesity, and Metabolism institute at the Icahn School of Medicine. Dr. Baumel-Alterzon received her PhD in 2014 from the Technion- Israel Institute of Technology, where she studied parasitic diseases. In 2018, Dr. Baumel-Alterzon joined Dr. Donald Scott's lab at Mount Sinai to study the underlying mechanisms that regulate the expansion of pancreatic β -cells with the idea of finding therapeutic targets that can regenerate β -cells in diabetes. Specifically, her work focuses on the role of Nrf2 transcription factor, a master regulator of anti-oxidative response, on adaptive β -cell expansion, survival and identity. Dr. Baumel-Alterzon has recently shown that Nrf2 is required for adaptive β -cell expansion under situations of overnutrition and that activation of the Nrf2



Sharon Baumel-Alterzon, PhD

Instructor, Medicine

Key Publications:

Baumel-Alterzon S, Katz S. L, Brill G, Jean-Pierre C, Li Y, Tse I, Biswal S, Garcia-Ocaña A, Scott K. D. [Nrf2 Regulates \$\beta\$ -cell Mass by Suppressing \$\beta\$ -Cell Death and Promoting \$\beta\$ -Cell Proliferation](#). *Diabetes*. 2022 May 1;71(5):989-1011.

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New Intramural Faculty- Continued

pathway using pharmacological agents increases human β -cell proliferation, highlighting the promising therapeutic potential of compounds that modulate Nrf2 to induce β -cell regeneration for diabetes. Since defects in maternal β -cell adaptive expansion can lead to gestational diabetes mellitus, Dr. Baumel-Alterzon has been recently awarded with a NIH/NIDDK KO1 award to study the role of Nrf2 in β -cell turnover during pregnancy. Additionally, due to the sharp increase in

the annual incidence of both type 1 (1.8%) and type 2 (4.8%) diabetes in the pediatric population in the last decades, as part of MCHDI trainee pilot award, Dr. Baumel-Alterzon began to explore the role of Nrf2 in regulating β -cell expansion at early stages of life. Dr. Sharon Baumel-Alterzon's final goal is to identify mechanistic targets for therapeutic intervention in diabetes.

New Extramural Faculty

Nathalie Chami, PhD

Nathalie Chami, PhD, is an instructor of Environmental Medicine and Public Health in the lab of Dr. Ruth Loos at the Icahn School of Medicine. The focus of her research has been on gene discovery in monogenic and polygenic traits and disorders including blood cell traits, familial dilated cardiomyopathies, obesity and related metabolic traits using genotype and sequencing data. She is currently leading one of the largest studies aimed to identify novel genes associated with BMI and obesity using whole exome and whole genome sequencing analysis in TOPMed and the UK Biobank, two of the largest datasets available to the research community. She is also leveraging these datasets to study the penetrance of variants that cause monogenic disease in order to improve interpretation of rare variants. In addition, she is interested in identifying genetic factors that increase the risk of obesity but otherwise decrease the risk of cardio-metabolic traits such as cholesterol and blood pressure and vice versa with the purpose of elucidating the mechanisms that uncouple weight gain from susceptibility to cardiovascular outcomes.



Nathalie Chami, PhD

Instructor, Environmental Medicine and Public Health

Dr. Chami received a BSc in Biomathematics and an MSc in Human Genetics from McGill University. She then pursued her doctoral studies at the Montreal Heart Institute. Dr. Chami received a postdoctoral grant from the Canadian Institute of Health Research from 2017-2020 and completed her post-doctoral training at the Icahn School of Medicine.

Key Publications:

Huang OL, Rauch A, Mazzaferro E, Preuss M, Carobbio S, Bayrak CS, **Chami N**, Wang Z, Schick UM, Yang N, Itan Y, Vidal-Puig A, den Hoed M, Mandrup S, Kilpeläinen TO, Loos R.J.F. [Genome-wide discovery of genetic loci that uncouple excess adiposity from its comorbidities](#). *Nat Metab*. 2021 Feb;3(2):228-243.

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Grants, Awards, and Honors

Faculty Grants/Honors/Awards

Sharon Baumel-Alterzon, PhD, NIH/NIDDK, KO1 Research Scientist Development Award, “The Role of Nrf2 in Beta Cell Expansion During Pregnancy”

Minji Byun, PhD, NIAID, R21, “Mechanistic Modeling of Epigenetic Modifier Mutations in Human Pluripotent Stem Cell-Derived Immune Cells”

Tirtha K. Das, PhD, Co-Chair and Speaker, 63rd Annual Drosophila Conference, “Human Disease Modeling” oral platform presentation section and “Flies on Drugs” workshop

David Dunkin, MD, American Gastroenterological Association, AGA Fellow

Bruce D. Gelb, MD, Promotion to Dean of Child Health at the Icahn School of Medicine at Mount Sinai

Yuval Itan, PhD, Elected as a member to the Henry Kunkel Society (HKS)

Yuval Itan, PhD, Leducq Foundation, “Brown Fat and Cardiovascular Health: Genetic Determinants and Molecular Mechanisms”

Yuval Itan, PhD (co-I), NIDDK, U24, “Precision IBD via Genetics and Genomics: Integrating International and Multi-omic Datasets, Expanding Studies in Diverse Populations, and Defining Mechanisms of Unmet Clinical Needs in IBD”

Yuval Itan, PhD (co-I), Helmsley Foundation, “Integrative Network Approaches for VEOIBD Target Gene Identification and Prioritization for Drug Discovery”

Amy R. Kontorovich, MD, PhD, Promotion to Director of the New Mount Sinai Center for Inherited Cardiovascular Diseases

Geming Lu, MD, MS, American Diabetes Association’s 82nd Scientific Sessions, Young Investigator Award

Lisa M. Satlin, MD and Thomas R. Kleyman (mPIs), NIDDK, R01, “Role of Piezo Channels in Intercalated Cells”

Trainee Grants/Honors/Awards

Tasneem Ebrahim, BA, American Heart Association and Children’s Heart Foundation, Congenital Heart Defect Predoctoral Fellowship, “Role of Retinoic Acid in Cardiac Progenitor Specification”

Vahe Khachadourian, PhD, International Society for Autism Research 2022, “Comorbidities in Autism Spectrum Disorder and Their Etiologies” oral presentation

Vahe Khachadourian, PhD, International Society for Autism Research 2022, “Diagnoses in Pregnancy and Risk of Autism Spectrum Disorder” oral presentation

Adele Mossa, PhD, FBI Postdoc Innovator Award 2022, “Sex-Specific mRNA Translation in a Mouse Model of Autism Spectrum Disorder”

Adele Mossa, PhD, International Society for Autism Research 2022, Molecular and Cellular Biology section, “The Intellectual Disability Gene DDX3X in Sex-Specific Neuronal Morphogenesis” poster presentation

Faculty Highlights

Publications

Baumel-Alterzon S, Katz LS, Brill G, Jean-Pierre C, Li Y, Tse I, Biswal S, **Garcia-Ocaña A**, **Scott DK**. Nrf2 regulates β -cell mass by suppressing β -cell death and promoting β -cell proliferation. *Diabetes*. 2022 May 1;71(5):989-1011.

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