InTouch
WITH RESEARCH
at Stanley Manne Children's Research Institute

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IN THIS ISSUE

Decoding the Cause of a Devastating Neonatal Disease Using a New Model System

The Tan laboratory. From left: Fangyi Liu, Xiao-Di Tan, MD, Heng-Fu Bu, PhD, Hua Geng, PhD, Xiao Wang, MD, PhD (photo: Jan Terry).

Necrotizing enterocolitis (NEC) is the most common neonatal life-threatening illness affecting preterm or very low birth weight infants. The disease is primarily featured with gut inflammatory injury-associated syndromes that are rapidly followed by devastating conditions such as sepsis and multiple organ failure in patients. Therefore, doctors always consider NEC as an emergency. They apply a set of strategies on premature babies to prevent NEC. When the disorder occurs, they often perform urgent surgery on babies with NEC to remove dead intestinal tissues in addition to comprehensive therapies such as draining fluids from the stomach and intestines, giving IV fluids, administering antibiotics, and intensive care.

Aside from its presentation and the resulting health consequences in neonates, NEC is problematic for other reasons: Therapeutic options are limited, the mortality rate of neonates with NEC remains high, and nobody has been able to figure out its causes despite many years of extensive research. Thus, physicians and experts in the field recognize that additional efforts and new research approaches for understanding the mystery of NEC are required.

Xiao-Di Tan, MD, a principal investigator at Stanley Manne Children's Research Institute, has led a research group supported by the National Institutes of Health (NIH) to study how sepsis and acute inflammation affect the gut barrier for a decade. He recently received a new NIH grant to decode the cause of NEC. Tan established this research project with NEC as the focus precisely because the stakes are so high. "About 14 to 40 percent of babies who develop the disease will undergo surgery management. The death rate is unacceptable. Furthermore, those who survive may have a lifetime of impact, such as short gut syndrome or nutritional deficiencies that can

A Model System for a Devastating Disease (continued from page 1)

Xiao-Di Tan, MD, is Research Professor of Pediatrics and Pathology at Northwestern University Feinberg School of Medicine, and Director of the Center for Intestinal and Liver Inflammation Research (CILIR) at the Manne Research Institute. Tan holds the Dorothy M. and Edward E. Burwell Professorship in Immunobiology at Ann & Robert H. Lurie Children's Hospital of Chicago. His new R01 research project entitled "Surgical studies of gut epithelial apoptosis-initiated critical illness" has been recently awarded by the National Institute of General Medical Sciences of the NIH.

cause developmental problems," he says.

Tan's efforts will concentrate on two related objectives: To develop an animal model that is consistent with NEC, and to discover what causes the disease – its pathogenesis.

In the past 30 years, much of the research in the field has focused on improving treatments for NEC patients. The experimental models currently in use are associated with the administration of risk factor-associated stresses – such as exposure to cold, asphyxia, enteral feeding and gavaging bacterial mixtures – to induce NEC. These models have improved greatly, thus advancing the science. However, several problems are inherent to the models – they rely on stimuli that may not be causative factors in NEC patients, they don't address the origins of the disease, and the approaches for delivery of stresses are extremely labor intensive.

To get to the heart of NEC pathogenesis, Tan intends to develop a robust animal model using a state-of-the-art genetic approach that induces scattered intestinal epithelial cell apoptosis (cell death) in mice. "The reason this is important is that scattered intestinal epithelial cell apoptotic injury is a well-identified hallmark of NEC. However, it is not clear whether this unique pathological change can lead to NEC development, and if so how the whole intestine is then subject to rapid necrosis after scattered intestinal epithelial cell apoptotic injury. With our new model, we can mimic what happens and provide answers," explains Tan.

So, his lab is busy trying to determine how apoptosis that is limited to a small area of the intestinal lining triggers necrosis throughout the entire organ. The scientists will induce apoptosis, which will cause injury to develop. Once this model is established, they will go on to study the role of other risk factors in NEC development, and to work with partners to investigate therapies that target the source of NEC pathogenesis.

Says Tan, "I am confident that we will find the mechanisms of apoptosis in intestinal focal areas of the lining leading to necrosis in the intestine, and that this model will be a novel research tool that pharmaceutical companies can use to develop drugs." Tan believes in the foundations of science – that one achieves success by building on the research of colleagues past and present. "Other investigators including the research group led by Isabelle De Plaen, an attending neonatologist at Lurie Children's, have elegantly demonstrated that certain stresses induce intestinal epithelial cell apoptosis prior to NEC development, suggesting the pathogenic role of this apoptosis in causing NEC. At the research institute, the De Plaen lab is adjacent to mine. I am excited that her group and my lab will collaborate on this newly initiated battle against NEC with strong support from the NIH," he says.

He goes on: "My mentor, Wei Hsueh, an emeritus professor at Northwestern University, conducted pioneering research in the pathogenesis of NEC during the 1980s and the 1990s. I was inspired by her passion for decoding the cause of this devastating neonatal disease. I so much appreciate all that this wonderful and unique hospital, Lurie Children's, has done to support my research, particularly the Warren and Eloise Batts Research Scholarship that supported my early career at the institution. More recently, I received a named title honoring the Burwell family. The people in my laboratory are wonderful, and what we do is truly a team effort. I am grateful for the support and strong motivation from Dr. Hsueh, collaborators such as Isabelle, the lab members, public generosity, and especially the parents and their babies who come to Lurie Children's, to get to the bottom of this terrible disease."

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

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Stanley Manne Children's Research Institute is the research arm of Ann & Robert H. Lurie Children's Hospital of Chicago, and 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 200 investigators and over $30 million in external funding for research, two-thirds from the NIH and other federal agencies.

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I am delighted to share with you our newest edition of InTouch. As you'll read, the past several months have been very productive for our investigators and historic for our city and country. Just as we finished recovering from our celebration of the Cubs' first World Championship in 108 years, we were faced with the usual unknowns of an incoming presidential administration. From the tenor of the campaign trail it is difficult to predict the implication of the Trump administration on child and adolescent healthcare and biomedical research. So as we do with every election, we will be keeping a close eye on the philosophy and principles espoused by this new team. It is encouraging that earlier this year, Mr. Trump was quoted as saying, "while there are increasing demands to curtail spending and to balance the federal budget, we must make the commitment to invest in science, engineering, healthcare and other areas that will make the lives of Americans better, safer and more prosperous." For its part, the NIH says it's ready for the transition. "NIH has a long history of bi-partisan support and stands ready to work with the new Administration to improve people's health and reduce the burden of disease through biomedical research," said Amanda Fine. Regardless of the external forces that we will face, our investigators and their teams at the Stanley Manne Children's Research Institute and across the Lurie Children's research enterprise will remain steadfast in their dedication to discovery that will improve the outcomes of children both today and in the future.

Sara Fossum, PhD

Sara Fossum successfully completes her graduate training

Sara Fossum, a graduate student in the laboratory of Ann Harris, PhD, successfully defended her thesis and presented her public defense in August. She is the 21st student to graduate from the laboratory.

After completing an undergraduate degree in Biology from the University of Notre Dame, Sara entered the Northwestern University Medical Scientist Training Program (MSTP), which prepares students for exciting and rewarding careers combining biomedical investigation and the practice of medicine. Sara joined the Harris laboratory in 2012, where she focused on the Ets homologous factor (EHF) and its involvement in lung function.

While in the Harris laboratory, Sara was awarded a grant from the National Heart, Lung, and Blood Institute, received the Junior Investigator Basic Science Semi-Finalist award at the North American Cystic Fibrosis Conference, was part of the Cellular and Molecular Basis of Disease Training Program at Northwestern University, and won the Heller Award for Excellence in the Pre-Clinical Curriculum from the Feinberg School. Sara plans to return to medical school to finish her third and fourth years.

Ann Harris, PhD, is Director of the Human Molecular Genetics Program at the Manne Research Institute, Valerie and George D. Kennedy Research Professor in Human Molecular Genetics at Lurie Children's, and Professor of Pediatrics at the Feinberg School.

Jutla presents at Loyola University Psychiatry Grand Rounds

Amandeep Jutla, MD, a fifth-year fellow in the Department of Child and Adolescent Psychiatry at Lurie Children's, presented at the Loyola University Medical Center Psychiatry Grand Rounds in September with James MacKenzie, DO, on the topic of Pediatric Conversion Disorder. MacKenzie is Medical Director of the Department's Consultation-Liaison Service and Assistant Professor in the Department of Psychiatry and Behavioral Sciences at the Feinberg School.

Geng recognized by AGA Institute Council

Hua Geng, PhD, a postdoctoral associate in the laboratory of Xiao-Di Tan, MD, was recently recognized as an accomplished early stage investigator by the American Gastroenterological Association (AGA) Institute Council for her outstanding presentation entitled "H19 long non-coding RNA contributes to promoting IGF1R expression and intestinal epithelial cell restitution following inflammatory injury" during Digestive Disease Week 2016.

Early career investigators receive TL1 awards to solve child health problems

Five clinical fellows in pediatrics and postdoctoral fellows in engineering or data science have received TL1 awards. The TL1 program was established by Northwestern University Clinical and Translational Sciences Institute (NUCATS) with the support of the NIH, with the goal of promoting multidisciplinary training to improve the health of children and adolescents. The awardees, selected by a committee of experts and NUCATS, will receive support from their mentors in engineering and medicine, complete formal coursework and receive protected research time, all with the goal of allowing them to build a strong foundation for a career in research. NUCATS promotes collaboration among early career investigators as they work to solve child health problems.

The TL1 scholars are:

Bimal Chaudhari, MD, MPH, fellow in the Division of Neonatology; Dan Fort, PhD, MPH, postdoctoral fellow in Health and Biomedical Informatics, Department of Preventive Medicine; Alicia Lenzen, MD, fellow in the Division of Hematology, Oncology, Neuro-oncology and Stem Cell Transplantation; Michael Sherenian, MD, fellow in the Division of Allergy and Immunology; and Matthieu Chardon, PhD, postdoctoral fellow in the Department of Physiology. Read more.

Tool for ED to Treat Feverish Infants

Many parents have experienced the indecision and worry over caring for their feverish and miserable infant. The parents can't get to the bottom of what is wrong and don't know what to do because their babies can't answer questions. Where are they hurting? Just how sick are they? And so on.

One option parents exercise is to bring their baby to the emergency department (ED). Although ED staff members are highly skilled professionals who are good at solving problems quickly, they are often faced with challenges in these types of cases. As mentioned, the baby can't talk to them. Secondly, results from the blood culture they order may take days.

Clinicians know that bacterial infections are common in feverish infants who are seen in the ED, and they often administer antibiotics to these babies. Because the antibiotics must be given intravenously, the infants are admitted to the hospital. In addition, if the illness is caused by a viral infection the antibiotics probably won't help.

What if there were a test that could quickly identify the pathogen – bacterial versus viral – and obviate the need for hospital admission and unnecessary antibiotics? Elizabeth Powell, MD, MPH, and Elizabeth Alpern, MD, participated in a study with other PECARN (Pediatric Emergency Care Applied Research Network) investigators to determine if host expression patterns – or RNA biosignatures – can be analyzed as a quicker and more accurate diagnostic approach. In a preliminary study published in *JAMA*, the investigators found that there is a unique response to a bacterial pathogen versus a viral pathogen. Samples from infants with bacterial infections tend to overexpress markers of inflammation while not overexpressing interferon markers, while samples from infants without bacterial infections showed different profiles.

Says Powell, "This study was a unique partnership between clinicians and basic scientists. Octavio Ramilo from Nationwide Children's Hospital and The Ohio State University, is the basic scientist in the group. Blood samples from participating sites across the country were sent to him for this work. We are encouraged because the results showed clear differences in biosignatures, which is promising."

However, Powell cautions that much more is needed. "The purpose of the study was to determine if the research was feasible, and if it demonstrated clear differences among types of infections. Now that we have analyzed the data on a small set of patients, we hope to study a larger set. This will help us refine our criteria and hopefully develop a reliable, sensitive tool that can be used in the ED," she says.

"We still have so much to learn," she continues. "How can we more clearly distinguish between bacterial infections in spinal fluid – the most serious – as opposed to those in blood and in urine? How do we know if the biosignature in a baby changes over time? We are already planning our next steps."

These next steps involve babies in the ED, and Powell has a request for parents. "We are sensitive to the fact that the ED is an extremely stressful place to be. It's so important and helpful to us that despite these stresses, parents can be patient with our interest in enrolling their babies in clinical studies. We make it clear to parents that they are doing this to help other babies, and that it won't necessarily help their baby. They are coming to Lurie Children's in part to receive the best cutting edge therapies for their children. This is critical to our mission. Having said this, I know that the ED is quite different from other environments when enrolling patients. Parents have so much on their minds, and they may not have the capacity to make another decision. We completely understand if they choose not to participate."

Elizabeth Powell, MD, MPH is an attending physician in the Division of Emergency Medicine at Lurie Children's and Professor of Pediatrics at the Feinberg School.

Emilie Johnson, MD, MPH

Bradley Kulat, CCP, LP

Laurie Sands, APN, NP, CPNP-PC, and Suzanne Kujawa Smith, RNC, MSN, CPNP-PC, both Advanced Practice Providers in the Division of Pediatric Surgery at Lurie Children's, have been selected to co-chair the National Trauma Special Interest Group for the American Pediatric Surgical Nurses Association (APSNA). As resources for the APSNA Board of Directors and general membership, this group will provide expertise for projects such as the development of position statements or educational materials including teaching sheets for parents; coordinate national in-service on driving safety; and serve as liaisons to other organizations.

Johnson appointed to PCORI Advisory Panel

Emilie Johnson, MD, MPH, has been appointed by the Patient-Centered Outcomes Research Institute (PCORI) as a member of its Advisory Panel on Communication and Dissemination Research. Johnson will join other members of the panel in applying her experience and expertise to help PCORI refine and prioritize research funding priorities and ensure that the research PCORI supports centers on the outcomes that matter to patients and other healthcare decision makers. PCORI is an independent, non-profit organization authorized by Congress to fund research that will provide patients, their caregivers, and clinicians with the evidence-based information needed to make informed healthcare decisions. Johnson is an attending physician in the Division of Urology at Lurie Children's and Assistant Professor of Urology at the Feinberg School.

Kulat receives award at Illinois State Perfusion Society Annual Meeting

Bradley Kulat, CCP, LP, was awarded the Suzanne H. DeWitt Perfusionist of the Year Award at the annual meeting of the Illinois State Perfusion Society in September. The award was established to honor a clinical perfusionist in Illinois who has consistently demonstrated strong leadership skills and has made significant contributions to the perfusion community both clinically and professionally. Kulat is Coordinator of Perfusion Services in the Heart Center at Lurie Children's.

Lulla appointed executive chair of Brain Tumor Consortium

The Children's Brain Tumor Tissue Consortium (CBTTC) has appointed Rishi R. Lulla, MD, MS, as its new executive chair. Lulla is an attending physician in the Division of Hematology, Oncology, Neuro-oncology and Stem Cell Transplantation at Lurie Children's. The CBTTC, a multi-institutional research partnership, maintains a state-of-the-art biorepository and informatics portal, which allows researchers to access high quality genomic and clinical tumor data. Lurie Children's was one of the founding core member institutions of CBTTC. Lulla is Assistant Professor of Pediatrics at the Feinberg School.

National Psoriasis Foundation honors Paller

The National Psoriasis Foundation honored Amy Paller, MD, and Mark Lillie, in its Commit to Cure Gala in October. The Gala celebrates the contributions of individuals who make a difference in the lives of people with psoriatic disease. The Gala is "also our glitziest fundraising event of the year for which we allocate all money raised toward advancing psoriatic disease research," according to the Foundation. Paller is Professor of Pediatrics and Dermatology, Chair of the Department of Dermatology, and Walter J. Hamlin Professor of Dermatology at the Feinberg School. She is an attending physician in the Division of Dermatology at Lurie Children's.

Robbins named Early Career Speaker for Perinatal Research Society meeting

Mary Robbins, MD, was named one of a select few Early Career Speakers for the Perinatal Research Society (PRS) annual meeting in September. Robbins, one of two Abbott Nutrition Early Career Speakers, presented on the role of microRNAs in neonatal lung disease models. Robbins' mentor is Kathryn Farrow, MD, PhD, an attending physician in the Division of Neonatology at Lurie Children's, Neonatal-Perinatal Medicine Fellowship Director, and Associate Professor of Pediatrics at the Feinberg School. Robbins is an attending physician in Neonatology at Lurie Children's and Instructor in Pediatrics at the Feinberg School.

Adler receives Society for Simulation in Healthcare Program Innovations Award

Mark Adler, MD, Associate Professor of Pediatrics and Medical Education at the Feinberg School, won the Society for Simulation in Healthcare Program Innovations Award for his article "Approach to confederate training within the context of simulation-based research." Adler is an attending physician in the Division of Emergency Medicine at Lurie Children's.

Barbara Lockart, MSN, APN, CPNP, CPON (above right), an Advanced Practice Provider in the Divisions of Pediatric Surgery and Hematology, Oncology, Neuro-oncology and Stem Cell Transplantation at Lurie Children's, has been honored with an "APHON Counts Writing Award," for her article entitled "Challenging conversations with adolescent and young adult patients." The award, which was presented by the Association of Pediatric Hematology/ Oncology Nurses (APHON) in September, recognizes excellence in writing and communication.

Zekas selected to serve on NAPNAP Health Policy Committee

Linda Zekas, MSN, APN, NP, an Advanced Practice Provider in the Division of Pediatric Surgery at Lurie Children's, has been selected to serve on the Health Policy Committee for the National Association of Pediatric Nurse Practitioners (NAPNAP). The committee oversees federal, state and grassroots government relations programs on behalf of the profession. It also evaluates proposed federal legislation and regulations for their implications on advanced practice nursing and child health. NAPNAP is the only national professional organization dedicated to advancing the pediatric nurse practitioner's role in providing care, and through that improving the quality of health care for children.

Backer appointed president of Congenital Heart Surgeons' Society

Carl Backer, MD, was installed as the president of the Congenital Heart Surgeons' Society (CHSS) at the 2016 CHSS Annual Meeting in October. He will serve in this role through 2018. Backer is head of the Division of Cardiovascular-Thoracic Surgery, Surgical Director of the Heart Transplant Program, and holds the A.C. Buehler Professorship in Surgery at Lurie Children's; and is Professor of Surgery at the Feinberg School.

Gosain named to American College of Surgeons' Board

Arun Gosain, MD, head of the Division of Plastic and Reconstructive Surgery at Lurie Children's, was recently named to the Board of Governors of the American College of Surgeons (ACS). As a Governor he is one of the leaders of the largest organization of surgeons in the world. As immediate past-president of the American Society of Maxillofacial Surgeons (ASMS), he represents that organization on the ACS Board. Gosain is Professor of Surgery at the Feinberg School and director of a laboratory in the Developmental Biology Program of the Manne Research Institute.

Appointments and Promotions

Lurie Children's faculty promotions by Northwestern University Feinberg School of Medicine

Rishi Agrawal, MD, MPH - Associate Professor of Pediatrics (Hospital-Based Medicine)

Lee Bass, MD - Associate Professor of Pediatrics (Gastroenterology, Hepatology and Nutrition)

Sonali Chaudhury, MD - Associate Professor of Pediatrics (Hematology, Oncology, Neuro-oncology and Stem Cell Transplantation)

John Costello, MD, MPH - Professor of Pediatrics (Cardiology)

Jie Deng, PhD - Research Associate Professor of Radiology

Mariana Glusman, MD - Associate Professor of Pediatrics (Academic General Pediatrics and Primary Care)

Shannon Haymond, PhD - Associate Professor of Pathology

Nancy Kuntz, MD - Professor of Pediatrics (Neurology) and Neurology - Ken and Ruth Davee Department

Jeffrey Rastatter, MD - Associate Professor of Otolaryngology - Head and Neck Surgery

Jennifer Schneiderman, MD - Associate Professor of Pediatrics (Hematology, Oncology, Neuro-oncology and Stem Cell Transplantation)

Anne Marie Singh, MD - Associate Professor of Pediatrics (Allergy and Immunology) and Medicine (Allergy and Immunology)

Lisa Sohn, MD - Associate Professor of Anesthesiology

Simone Treiger Sredni, MD, PhD - Research Associate Professor of Neurological Surgery

Jill Weissberg-Benchell, PhD - Professor of Psychiatry and Behavioral Sciences

Katherine Barsness MD, MS

Barsness receives PCORI award to develop patient and family advisory board to help improve patient experience

Katherine Barsness, MD, MS, pediatric surgeon at Lurie Children's and Associate Professor of Surgery and Medical Education at the Feinberg School, has received a funding award from the Patient-Centered Outcomes Research Institute (PCORI). The $15,000 award, provided through PCORI's "Pipeline to Proposal" program, will support a project that brings together patients and clinicians to discuss ways to improve the pediatric surgery patient experience. Through this project, titled "Developing a patient and family-centered pediatric surgical collaborative," a patient-focused advisory board will be developed, comprised of individuals and groups who share a desire to improve patient/family experiences.

Together, these advisory board members will develop interventions based on identified patient and stakeholder priorities, which can improve compliance with treatment recommendations and ultimately improve the patient experience. In addition, these interventions can help decrease psychosocial stressors experienced during the surgical experience such as preoperative anxiety in the child and adult caregiver, and guide appropriate support for patients.

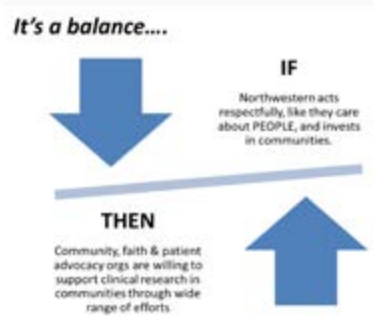
Barsness' study was one of only 46 Tier 1 projects recently funded through this program. All approved projects are intended to develop the capacity for patients, caregivers, and other stakeholders to participate in patient-centered clinical comparative effectiveness (CER) research.

Review of Down syndrome and acute lymphoblastic leukemia

Down syndrome (DS), a common chromosomal disorder, is associated with a number of morbidities, including leukemia. Children with DS are twenty times as likely as other children to develop acute lymphoblastic leukemia (abbreviated DS-ALL). In a review article published in the September 2016 issue of *Leukemia*, a group from Lurie Children's, the Feinberg School and Tel Aviv University discuss the clinical features, genetics and biology of DS-ALL patients. Based on their review of recent findings, the authors conclude that DS-ALL is unique in its distinct subset of mutations, causing children with this condition to relapse and to suffer severe side effects from standard therapies. They discuss studies – either ongoing or needed – that will be required for the development of effective therapies. First author Paul Lee, MD, PhD is a fellow in the Division of Hematology, Oncology, Neuro-oncology and Stem Cell Transplantation and is supported by the Children's Research Fund Junior Board at Lurie Children's. His mentor, John Crispino, PhD, is co-senior author on the publication. Crispino is Professor of Medicine (Hematology/Oncology) and Biochemistry and Molecular Genetics, and the Robert I. Lurie, MD, and Lora S. Lurie Professor at the Feinberg School. Co-senior author Nobuko Hijiya, MD, is an attending physician in Hematology, Oncology, Neuro-oncology and Stem Cell Transplantation at Lurie Children's and Professor of Pediatrics at the Feinberg School.

Acetaminophen for children with mild persistent asthma

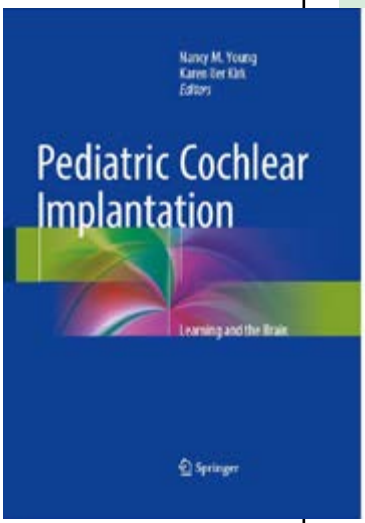
Based on studies that have suggested an association between frequent acetaminophen use and asthma-related complications in children, some physicians recommend that acetaminophen be avoided in children with asthma. However, it is the most commonly used medication in U.S. children, and no appropriately designed studies have tested whether this observed association is real. Jacqueline Pongracic, MD, and Rachel Robison, MD, were co-investigators on a clinical study of asthma exacerbations in children receiving acetaminophen versus ibuprofen. The results, published in the *New England Journal of Medicine*, found no significant differences in asthma exacerbation or asthma control between the two groups. Pongracic is head of, and Robison is an attending physician, in the Division of Allergy and Immunology at Lurie Children's. Pongracic is Professor of Pediatrics, and Robison is Assistant Professor of Pediatrics at the Feinberg School.



ARCC presents poster at Advancing the Science of CEnR Conference

The Center for Community Health's Alliance for Research in Chicagoland Communities (ARCC) Steering Committee member Melvin Thompson of Endeleo Institute and Maryann Mason, PhD, Research Assistant Professor of Pediatrics and Preventive Medicine at the Feinberg School, presented a poster entitled "Community perspectives on supporting clinical research" at the Advancing the Science of Community Engaged Research Conference in August. The poster presents findings of ARCC focus groups with staff representing community-based, faith-based and patient advocacy organizations to learn more about how community organizations view partnering with research institutions for the purpose of educating community members about clinical research participation and/or giving input on the design and conduct of clinical research. Mason is co-director of the Center on Obesity Management and Prevention (COMP), Community and Evaluation Research Director for the Consortium to Lower Obesity in Chicago Children (CLOCC) and principal investigator of the Illinois Violent Death Reporting System (IVDRS), all part of the Mary Ann & J. Milburn Smith Child Health Research Program at the Manne Research Institute.

Books by Lurie Children's authors



Amy Paller, MD, and Anthony Mancini, MD, are co-authors of the leading textbook in pediatric dermatology internationally, the 5th edition of Hurwitz Clinical Pediatric Dermatology. The publication won first prize in the Paediatrics category at the British Medical Association Book Awards in September. Mancini is head of the Division of Dermatology at Lurie Children's and Professor of Pediatrics and Dermatology at the Feinberg School.

Nancy Young, MD, and Karen Iler Kirk are co-editors of a new book entitled Pediatric Cochlear Implantation: Learning and the Brain. This book is intended to educate clinicians about current and emerging best practices and to inspire research in new areas of importance, such as the relationship between cognitive processing and pediatric cochlear implant outcomes. Lurie Children's chapter authors include Tina Tan, MD, Constance Weil, PhD, and Young. Leading researchers in the field also contributed to the book. Contributor Blake Wilson was the recipient of the 2013 Lasker Foundation Clinical Medical Research award for advancement of signal processing essential to development of the modern cochlear implant. Young is Section Head of Otology/Neurotology and Medical Director of the Cochlear Implant Program, the Lillian S. Wells Chair in Pediatric Otolaryngology at Lurie Children's, Professor of Otolaryngology - Head and Neck Surgery at the Feinberg School, and Professor and Fellow of the Knowles Hearing Center in the Roxelyn and Richard Pepper Department of Communication Sciences and Disorders at Northwestern University.

Study finds gene associated with asthma in children who had a viral illness early in life

Results of a study published in *PLoS ONE* show that asthma risk increased 17 times when children who had bronchiolitis in the first two years of life also had a common variation of the Plasminogen activator inhibitor-1 (PAI-1) gene. Similarly, children with this genetic variation were 12 times more likely to develop asthma after any lower respiratory tract infections requiring medical contact early in life (including those that were potentially less severe). "Our findings suggest that genetic influences on asthma might be more pronounced in the context of early life environmental exposures, especially viral respiratory infections," says Rajesh Kumar, MD, senior author and allergist at Lurie Children's, as well as Associate Professor of Pediatrics at the Feinberg School. Read the full press release.

Tomita introduces new journal

Tadanori Tomita, MD, who holds the Yeager Professorship in Pediatric Neurosurgery and is head of the Division of Pediatric Neurosurgery at Lurie

Children's, and Professor and Vice Chair of the Department of Neurological Surgery at the Feinberg School, has founded the *Journal of Neurosurgery Imaging and Techniques* — a new open access international peer reviewed scientific journal. It seeks to provide a platform for surgeons worldwide to contemplate the anatomy of a patient's brain during surgery and route the location of their surgical instruments in relation to the anatomy.

Nancy Kuntz, MD

First treatment for Spinal Muscular Atrophy to be submitted to FDA for approval

Lurie Children's participated in a Phase 3 clinical trial for a drug to treat Spinal Muscular Atrophy that is going before the FDA for approval. Nancy Kuntz, MD, the site principal investigator, Leon Epstein, MD, Jonathan Kurz, MD, PhD, Kristin Krosschell, DPT, Laurey Brown, DPT, and Lurie Children's Clinical Research Unit staff played key roles in the clinical trial. Kuntz is medical director of the Mazza Foundation Neuromuscular Program and director of the Muscular Dystrophy Association (MDA) Clinic at Lurie Children's; and Professor of Pediatrics and Neurology at the Feinberg School. Epstein is head of the Division of Neurology and holds the Derry A. and Donald L. Shoemaker Professorship in Pediatric Neurology at Lurie Children's; he is Professor of Pediatrics and Neurology, and Associate Chair for Research for the Department of Pediatrics at the Feinberg School. Read the full press release.

Full re-accreditation for protecting research participants

Lurie Children's and the Manne Research Institute were awarded full re-accreditation by the Association for the Accreditation of Human Research Protection Programs (AAHRPP) at the September meeting of its Council on Accreditation. An independent, non-profit organization, AAHRPP uses a voluntary, peer-driven model to ensure that human research protection programs meet highest standards for quality and can demonstrate that their protections exceed the safeguards required by the U.S. regulations. Lurie Children's earned its initial full accreditation in September 2013, the fourth institution in Illinois to receive this "gold seal." With over 1,600 active studies involving research participants, the AAHRPP re-accreditation signifies that through established policies, procedures and practices, Lurie Children's is committed to scientifically and ethically sound research and to continuous improvement.

What are the trends for children in Medicaid who are high resource users?

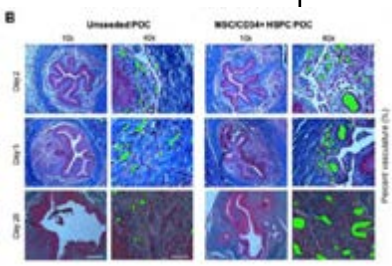
Little is known about trends in healthcare spending associated with children who are high resource users enrolled in Medicaid. These children are prioritized by the Center for Medicare & Medicaid Innovation for the development of new models of care to optimize health and contain spending. However, lack of knowledge about these children's demographic and clinical information presents obstacles to designing effective programs.

Rishi Agrawal, MD, MPH, led a study published in *Pediatrics* that retrospectively analyzed data to determine demographic and clinical characteristics of child high resource users. The data from 48,743 children ages 1 to 18 years and continuously enrolled in 10 state Medicaid programs from 2009 to 2013 were studied. This group represents those in the top 5 percent for Medicaid spending in 2010 (index year). Agrawal and colleagues determined that almost one-third of the children consistently remained in the top 5 percent of spending throughout the study period (persistent group). The highest likelihood of persistent spending occurred in children ages 13 to 18 years; and in children with 6 or more chronic conditions, a respiratory complex chronic condition, or a neuromuscular complex chronic condition. Those children who were hospitalized or used an emergency department were less likely to be categorized in the persistent spending group.

"These data have important implications for how we implement new models of health financing in

children with high resource use," says Agrawal. "Health systems will have to account for substantial year-to-year variability in spending incurred by these vulnerable children as well as the fact that much of the spending occurs outside the hospital setting."

Agrawal is a member of the Division of Hospital-Based Medicine at Lurie Children's and Associate Professor of Pediatrics at the Feinberg School. He is also a hospitalist at La Rabida Children's Hospital.



Staining demonstrate differences in vessel number and size (vessels marked with green) over time between seeded and control animals at the surgical site. Vessels tended to increase in size in seeded animals with time, compared to persistently small vessels in the control group. (Figure courtesy of Arun Sharma, PhD).

Study shows promise to repair urethra using bone marrow stem cells

A study published in *Scientific Reports* describes a new strategy that may be utilized to correct hypospadias, a birth defect found in up to one in every 200 boys. Using an animal model, scientists have demonstrated that it can be feasible and effective to use a graft made from an individual's own bone marrow stem cells. These stem cells were seeded onto a novel synthetic scaffold that is nontoxic, biodegradable and able to stretch and contract. The resulting graft aided in the regeneration of the damaged tissue on multiple biological levels. Senior author Arun Sharma, PhD, is Director of Pediatric Urological Regenerative Medicine in the Division of Urology at Lurie Children's, director of a laboratory in the Developmental Biology Program and Director of Surgical Research at the Manne Research Institute, and Research Associate Professor of Urology at the Feinberg School. Read the full press release.

Technology to help control asthma

Ruchi Gupta, MD, MPH, is conducting a study entitled "iTRACC (Improving Technology-Assisted Recording of Asthma Control in Children)." The purpose is to determine whether a sensor-enabled, clinically integrated, mobile health asthma program can improve asthma outcomes among 4 to 11 year old children with moderate to severe asthma. The randomized clinical trial will compare asthma inhaler use and asthma-related outcomes between children who either receive an intervention, the Remote Health Management Platform, or standardized education for asthma management. The Remote Health Management Platform will be used to transmit data to the caregiver's smartphone app or to a web portal and to the physician and care team to help facilitate improved asthma management. This constant feedback and reinforcement may lead to improved asthma control, therefore reducing frequency and severity of asthma exacerbations. Gupta is an attending physician in the Division of Academic General Pediatrics and Primary Care at Lurie Children's, and Associate Professor of Pediatrics and Medicine at the Feinberg School.

Competitive renewal received by Farrow

Kathryn Farrow, MD, PhD, has received a competitive renewal for a NIH R01 grant entitled "Redox regulation of vascular cGMP signaling in neonatal lungs." This project is an extension of initial studies investigating the role of cGMP signaling in the development of brochopulmonary dysplasia-associated pulmonary hypertension, a disease seen in premature infants with high rates of morbidity and mortality. A unique aspect of the proposal is the group's focus on infants who are born smaller than expected for their gestational age, and who have a higher risk for the disease. In order to accomplish this, the Farrow group has established a collaboration with Camille Fung, MD, a neonatologist at the University of Utah, who has extensive expertise in studying growth restriction in utero.

Healthy Communities Initiative

Lurie Children's Healthy Communities is a new initiative that consolidates the hospital's wide ranging activities in public health, child health research, policy and advocacy, as well as community partnerships and clinical programs in the community. It will strategically align and integrate goals to support the hospital's vision of helping achieve a healthier future for every child at the community level. To achieve maximum measurable impact, data from the Community Health Needs Assessment and other public health research will be used to guide its efforts.

Welcome to new members of the Stanley Manne Children's Research Institute Board of Directors, who were elected at the August 18 Medical Center Board meeting.

- Pran Jha, Partner, Sidley Austin; Foundation Board Member
- Sharon L. Manne, PhD, Associate Director for Cancer Prevention, Control and Population Science; Co-Leader, Cancer Prevention and Control Research Program, Rutgers Cancer Institute of New Jersey
- H. Thomas Watkins III, Former President/Chief Executive Officer, Human Genome Sciences, Inc.; Vice Chair, QMPS; Medical Center Board Member

The Children's Ball is around the corner!

The Children's Research Fund's annual philanthropic highlight is almost here, made even more special this year by the celebration of the organization's 25th anniversary of affiliating with Lurie Children's. The Children's Ball, which supports pediatric medical research at the Manne Research Institute, is set for Saturday, December 3, at the Hilton Chicago. This year's theme is "Moments: Yesterday, Today & Tomorrow," celebrating all the moments, big and small, made possible by research. Co-chairs Ann and John Amboian and Ashley Hemphill Netzky and Pam Netzky have planned a truly special event for this year's Ball guests. For ticket information, visit www.childrensresearchfund.org, or call Katie Cerone at 312.227.7299.

From left: Barneys New York Shopping Event Co-chairs Phillip and Nancy Resnick, Kyle and Sage Kamin and Enzo and Colleen Incandela.

Barneys New York Shopping Event

On October 20, Children's Research Fund board members, supporters and friends gathered at Barneys New York for a festive evening of cocktails, hors d'oeuvres, shopping and raffle prizes. A portion of shopping proceeds were donated to support the Children's Research Fund's current fundraising commitment to precision medicine. This year's successful event was co-chaired by Barneys New York Creative Ambassador-at-Large Simon Doonan along with Enzo and Colleen Incandela, Sage and Kyle Kamin and Nancy and Phillip Resnick. The evening included opportunities to shop with Barneys New York designers Brooke Garber Neidich, Tabitha Simmons and Nannette De Gaspé Beaubien.

Waldorf Astoria Holiday Tree Lighting

The Children's Research Fund encourages you to participate in a special Holiday Tree Lighting ceremony in support of Lurie Children's on November 16, from 5:30 to 7:30 p.m., at The Waldorf Astoria Chicago, 11 E. Walton Street. Guests are encouraged to bring a gift card or unwrapped toy to be donated to children and their families cared for by the hospital's Center for Cancer and Blood Disorders. To RSVP, contact Carrie Plungis at carrie.plungis@waldorfastoria.com.

About the Children's Research Fund

The Children's Research Fund is one of Chicago's leading philanthropic organizations dedicated to funding basic, translational 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 Lurie Children's in 1991, the Children's Research Fund has contributed more than $67 million.

To get the latest information on Children's Research Fund events and fundraising campaigns, please visit: www.childrensresearchfund.org.