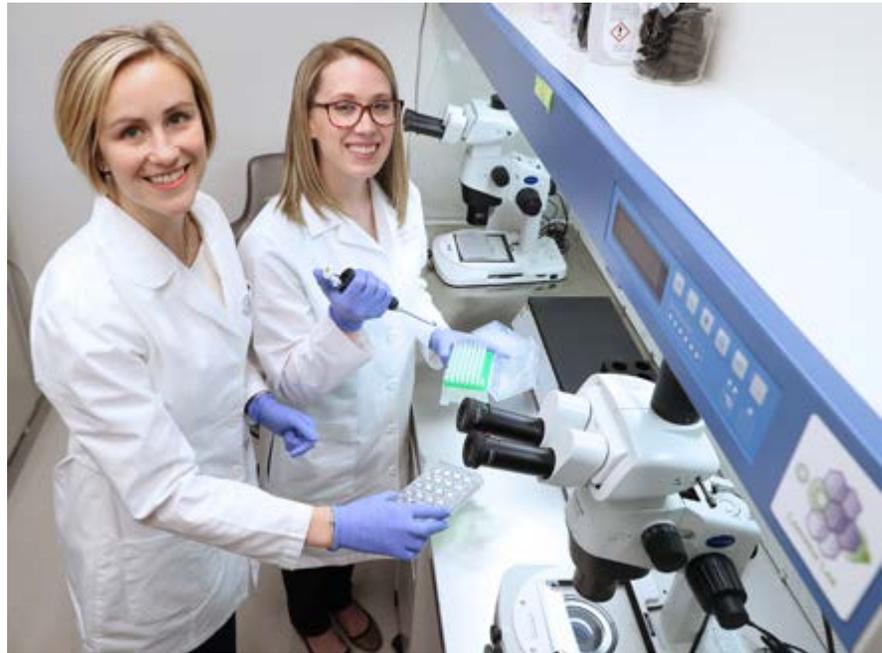


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Preserving Fertility and Hormone Balance After Therapy

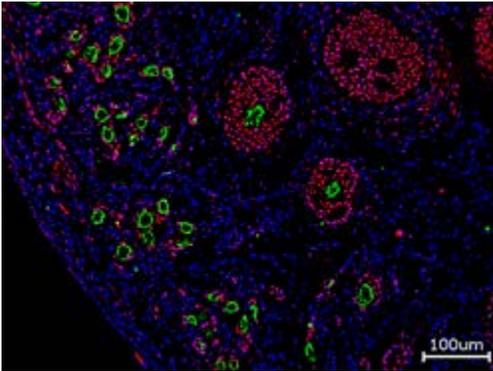


Monica Laronda, PhD (left) with lab manager Kelly Even. Photo: Jan Terry

Monica Laronda, PhD, came to Stanley Manne Children's Research Institute at Ann & Robert H. Lurie Children's Hospital of Chicago from Northwestern University in 2016 with a mandate to lead basic and translational research for the **Fertility & Hormone Preservation & Restoration Program**. One of a few pioneering programs in this field, the center's objective is to advance fertility options and more for the youngest patients. Babies and pre-pubescent children who receive certain treatments – such as therapies for cancer or rheumatologic diseases – could experience deficits to their sexual development or reproductive viability. As the program's research scientist, Laronda seeks to develop a patient-specific bioengineered ovary – what she calls a bioprosthesis ovary – to overcome these deficits.

In a **TEDx Talk** from 2016, Laronda explained why fertility preservation in childhood may be necessary: "Forty-three children per day are diagnosed with cancer, but fortunately 85 percent of them have survival out to five years, and many go on to enjoy normal lifespans. But there are off-target effects to cancer therapy, including to the ovaries or testes. Adults who received these therapies as children may be less likely than their siblings to get pregnant and produce sex hormones."

She stresses this last point: "The endocrinology of having an ovary is not just about fertility. Morbidities associated with reduced ovarian function can affect women's long-term health."



Ovary section stained with a nuclear stain (blue), marker for oocytes (DDX4, green) and marker for granulosa cells (supportive hormone-producing, FOXL2 red).

Monica Laronda, PhD, is Director of Basic and Translational Research for the Fertility & Hormone Preservation & Restoration Program at Lurie Children's, Warren and Eloise Batts Research Scholar at the Manne Research Institute, and Assistant Professor of Pediatrics at Northwestern University Feinberg School of Medicine.

The Fertility & Hormone Preservation & Restoration Program's members include specialists in Pediatric Surgery, Oncology, Endocrinology, Urology and Adolescent Medicine at Lurie Children's, and Obstetrics and Gynecology/ Reproductive Endocrinology and Infertility at the Feinberg School.

We want to be able to identify problems and help patients at the time of need." One example is the development of osteoporosis, which commonly affects post-menopausal women, but which could be avoided in younger patients if the production of sex hormones were restored.

One of Laronda's first and greatest challenges is to create a bioprosthetic ovary. Unlike prosthetics made exclusively from artificial materials, the replacement ovary needs to begin with a scaffold on which patient-derived substances can dock, thrive, and signal. "In the female reproductive system, there is a complicated interplay among the ovarian follicles and the pituitary gland," she explains. "The follicle is the centralized oocyte and the support cells that produce sex hormones in response to the pituitary." Not only that, the follicle grows to over 600 times its original size as it matures just before ovulation. "All of these dynamic interactions require a scaffold that is porous, allows nutrient flow and is bioactive," Laronda explains.

While she was a postdoctoral fellow under the mentorship of Teresa Woodruff, PhD, Laronda collaborated with Ramille Shah, PhD, and her group to successfully engineer a system that works in laboratory mice. They showed its effectiveness by seeding the scaffold with green fluorescent protein (GFP) tagged follicles and transplanting them into a recipient female whose ovaries were removed. "We were very excited to get a litter of green pups, which demonstrated that the mom ovulated, became pregnant and gave birth from our bioprosthetic ovary," she comments. [Read more](#) about results published on May 16 in *Nature Communications*.

Translating this success to humans will require many more steps. Says Laronda, "One of our priorities is to develop methods that will avoid re-introducing cancer cells back into the patient. We are also developing protocols to produce stem cells from patients that are then differentiated into ovarian hormone-producing cells." In addition, the program will need a way to identify fertility potential in pediatric patients. "Our colleague on the adult side, and founder of the [Oncofertility](#)

[Consortium](#) at Northwestern University, Woodruff has pioneered a lot of this research. She has shown, among other things, that the level of AMH – anti-Mullerian hormone – can be detected within a small blood spot. If this also proves to be the case in children, we can check girls, including those in the peri-pubertal and pubertal ages, on a regular basis to determine if and when we should take action to restore their hormones," she says.

More exciting research is on the horizon, including the curation and mining of a patient registry – which, as Laronda points out, will allow a number of questions to be asked and answered. In addition, she envisions mentoring opportunities to train the next generation of fertility specialists. "I think that our trainees will welcome projects that allow them to develop innovative web apps or to design surveys. They can be our ambassadors to get the word out to our clinics and our families that these services are available," she says.

Laronda credits her colleague and "a real champion," [Erin Rowell, MD](#), Director of the Fertility & Hormone Preservation & Restoration Program, who has garnered support for expansion and innovation within basic and clinical research from other units. These areas include the Divisions of Hematology, Oncology, Neuro-oncology and Stem Cell Transplant, Endocrinology, Gender and Sex Development, Urology, and the Department of Surgery at Lurie Children's. Says Laronda, "Basic science is fundamental and completely necessary, and having that link to the hospital is what motivates me. We are able to build on concepts that impact human health when we go from the bench to the bedside and back to the bench. Erin and I have different perspectives, which allows us to bounce ideas off of each other. We are both passionate about getting to the same end points with this program, which is to offer safe ways for preserving and restoring fertility and hormone function in pediatric patients."

Funding comes from the Warren and Eloise Batts Research Scholar endowed position, Burroughs Wellcome Fund Career Award at the Scientific Interface, a Faculty Practice Plan grant, the National Institutes of Health, the Children's Research Fund, the Founders' Board and Mary and Ralph Gesualdo.

Chief Research Officer's Message



Thomas P. Shanley, MD, is Chairman of the Department of Pediatrics
Chief Research Officer, Stanley Manne Children's Research Institute
Founders' Board Centennial Professor in Pediatrics
Ann & Robert H. Lurie Children's Hospital of Chicago
Northwestern University Feinberg School of Medicine

Discovery

RESEARCH
at Stanley Manne Children's Research Institute

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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.

Please send questions and comments to Peggy Murphy:
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Celebrating our scholars

I want to take this opportunity to congratulate those who participated in **Research Scholar Day**, hosted by Lurie Children's and the Manne Research Institute on May 11. Our scholars at the graduate student, postdoctoral associate, clinical fellow, research technician and resident levels presented eighty-six posters on research in areas spanning the translational research spectrum and ranging from cancer biology to simulation to medical education.

This day would not have been a success without the participation of faculty judges who listened to poster presentations, asked questions and scored the posters on their scientific merit, hypotheses and experimental design. Many thanks to Nancy Irizarry, Melissa Kroll, Denise Lilly, Brad Lynk and Peg Rainey for organizing and running the event to perfection.

At the poster awards announcement, **Jennifer Trainor, MD**, congratulated all presenters "for a very high level of scholarship, insight, and polish." In addition to Dr. Trainor, Drs. Meredith Bone, Pat Seed and Phil Iannaccone were also instrumental to the successful planning and execution of the day. In addition, many thanks to our prize committee members: Drs. Bone, Trainor and Seed as well as Drs. Susanna McColley, Estella Alonzo, and Mark Adler and the forty faculty members who served as reviewers.

The keynote address was presented by **Margaret Rita Karagas, PhD**, director of the Children's Environmental Health and Disease Prevention Research Center and the Center for Molecular Epidemiology at the Geisel School of Medicine at Dartmouth. Karagas' research encompasses studies focusing on the etiology and prevention of human cancers, as well as adverse pregnancy and children's health outcomes. Her keynote, "Identifying the Human Health Impacts of Early Life Exposures: A Collaborative Investigation," was a fascinating discussion of the impact of arsenic and other toxic substances in food and water on the health of pregnant women, babies and children. This is clearly an area of rapid development as we continue to unravel the environmental consequences on gene expression through epigenetic modifications.

Research Scholar Day 2017 Award Winners

Resident Research Award: "Lollapalooza Longitudinally: An Annual Binge Drinking Epidemic" | Nina Alfieri, MD | Pediatric Residency Program | Mentor: Robert R. Tanz, MD

First Year Fellow Basic Research Award: "Cord Blood Cleaved Fibroblast Growth Factor 23 (cFGF23) is Increased with Intrauterine Growth Restricted (IUGR)" | Andrew Franklin, MD | Neonatology | Mentor: Karen Mestan, MD

First Year Fellow Clinical Research Award: "National and Local Trends in Intravenous Acetaminophen Use in Pediatric Hospitals" | Kate Lucey, MD | Hospital Based Medicine | Mentor: Craig Garfield, MD

Second Year Fellow Basic Research Award: "A siRNA Approach for Targeting Immunosuppressive IDO1 in Pediatric Diffuse Intrinsic Pontine Glioma" | Alicia Lenzen, MD | Hematology, Oncology, Neuro-oncology and Stem Cell Transplant | Mentor: Derek Wainwright, PhD

Second Year Fellow Clinical Research Award: "Universal Screening for Toxic Stress During Well-Child Visits: The Addressing Social Key (ASK) Questions for Health Study" | Kavitha Selvaraj, MD, MAEd | Academic General Pediatrics and Primary Care | Mentor: Barbara Bayldon, MD

Third Year Fellow Basic Research Award: "Targeting GLI1 via PI3k/mTOR Inhibition in Medulloblastoma and Ewing Sarcoma" | Jessica Clymer, MD | Hematology, Oncology, Neuro-oncology and Stem Cell Transplant | Mentor: Leonidas Platanius, MD, PhD

Third Year Fellow Clinical Research Award: "Risk of Pediatric Intensive Care Unit Admission in Anthracycline-Exposed Oncology Patients" | Katie Wolfe, MD | Critical Care | Mentor: Lauren E. Marsillio, MD

Graduate Student Research Award: "Pathogenic UBQLN2 Deregulates mTOR Kinase Signaling by Attenuating its Degradation to Affect Neuronal Development and Disease" | Brittany Edens, BA | Developmental Biology | Yong-Chao Ma, PhD

Research Tech Award: "Anti-inflammatory Nanomolecules to Modulate Inflammation in Crohn's Disease" | Matthew Bury, MS | Developmental Biology | Mentor: Arun Sharma, PhD

Postdoc Research Award: "Functional Analysis of KCNT1 Mutation in Epileptic Encephalopathy" | Tracy Gertler, MD, PhD | Neurology | Mentor: Alfred L. George, Jr., MD

Judges' Award: "Rho Kinase Inhibitors as a Novel Therapeutic for NEC" | Justyna Grothaus, MD | Neonatology | Mentor: Catherine Hunter MD

Judges' Award: "Predicting Survival after Pediatric Cardiac Extracorporeal Membrane Oxygenation" | Diana Geisser, MD | Cardiology | Mentor: Bradley Marino, MD, MPP, MSCE



Ma laboratory (from left): Yongchao Ma, PhD, Brittany Edens, Nimrod Miller, PhD, and Han Shi, PhD.

Han Shi, a graduate student in the laboratory of Yongchao Ma, PhD, presented his public thesis defense on April 12. The title of his seminar was "Sirtuin-dependent protein deacetylation regulates mitochondrial oxidative stress and dopaminergic neuron degeneration." Han completed his PhD work in the Walter S. and Lucienne Driskill Graduate Program in Life Sciences at Northwestern University. Says Ma of his first graduate student, "Han independently developed a project on how aging affects dopaminergic neurons in Parkinson disease. During his time in my lab, Han has been a co-author on three publications and has won numerous awards." In addition to receiving an award of excellence at the research institute's Biomedical Research Symposium, Han was named a Children's Research Fund Outstanding Graduate Student and received an outstanding presentation award at a Northwestern University symposium. Han will join a biotech company in San Diego.

The Ma laboratory recently published a paper in *Human Molecular Genetics* on Han's thesis topic. The study results suggest that an age-related decline in Sirtuin 3 (Sirt3) protective function is a major factor underlying increasing mitochondrial oxidative stress and loss of substantia nigra dopaminergic neurons in Parkinson disease. The studies were conducted with David Gius, MD, PhD, Professor of Radiation Oncology and Pharmacology; Paul Schumacker, PhD, Professor of Pediatrics, Cell & Molecular Biology and Medicine;

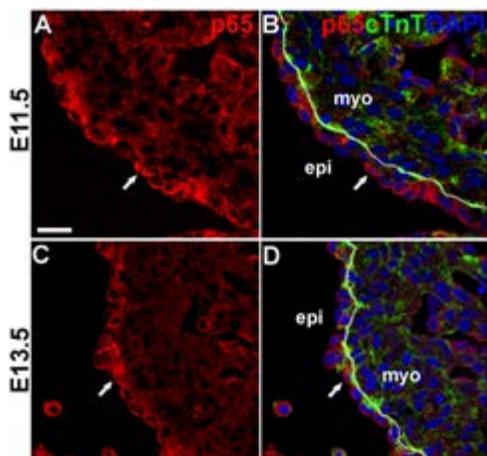
and D. James Surmeier, PhD, Nathan Smith Davis Professor of Physiology, at the Feinberg School. Yongchao Ma is Assistant Professor of Pediatrics, Neurology - Ken and Ruth Davee Department, and Physiology at the Feinberg School, and Ann Marie and Francis Klocke, MD Research Scholar at the Manne Research Institute. He is a member of the Developmental Biology Program at the research institute.

The 13th Annual Lewis Landsberg Research Day broke records with more than 400 abstract presentations that showcased the diversity of innovative research taking place at the Feinberg School. Manne Research Institute scientists were well represented among the poster presentations in four categories: Basic Science (9 posters), Clinical Science (13 posters), Education (1 poster) and Public Health (5 posters). Research Day is a campus-wide Feinberg School event to promote faculty and trainee development through the sharing of exciting research and conversation with colleagues.



Elizabeth Martinez, BA, and Danica Aniciete, MS (pictured from left), at Research Day. They presented a poster entitled: "Improving Communication in the PICU: PICU Supports Pilot Study" (principal investigator: Kelly Michelson, MD, MPH). Michelson is an attending physician in the Division of Critical Care at Lurie Children's, Associate Professor of Pediatrics, Director of the Center for Bioethics and Medical Humanities, and Julia and David Uihlein Professor of Bioethics and Medical Humanities at the Feinberg School.

Repairing the Damaged Heart



NF- κ B p65 is expressed in embryonic epicardium. From: Li Y, Urban A, Midura D, Simon H-G, Wang QT (2017) Proteomic characterization of epicardial-myocardial signaling reveals novel regulatory networks including a role for NF- κ B in epicardial EMT. *PLoS ONE* 12(3): e0174563. <https://doi.org/10.1371/journal.pone.0174563>. Image by Yanyang Li.

*The **secretome** is defined as “the totality of secreted organic molecules and inorganic elements by biological cells, tissues, organs, and organisms.” Wikipedia (accessed 5/1/2017).

Hans-Georg Simon, PhD, is a member of the **Developmental Biology Program** at the Manne Research Institute and Associate Professor of **Pediatrics** at the Feinberg School. This work was funded by a Catalyst Award of the Chicago Biomedical Consortium with support from the Searle Funds at The Chicago Community Trust.

Researcher **Hans-Georg Simon**, PhD, studies heart development in the embryonic stages of life, and heart repair in adults. His aim is to understand regulatory pathways that will lead to the correction of congenital heart defects (CHD) and the repair of damaged heart tissue.

In the U.S., heart attack survival rates are improving year to year, but the damaged muscle tissue remains compromised by a scar. The loss of muscle can have severe consequences over time, often leading to congestive heart failure and death. In addition, CHD, the most common type of birth defect, can significantly alter the long-term health of children born with these defects. Since the infarcted or structurally abnormal heart cannot fix itself, Simon’s goal is to replace the damaged tissue with viable muscle that is normal in its contractile and conductive properties.

As the heart develops, the epicardium – the outer layer of cells that cover the heart muscle – gives rise to progenitor cells that migrate into the myocardium and differentiate into multiple cell types, including cardiomyocytes – the heart muscle cells. This process is called epithelial-to-mesenchymal transition, or EMT. Both the epicardium and myocardium produce and secrete factors that regulate the EMT process and subsequent differentiation of epicardial-derived cells. In addition, epicardium-derived signals stimulate cardiomyocyte proliferation and coronary blood vessel formation within the myocardium. These developmental processes stop shortly after the first month of life, leaving the adult heart unable to repair damaged tissue. Recent data revealed that after heart attack the epicardium can become partially re-activated, producing factors that promote blood vessel formation, reduce infarct size and improve short term heart function.

Simon notes, “Our approach builds on this paradigm of resident-cell-based cardiac repair, and integrates novel genetic tools with mass spectrometry. The

project holds the potential for the development of new treatments to enhance regenerative wound healing in human hearts.”

The **Simon laboratory** teamed up with the lab of Q. Tian Wang, PhD, at the University of Illinois at Chicago, to identify novel protein targets for the stimulation of epicardial cells for resident-cell-based cardiac repair. The objective of the collaboration is to systematically identify protein factors that mediate signaling between the layers of epicardial and underlying myocardial cells. “We think that the secretome* of embryonic epicardium and neighboring myocardium contains factors that are critical for progenitor cell generation, but are missing in the adult heart. We are using a direct proteomic approach to identify and evaluate the activity of selected factors,” says Simon.

Drawing from the strengths of both labs, the team of graduate students and research associates integrated a unique set of methodologies. These include liquid chromatography tandem mass spectrometry to analyze conditioned media of co-cultured embryonic epicardial and myocardial cells. To functionally link specific protein factors with epicardial activity, they are determining conserved expression of factors in relation to space and time in embryonic chicken and mouse hearts with different levels of epicardial activity. The expression profiles and pathway associations of the identified proteins are helping to narrow down candidate proteins for further functional characterization.

The results of their first functional characterization were **published this March** in the journal *PLoS ONE*. “Our work identified a growth factor, NF- κ B, that plays a yet unknown essential role in cardiac EMT. To the best of our knowledge, no other group has conducted a comprehensive characterization of the embryonic epicardium-myocardium secretome to date,” comments Simon. He continues, “Using these tools and the knowledge we acquire, our group hopes to further define factors that can be targeted to enhance the repair of damaged human hearts.”

Awards & Honors



Dana Thompson, MD

This year marks the centennial of the American Broncho-Esophagological Association (ABEA). Dana Thompson, MD, division head of Otolaryngology-Head & Neck Surgery at Lurie Children's, is the president of the ABEA and has the distinct honor of serving in this role in the association's 100th year. She continues the legacy of all four prior division heads of Otorhinolaryngology: Lauren Holinger (ABEA president, 1992); Joyce Schild (1979); Gabriel Tucker, Jr. (1973); and Paul Holinger (1948). Thompson holds the Lauren D. Holinger, MD Professorship in Pediatric Otolaryngology and is Professor of Otolaryngology - Head and Neck Surgery at the Feinberg School.

Kathleen Billings, MD, James Schroeder Jr., MD, and Dana Thompson, MD, have been invited to speak and participate at the International Federation of Oto-Rhino-Laryngological Societies (IFOS) World Congress this June in Paris, France. IFOS is the world's largest gathering of otolaryngologists. It has evolved to deal on a global basis with the problems of people with otorhinolaryngological disease by means of an active secretariat and committee structure, lobbying the World Health Organization, leading the global program for hearing loss prevention, and providing interchange between centers. IFOS has a continuing medical educational role, has developed a model undergraduate curricula and has recently begun CME conferences between congresses. Billings and Schroeder are attending physicians in the Division of Otolaryngology-Head & Neck Surgery at Lurie Children's, and Associate Professors of Otolaryngology - Head and Neck Surgery at the Feinberg School.

Twenty-six practices in the Pediatric Practice Research Group (PPRG) participated in a study funded by the Center for Community Health Research Seed Grant, "Hypertension in premature infants in the pediatric office." Benjamin Kornfeld, MD, of North Suburban Pediatrics and a member of the Division of Academic



General Pediatrics and Primary Care at Lurie Children's, Gal Finer, MD, PhD, and PPRG director Adolfo Ariza, MD, documented screening practices and incidence of abnormally elevated blood pressure measurements in premature infants seen in community sites. Reports to participating practices, which were designed in collaboration with community clinicians, included study results and information needed to implement practice change. The study team plan assessed the impact of the reports on practice behavior. Finer is an attending physician in Kidney Diseases at Lurie Children's and Assistant Professor of Pediatrics at the Feinberg School. Ariza is co-director of the Center on Obesity Management and Prevention (COMP) and Research Associate Professor of Pediatrics at the Feinberg School. Both PPRG and COMP are part of the Smith Child Health Research Program at the Manne Research Institute. [Read more.](#)

Robert Liem, MD, has received a 5-year R01 grant from the National Heart, Lung, and Blood Institute (NHLBI) for a multicenter study entitled: "The pro-inflammatory effects of acute exercise in children with sickle cell anemia." These children suffer from complications that lead to significantly reduced physical functioning and exercise capacity. As a result, they may be advised to exercise less often or with lower intensity than children without SCA. Liem's long term goal is to address the safety and health impact of regular exercise in these children. He says, "For the first time in SCA, our group of investigators in hematology, exercise science and exercise immunology will provide the critical prerequisite toward developing evidence-based guidelines for exercise prescription as a transformative strategy to maintain physical functioning and health in children with SCA." Liem is director of the Comprehensive Sickle Cell Program and an attending physician in the Center for Cancer and Blood Disorders at Lurie Children's. He is also Associate Professor of Pediatrics at the Feinberg School.



Walter Eppich, MD, MEd, Associate Professor of Pediatrics in the Division of Emergency Medicine and of Medical Education, has been named a member of the inaugural group of fellows for the Society for Simulation in Healthcare (SSH) Academy. Fellows are elected based on their outstanding contributions to the development of SSH and the field of healthcare simulation.

Young adults with uncomplicated epilepsy fare as well as their siblings

Lurie Children's [news release](#) April 25, 2017

A 15-year follow-up study of young adults with epilepsy found that those with uncomplicated epilepsy who were seizure-free for five years or more did as well as their siblings without epilepsy in measures of education, employment, family arrangements and driving status. Youth with complicated epilepsy had worse social outcomes and were less likely to drive, even if living without seizures. Results were [published in *Epilepsia*](#).

"So far there has been conflicting data on whether adults with uncomplicated childhood-onset epilepsy have worse social outcomes compared to people without epilepsy," said senior author [Anne Berg, PhD](#). "Our study provides further evidence that children growing up with uncomplicated epilepsy who stay seizure-free have a favorable prognosis. However, if they do not achieve five-year seizure remission, young adults with uncomplicated epilepsy are less likely to drive and graduate high school. They also tend to be less productively engaged and not live independently. These results show how critically important it is to control seizures."

In the study, patients with epilepsy were designated as having "uncomplicated" disease if they had no other neurologic impairments, no intellectual disability and no history of conditions such as meningitis or stroke that might have caused epilepsy. Researchers conducted structured interviews with 361 individuals with epilepsy and 173 siblings without epilepsy to compare their social outcomes.

"The fact that teens with uncomplicated epilepsy who were seizure free finished high school at rates comparable to their siblings might be a reflection of the special education services many of them have received," said Berg, who is Research Professor of Neurology at the Feinberg School. "These services can have tremendous impact."

This study was supported by a grant from the [National Institutes of Health](#).



Both low and high birth weight linked to fatty liver disease in children

Lurie Children's [news release](#) April 20, 2017

A study [published in the *Journal of Pediatrics*](#) suggests that children born with lower or higher weight than normal may be at increased risk for developing nonalcoholic fatty liver disease (NAFLD). These children also were at higher risk for more severe disease, but in different ways. Advanced scarring of the liver was associated with low birth weight, while more inflammation was linked to high birth weight. The study is the first to characterize the relationship between high birth weight and NAFLD.

"With the obesity epidemic, we are seeing more babies with high birth weight than ever before," said co-author [Mark Fishbein, MD](#), an attending physician in the Division of Gastroenterology, Hepatology and Nutrition at Lurie Children's. "Our study shows that these kids are more likely to have serious liver damage by the time they are teenagers."

NAFLD is the most common cause of chronic liver disease in children and typically is diagnosed in early adolescence. "Being able to identify at birth infants at risk for severe liver disease will help initiate earlier interventions," said Fishbein, who is Associate Professor of Pediatrics at the Feinberg School. "Maintaining a healthy weight is the main strategy for preventing NAFLD in children."

The multicenter study included children who were enrolled in the database of the [National Institute of Diabetes and Digestive and Kidney Diseases \(NIDDK\)](#) NASH Clinical Research Network and were diagnosed with NAFLD. Birth weights were categorized as low, normal or high, and compared with the birth weight distribution in the general U.S. population. The severity of liver disease was assessed by birth weight category.

The study was supported by the NIDDK and the [National Center for Advancing Translational Sciences](#).

In the News (continued from page 7)

Transgender youth face major barriers to fertility preservation

Lurie Children's [news release](#), March 29, 2017
Few transgender adolescents opt to pursue fertility preservation, according to a report [published in the *Journal of Adolescent Health*](#). While all patients were counseled about available options for fertility preservation prior to initiating hormones for medical transition, only 12 percent chose to see a fertility specialist and less than 5 percent completed fertility preservation procedures.

Lead author [Diane Chen, PhD](#), and colleagues identified the major barriers to fertility preservation in transgender youth as cost, invasiveness of procedures and reluctance to delay initiating hormone therapy for medical transition. "Not surprisingly, procedure invasiveness was a frequent concern for transgender men, who are assigned female at birth and identify as male. They often experience significant body dysphoria that can be exacerbated by fertility preservation procedures," said Chen, a pediatric psychologist with the Gender & Sex Development Program at Lurie Children's and Instructor in the Department of Psychiatry and Behavioral Sciences at the Feinberg School.

The study involved a retrospective chart review of all patients initiating hormones with the Gender & Sex Development Program between July 2013 and July 2016. Out of 105 transgender adolescents, 13 saw a fertility specialist for formal consultation and five underwent fertility preservation.

"Anecdotally, we have heard from a few transgender youth after starting hormones, when they are more comfortable in their bodies, that they felt more ready to consider becoming parents in the future," said Chen. "Better understanding how these youth approach fertility-related decision-making and what information they may need from providers is important, which is why we are currently recruiting for a study looking at fertility-related knowledge, attitudes, and beliefs among transgender youth and their parents," she said.

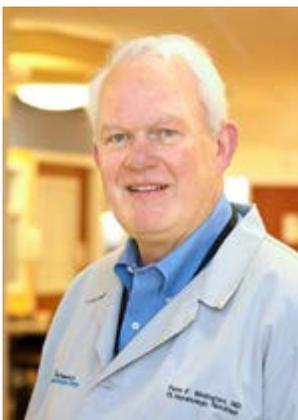
Mental health workers tackle unseen effects of Chicago violence

[WTTW Chicago Tonight](#), March 30, 2017

The staggering violence in some Chicago neighborhoods can't be measured by statistics alone. There are lingering mental health effects on those impacted by the shootings and deaths, and Chicago researchers are reporting some disturbing findings related to psychological trauma. One study found that cases of post-traumatic stress disorder are especially high among women in neighborhoods with high rates of violence. Eddie Arruza of WTTW Chicago Tonight took a closer look at the issue with JaShawn Hill, a social worker and family support specialist at Chicago Survivors; Inger Burnett-Zeigler, a clinical psychologist and Assistant Professor of Psychiatry and Behavioral Sciences at Northwestern Medicine; and Tara Gill, PhD, a clinical psychologist at Lurie Children's [Center for Childhood Resilience](#). [See the video here.](#)

Peter Whittington, MD, retires

After a distinguished career of 45 years as a physician, and 20 years at Lurie Children's (formerly Children's Memorial), Peter Whittington, MD, in the [Division of Gastroenterology, Hepatology and Nutrition](#), has retired. In 1997, Children's Memorial recruited Whittington to create and launch a world-class pediatric transplant program. Envisioning a unique partnership, he assembled top medical and surgical transplant teams to care for patients. In 1997, the first liver transplant was performed at Children's Memorial. In 1999, Dr. Whittington received a significant funding commitment from the Siragusa family and established the [Siragusa Transplantation Center](#). The Center ranks among the top pediatric transplant centers in the country, not just in volume, but also in patient survival rates. Dr. Whittington has been a tremendous mentor to many young researchers and is known for his scientific expertise in rare and often lethal liver diseases. [Read this touching tribute to Dr. Whittington.](#)



Peter Whittington, MD, also held the Sally Burnett Searle Professorship in Pediatrics and Transplantation at the time of his retirement.



From left: Children's Ball Co-chairs John Simpson, Laura Keidan Martin and Craig Martin unveiled the 2017 annual campaign theme on May 9.

About the Children's Research Fund

The Children's Research Fund has firmly established itself as one of Chicago's leading philanthropic organizations dedicated to funding basic and clinical medical research. Over the years, Children's Research Fund support has led to advanced investigation in cancer, heart disease, genetics, microbiology and neonatology. Since its affiliation with Ann & Robert H. Lurie Children's Hospital of Chicago in 1991, the Children's Research Fund has contributed more than \$70 million in support of research conducted at the Manne Research Institute. To get the latest information on Children's Research Fund events and fundraising campaigns, please visit www.childrensresearchfund.org.

Planning for 2017 Children's Ball underway

Planning for the 2017 Children's Ball formally kicked off on May 9 with a reception at the Arts Club and the energy level in the room was high. Over cocktails and hors d'oeuvres, Lurie Children's President and CEO Patrick M. Magoon made a compelling case for supporting research, the 2017 Children's Ball co-chairs were introduced and the theme for the annual campaign and Ball was unveiled.

Meet the 2017 Children's Ball Co-chairs

This year's Children's Ball co-chairs are a trio of enthusiastic supporters of pediatric medical research and the Manne Research Institute. All are active in the community and serve on nonprofit boards and all, coincidentally, are graduates of Harvard Law School. They are parents and understand the importance of high-quality pediatric healthcare and research.

- Laura Keidan Martin is prominent in the legal community as the national head of health care practice for Katten Muchin Rosenman, where she serves as a member of the firm's Board of Directors and Executive Committee. She has worked as outside counsel with Lurie Children's for several years.

- Craig Martin is the Chair of Jenner & Block's Litigation Department and is a member of the firm's Policy Committee.

- John Simpson is a Partner at Broadhaven Capital Partners in Chicago, an international merchant banking firm and growth equity investor. He serves on the Lurie Children's Medical Center board.

Theme unveiled for December 2 Children's Ball

Laura Keidan Martin spoke on behalf of the co-chairs to reveal and explain the campaign's theme. "Stories: Rewriting the Possibilities" is the theme they chose to reflect and encompass all the stories made possible for patients and families thanks to medical research and support from donors. The theme recognizes the role that research plays in opening new possibilities and changing outcomes for patients. The co-chairs are already rewriting some possibilities for fundraising, crediting their naturally competitive natures with significant early fundraising success: the annual campaign is already nearing the \$1 million raised mark.

For more information about the Children's Ball, please [visit the website](#) or contact [Katie Cerone](#) at 312.227.7299 or via email.

Children's Research Fund Members will Move for the Kids on June 10

For the fifth consecutive year, the Children's Research Fund is fielding a team for Move for the Kids Walk/Run 5K on Chicago's lakefront, on Saturday, June 10. It's a fun opportunity to join with other Children's Research Fund members and friends and family to run or walk in support of the Children's Research Fund's current fundraising commitment. This year's team is captained by [Devanee Washington](#). Email her for information about joining the team.



Susanna McColley, MD, is an attending physician in the Division of Pulmonary Medicine at Lurie Children's; Associate Chief Research Officer for Clinical Trials at the Manne Research Institute; and Associate Clinical Director for Child Health at the Translational Sciences Institute and Professor of Pediatrics at the Feinberg School.

Revised guidelines on the diagnosis of cystic fibrosis to help physicians

Cystic fibrosis (CF) is genetic disease that affects approximately 1 in 4,000 newborns in the U.S. each year. As of 2010, all U.S. states are performing newborn screening (NBS) for CF in order to diagnose and start treatment early. Babies who test positive receive confirmatory tests: those that show the level of sweat chloride concentration, and genetic testing to confirm mutations in the gene for the CF transmembrane conductance regulator (CFTR).

Although many screened infants can be clearly diagnosed using these tests, the results may prove inconclusive, or yield no evidence of the disease. Physicians without specialized knowledge about CF are often the first to receive abnormal NBS results, and need information about next steps.

In recent years, less common CFTR mutations have been elucidated, and some don't correlate neatly with symptoms and levels of disease in affected individuals. Experts also discovered that some CF-related conditions have different names based on country of diagnosis, and that the original guidelines are not being used consistently.

To improve diagnosis and achieve standardization in definitions worldwide, the Cystic Fibrosis Foundation convened an international committee of experts to develop clear and actionable consensus guidelines on diagnosis, and to clarify diagnostic criteria and terminology for associated disorders. The consensus statements resulting from the committee's deliberations are published in the *Journal of Pediatrics*.

Says Susanna McColley, MD, Associate Director of the CF Center at Lurie Children's, "It's most important for physicians to be aware of the changes in the diagnostic criteria, so that they are diagnosing and treating patients with CF as early

as possible, and avoiding treatment of individuals who don't need it. In cases where the diagnosis is unclear, we strongly encourage physicians to consult with experts at CF centers. We have trained clinicians and staff members who are ready to help with diagnosis and treatment." McColley served on the consensus committee and is a co-author on two of the resulting publications.

Overuse injuries more common in kids who specialize in individual sport

Young athletes who specialize in an individual sport are at higher risk for overuse injuries compared to those who focus on a single team sport, according to a study published in *The Physician and Sportsmedicine*.

"Kids in an individual sport usually start specializing at a younger age and tend to spend more hours per week training than those in team sports, which might explain why we see a greater proportion of overuse injuries among these athletes," said senior author Cynthia LaBella, MD, Medical Director of the Institute for Sports Medicine at Lurie Children's and Associate Professor of Pediatrics at the Feinberg School.

More than 25 percent of the young athletes enrolled in the study reported participating in a single sport and training in that sport more than eight months of the year. Sports with the highest proportion of single sport specialized athletes – tennis, gymnastics and dance – also had the highest rate of serious overuse injury. The youngest age of sports specialization was seen in gymnastics, dance and soccer.

"Better understanding of the relationships between sports specialization and injury risk can help us design more effective injury prevention strategies," said LaBella. "Our data from previous studies suggest that young athletes specializing in individual sports may reap the greatest benefits from preventive neuromuscular training." The study was funded by the American Medical Society for Sports Medicine Foundation.



Cynthia LaBella, MD

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Charlene Wong, MD, MSHP, is Assistant Professor of Pediatrics and a health policy researcher at Duke University.

Pediatric specialty physicians more likely to be missing from ACA provider networks

Concerns have been raised about patient access under plans in the Patient Protection and Affordable Care Act (ACA) because of limited or narrow physician networks. As of now, no studies have examined the supply and geographic distribution of pediatric specialty physicians in these networks.

In a publication appearing in *Pediatrics*, Charlene Wong, MD, MSHP, Kristin Kan, MD, MPH, MSc, and colleagues collected and

analyzed data from the ACA silver-level health insurance plans to describe the physician networks of specialists covered by the plans. By quantifying networks into categories, they were able to identify “narrow networks” – those with no or limited numbers of physicians. They also categorized physicians into specialties, such as pediatric cardiology and adult cardiology, and determined the availability of those specialists in the networks. The findings show that narrow networks were more prevalent among pediatric than among adult specialty providers. In addition, the proportions of networks where no specialists were included, even if they practiced in the area covered, were significantly higher for all pediatric than adult specialties except nephrology.

Wong, who conducted this research as an Adolescent Medicine fellow at the Children’s Hospital of Philadelphia and a Senior Fellow at the Leonard Davis Institute of Health Economics at the University of Pennsylvania, says, “Even before the ACA was adopted, narrow networks were being used as a way to control healthcare costs. We didn’t know to what extent the increase in narrow networks might affect pediatric compared to adult healthcare access until we analyzed the data. Our hope is that these results catalyze a policy discussion around network adequacy standards.”

“Studies such as ours show that there are

implications to how networks are designed. Children, particularly those with chronic medical conditions, have unique needs when it comes to access to pediatric specialists through the health insurance marketplace,” said Kan. “We are concerned that referring physicians might not recognize that pediatric specialty care may only be available to some families out of network, leading to considerable out-of-pocket costs. It is also critical for families to have tools to evaluate network size and access when shopping for health insurance plans so that they are able to make the right decisions regarding coverage.”

The authors believe that children’s access to healthcare should be included in broader health policy discussions moving forward. “The availability of pediatric providers in any network, whether it be employer-sponsored insurance, a public insurance program, or the next generation of individual marketplaces under the Trump administration, is critical to ensuring high quality healthcare for our country’s children and youth,” said Wong.

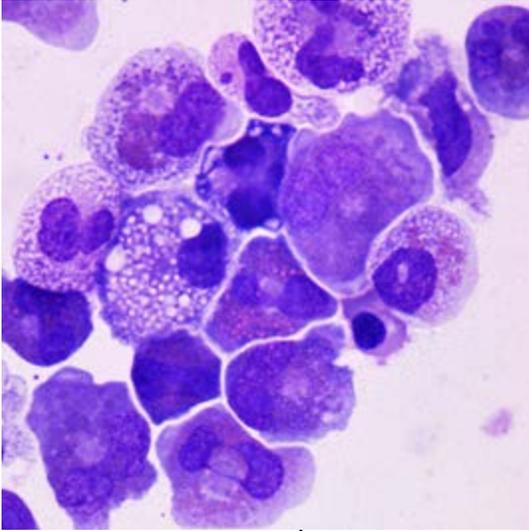
Patient-matched blood cells for therapies and other applications

The Galat laboratory at the Manne Research Institute has developed an elegant system to derive blood cell precursors from human pluripotent stem cells (hPSC). This type of stem cell has the potential to develop into many different kinds of cells in the body, and is capable of participating in organ repair and function. These qualities have prompted scientists to test the use of hPSC to treat some diseases. However, developing a fully defined system to generate functional blood cell precursors has proven to be a significant challenge. The findings hold promise to overcome this challenge.

The approach is reliable, cost-effective and relatively simple. By eliminating variables used in other systems, the lab has streamlined the process of developing blood cell precursors. This allows scientists to study the factors that affect early stages of blood cell development, and provides a mechanism for clinician-researchers to develop therapies for patients.



Kristin Kan, MD, MPH, MSc, is an attending physician in Academic General Pediatrics and Primary Care at Lurie Children’s and Instructor of Pediatrics at the Feinberg School. She is a member of the Smith Child Health Research Program at the Manne Research Institute.



Blood cells produced from induced pluripotent stem cells (iPSC). Image courtesy of Vasil Galat, PhD. Galat is Director of the Human iPSC and Stem Cell Core at the Manne Research Institute and Research Assistant Professor of Pathology at the Feinberg School.

Members of the Fertility & Hormone Preservation & Restoration Program who authored chapters in the new *Pediatric and Adolescent Oncofertility* book include Erin Rowell, MD, Program Director, Emilie Johnson, MD, MPH, Barbara Lockart, DPN, APN, CNP, CPON, as well as Monica Laronda, PhD. Rowell is an attending physician in Pediatric Surgery at Lurie Children's and Assistant Professor of Surgery at the Feinberg School. Johnson is an attending physician in Urology at Lurie Children's and Assistant Professor of Urology at the Feinberg School. Lockart is a pediatric nurse practitioner in Hematology, Oncology, Neuro-oncology and Stem Cell Transplant and General Pediatric Surgery at Lurie Children's.

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In a series of experiments, the lab converted adult skin cells into hPSC and then used these patient specific cells to optimize their platform of blood cell precursor derivation. Assays were employed to demonstrate the ability of blood cell precursors to form mature cells of blood lineage. The cells were identified in collaboration with immunology labs at Lurie Children's and

Rosalind Franklin University. A description of the work is published in *Stem Cell Research & Therapy*.

Previously, scientists relied on the introduction of external factors – proteins or cells – to induce hPSC to differentiate. In addition to potentially changing the outcomes, these factors can complicate the experimental setup and cause inefficiencies or bias in the generation of blood cell precursors.

“We designed the platform to exclude as many sources for variability in the differentiation outcome as possible. These factors include co-culturing the hPSC with other cells that secrete an unmeasurable amount of substances into the media. We also excluded cytokines – proteins that affect hPSC differentiation in various ways,” says first author Yekaterina Galat. “We demonstrated that the approach efficiently promotes differentiation of hPSC to blood cell precursors, while eliminating many complications,” she continues.

Says corresponding author and laboratory director Vasil Galat, PhD, “Our hope is to leverage this platform in order to help other scientists and clinicians. The cells we derive can be used to test the effects of factors on hPSC differentiation, paving the way for studies of drug efficacy and toxicity, and to model diseases.”

First book on pediatric and adolescent oncofertility published

A recently released book, *Pediatric and Adolescent Oncofertility*, is the first of its kind to present a comprehensive discussion of pediatric and adolescent

oncofertility. It examines the impact of pediatric cancer and cancer therapy on fertility and presents both current and emerging fertility preservation techniques for both males and females.

Edited by Teresa Woodruff, PhD, and Yasmin Gosiengfiao, MD, this book includes chapters written by members of the Fertility & Hormone Preservation & Restoration Program at Lurie Children's. Woodruff is Director of the Women's Health Research Institute, Chief of Reproductive Biology Research in the Department of Obstetrics and Gynecology, Thomas J. Watkins Memorial Professor of Obstetrics and Gynecology, Professor of Obstetrics and Gynecology (Reproductive Science in Medicine), McCormick School of Engineering, Medical Social Sciences and Medicine (Endocrinology) at the Feinberg School. Gosiengfiao is an attending physician in the Division of Hematology, Oncology, Neuro-oncology and Stem Cell Transplant at Lurie Children's and Assistant Professor of Pediatrics at the Feinberg School.

Cord blood test might help predict fatal lung disease in preemies

Findings published in the *Journal of Pediatrics* describe growth factors in cord blood that may identify premature infants at risk for bronchopulmonary dysplasia-associated pulmonary hypertension (BPDPH) – an often fatal lung disease in which the vessels carrying blood from the heart to the lungs become narrowed and dysfunctional. Identifying these babies at birth would allow interventions to prevent the disease that manifests in some preemies months after birth.

“We have many promising interventions and it would be exciting to start them at birth in babies at risk,” said lead author Karen Mestan, MD, MSCI, a neonatologist at Lurie Children's and Associate Professor of Pediatrics at the Feinberg School. “Our study shows that using cord blood for prediction of disease has tremendous potential to save lives.” This research was supported in part by grants from the NHLBI. [Read more.](#)