The virus that causes COVID-19 uses angiotensin converting enzyme 2 (ACE2) for host entry. ACE2, which stands for angiotensin converting enzyme 2, is a receptor that some might be familiar with because of its role in blood pressure regulation. The coronavirus uses ACE2 to enter the human body, where it spreads. ACE2 is known to be present in our airway, kidneys, heart, and gut. MCHDI and pediatric researchers Supinda Bunyavanich, MD, MPH, Anh Do, PhD, and Alfin Vicencio, MD took this knowledge a step further, finding that compared to adults, children have lower levels of ACE2 gene expression in their nasal passages. The team’s finding may help explain children’s lower risk of COVID-19 infection and mortality. These results, published in JAMA on May 20, 2020, may point to a potential biomarker of susceptibility to the SARS-CoV-2 virus.

“Why children get COVID-19 less than adults has been a puzzle,” says MCHDI faculty member Supinda Bunyavanich, MD, MPH, Professor of Genetics and Genomic Sciences and Pediatrics. “Researchers have hypothesized that lower expression of ACE2 might explain why children are less likely to get COVID-19. Our study shows that ACE2 expression in the nasal epithelium is lowest in younger children and increases with age into adulthood. These results may help explain why children account for less than 2% of identified cases of COVID-19. A biomarker of COVID-19 susceptibility based on ACE2 expression might be possible.”

The research focused on ACE2 due to its significance in COVID-19 infection. The nasal passages are usually the first point of contact for SARS-CoV-2 and the human body. The Bunyavanich team’s study is one of only a few examining the relationship between ACE2 in the airway and age.

The retrospective analysis examined nasal brushings collected from Mount Sinai Health System patients aged 4 to 60. The researchers found ACE2 gene expression in nasal epithelium was age-dependent, lowest in younger children and increasing with age into adulthood.
Eyal Shemesh, MD, a faculty member of MCHDI, in collaboration
with Sudipto Srivastava, a Senior Director in the Mount Sinai
health IT department, on behalf of the Mount Sinai medical
Center, received an award of $862,950 to provide more than
700 connectivity devices to pediatric patients within the health
care system. The award, a part of an innovative and competitive
extension to the Cares Act allocation, is hosted and managed by
the Federal Communications Commission (FCC). Those devices
are expected to help connect families of children with chronic
health care needs to their Doctors and care providers within Mount
Sinai's health system.

Mount Sinai pediatric practices treat more than 10,000 children
from disadvantaged backgrounds with pre-existing, chronic
conditions such as asthma, cardiac disease, diabetes, obesity, or
immune-compromise, all of which meet CDC criteria for COVID-19
monitoring, patients who cannot take care of themselves, and
patients whose families may be affected by the virus as well.
The funding allows for purchase, shipment, and maintenance
and support services to a unique device that is provided to those
families without charge. This device, which has been used in the
health system before, is customized to the particular needs of each
patient group, under oversight of our specialists.
The PadInMotion device (Picture) has been especially built to
provide telehealth, educational, and connectivity services to
populations that have serious barriers to participation in remote
access health-promotion encounters: it is easy to use, and comes
pre-loaded with the applications, including the required Mount Sinai
interfaces. The platform is multi-lingual and HIPAA compliant. It
comes with pre-loaded, fully paid for wireless or mobile broadband
options.

While providing the connectivity devices, a robust evaluation of
their use to inform future implementation of telehealth practices
within the health system will also be performed. The knowledge
gained as well as the actual services rendered are expected to help
in moving Mount Sinai’s pediatric practices into a new and exciting
era of providing integrated, highly personalized, remote and home-
based surveillance and care. In this care model, clinic visits are still
important but constitute only one component of a general strategy
aimed at keeping our patients healthy at their home and in the
community.
Faculty Highlights

Pilot Project 2019-2020 Awardees

**Project Title: Neural Control of Pancreatic Endocrine Function in the Development of Type 1 Diabetes**

**Principal Investigators:** Adolfo Garcia-Ocaña, PhD, MCHDI Investigator and Professor of Medicine; Sarah A. Stanley, MBBCh, PhD, Assistant Professor of Medicine

Abstract: Type 1 diabetes (T1D) is a common chronic disease in childhood with significant effects on quality of life. New approaches to treating T1D can be created by controlling activity in pancreatic nerves to regulate blood glucose. However, there is a lack of detailed knowledge of pancreatic nerve structure, function, and the effects of T1D required to achieve this. Without this, the likelihood of successfully targeting neural pathways to control blood glucose in diabetes is remote. This proposal aims to understand the effects of T1D on the structure and function of pancreatic sympathetic nerves. Their central hypothesis is that T1D increases islet sympathetic innervation leading to excess glucagon and insufficient insulin to maintain normal glucose. Pancreatic islets are high innervated by sympathetic nerves and T1D disrupts pancreatic nerve structure and function. However, it is not known if the structural changes from T1D are uniform, which endocrine cells are affected or the time course. In addition, the precise functions of pancreatic sympathetic nerves or the effects of T1D on these physiological roles are unknown. To test this hypothesis, the investigators will determine the effects of T1D on a) the 3D structure of islet sympathetic nerves and their associations with immune infiltration and b) the function of islet sympathetic nerves to regulate blood glucose in juvenile mice. They will determine the effects of T1D on pancreatic sympathetic nerve function by measuring blood glucose and pancreatic hormone release in response to activation or inhibition of pancreatic sympathetic nerves. The proposed studies will provide a comprehensive understanding of pancreatic sympathetic nerve structure and function in T1D and form a critical foundation for future studies identifying mechanism and therapeutic targets to treat T1D.

**Adolfo Garcia-Ocaña, PhD**
Professor, Medicine

**Sarah A. Stanley, MBBCh, PhD**
Assistant Professor, Medicine

**Project Title: Identifying the Role of Early Environmental Toxicants in Newborns with Biliary Atresia**

**Principal Investigators:** Jaime Chu, MD, MCHDI Investigator and Assistant Professor of Pediatrics; Lauren Petrick, PhD, Assistant Professor of Environmental Medicine and Public Health; Sanjiv Harpavat, MD, PhD, Assistant Professor of Pediatrics (Texas Children’s Hospital, Baylor College of Medicine)

Abstract: Biliary atresia (BA) is the rapid and progressive destruction of bile ducts in neonates and results in 100% mortality by 1 year if misdiagnosed and left untreated. BA has long been the most common indication for pediatric liver transplantation, yet its etiology remains elusive and the field lacks any biomarkers to aid in early diagnosis. Research focused on GWAS and transcriptomic signatures at 6-8 weeks of age, the typical emergence of visible symptoms, have been unsuccessful at predicting cases of BA. The paradigm is shifting with recent data suggesting 1) a prenatal injury and the need for biomarkers at birth and 2) a role for environmental toxins in BA. Therefore, the investigators propose the first study to investigate toxicant exposure and endogenous biomarker levels in newborns with biliary atresia and perform untargeted metabolomics analysis to identify differences in metabolite profiles at birth between neonates that later developed biliary atresia compared to healthy neonate controls and ascertain which combination(s) of DBS metabolites increase BA risk as potential pre-diagnosis biomarkers. This proposal addresses the critical unmet need for early and effective biomarkers in BA. They will leverage diverse and complementary expertise in pediatric liver disease and innovative ability to extract small molecule data from DBS to establish a metabolic signature of infants with BA and introduce the novel prospect that analysis of newborn DBS can offer a window into etiology and earlier diagnosis, and potential transplant-sparing interventions.

**Jaime Chu, MD**
Associate Professor, Pediatrics
Associate Chief, Division of Pediatric Hepatology
Director, Pediatric Physician-Scientist Residency Program

**Lauren M. Petrick, PhD**
Assistant Professor, Department of Environmental Medicine and Public Health

**Sanjiv Harpavat, MD, PhD**
Assistant Professor, Department of Pediatrics
Texas Children’s Hospital
Baylor College of Medicine
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.

New Extramural Faculty

Fernando Ferrer, MD, FACS, FAAP
Professor, Urology

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 their 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.

They combine genetics and drug screening to rationally improve lead compounds and clinical therapeutics. Their work 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.

New Intramural Faculty

Tirtha Kamal Das, PhD
Assistant Professor, Department of Cell, Developmental & Regenerative Biology

Key Publications:

Cancer Mechanisms:


Cancer Therapeutics:


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.
Faculty Grants

M. Cecilia Berin, PhD and Maria Curotto de Lafaille, PhD, NIAID, R01, “Heterogeneity of T cell phenotype and function in food allergy”

Dusan Bogunovic, PhD, NIAID-R01, “Inborn Errors of Immunity Leading to Autoinflammatory Syndromes”

Minji Byun, PhD, Castleman Disease Collaborative Network, Research Award, “The hyperinflammatory response associated with DNMT3A mutations in idiopathic multicentric Castleman disease”

Jaime Chu, MD, NIDDK, R01, “Mannose metabolism as a regulator of hepatic stellate cell activation and fibrosis”

Hala Harony-Nicolas, PhD, United State–Israel Binational Science Foundation, “Studying the relationship between socio-emotional valence, oxytocin and social brain activity in health and disease”

Ruth J.F. Loos, PhD, NIDDK, R01, “Resilience to obesity in carriers of monogenic obesity mutations - a study on the underlying mechanisms”

Eyal Shemesh, MD, Federal Communications Commission, COVID-19 Telehealth Program Grant

Faculty Highlights

Publications


Breen MS, Garg P, Tang L, Mendonca D, Levy T, Barbosa M, Arnett AB, ... Gorce DE, ... Kolevzon A, Sharp AJ, Buxbaum JD, Siper PM, De Rubeis S. Episignatures stratifying Helsmoortel-Van Der Aa syndrome show modest correlation with phenotype. Am J Hum Genet. [In Press]


Lorenzini T, Fleigauf M, Klanner M, Frede N, Proietti M, Bulashevska A, ... Cunningham-Rundles C, ... Grimbach B. Characterization of the clinical and immunologic phenotype and management of 157 individuals with 56 distinct heterozygous nkbf1 mutations. J Allergy Clin Immunol. 2020 Apr 9;S0091-6749(20)30422-X. [Online Ahead of Print]


Lu G, Rausell-Palamos F, Zhang Z, Vasavada BC, Valle S, Spindler M, ... Garcia-Ocanas A. Dextran Sulfate Ameliorates Type 1 Diabetes, pancreatic beta cell death and autoimmunity. Diabetes. [In Press]


Zhang X, Spear E, Gennings C, Curtin PC, Just AC, Bragg JB, Stroustrup A. The association of prenatal exposure to intensive traffic with early preterm infant neurobehavioral development as reflected by the nicu network neurobehavioral scale (nnns). Environ Res. 2020 Apr;183:109204.


Wang T, Nichols HB, Nyante SJ, Bradshaw PT, Moorman PG, Kabat GC, ... Teitelbaum SL, ... Gammon MD. Urinary estrogen metabolites and long-term mortality following breast cancer. JNCI Cancer Spectr. 2020 Jun;5(6):pkaa014.


---

Events / Announcements

**Save the Date**

8th Annual MCHDI Retreat

Date: November 20, 2020

Time: TBA

---

Website: [www.mountsinai.org/mchdi](http://www.mountsinai.org/mchdi)

Email: mchdi@mssm.edu

Facebook: [www.facebook.com/mindichdhi](http://www.facebook.com/mindichdhi)

Twitter: [@MindichCHDI](https://twitter.com/MindichCHDI)

Contact: Tel: (212) 824-8938 Fax: (212) 241-3310

Address: 1470 Madison Avenue, 8th Floor

Hess Center for Science and Medicine at Mount Sinai

New York, NY 10029-6542