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Discovery

RESEARCH
at Stanley Manne Children's Research Institute

Published by Stanley Manne Children's Research Institute

Fall 2017

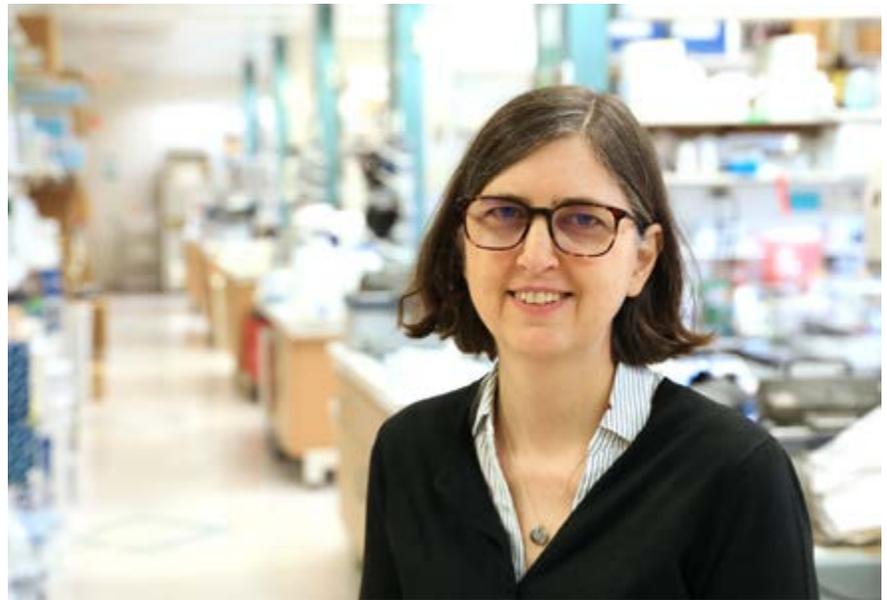
Volume 14: Issue 3

luriechildrens.org/research

Research at Ann & Robert H. Lurie Children's Hospital of Chicago is conducted through the Stanley Manne Children's Research Institute. The Manne Research Institute is focused on improving child health, transforming pediatric medicine and ensuring healthier futures through the relentless pursuit of knowledge. The research institute is a virtual center for pediatric research at Northwestern University Feinberg School of Medicine. Founded in 1989, the research enterprise has grown to include more than 500 investigators and over \$30 million in external funding for research, two-thirds from the NIH and other federal agencies.

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Protecting Premies from Intestinal Injury



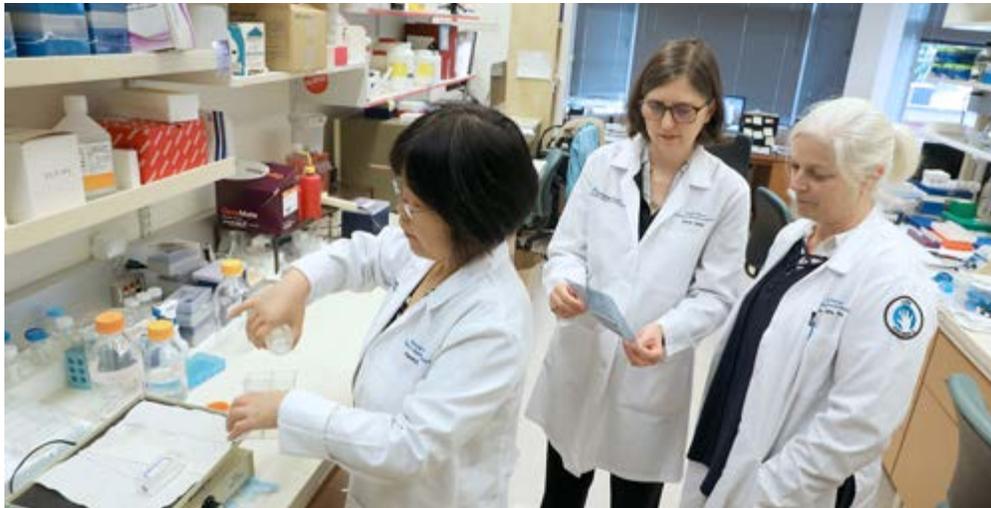
Isabelle De Plaen, MD.
Photo: Jan Terry.

Imagine a new mom whose preterm baby – who was fine initially – suddenly won't tolerate his feeds anymore and seems very sick. Nothing happens as planned – the feedings come back up, the baby appears in pain and has bloody stools. What is most worrisome is that he is now pale and no longer active. The mom, understandably, is upset – frightened, troubled, confused. Her baby who only hours or days before was healthy is now extremely ill.

Newborns who are very preterm are at risk of developing serious and potentially life-threatening conditions that only rarely occur in full term infants. Among these is necrotizing enterocolitis (NEC), the most common and difficult intestinal disease in preemies. Indeed, NEC affects approximately 7 to 10 percent of very low birth weight infants (weighting less than 3.3 pounds). In NEC, the intestinal tissues die off, leading to passage of bacterial products through the intestinal wall into the bloodstream, which causes the baby to go into shock.

Infants with NEC experience a variety of health issues and cannot eat by mouth for extended periods of time. Surgeons may need to remove dead intestinal tissues, resulting in the inability of these babies to digest food normally, which in turn necessitates long-term intravenous nutrition. Although the condition can resolve, some babies succumb. Those who survive could suffer from significant and lasting effects including poor growth, neurological or neurodevelopmental deficits, and visual or hearing impairments. There is currently no cure for NEC, and the therapeutic options are limited.

Isabelle De Plaen, MD, has been studying NEC at the bedside and in the lab for her entire career. As a neonatologist, she has cared for infants with NEC and their families. "These parents," she says, "feel



Isabelle De Plaen (center) with research associate Xiaocai Yan, PhD, and postdoctoral fellow Elizabeth Managlia, PhD. Photo: Jan Terry.

Isabelle De Plaen, MD, is an attending physician in the **Division of Neonatology** (Neonatal Intensive Care Unit) at Lurie Children's, Associate Professor of **Pediatrics (Neonatology)** at Northwestern University Feinberg School of Medicine, and a member of the **Center for Intestinal and Liver Inflammation Research** at Stanley Manne Children's Research Institute.

helpless to make things better for their newborns. Our goal is to prevent NEC from ever happening."

Her laboratory recently showed evidence that insufficient intestinal microvasculature – a fine network of blood vessels – may be critical in the development of NEC. She has hypothesized that maintaining low levels of oxygen during fetal development is essential for proper formation of the tiny blood vessels feeding the intestinal tissue. During premature birth the growth of these incompletely formed intestinal blood vessels slows down, increasing the susceptibility of the intestines to NEC.

In a **new study** published in *Pediatric Research*, the De Plaen lab tested a novel agent called DMOG, which increases the stability of a signaling molecule called hypoxia inducible factor-1 (HIF-1), which is triggered by low oxygen levels. They found that mice treated with DMOG produce higher levels of VEGF, a key vascular growth-promoting factor, in their intestines. Furthermore, DMOG treated mice maintain intestinal blood vessel growth and are protected against intestinal injury when exposed to an experimental NEC model.

"Several factors may affect the growth of the intestinal tiny blood vessels in the developing fetus," says De Plaen. "The problem is that we don't know exactly what roles these factors play, and without that knowledge it is difficult to design models for improving outcomes in babies with NEC. It is critical for us to continue these studies so as to find ways to best stimulate molecular pathways that promote intestinal vascular development. Also, we want to prevent conditions that would interfere with vascular development, so that intestinal tiny vessel development

is maintained in premature infants and NEC does not happen."

De Plaen is encouraged by but realistic about the findings. She explains, "Despite many years of research, there are still no significant advances in therapy for NEC. The goal of our research is to identify key molecules or pathways that cause or prevent the disease. This is why we continue to do research, because we know it's badly needed. By comparison, inflammatory bowel disease – an adult condition – now has an effective treatment, all due to animal-based research. This gives me hope that the same can be said of NEC in the near future."

She continues, "I am grateful to be surrounded by such talented researcher associates including Drs. Xiaocai Yan and Elizabeth Managlia, whose work is key to this research. In addition, I want to acknowledge Dr. Rakhee Bowker, a former neonatology fellow who is now Assistant Professor and a neonatologist at Rush University, and who was instrumental in the recently published study in *Pediatric Research*. Finally, I am grateful for the friendship and advice of my former mentor, Dr. Wei Hsueh, and of my long time collaborator, Dr. Xiao-Di Tan."

When asked about success stories with former patients, De Plaen's face lights up. "Our parents like to send us news about how well NEC graduates are doing. We had a very preterm baby whose family moved out of the U.S. They came back to visit recently, and this once sick baby is now a happy and thriving young person. It is extremely gratifying to receive updates like that," she says.

Trainee News



Jordan Vaught

As part of her Area of Scholarly Concentration (AOSC) Jordan Vaught, a second year medical student at the Feinberg School, presented her work entitled "Practitioner Perceptions Surrounding the Willingness of



Justin Ideozu

* This work was supported by the National Institutes of Health (NIH). Senior author **Hara Levy, MD**, is an attending physician in the **Division of Pulmonary Medicine** at Lurie Children's and Associate Professor of **Pediatrics (Pulmonary Medicine)** at the Feinberg School. She is a member of the **Human Molecular Genetics Program** of the Manne Research Institute. Co-authors Xi Zhang and Zainub Ashrafi are part of Pulmonary Medicine. Co-authors Amy Pan, PhD, Katherine Woods, Martin Hessner, PhD, and Pippa Simpson, PhD, are from the Medical College of Wisconsin.

Parents to Participate in Fertility Preservation for Their Children" at the Robert H. Lurie Medical Research Center on October 13. Vaught is mentored by **Erin Rowell, MD**, director of the **Fertility & Hormone Preservation & Restoration (FHPR) Program**, and focuses on the clinical and ethical aspects of fertility preservation for children through identifying patient, parent and provider preferences.

Kristine Corkum, MD, who is also mentored by Rowell and is completing her surgical research fellowship with the FHPR Program, was awarded a Stanley Manne Children's Research Institute Trainee Travel Award to present "Laparoscopic Oophorectomy for Ovarian Tissue Cryopreservation in Prepubertal and Young Adolescent Females: A Review of Surgical Outcomes" at the **International Pediatric Endosurgery Group's 26th Annual Congress for Endosurgery in Children** in London.

Justin Ideozu, a postdoctoral fellow in the **laboratory of Hara Levy, MD**, received a travel award from the **American Society of Human Genetics** to attend its annual meeting in October. Ideozu presented a poster entitled "Transcriptome Analysis of Cystic Fibrosis Molecular Signatures."

Ideozu is first author on a **publication that appeared** in the August issue of the *International Journal of Molecular Sciences*. Cystic fibrosis (CF) is a multisystem disorder caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. Many organs are affected by CF, most importantly the lungs, pancreas and digestive system, as is the patient's

ability to fight infections. Advances in newborn screening and treatments have improved outcomes, but researchers ultimately hope to establish a direct correlation between patients' genetic makeup and therapies targeted to their mutations. So far, these efforts have not proven effective.

Using a variety of methods, Ideozu and colleagues sought to determine the relationship between ABCC1 – a gene that is structurally and functionally related to CFTR, and associated with multidrug resistance – and clinical status in CF patients. Upregulation of ABCC1 is thought to improve lung function in patients with CF, but the mechanism underlying this effect is unknown. The lab investigated ABCC1 mRNA expression levels and methylation status, and their correlation with clinical variables among CF subjects with differing CFTR mutations. They also analyzed the ABCC1 promoter single-nucleotide polymorphism (SNP) rs504348 genotypes and various markers of CF disease severity, such as a commonly used disease severity equation classification, pancreatic status, and colonization with *Pseudomonas aeruginosa*, but found no significant association.

However, the group showed that CF subjects with CFTR genotypes associated with pancreatic insufficiency were more likely to be colonized with *P. aeruginosa* or the mucoid form of *P. aeruginosa* than those with genotypes associated with pancreatic sufficiency. Knowing that plasma-induced transcriptional signatures are capable of characterizing CF disease severity, the scientists measured plasma-induced ABCC1 expression in peripheral blood mononuclear cells (PBMCs) and showed it to be significantly higher with the plasma of CF subjects compared to that of healthy controls.

"Based on the limited sample size and a variety of unanswered questions the results raised, this study is just a small step in the right direction," says Levy. "We are encouraged, though, by our results suggesting that ABCC1 expression has a role in CFTR activity. This increases our understanding of the molecular underpinnings of the clinical heterogeneity in CF," she concludes.*

Awards & Honors

Pediatric nurse practitioner **Barbara Lockart, APN**, received the Daisy Award at Lurie Children's in July. The **Daisy Award** is a national award given in memory of J. Patrick Barnes. It celebrates nurses who provide extraordinary, compassionate and skillful care every day, recognizing exceptional nurses around the country. Lockart is in the Divisions of **General Pediatric Surgery** and **Hematology, Oncology, Neuro-Oncology & Stem Cell Transplantation** at Lurie Children's.



Gal Finer, MD, PhD

Gal Finer, MD, PhD, has received a **Research Grant for the Young Investigator** from the National Kidney Foundation of Illinois. The title of her project is "Elucidating the Role of Transcription Factor 21 in Kidney Development - Implications for Congenital Anomalies of the Kidney and Urinary Tract". The foundation's Research Grant program funds young investigators who have research projects that will increase the understanding of kidney, urologic and related diseases and transplantation as well as improve the clinical management and treatment or cure of these diseases. Finer is an attending physician in the **Division of Kidney Diseases** at Lurie Children's and Assistant Professor of **Pediatrics (Kidney Diseases)** at the Feinberg School.



Tracy Gertler, MD, PhD

Tracy Gertler, MD, PhD, has been awarded a **KL2 Scholarship** from the Northwestern University Clinical and Translational Sciences Institute (NUCATS). The award is a multidisciplinary mentored career development program that will provide Gertler and Sadiya Khan, MD, MS, with resources, educational opportunities, salary support and career guidance.

Gertler, who is an attending physician in the **Division of Neurology** at Lurie Children's and Instructor of **Pediatrics (Neurology)** at the Feinberg School, will use KL2 funding to further investigate the relationship between malignant migrating partial epilepsy of infancy (MMPEI), a type of epileptic encephalopathy (EE) and a mutation

within the KCNT1 gene encoding Slack, a sodium-activated potassium channel.

Quinidine has been reported as a uniquely efficacious anticonvulsant, suggesting that targeting neuronal excitability in EE is therapeutically beneficial, yet its use is limited in the brain and heart due to safety concerns. Advances in EE are further complicated by a lack of understanding of the neuronal subtype within the brain driving the development of epilepsy.

This project seeks to delineate the molecular mechanisms governing gain-of-function of Slack channels in a mammalian system and in human neurons differentiated from patient-derived induced pluripotent stem cells (iPSCs), representing a novel attempt to model pathogenic ion channels in mammalian cells and human neurons.

By identifying the mechanism of "overactive" Slack channels and developing a select panel of drugs that block its gain-of-function, Gertler hopes to refine a more precise approach to treating patients with severe global impairment and intractable epilepsy due to KCNT1 mutation.

An **anonymous \$12 million donation** to Lurie Children's will be used to treat child abuse, mental health issues and the direct and indirect effects of violence on Chicago's youth. The gift will go towards the hospital's **Healthy Communities** program, which partners health care providers and outreach organizations to mentor and treat youth and adolescents in some of Chicago's underserved communities.

Matthew Davis, MD, MAPP, head of the **Division of Academic General Pediatrics and Primary Care** at Lurie Children's, said child abuse and its mental health impact are naturally connected items in a cyclical pattern of violence. "When a child is maltreated in life, that child is more likely to have mental health challenges in childhood, adolescence and young adulthood," Davis said. "Mental health challenges may lead an adolescent or young adult to turn to violence and in turn, may put that young adult at risk of maltreating a child when he or she becomes a parent."

Awards & Honors (continued from page 4)



Matthew Davis, MD, MAPP



Debra Weese-Mayer, MD



Xiao-Di Tan, MD, is director of the **Center for Intestinal and Liver Inflammation Research (CILIR)** and holds the Dorothy M. and Edward E. Burwell Professorship in Immunobiology at the Manne Research Institute; and Research Professor of **Pediatrics** and **Pathology** at the Feinberg School.

The violence prevention program within the social services nonprofit **UCAN** will be one of several organizations partnering with the hospital. The program connects young people to mental health professionals and provides mentoring in the North Lawndale neighborhood. Norman Livingston Kerr, Vice President of UCAN's Violence Intervention and Prevention Services, said young people who have experienced trauma often suffer from post-traumatic stress disorder and carry the mental scars of violence in their communities. "Many of them have seen people abused verbally and physically – they've seen people shot," Kerr said.

The donation will also go towards making Humagram, software used to identify child abuse that was developed at Lurie Children's, available to hospitals across the U.S. The app helps health care providers determine if a patient's injury is intentional or accidental – a sometimes difficult distinction to make. "In the vast majority of cases when a child is diagnosed with child abuse, that child has been seen by a medical provider within the last six months and the diagnosis was missed," Davis said. "So we want to try to reduce children's risks for maltreatment by helping clinicians make the right diagnosis the first time."

Davis is director of the **Mary Ann & J. Milburn Smith Child Health Research, Outreach and Advocacy Center** and Associate Chief Research Officer for Health Services and Policy Research at the Manne Research Institute, A Todd Davis, MD Professor in General Academic Pediatrics, Mary Ann & J. Milburn Smith Research Professor for the Director of Child Health Research, and Professor of **Pediatrics (Academic General Pediatrics and Primary Care)** at the Feinberg School. [Read more.](#)

Lurie Children's is a **Grand Challenges Explorations** winner, an initiative funded by the Bill & Melinda

Gates Foundation that supports innovative thinkers worldwide to explore ideas that can break the mold in how we solve persistent global health and development challenges. **Debra Weese-Mayer, MD**, chief of the **Center for Autonomic Medicine in Pediatrics (CAMP)** at Lurie Children's, is the principal investigator for one of 51 Grand Challenges Explorations Round 19 grants announced by the Gates Foundation.

To receive funding, Weese-Mayer had to demonstrate a bold idea in one of four critical global health and development topic areas. Weese-Mayer is recognized internationally for her clinical and research work in the emerging discipline of pediatric autonomic medicine and is a lead translational researcher at Lurie Children's and the Manne Research Institute. She is the Beatrice Cummings Mayer Professor of Pediatric Autonomic Medicine and Professor of **Pediatrics (Neurology)** at the Feinberg School.

Weese-Mayer's collaborators for the Gates grant include Roozbeh Ghaffari and John Rogers in the **Center for Bio-Integrated Electronics** at the Simpson Querrey Institute for Bionanotechnology at Northwestern University, both lead internationally recognized researchers in the growing discipline of wearable technology. [Read about this project.](#)

Xiao-Di Tan, MD, has received an **RO1 award** from the National Institute of General Medical Sciences entitled "Mechanisms Underlying Disruption of Intestinal Epithelial Barrier in Critical Illness". The loss of gut barrier function takes place in critically ill patients, which contributes to the onset of multiple vital organ failure. To date, there is an urgent need to develop novel therapies for gut barrier dysfunction because few effective treatments are available. Says Tan, "In this project, we will specially address the molecular mechanism that underlies disrupting of gut epithelial barrier integrity under critical surgical circumstances, which will lead to the identification of novel molecular targets and will ultimately advance strategies for prevention and treatment of gut barrier dysfunction in patients with critical illness."

Appointments & Promotions



Congratulations to the Lurie Children's physicians and scientists who have been appointed to or promoted in **faculty positions at the Feinberg School**. In addition to seeing patients, our physicians engage in scholarly activities, teach or serve on committees; similarly, our scientists conduct research while pursuing other scholarly activities. Lurie Children's is proud of the commitment our faculty have to caring for patients and pursuing a healthier future for all children.

Professor

- Mark Adler, MD – Pediatrics (Emergency Medicine) and Medical Education
- Steven Boas, MD – Clinical Professor of Pediatrics (Pulmonary Medicine)
- Amir Kagalwalla, MD – Pediatrics (Gastroenterology, Hepatology and Nutrition)
- Ronald Kallen, MD – Clinical Professor of Pediatrics
- Cynthia LaBella, MD – Pediatrics (Academic General Pediatrics and Primary Care)
- Kathleen Malee, PhD – Psychiatry and Behavioral Sciences

Associate Professor

- Mariana Morais Cajaiba, MD – Pathology
- Leslie Caldarelli, MD – Pediatrics (Neonatology)
- Valeria Cohran, MD – Pediatrics (Gastroenterology, Hepatology and Nutrition)
- Reema Habiby, MD – Pediatrics (Endocrinology)
- Russell Horowitz, MD – Pediatrics (Emergency Medicine)
- Catherine Hunter, MD – Surgery (Pediatric Surgery) and Pediatrics
- Lisa Kuhns, PhD, MPH – Research Associate Professor of Pediatrics (Adolescent Medicine)

- Rishi Lulla, MD, MS – Pediatrics (Hematology, Oncology, Neuro-oncology, and Stem Cell Transplantation)
- Sameer Patel, MD – Pediatrics (Infectious Diseases)
- Maura Ryan, MD – Radiology
- Amod Sawardekar, MD – Anesthesiology
- Ravi Shah, MD – Anesthesiology
- Lisa Sorensen, PhD – Psychiatry and Behavioral Sciences
- Jennifer Strople, MD – Pediatrics (Gastroenterology, Hepatology and Nutrition)

Assistant Professor

- Eric Cheon, MD – Anesthesiology
- Bria Marielle Coates, MD – Pediatrics (Critical Care)
- Meghan Coghlan, MD – Pediatrics (Neonatology)
- Ann Gallagher Downey, MD – Pediatrics (Neonatology)
- Gustave Falciglia, MD – Pediatrics (Neonatology)
- Jessica Teresa Fry, MD – Pediatrics (Neonatology)
- Bessey Geevarghese, DO – Pediatrics (Infectious Diseases)
- Arika Gupta, MD – Pediatrics (Neonatology)
- Natalia Henner, MD – Pediatrics (Neonatology)
- Clayton Hinkle, PhD – Psychiatry and Behavioral Sciences
- Nazia Husain, MD – Pediatrics (Cardiology)
- Irini Kolaitis, MD – Pediatrics (Hospital-Based Medicine)
- Dennis Liu, MD – Urology
- Vanessa Ng, MD – Anesthesiology
- Mary Robbins, MD – Pediatrics (Neonatology)
- Lisa Simons, MD – Pediatrics (Adolescent Medicine)

Alonso appointed Medical Director of the Siragusa Transplantation Center

Estella Alonso, MD, has been appointed Medical Director of the **Siragusa Transplantation Center** at Lurie Children's. She looks forward to ensuring that each



Estella Alonso, MD, is Professor of **Pediatrics (Gastroenterology, Hepatology, and Nutrition)** and **Medical Social Sciences** at the Feinberg School.

transplant program sustains and grows as a leader in pediatric transplantation. The Transplantation Center consistently ranks among the top pediatric transplant centers in the nation.

Alonso has authored multiple papers examining survival, long term complications and recommendations for ongoing medical management of children following liver transplantation, and is recognized for her work in pediatric acute liver failure. She has held leadership roles in multiple NIH funded research consortia and since 2000 has sustained NIH funding for research in clinical aspects of pediatric liver disease and transplantation. Lurie Children's was one of the first pediatric liver programs in the country to offer a fourth year of intensive training in pediatric liver disease and has trained pediatric hepatologists who practice at top ranked transplant programs across the U.S.

The Siragusa Transplantation Center is home to five transplant programs: pediatric heart, kidney, liver, intestinal and stem cell transplant.

areas – Host-Microbial Interactions, Inflammation and Immunity Program – which aims to identify patient-specific immunologic therapies to improve health outcomes. His research is supported by the NIH and multiple foundations.

Seed received both his doctorate in microbiology and his medical degree from the University of Rochester. He was chief resident at the University of Michigan, followed by a fellowship in infectious diseases at Washington University. During his fellowship, he was the recipient of the prestigious Pediatric Scientist Development Program award.

Seed's prior appointment was at Duke University, where he served as an attending physician in Pediatric Infectious Diseases and was Associate Professor of Pediatrics, Molecular Genetics and Microbiology, and Surgery. He has authored over 50 peer-reviewed journal publications and book chapters, and has served as a reviewer on numerous NIH committees and academic journals. Seed is Professor of **Pediatrics (Infectious Diseases)** and **Microbiology-Immunology** at the Feinberg School.

Internationally Recognized Cancer Biologist Joins Lurie Children's

Xiao-Nan Li, MD, PhD, will join Lurie Children's in January 2018. He will assume the new role of director of Pediatric Xenograft Modeling at the Manne Research Institute. Li comes from **Baylor College of Medicine** in Houston. His expertise and substantial research funding will allow Lurie Children's to advance its Precision Medicine initiative through the development of animal models for preclinical drug screening and biological studies of pediatric tumors. Li received his MD and PhD degrees from Suzhou Medical College, Suzhou, China, and completed his postdoctoral research fellowship at Baylor College of Medicine. He actively participates in National Cancer Institute sponsored research consortia, including serving as chair of the High Grade Glioma Committee of the Pediatric Brain Tumor Consortium.

New Head of the Division of Infectious Diseases

Patrick Seed, MD, PhD, has accepted the position of Division Head of **Infectious Diseases** at Lurie Children's. Seed joined Lurie Children's in 2016 as an attending physician in Infectious Diseases, Associate Chief Research Officer for Basic Science Research and Children's Research Fund Chair in Basic Science at the Manne Research Institute. He will continue in his research role while assuming leadership of the division.

Seed's diverse research examines molecular mechanisms by which a child's immune system interacts with germs, including the body's own microorganisms, the microbiome. He is leading one of Lurie Children's research priority



Patrick Seed, MD, PhD



Do Medicaid managed care structures succeed in coordinating care?

Enrollment in Medicaid has increased significantly in recent years, and children are part of this trend. Medicaid managed care (MMC) is used by states to control costs and increase access to services. Care coordination is a key metric in MMC evaluation because it drives much of the proposed cost savings and may be associated with improved health outcomes and utilization. However, it is unknown if MMC actually delivers on its promise to coordinate care for children.

Rishi Agrawal, MD, MPH, a hospital-based medicine specialist at Lurie Children's, has been studying medically complex patients for years. "Children with medical complexity can have multiple health issues, chronic conditions, or other issues that make it difficult to manage their diseases. Good care coordination is extremely important for these patients to remain as healthy as possible," he explains.

Agrawal is the lead author on a study that evaluated the relationships between enrollment in two MMC structures – primary care case management (PCCM) and health maintenance organization (HMO) – and access to and receipt of care coordination by children. **The study was published in *Pediatrics*.**

Agrawal's biggest takeaway from the study is that the form of MMC made a difference in terms of care coordination. He says, "While the PCCM demonstrated both increased access to and receipt of care

coordination, the HMO structure was associated with lower access to and receipt of care coordination.

"Our results demonstrate a significant, national-level correlation between the form of MMC used by states and the odds that a child living within that state will have access to adequate care coordination and that he or she will receive care coordination when needed. This is especially important to the children with medical complexity whom I serve," he continues.

Agrawal points out that the study wasn't designed to capture specific reasons for these disparities. "We don't know why there are differences between these two structures. We also don't have answers yet to a critical question – Does access to and receipt of care coordination actually improve the health of children who receive it? We hope to expand on our studies with this objective in mind." One thing he is confident about, though. "Primary care case management seems to be a better option if we are interested in coordinating care. States should consider this when structuring their Medicaid programs," he says.

This study was conducted with researchers from Northwestern University and the University of Colorado. Rishi Agrawal, MD, MPH, is an attending physician in Hospital-Based Medicine at Lurie Children's and Associate Professor of **Pediatrics (Hospital-Based Medicine)** at the Feinberg School.

Rotational deformities of the tibia - also called tibial torsion - are common among children with spina bifida and cerebral palsy. In these and other conditions, surgery is often necessary to correct the deformities. Although these surgeries result in demonstrable clinical benefits to patients, the risk of complications and the need to perform additional surgeries to re-correct the defects are troubling to many pediatric orthopaedic surgeons.

In reviewing the existing literature on the topic, **Vineeta Swaroop, MD**, and colleagues were concerned that the percentage of complications and the need for re-operations may have been overstated because



Vineeta Swaroop, MD

outcomes in patients with a wide array of neuromuscular conditions had been grouped together. The team identified cases and stratified the cause of rotational deformities into groups, then compared two conditions: spina bifida and cerebral palsy.

Despite profound differences in the causes and disease processes of these conditions, the groups demonstrated a remarkable similarity in response to surgical management of tibial torsion in terms of complications and need for re-derotational osteotomy. A surgical technique previously published by the authors resulted in complication rates and need for re-surgery that were well within acceptable limits. The authors also found that the age at which such surgeries are performed is critical: younger patients tend to have more complications and need a follow up surgery as compared to older patients.

The **study was published** in the August issue of the *Journal of Children's Orthopaedics*. Swaroop is an attending physician in the **Division of Orthopaedic Surgery** at Lurie Children's and Assistant Professor of **Orthopaedic Surgery** and **Physical Medicine and Rehabilitation** at the Feinberg School. Her co-authors are from the University of California Los Angeles, the Feinberg School and the Shirley Ryan AbilityLab (formerly the Rehabilitation Institute of Chicago).



Ben Katz, MD

Ben Katz, MD, is the author of a chapter entitled "Epstein-Barr Virus (Mononucleosis and Lymphoproliferative Disorders)" in the 5th edition of **Principles and Practice of Pediatric Infectious Diseases**. The book is edited by Sarah S. Long, Charles G. Prober and Marc Fischer, and is published by Elsevier. Katz is an attending physician in the **Division of Infectious Diseases**, medical director of the **Travel Immunizations Program** and co-medical director of the **International Adoptee Program** at Lurie Children's, and Professor of **Pediatrics (Infectious Diseases)** at the Feinberg School.

The **Center on Obesity Management and Prevention (COMP)**, part of the Smith Child Health Research, Outreach and Advocacy Center at the Manne Research Institute, recently completed a study entitled "Health Service Utilization and Body Mass Index Changes in Children Attending Subspecialty Clinics at a Tertiary Children's Hospital: a Retrospective Cohort Study". Leading the study was **Kavitha Selvaraj, MD**, now Instructor of Pediatrics (**Academic General Pediatrics and Primary Care**) at the Feinberg School and at the time a third-year fellow in the **Division of Academic General Pediatrics and Primary Care** at Lurie Children's.

This study evaluated body mass index (BMI) trajectory over two years from children who were new to Lurie Children's subspecialty clinics. One of the preliminary findings is that obese patients with high health service utilization (more clinic visits and more subspecialties seen) did not decrease their BMI over the two-year period compared to obese patients with low health service utilization. An abstract from the study was accepted for the annual **ObesityWeek conference** in Washington, D.C., held in October. This project was supported through a Cooperative Research Agreement between Lurie Children's and the **Williams Heart Foundation**.



Kavitha Selvaraj, MD



Mary McBride, MD, MEd



Walter Eppich, MD, MEd

Medical Education Day Celebrates Feinberg Educators and Provides Teaching Tools

Northwestern Medicine News Center

by Will Doss, October 4, 2017

The seventh annual Medical Education Day was held September 29 and sponsored by the **Department of Medical Education**, **Northwestern Simulation** and the Feinberg Academy of Medical Educators (**FAME**).

The conference featured didactic lectures and activities on researching and improving medical education, the induction of 34 new Feinberg faculty members into FAME and the presentation of **Mary McBride, MD, MEd**, Assistant Professor of **Pediatrics (Cardiology)**, as the new associate director of FAME.

"I think Medical Education Day makes a statement of how important we believe the educational mission is at the Feinberg School," said **Walter Eppich, MD, MEd**, Associate Professor of **Pediatrics (Emergency Medicine)** and director of FAME. "Without the excellence of medical educators who work every day with our students and residents, we would not be producing high-quality physicians — so I appreciate that we pause and recognize educational excellence."

McBride and Eppich are also faculty in the Department of Medical Education.

The following Lurie Children's faculty members received the John X. Thomas, Jr. Best Teachers of Feinberg Award:

- **Ronit Lever, MD**, Instructor of Pediatrics (Hospital-Based Medicine)
- **Karen Mangold, MD, MEd**, '11 GME, Assistant Professor of Pediatrics (Emergency Medicine) and Medical Education
- **Kavitha Selvaraj, MD**, '15 GME, Instructor of Pediatrics (Academic General Pediatrics and Primary Care). [Read more.](#)

Combatting Obesity in Kids: Less Screen Time and More Vigorous Exercise

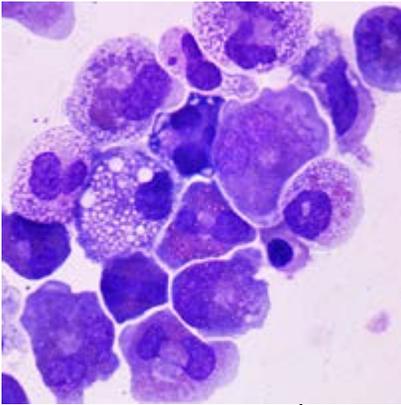
The battle against childhood obesity has been raging for a long time. Experts have cited many reasons for the growing number of overweight and obese kids: unhealthy diets, less exercise, more time spent on electronic devices, poor sleep patterns, etc. A new study is shedding some light on where obesity prevention and reduction programs should target their efforts.

Scientists at the University of Iowa and **Soyang Kwon, PhD**, at Lurie Children's, developed a powerful statistical model to analyze 14 years of prospective data in the Iowa Bone Development Study. They looked at height and weight adjusted for age, physical activity (PA), TV viewing (TV) and adiposity — total fat mass (FAT) and visceral adipose tissue mass (VAT), analyzing all the data to determine statistical significance.

"Children experience different patterns of growth, body composition, exercise and sedentary time depending on their developmental stage, so we needed to thoroughly account for these factors. By using the model, we were able to determine the contributions of PA, sedentary time (SED) and TV to adiposity throughout childhood," says Kwon.

The authors found that TV viewing was a clear contributor to increased body fat. Kwon explains, "Across levels of exercise and sedentary time, kids seem to develop fat mass and visceral adipose tissue mass when they watch more television. We think this has to do with more time spent in a sedentary activity, but also with the increased snacking that kids do when they are watching TV."

The findings, **published** in *Medicine & Science in Sports & Exercise*, indicate that the correct target for reducing childhood obesity is at least moderate-intensity PA, and that TV viewing has an even more powerful influence on adiposity than moderate-intensity PA. "Previously, it was thought that activity at any level was enough to deter adiposity, and that any kind of sedentary activity contributed to adiposity. Using these data, we now think that it's not enough for



Induced pluripotent stem cells produced in the Human iPS & Stem Cell Core.

In the News (continued from page 10)

childhood obesity prevention and reduction programs to encourage more exercise,” Kwon says. “These programs will need to emphasize more vigorous exercise and reduced screen time to make a real difference.”*

Novel RNA Discoveries Could Improve Stem Cell Research

Northwestern Medicine News Center

by Will Doss, August 24, 2017

A recently described variety of RNA closely associated with gene expression was found to be largely cell-type specific, raising the possibility this variety of RNA sequences could be used as a marker in stem cell research. The [study was published](#) in *Nature Structural and Molecular Biology* and co-authored by [Vasil Galat, PhD](#), director of the [Human iPS & Stem Cell Core](#) at the Manne Research Institute and Research Assistant Professor of [Pathology](#) at the Feinberg School.

Only about 20 percent of RNA codes for proteins, and the remaining 80 percent, called non-coding RNA, is thought to be involved in a variety of cellular processes. Non-coding RNA can be further divided into micro RNA and long non-coding RNA, and over half of long non-coding RNA is chromatin-enriched (cherNA), where chromatin loops around strands of RNA, which are then bound by RNA polymerase II near the sites of gene promoters. This physical proximity translates to functional connectivity, according to Galat.

Galat and colleagues discovered that the cherNA sequences are also specifically associated with cell specific genetic expression. “Because they are so well associated with a promotor region, they can be used as a predictor of the promotor region’s particular genes,” Galat said. “Once you see the cherNA expressed, you can judge the location of genes.”

There are several methods biologists currently use to locate gene promotor regions, but this method could be more reliable and precise, according to Galat. Now, the discovery that cherNA is cell-type specific has particularly tantalizing applications in his primary line of research: pluripotent stem cells.

Pluripotent stem cells are undifferentiated, meaning they could develop into almost any type of cell in the human body. It can be tricky to keep them in the pluripotent stage, which is why [Galat’s lab](#) was invited to collaborate with this University of Chicago-led project. “Our lab has a great deal of experience working with pluripotent cells,” Galat said. “These cells require experience to maintain. They are spontaneously differentiating all the time in culture.” [Read more.](#)

Rare Disease Experts: Worth the Cost?

excerpted from [Medium](#)

by Grace Niewijk, October 20, 2017

When you play sports or go for a run, your body needs extra oxygen and starts to feel hot. In response, your heart beats faster, your breath quickens, and you sweat to cool your body. But have you ever had to think about making those things happen? Chances are, you haven’t—you probably have a functioning autonomic nervous system.

Children with rare autonomic disorders lack the ability to adjust, or even to sense the need for adjustment. These children can stop breathing in their sleep, when automatic control is supposed to take over completely; they’ll turn blue when they try to run and play with their friends; they might run out into the snow with bare feet, risking frostbite, because snow doesn’t feel as cold to them.

Rare diseases that affect the autonomic nervous system can be confusing and difficult for nonexperts to diagnose, because they affect so many different organ systems in the body. But on the day their child finally receives a rare autonomic disease diagnosis, dozens of parents across the globe each year hear the same sentence: “You need to go to Chicago.”

The [Center for Autonomic Medicine in Pediatrics](#) (CAMP) at Lurie Children’s is a one-stop shop for children with these diseases. Without CAMP, these children and their families would spend their lives being shuttled between specialists, each of whom would treat only one symptom at a time. Centralized care not only improves efficiency but also helps individual children get the care they actually need. [Read more.](#)**

* Soyang Kwon, PhD, is Research Assistant Professor of [Pediatrics](#) at the Feinberg School. She is the senior statistician for the [Center on Obesity Management & Prevention](#), part of the Smith Child Health Research, Outreach and Advocacy Center at the Manne Research Institute. Kwon is a member of the [Center for Community Health](#) and the [Center for Behavior and Health](#), both part of the [Institute for Public Health and Medicine](#) at the Feinberg School.

** Grace Niewijk is a former CAMP summer student who is pursuing her undergraduate degree at Yale University. Grace studies molecular biophysics and biochemistry.