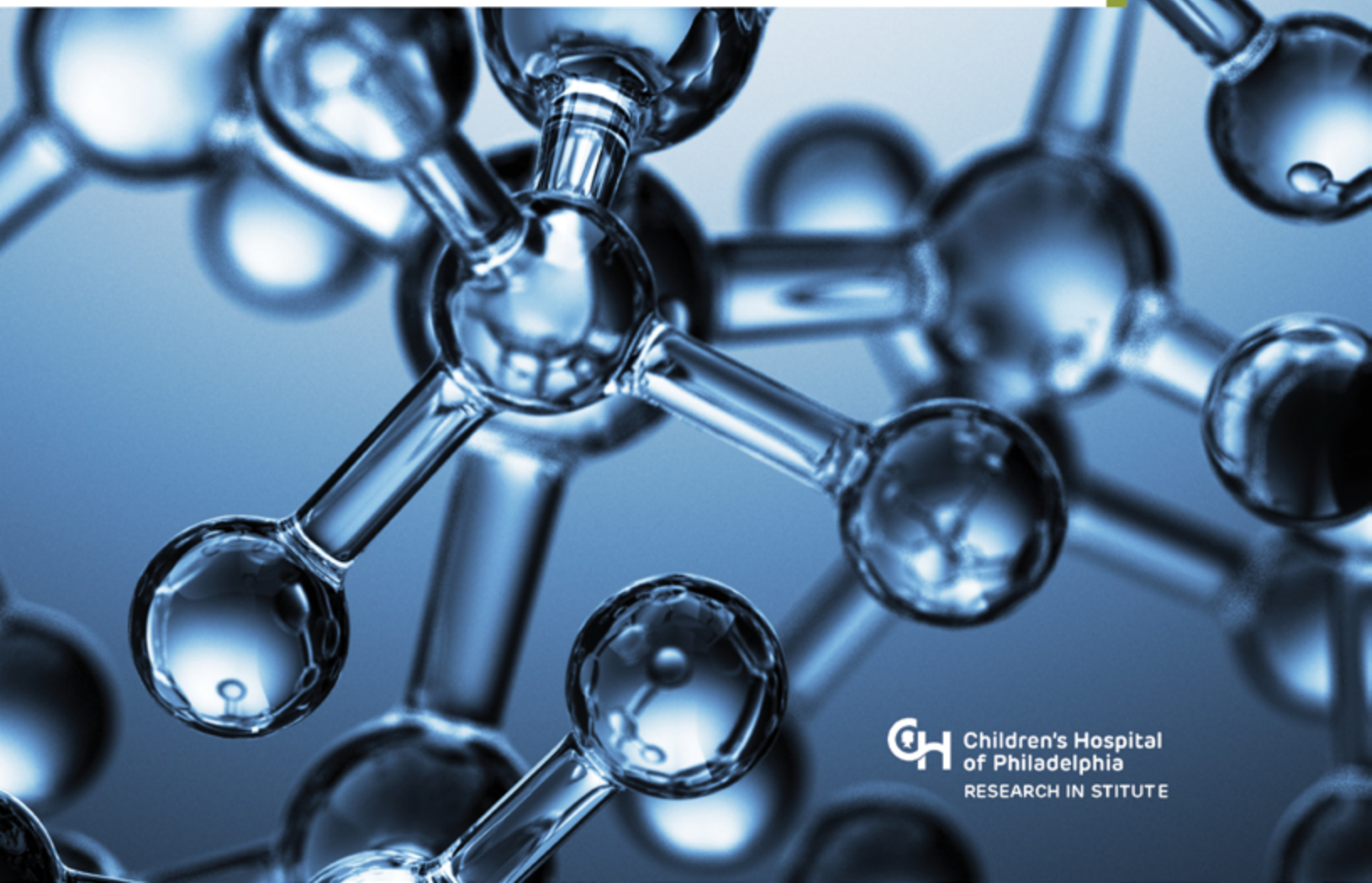
17-18
RESEARCH ANNUAL REPORT



Children's Hospital of Philadelphia
RESEARCH IN STITUTE

17-18 RESEARCH ANNUAL REPORT

MILESTONES ›

MILESTONES

INITIATIVES ›

GAME CHANGER: FIRST-EVER FDA APPROVAL FOR A CAR-T CELL THERAPY

The U.S. Food and Drug Administration (FDA) approved a game-changing cellular therapy in August 2017 to treat cancer with a patient's own immune system. Kymriah™, the first therapy based on gene transfer to be approved by the agency, targets patients age 25 and under who are battling an aggressive blood cancer known as B-cell precursor acute lymphoblastic leukemia (ALL).

Developed by CHOP and the University of Pennsylvania in partnership with Novartis, Kymriah is a chimeric antigen receptor (CAR) T-cell therapy that modifies patients' own immune T cells. The modified cells are collected and reprogrammed at a Novartis facility and then infused back into the patients' bodies to seek and destroy the leukemia cells.

In 2012, CHOP became the first institution to investigate how CAR T-cell therapy could be used to treat pediatric patients who have ALL. While ALL is the most common childhood cancer, an effective treatment has been elusive.

Updated results from a global clinical trial of the CAR T-cell therapy, also known as tisagenlecleucel, reveal that children and young adults continued to show high rates of durable, complete remission of their disease. Most side effects were short-lived and reversible, according to a study published in the *New England Journal of Medicine*.

"This expanded, global study of CAR T-cell therapy gives us further evidence of how remarkable this treatment can be for our young patients in whom all other treatments failed," said lead author Shannon L. Maude, MD, PhD, a pediatric oncologist at CHOP and assistant professor of Pediatrics in the Perelman School of Medicine at the University of Pennsylvania. "Our data show not only can we can achieve longer-term durable remissions, and longer-term survival for our patients, but that these personalized, cancer-fighting cells can remain in the body for months or even years, effectively doing their job."

In the "Inspiration" section of this Annual report, read the story of 9-year-old Austin Schuetz, a Cub Scout, collector, and cancer survivor from Wisconsin who participated in early clinical trials at CHOP for the treatment.

ROTAVIRUS VACCINE: A DECADE OF SAVING LIVES

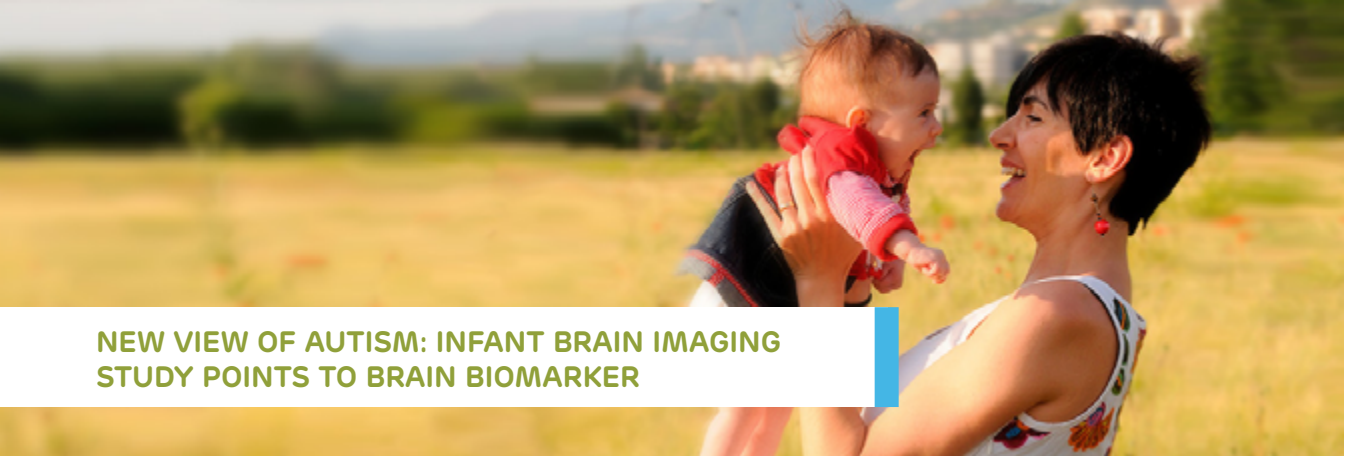
CHOP and The Wistar Institute celebrated the 10th anniversary of a vaccine against rotavirus, a major worldwide killer of children under age 5. Rotavirus is a widespread microbe that infects the gastrointestinal system, causing severe diarrhea and vomiting, which can be life-threatening in young children.

Research conducted by CHOP and Wistar scientists starting in the 1980s culminated in FDA approval of the Rotateq® vaccine in 2006. Before Rotateq, approximately half a million children ended up in the emergency room with rotavirus every year, with 75,000 hospitalized with severe dehydration. Up to 60 children hospitalized died each year. Thanks to Rotateq, today, child hospitalizations from rotavirus have dropped by 85 percent in the U.S. The vaccine is also saving children's lives around the world.

DRIVING CHANGE: PARTNERS FOR CHILD PASSENGER SAFETY TURNS 20

CHOP's Partners for Child Passenger Safety (PCPS) program, the nation's first large-scale child-focused crash surveillance system, turned 20 in 2017. In its first 10 years of existence, PCPS conducted the world's largest research project focused on children in motor vehicle accidents, studying more than 875,000 children involved in 600,000 crashes, conducting 33,000 interviews, and analyzing over 800 on-site investigations.

Created in collaboration with State Farm Insurance, PCPS used its study findings to make recommendations about child safety that have shaped and advanced the future of vehicle design, legislation, and public health education. Most importantly, PCPS has contributed to reducing the number of children dying in automobile crashes each year from more than 2,000 in the 1990s to approximately 1,000 in 2017. PCPS also has helped save many more children from serious injury.



NEW VIEW OF AUTISM: INFANT BRAIN IMAGING STUDY POINTS TO BRAIN BIOMARKER

CHOP's Center for Autism Research took part in the Infant Brain Imaging Study network, which discovered a brain biomarker that may help identify children with autism spectrum disorder (ASD) earlier in life with the help of a computer-generated algorithm. The findings seem to confirm what researchers have long suspected — that changes in the brain may precede behavioral manifestations of ASD.

Autism is typically diagnosed in children around age 4 in the U.S., but by that time, their brains have already changed substantially and tend to be enlarged. Increased brain size was one of the earliest brain markers discovered in autism, which is characterized by difficulties in social interaction, verbal and nonverbal communication, repetitive behaviors, and restricted interests.

Previously, brain size had only been studied in children and adults after the full onset of autism. The study findings could result in diagnosing a child with autism much earlier, before the full onset of symptoms. The ability to intervene as early as a child's first year of life could offer the potential to mitigate the development of autism and improve long-term outcomes.

ENDING A DIAGNOSTIC ODYSSEY: MULCHANDANI-BHOJ-CONLIN SYNDROME

A rare genetic growth condition was named after the three scientists at CHOP who extensively studied and defined it as a recognizable disorder. Mulchandani-Bhoj-Conlin Syndrome (MBCS) is characterized by mild prenatal growth deficiency, slow growth, and the lack of desire to eat.

MBCS takes its name from Surabhi Mulchandani, MS, genetic counselor and manager of the Genomic Diagnostics Laboratory; Elizabeth Bhoj, MD, PhD, clinician-researcher in the Division of Human Genetics; and Laura Conlin, PhD, director in the Genomic Diagnostics Laboratory. In defining the characteristics of MBCS, including the unusual chromosomal pattern, the three scientists conducted 13,000 genetic tests over eight years and published a research article on their findings.

Normally, children inherit one copy of each chromosome from each parent, but children with MBCS receive both copies of chromosome 20 from their mother only. Researchers don't know yet what causes the absence of paternally inherited genes on chromosome 20.

But the recognition of a clear, definable disorder with an official name brings hope to families. The CHOP scientists found that children treated with growth hormones put them back on track developmentally, and none experienced long-term delays. It also brings clarity for physicians because many conditions cause babies to have trouble gaining weight.

LANDMARK APPROVAL: REVOLUTIONARY GENE THERAPY FOR INHERITED BLINDNESS

The U.S. Food and Drug Administration landmark approval of Luxturna™ marked the nation's first gene therapy approved for the treatment of a genetic disease, and it was the culmination of more than a decade of dedication and perseverance by the CHOP-Penn-Spark research team and the commitment of the patients and families who participated in the clinical studies.

"The FDA's approval of Luxturna highlights the vital role of pediatric research in developing breakthrough cures," stated Bryan Wolf, MD, PhD, Executive Vice President and Chief Scientific Officer of CHOP Research Institute. "Spanning the course of 10 years, the research conducted at CHOP's Center for Cellular and Molecular Therapeutics laid the groundwork for this revolutionary gene therapy."

The one-time gene therapy product is indicated for the treatment of patients with a rare, inherited form of retinal blindness called biallelic RPE65 mutation-associated retinal dystrophy. An estimated 1,000 to 2,000 patients in the U.S. with RPE65 mutations experience visual impairment at infancy or early childhood and become totally blind by mid-life. The therapy delivers corrected versions of the RPE65 gene in a single injection using a genetically engineered, benign adeno-associated virus to carry the genes to the retina.

Spark Therapeutics, a Philadelphia biotechnology company created in 2013 by CHOP to accelerate the timeline for bringing new gene therapies to market, led the late-stage clinical development of the therapy. Spark was built on the foundational research conducted at CHOP's Raymond G. Perelman Center for Cellular and Molecular Therapeutics under the direction of then-CHOP-researcher Katherine High, MD, a gene therapy pioneer who is now Spark's president and head of research and development.

The initial research also was spearheaded by Jean Bennett, MD, PhD, F.M. Kirby professor of Ophthalmology at the Perelman School of Medicine at the University of Pennsylvania's Scheie Eye Institute, and Albert Maguire, MD, a professor of Ophthalmology at Penn Medicine and an attending physician at CHOP, who served as a principal investigator of the therapy's clinical trials.

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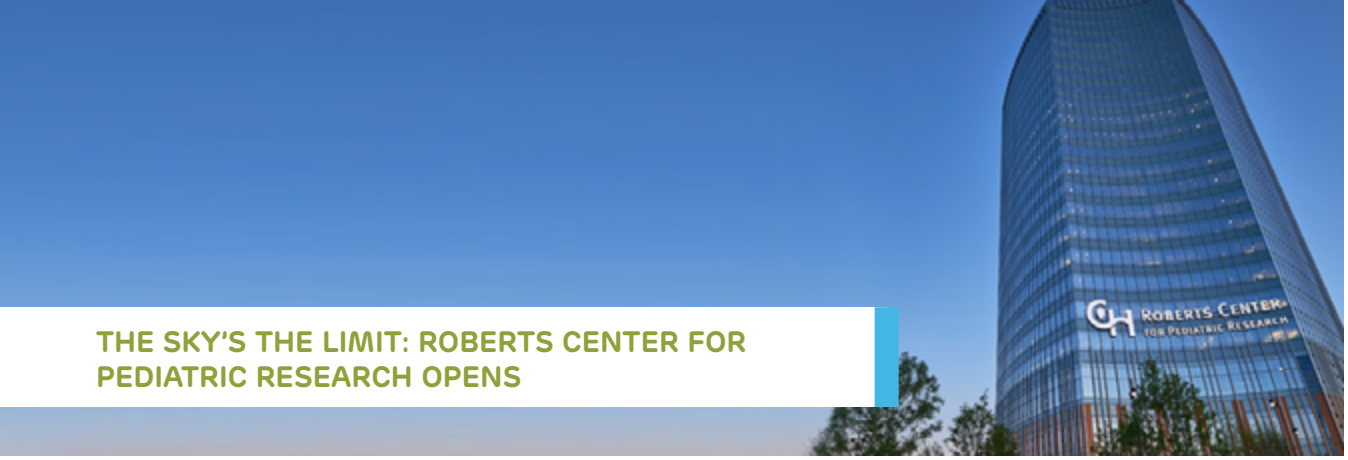


THE SKY'S THE LIMIT: ROBERTS CENTER FOR PEDIATRIC RESEARCH OPENS

With a completed 21 floors, 466,000 square feet, and a breathtaking view of Philadelphia's Schuylkill River, the Roberts Center for Pediatric Research officially opened in May 2017. The curvy building has open floor plans that foster collaboration among research and administrative personnel. And the Family Research Center in the Roberts Building allows for a range of specialized evaluations of children and families, typically through direct observation, survey, or even CHOP's driving simulator.

The latest addition to CHOP's campus is named after the Roberts Family, who generously donated $25 million toward the Roberts Collaborative for Genetic and Individualized Medicine in 2016. The Collaborative combines existing genetics and genomics centers at CHOP for a multidisciplinary approach to developing novel treatments and understanding of rare and complex diseases. Both the Collaborative and the Roberts Center at which it is headquartered are a nod to the exciting potential that genetics and genomics research hold in current investigations as well as in years to come. At the Roberts Center grand opening, Bryan Wolf, MD, Executive Vice President and Chief Scientific Officer at CHOP Research Institute, said that the Roberts Center and the Collaborative will help transform our efforts to progress personalized medicine.

The Hospital acquired the property in 2010 and began planning for construction. The ground-level spaces outside the building offer new possibilities for neighbors to gather as a community, and a pedestrian bridge connects to the popular Schuylkill River Trail.

PIONEERING TREATMENTS: THREE NEW FRONTIERS PROGRAMS ANNOUNCED

Bringing a research breakthrough from the bench to the bedside often takes years of hard work and support. In 2015, CHOP launched the Frontiers Program Initiative to support large internal programs in fast-tracking cutting-edge research pioneered in their labs and clinics. This year, an oversight panel selected three new Frontier Programs: the Mitochondrial Medicine Center, the Newborn and Infant Chronic Lung Disease Program, and the Center for Pediatric Airways Disorders. The programs receive funding from the hospital and programmatic guidance from a multidisciplinary steering committee.

With its new designation as a Frontier Program, the Mitochondrial Medicine Center aims to address the growing prevalence and heterogeneity of mitochondrial disorders, genetic conditions that result from dysfunction in our body's tiny cellular batteries. The Center will drive research and clinical care forward by improving communication among clinicians from multiple disciplines who treat mitochondrial patients, finding novel ways to diagnose children with mitochondrial conditions, and developing new therapies, according to Marni Falk, MD, director of the Mitochondrial Medicine Frontier Program.

Meanwhile, the Center for Pediatric Airway Disorders, the largest multidisciplinary center in the world for treating airway conditions, will use its new Frontier designation to expand both its research effort and its clinical reach. A new bioengineering materials scientist will lead and develop a new cartilage and bioengineering materials laboratory. Frontier funding will also help to further develop a number of novel treatments and devices, according to Ian Jacobs, MD, medical director of the Center. These include the identification of the most ideal beverage or solution for mitigating button battery injuries and the commercialization of a 3-D printed tracheal model to be used in simulation training for teaching tracheostomy care to healthcare professionals and parents.

Finally, the Newborn and Infant Chronic Lung Disease Program (NeoCLD), one of the largest specialty programs in the country, will focus on advancing translational research and continue developing liquid ventilation — a therapeutic innovation 25 years in the making. Liquid ventilation aims to give infants who develop severe breathing problems a stronger chance of survival by delivering oxygen to their lungs through liquid instead of air.

"The Frontier Program will take us to the next step, which includes multicenter trials, and it will allow us to expand several trials simultaneously," said William Fox, MD, medical director of the Infant Breathing Disorder Center at CHOP and a neonatologist within NeoCLD.

Learn more about the new Frontier Programs on *Bench to Bedside*.

NEXT GENERATION COLLABORATION: CENTER FOR APPLIED GENOMICS ACHIEVES MILESTONE

As next-generation sequencing has quickly become more sophisticated, less expensive, and faster in the last decade, the Center for Applied Genomics (CAG) at CHOP is pioneering its use to diagnose, prevent, and manage rare pediatric diseases with the help of reliable informatics. In December 2016, the CAG reached an important milestone: It received Clinical Laboratory Improvements Amendments (CLIA) certification. Mandated by the Centers for Medicare & Medicaid Services, CLIA certification ensures that a laboratory team continuously adheres to high standards in all aspects of their work—from the integrity of lab procedures to the safety of research participants—and can prove it through bi-annual proficiency tests.

"This reflects a major accomplishment from the entire team at CAG who worked tirelessly for many months to achieve this milestone," said Avni Santani, PhD, director of Clinical Laboratories, Strategic Partnerships, and Innovation at the CAG. "The CAG team is excellent and dedicated to the pursuit of quality in every step of the pathway from specimen collection to data analysis."

Now positioned as the only CLIA-certified high throughput sequencing and SNP-array facility that operates within a robust children's research institute, CAG can join and lead collaborations with other academic, biotechnology, and pharmaceutical organizations worldwide by supporting large clinical research studies. The Center's new CLIA status might also pave the way for future third-party collaborations with genetic carrier screening services, as mainstream interest into genomics grows, according to Hakon Hakonarson, MD, PhD, director of CAG. In this case, the CAG would work on the complex genomic work of isolating DNA and then provide the third-party company with information about its client's results. Genetic counselors would help to interpret the findings and explain them to concerned families.

These new partnerships also could speed discovery about rare and complex pediatric diseases. "We will always ask for the opportunity to use the samples and information we gather in a de-identified way for research," Dr. Hakonarson said. "This will allow for our biobank to grow much faster and allow far more productive research to be done."

Learn more about how the CAG plans to drive breakthroughs with their new CLIA certification on *Bench to Bedside*.

TIME OF OPPORTUNITY: CHANGING HOW WE TALK ABOUT THE TEEN YEARS

As new technologies transform the way researchers communicate information to the wider world, a new center is taking the opportunity to chip away at the ongoing narrative that depicts the teen years as one of stress and strain for parents. Two experts in the division of Adolescent Medicine at CHOP launched the new Center for Parent and Teen Communication (CPTC) with a three-year grant from the John Templeton Foundation and funding from the HIVE at Spring Point and Drs. Kathy Fields and Garry Rayant. Through the CPTC, a multi-disciplinary team of clinicians, researchers, and social media strategists will work together to promote the health, well-being, and character of adolescents through research, education, and advocacy.

"Adolescents quite literally represent our future, and it is critical that we create the right developmental milieu for them to become their best selves," said Ken Ginsburg, MD, physician in the division of Adolescent Medicine and co-founder of the CPTC. "Core to that development is their relationship with their parents. With so many undermining messages about that relationship, we want to give positive developmental messages that will change the tone and tenor of the conversation."

The Center currently houses a Research Core focused on improving parent-teen communication at the doctor's office, and a Translation and Dissemination Core that will translate evidence-informed information into written and video materials that are easily accessible and consumer-friendly. Through the Research Core, Carol Ford, MD, chief of the division of Adolescent Medicine and co-founder of the CPTC, conducts primary research on the important role doctors and nurses play in improving parent-teen communication.

"Parents and doctors both want the best health outcomes for their teens, and we really need to understand how doctors and nurses can better partner with parents, while also respecting their values, culture, and parenting styles," Dr. Ford said.

Dr. Ginsburg leads the effort to translate and disseminate existing research about positive youth development and parenting through a comprehensive website and the online social community.

"Social media now sets the discourse for conversation," Dr. Ginsburg said. "It's where people now turn to for information. The challenge is that the information is not always rooted in research and doesn't always give the most developmentally appropriate advice."

Learn more about the new Center for Parent and Teen Communication at CHOP on *Bench to Bedside*.

SMART SOLUTIONS: ENHANCEMENTS TO CLINICAL RESEARCH PROGRAM INTRODUCED

Since 2013, the number of interventional clinical trials approved by CHOP's Institutional Review Board has doubled to 600, encompassing a broader range of studies than ever before. In line with this growth, the Oncore Clinical Trial Management System rolled out across CHOP's enterprise in 2017. It is a powerful and comprehensive platform for managing a clinical trial throughout its lifecycle, simplifying data management, and improving compliance. OnCore is a testament to the Research Institute's continued commitment in its strategic plan to enhance and improve clinical trials for the benefit of both researchers and the patients and families who join our studies with the hope of advancing pediatric health.

Another exciting initiative to enhance clinical research strategies that began in early summer is a partnership with the hospital's division of Language Services that brought interpreter services to non-English speaking study participants. This language support improves accessibility to clinical trials for a diverse group of families. And the newly rebranded Center for Human Phenomic Science (CHPS) opened in the Wood Building, improving and expanding patient/family evaluation and in-house laboratory space. The goal of the CHPS is to provide the resources, environment, operations, and training to support and promote high-quality clinical and translational research by qualified investigators.

POSSIBILITIES FOR PREVENTION: LIFESPAN BRAIN INSTITUTE LAUNCHES

The new Lifespan Brain Institute (LiBI) is uniquely positioned as a broad collaboration between CHOP and the Perelman School of Medicine at the University of Pennsylvania that supports research across the fetal-adult continuum, which is a pillar of CHOP Research Institute's strategic plan. By studying the brain's development — and tracking psychiatric symptoms as they emerge from childhood to adulthood — researchers can get to the root of mental health conditions.

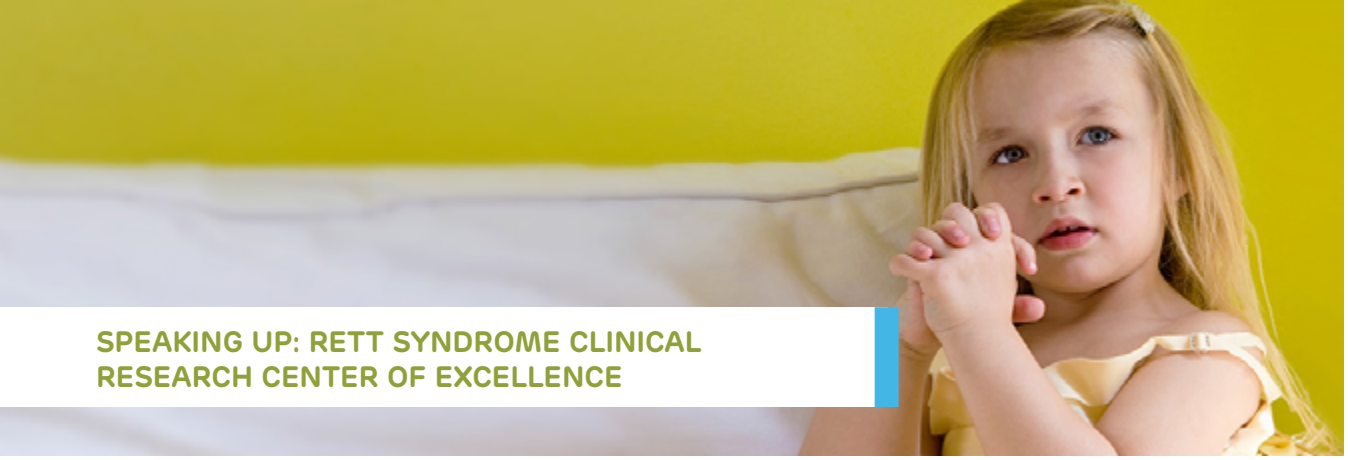
Co-directed by Raquel Gur, MD, PhD, professor of Psychiatry Neurology and Radiology at Penn, and Stewart Anderson, MD, a CHOP research psychiatrist and professor of Psychiatry at Penn, LiBI has assembled large data sets that allow researchers from multiple specialties to study the underlying genetic, molecular, cellular, system, and behavioral functions that likely intersect with environmental factors and contribute to the development of psychiatric illnesses.

"We know that neuropsychiatric illnesses that present in later childhood, adolescence or adulthood, have pathological antecedents that start way before symptoms begin," Dr. Anderson said. "Ideally, we'd really like to intercept the pathological process before people get sick, or before they get any sicker than necessary."

LiBI held its first mental health research symposium, "Pathological Antecedents to Neuropsychiatric Disorders," March 12, 2018, at the Smilow Center for Translational Research. The event gathered 200 attendees, including basic to translational scientists and child to adult psychiatrists, in order to discuss the importance of studying mental illness throughout the lifespan.

Several LiBI researchers are using data from the Philadelphia Neurodevelopmental Cohort (PNC) to conduct longitudinal analyses and dig deeply into the neurobiological development of mental illness. Funded by the National Institutes of Mental Health, the PNC is a collaboration between the Center for Applied Genomics at CHOP and the Brain Behavior Laboratory at the University of Pennsylvania. The cohort includes a population-based sample of over 9,500 individuals, ranging from 8 to 21 years old, who received medical care at the CHOP network.

For example, Ted Satterthwaite, MD, director of Imaging Analytics at LiBI, and David Roalf, PhD, research assistant professor at LiBI, are using multimodal imaging efforts through LiBI and the PNC to understand how the brain develops normally, so that investigators can plot types of development and understand how abnormal development is associated with risk and resilience. While Dr. Roalf focuses on advances in translational neuroimaging, particularly imaging brain glutamate, Dr. Satterthwaite focuses on executive deficits in psychiatric syndromes.



SPEAKING UP: RETT SYNDROME CLINICAL RESEARCH CENTER OF EXCELLENCE

With designation as a Rett Syndrome Clinical Research Center of Excellence by the nonprofit organization RettSyndrome.org, scientists at CHOP joined forces with 13 other clinics across the U.S. to dig deeper into the neurodevelopmental disorder's biology and pathology. Eric Marsh, MD, director of the Neurogenetics Program at CHOP, currently leads the Center of Excellence through a natural history study and other associated projects.

"It's an honor to be chosen, and it shows that we're doing good work," said Dr. Marsh of the new designation. "There is a lot of research activity going on that we hope to be a part of into the future to really see a change for the care of these girls and kids with related diseases too."

With all 14 Centers of Excellence working collaboratively, the Natural History of Rett Syndrome and Related Disorders study tracks and gathers data from Rett patients to examine the phenotypic differences and similarities of children with the MECP2 mutation that is at the root of the syndrome. The information will hopefully provide a baseline by which clinicians can compare patients to, especially as research gets closer to discovering treatments, according to Dr. Marsh.

As a subproject of that study, Dr. Marsh is also taking a closer look into the brain biomarkers of Rett symptoms by using visual and auditory evoked potential tests. Preliminary studies show that the brain responds differently for children with Rett compared to healthy, age matched controls. By placing electrodes on Rett patients' scalps, researchers can measure the brain's electrical activity and signature in response to the stimulation, or "evoking," of certain sensory nerve pathways.

"Our hypothesis is that the signature will be more different and get worse over time," Dr. Marsh said. "If that does happen, you can imagine that if you give a patient a particular drug and you see the signature go closer toward the normal response, then it would suggest that your intervention is working."

CHOP was also chosen to be an initial site of the Rett Syndrome Research Trust Clinical Trial Consortium. The initiative, launched in the fall of 2017, seeks to give expert Rett physicians from a number of institutions the resources and personnel they need to conduct high-quality clinical trials with efficiency and eliminate barriers to sharing important information to advance Rett research and treatment.

Read more about our research to end Rett from the perspective of the Connors, a patient family participating in the natural history study and other trials at CHOP, on *Cornerstone*. Learn more about CHOP's designation as a Rett Syndrome Clinical Research Center of Excellence on *Bench to Bedside*.

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COLLABORATION ›

THE GIFT OF TIME: ARTIFICIAL ENVIRONMENT MIMICS LIFE IN THE WOMB

Four years ago, spurred by the desire to give premature babies a better chance for a healthy life, a team of multidisciplinary researchers at CHOP began to develop a fluid-filled system that would imitate life for a fetus in the womb. Containing the necessary nutrients that a fetus requires to develop and thrive, the environment would support and stabilize babies born too soon, particularly between 23 and 26 weeks. Because extremely premature infants often have underdeveloped lungs that cannot adapt to gas ventilation, the system would give them a valuable few weeks to mature these and other vital organs — just as if they were still being carried in their mother's uterus.

The research team led by Alan Flake, MD, fetal surgeon at CHOP, reported on their most recent prototype in *Nature Communications*. The study captivated both the scientific community and the mainstream media as it described how the current preclinical model supported eight fetal lambs for as long as 28 days, keeping them healthy as indicated by vital signs, blood flow, fetal blood gases, and other parameters monitored 24 hours a day.

"This system is potentially far superior to what hospitals can currently do for a 23-week-old baby born at the cusp of viability," said Dr. Flake who is also a professor of Surgery at the University of Pennsylvania's Perelman School of Medicine. "This could establish a new standard of care for this subset of extremely premature infants."

After four rounds of prototypes, the current system is a sealed, sterile, fluid-filled container custom-made to fit each fetus and insulated from fluctuations in temperature, pressure, light, and hazardous infections. It provides nutrients and growth factors to each fetal lamb through a continuous amniotic fluid exchange system developed by Marcus Davey, PhD, a fetal physiologist at CHOP and associate professor of Surgery at Penn. Meanwhile, the lamb's heart pumps blood via its umbilical cord into a low-resistance external oxygenator that substitutes for the mother's placenta. Mimicking the normal physiology of a fetus, this flow of blood is driven entirely by the fetal lamb itself.

While the system has only been tested in animals, Dr. Flake believes that if more research shows that the system can translate into clinical care, it could help reduce mortality and disability for extremely premature babies by bridging their time from the womb to the world.

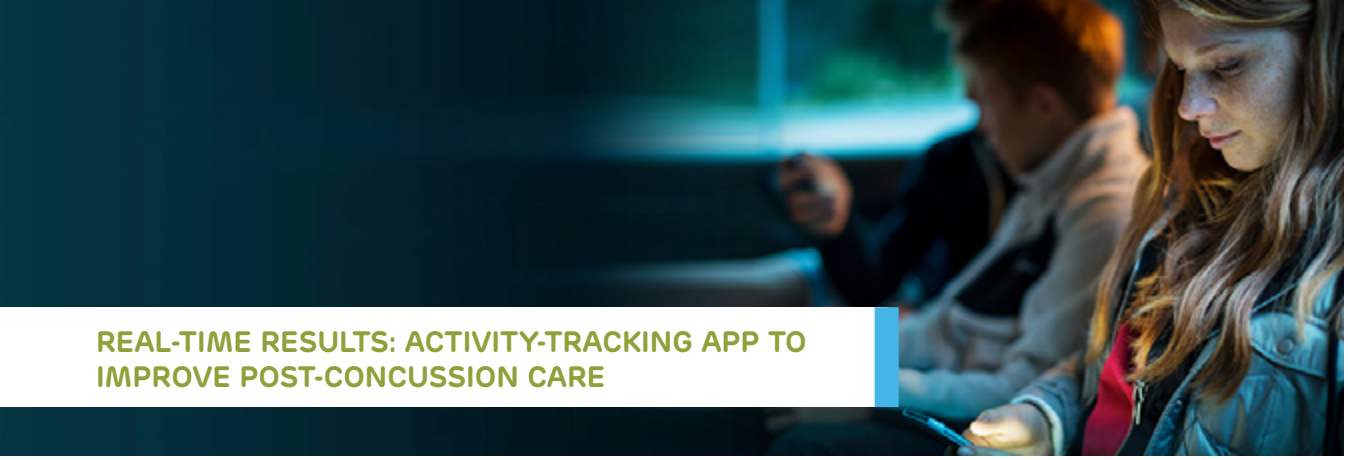
SNAPSHOT OF A SYNDROME: FACIAL RECOGNITION HELPS DIAGNOSE 22Q11.2 DS

Snapping a photo could soon be a simple way to help clinicians recognize rare, genetic diseases such as 22q11.2 deletion syndrome (22q11.2 DS). Children who inherit 22q11.2 DS often have multiple birth defects — from congenital heart disease, to endocrine problems, to developmental differences such as autism, and more. In collaboration with the National Institutes of Health (NIH), researchers at CHOP contributed to the development of a unique facial recognition software, which is similar to systems used by airports and Facebook, to facilitate earlier diagnosis of 22q11.2 DS. Further-refined models of the technology may allow providers to take a cell phone photo of their patient to be analyzed and accurately diagnosed when confirmatory laboratory studies are unavailable.

The team published a report of the current software in the *American Journal of Medical Genetics* with Elaine Zackai, MD, director of clinical genetics at CHOP and professor of Pediatrics in Genetics at Penn, and Donna McDonald-McGinn, MS, LCGC, associate director of Clinical Genetics and director of the 22q and You Center at CHOP, as well as T. Blaine Crowley, data manager, and Daniel E. McGinn, Davidson College undergraduate student, as co-authors. The study compared photos of 156 children and adults with 22q11.2 DS to 156 photos of individuals in a control group matched for age and gender.

Altogether, the participants represented 11 different countries. Based on 126 distinct facial features, the researchers made correct diagnoses 96 percent of the time for participants from all ethnic groups using the facial analysis software. The diversity of this cohort — and the software's sensitivity to ethnicity — is significant: Dr. McDonald-McGinn noted that in a previous study, she and her colleagues observed that diverse populations may be underdiagnosed for 22q11.2 DS. The research is also part of the NIH Atlas of Human Malformations in Diverse Populations, which will contain pictures and written descriptions of individuals from diverse ancestries.

"Healthcare providers here in the United States as well as those in other countries with fewer resources will be able to use the atlas and the facial recognition software for early diagnoses," said senior author Maximilian Muenke, MD, a former trainee and attending geneticist at CHOP and currently chief of the National Human Genome Research Institute's Medical Genetics Branch. "Early diagnosis means early treatment along with the potential for reducing pain and suffering experienced by these children and their families."



REAL-TIME RESULTS: ACTIVITY-TRACKING APP TO IMPROVE POST-CONCUSSION CARE

Families often wonder how long a child who has experienced a concussion should rest and which activities to avoid. When it comes to putting an exact number to recovery, however, the optimal timeframe varies for each individual. A CHOP research team harnessed the power of "real-time" updates found in today's mobile apps, in order to gain ground in personalizing pediatric post-concussion care.

The team led by Christina Master, MD, sports medicine pediatrician at CHOP and professor of Clinical Pediatrics at Penn, in collaboration with Douglas Wiebe, PhD, at Penn's Center for Clinical Epidemiology and Biostatistics, developed an app and monitoring system using Ecologic Momentary Assessment (EMA) that tracked the activity and concussion symptoms of 34 children ages 11 to 19 who had just sustained a concussion. The app prompted the patients to report their symptoms in real time at random intervals during the day, as well as report how much time they spent performing cognitive activities such as reading, gaming, or using the computer. In addition to carrying an Ipod Touch® for the app, the patients also wore accelerometers (step counters) to track their physical activity.

In results published in *JAMA Pediatrics*, Dr. Master and her team found that generally, symptoms decreased as the two-week follow-up period progressed. Regardless of their activity levels, more than 68 percent of study participants had acute symptoms resolve by the end of the follow-up. Additionally, the team discovered that cognitive activities often increased symptoms, while physical exercise lowered them.

As a research strategy, EMA could be used in future studies to further explore the relationship between activity and symptoms over the course of concussion recovery. In clinical care, EMA could help physicians adjust their care plans according to updates from their patients in real time. This new method of communication and care management could eliminate the wait for follow-up visits, and it also could prevent physicians from having to rely on what patients or parents remember about concussion symptoms.

STRENGTH IN NUMBERS: FIGHTING CANCER WITH BIG DATA

Many serious pediatric diseases are so rare that no individual institution can accumulate enough samples or data to gain significant insights into what drives the conditions at a molecular level. In the last few years, however, CHOP investigators have teamed up to build networks across the nation that break down these research silos and encourage the collaborative use of shared patient data.

For example, Adam Resnick, PhD, co-director of the Center for Data-Driven Discovery in Biomedicine (D3b), is currently the scientific chair of the Children's Brain Tumor Tissue Consortium (CBTTC), headquartered at CHOP, and the Pacific Pediatric Neuro-Oncology Consortium (PNOC). Meanwhile, D3b, which is co-led by Phillip 'Jay' Storm, MD, chief of the division of Neurosurgery and associate professor of Neurosurgery at Penn, drives forward a data-based ecosystem on behalf of CHOP's diverse patient population. D3b leads the Kids First Data Resource Center, a new NIH program supported by a nearly $15,000,000 grant, representing one of the largest initiatives of its kind focused on "big data genomics" in pediatric cancers and birth defects.

In October 2016, CBTTC and PNOC announced the release of CAVATICA, an open-access, cloud-based biomedical data analysis platform created in partnership with Seven Bridges, to give clinicians and scientists across CHOP and the world rapid access to large amounts of genomics data and other types of information about pediatric diseases. The data collectively represents more than 20 pediatric hospitals and covers a range of illnesses including cancer, congenital disorders, epilepsy, and autism. It is the first time that the information will exist in one single and accessible environment in the cloud, giving researchers the ability to move beyond the study of one disease and instead, analyze data from a number of rare diseases, in order to learn about their potential shared mechanisms. Under the Kids First Data Resource Program, CAVATICA and its associated portals will expand to include more than 25,000 patients and family members.

"CAVATICA gives us an unprecedented opportunity to research a number of childhood diseases, ranging from pediatric brain tumors that are the leading cause of disease-related death in children to rare pediatric disorders that get limited attention and resources," stated Dr. Resnick in a press release.

ESTIMATING CELL ENERGY: NOVEL IMAGING TOOL MEASURES MITOCHONDRIAL ACTIVITY

Mitochondria, the power plants of a cell, generate the energy we need for nearly every organ or system in the body to function properly. Shana McCormack, MD, an attending physician in the division of Endocrinology and Diabetes at CHOP and assistant professor of Pediatrics at Penn, along with colleagues at the University of Pennsylvania's Center for Magnetic Resonance and Optical Imaging, developed a noninvasive way to track mitochondria and gain insights into their bioenergetics.

The new approach is a unique magnetic resource imaging tool, called creatine chemical exchange saturation transfer (CrCEST) MRI, that could help researchers study the impact of metabolic disease longitudinally in children. CrCEST detects changes in muscle creatine content before and after exercise. These changes allow researchers to estimate mitochondrial oxidative phosphorylation (OXPHOS) capacity, which is an important indicator of how the body generates energy.

In their study published in *JCI Insight*, Dr. McCormack and her colleagues demonstrated that CrCEST was a viable technique for measuring OXPHOS capacity after exercise in individuals with genetic mitochondrial disease, a group of conditions that can produce symptoms in many different organs, including fatigue, cardiac problems, diabetes, hearing and vision impairment, and more — depending on which cells within the body have disrupted mitochondria.

CrCEST has several benefits beyond the current techniques used to measure mitochondrial function, which often require a muscle biopsy. Along with being noninvasive, CrCEST gives researchers a high-resolution picture of mitochondrial function in different muscle groups simultaneously. With further development, the new tool may give physicians an objective biomarker to determine whether a particular intervention is truly helping a patient's mitochondria to function better.

Investigators also could take the tool in new directions. For example, CrCEST could be used to address one of Dr. McCormack's research questions: How does muscle mitochondria dysfunction contribute to precipitating diabetes?

"In order for me to study diabetes risk in these individuals, it's helpful to have a measure of muscle mitochondrial dysfunction," Dr. McCormack said. "Then, the next question is: 'Does muscle uptake of glucose depend on the degree of OXPHOS capacity?' And if it does, this might be an area to intervene to prevent the development of diabetes, in individuals with mitochondrial diseases as well as individuals with 'common' type 2 diabetes."

IMAGING IN THE OR: ECHOCARDIOGRAPHY DETECTS HEART DEFECTS DURING SURGERY

When surgeons repair a type of heart condition known as a conotruncal defect, residual holes can appear between a patient's two heart chambers — a rare but life-threatening complication known as intramural ventricular septal defects (VSDs). Researchers from the Cardiac Center at CHOP investigated a novel approach to detecting VSDs that would give surgeons the powerful ability to repair the complication during the same operation.

Transesophageal echocardiography (TEE) is a type of echocardiography that takes pictures of the heart by inserting a small transducer into a patient's esophagus. Though the imaging tool is typically used in exams, TEE had not yet been studied as a way to detect VSDs during surgery. The CHOP research team is the first to do so, publishing their findings in the *Journal of Thoracic and Cardiovascular Surgery*. Meryl Cohen, MD, a pediatric cardiologist at CHOP and professor of Pediatrics at the Perelman School of Medicine, led the research.

In a retrospective analysis of 337 children, mostly infants, who underwent surgery for conotruncal defects between 2006 and 2013, Dr. Cohen and her fellow researchers compared the use of TEE during surgery with that of another echocardiography tool, transthoracic echocardiography (TTE) after surgery. Unlike TEE, TTE is noninvasive. In their results, the team found that both TTE and TEE identified 19 VSDs out of 34 surgical patients who had the intramural defect, while only TTE identified an additional 15. Overall, the data showed that TEE had modest sensitivity (56 percent) but high specificity (100 percent) for identifying intramural VSDs.

The findings build on a previous study from the Cardiac Center and led by Dr. Cohen that recognized intramural VSDs as distinct from other types of residual holes. In that study, published in *Circulation* in 2015, the research team concluded that intramural VSDs were uniquely associated with an increased risk of complications and mortality in children with heart disease, making it important to address and identify the defects as quickly as possible.

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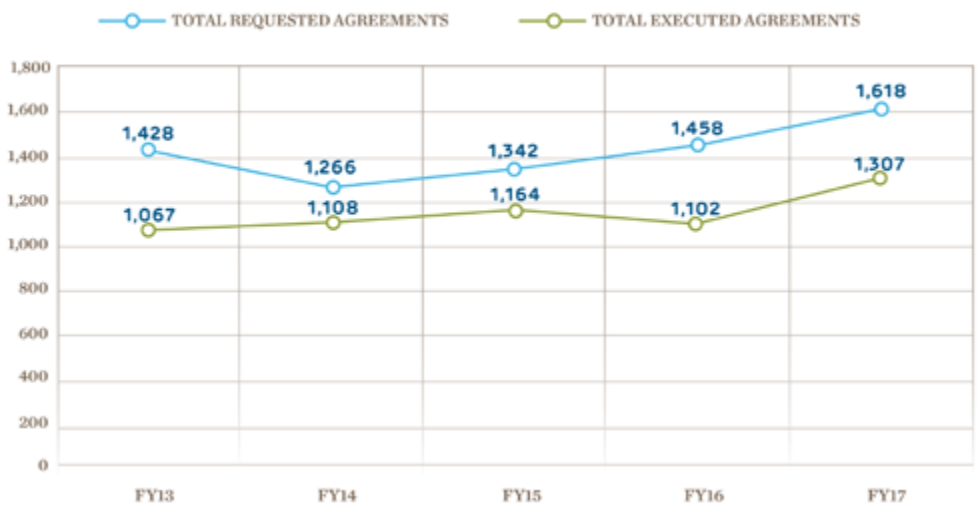

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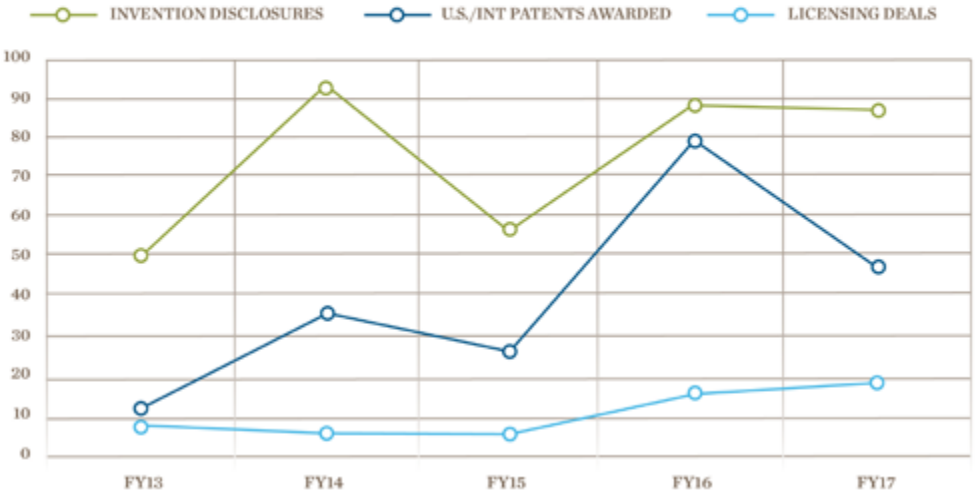

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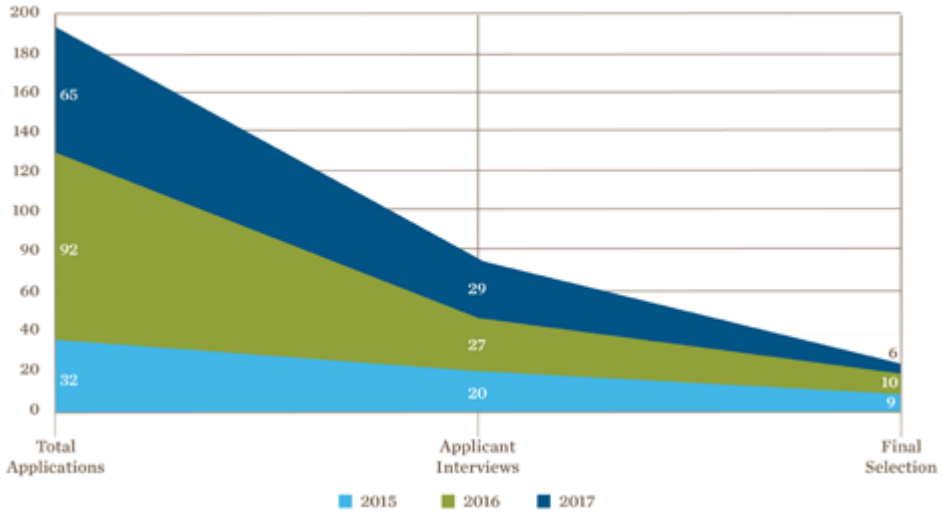


TECH TRANSFER BY THE NUMBERS	FY 2016	FY 2017
Licensing Deals	15	18
Invention Disclosures Received from Inventors	88	87
U.S. Patent Applications Filed (Provisional)	36	29
U.S. Patent Applications Filed (Utility and Nationalized PCT)	33	29
U.S. Patents Awarded to CHOP	14	6
International Patent Applications Filed (PCT and Foreign)	155	62
International Patents Awarded to CHOP	65	41

AGREEMENTS	FY 2016	FY 2017
Material Transfer Agreements (MTAs)	450	488
Confidential Disclosure Agreements (CDAs)	284	288
Data Use & Data Transfer Agreements (DUAs & DTAs)	143	186
Consulting Agreements	79	142
Other Agreements	146	203
TOTAL AGREEMENTS FULLY EXECUTED	**1102**	**1307**

COLLABORATION

HONORS ›

SOMETHING TO SMILE ABOUT: GENOMICS RESEARCH AND INNOVATION NETWORK

Going it alone to create a patient cohort population that is large enough to study can be a time-consuming process for an individual genetic scientist who wants to make a difference in a pediatric disease. That's why three premier pediatric academic medical institutions — Children's Hospital of Philadelphia, Cincinnati Children's Hospital Medical Center, and Boston Children's Hospital — formed the new Genomics Research and Innovation Network (GRIN) to foster a culture of data sharing.

"The ultimate goal is to have this resource populated with over 100,000 cases that would include individuals' clinical data at a high resolution, genotyping data, and associated biospecimens so that you can move discovery forward," said Ian Krantz, MD, an attending physician in the division of Human Genetics at CHOP who serves on GRIN's executive team.

The new initiative helps to overcome barriers to research in pediatric genomics by addressing the problem of too much data and too little time. A wealth of data is available through electronic health records, clinical trials, and data registries, but it is not feasible for individual researchers to comb through all this information and extract what they need to identify large patient cohorts with deep phenotyping. GRIN aims to make this process more consistent, precise, and seamless for its members by establishing a data trust that will allow for more comprehensive analysis of complex disease.

While GRIN is getting up and running, it currently is only open to investigators at the three member institutions, but the idea is to invite other institutions to join GRIN in the future. Before any investigator dives into this unparalleled resource, GRIN's scientific committee will vet their research proposals. The network's sustainability committee also is considering how to handle commercial interest, such as from pharmaceutical companies.

"This is a very valuable resource that could be leveraged for drug discovery and therapeutic trials," Dr. Krantz said. "Having access to this type of well-characterized and accessible cohort with available biological samples is very appealing."

PALLIATIVE CARE JOURNEY: SHARE AIMS TO HELP GUIDE FAMILIES

One of the challenges to pediatric palliative care research is that no one hospital is likely to have a sufficient number of children with a particular condition to be able to fully explore epidemiologic and health services questions. That is why CHOP and three other hospitals that are part of the Pediatric Palliative Care Research Network are launching an innovative multicenter project called SHAred Data and REsearch (SHARE).

CHOP, Boston Children's Hospital, Seattle Children's Hospital, and Children's Hospitals and Clinics of Minnesota all have "remarkably good" pediatric palliative care programs, according to SHARE Principal Investigator Chris Feudtner, MD, PhD, MPH, director of the department of Medical Ethics at CHOP and director of Research for the Pediatric Advanced Care Team. They will collaborate to build a standardized and organized infrastructure to collect and merge patient- and parent-reported clinical data with hospital administrative data into a SHARE database.

The resulting dataset will provide a wealth of information regarding hospital-based care for a cohort of 800 patients receiving pediatric palliative care, including patient demographic and diagnostic information, patient or parent reported symptoms, and parent reports on their levels of distress and how their goals of palliative care change as their child's serious illness progresses.

"We will follow them over time to identify distinct patterns of how things play out, and how those patterns affect the ways that they think about making decisions for their child," Dr. Feudtner said. "All of this will hopefully improve the care the kids get and the outcomes for them, their parents, and family members."

Dr. Feudtner expects that the collaborative SHARE project will be a catalyst for many future studies using the SHARE data and research infrastructure. He envisions large multicenter studies could be accomplished to perform intervention research — such as drug treatment studies or evaluating bundled therapies for symptom control— and quality improvement work within and across hospitals, such as identifying the best care delivery model to transition patients seamlessly from hospital to home care.

UNIQUE VANTAGE POINT: RESEARCHERS TACKLE CONCUSSIONS

While the heft of concussion research has looked at college-aged and professional athletes, a new $4.5 million grant from the National Institute of Neurological Disorder and Stroke will allow researchers from CHOP and Penn team to study a high school population, for whom there is little available data on injury criteria and thresholds. Their goal: Design evidence-based, diagnostic assessment tools for the clinic and the sidelines, as well as create the foundation for better headgear and other protective equipment.

The biggest strength of the study lies in its collaborative nature. The five-year project combined bioengineering and sports medicine expertise under the leadership of Kristy Arbogast, PhD, co-scientific director and director of engineering for the Center for Injury Research and Prevention at CHOP and a research professor of Pediatrics at the University of Pennsylvania; Christina Master, MD, primary care sports medicine specialist and co-director of the Concussion Care for Kids: Minds Matter Program; Catherine C. McDonald, PhD, RN, assistant professor at the Penn School of Nursing, and Susan Margulies, PhD, formerly a professor of Bioengineering at the University of Pennsylvania's School of Engineering and currently Wallace H. Coulter Chair of the Coulter Department of Biomedical Engineering (BME) at Georgia Tech and Emory University. Together, the team can take a holistic and thorough view of concussion treatment.

"The research questions being addressed by this project can only be answered by interconnected study across the clinic, the lab, and on the field," Dr. Arbogast said. "Each component informs the other's research in important ways."

Their evidence-based findings will help clinicians move away from subjective symptoms and toward more accurate, evidence-based guidelines for diagnosing and managing youth concussions. The study team will use objective metrics that measure a child's brain function. Enrolling participants from CHOP's Concussion Care for Kids: Minds Matter program, the researchers will measure and track the objective metrics of balance, neurosensory processing (such as eye tracking), and cerebral blood flow in adolescents ages 14 to 18 with a diagnosed concussion, and then compare those metrics to healthy controls. The resulting data will facilitate the development of a suite of quantitative assessment tools and guidelines that can help clinicians determine how long a child will take to recover, or when a young athlete can return to play.

The researchers also plan to track the magnitude and direction of head impacts of youth on the sports field. Equipped with head-impact sensors, the high school athletes will go about their play while the researchers take pre-and post-season objective clinical metrics data and analyze head impacts from the sensors. The head impact sensor component of the study will enroll research participants from suburban Philadelphia's The Shipley School.

OPEN SCIENCE INITIATIVE: STREAMLINE BRAIN TUMOR PRECISION MEDICINE RESEARCH

Five regional cancer academic treatment centers and two pediatric hospitals announced a collaboration in February 2017 called the Philadelphia Coalition for a Cure (PC4C) that is the nation's first city-wide brain tumor precision-medicine research partnership to benefit both adult and pediatric brain tumor patients. In time, the PC4C plans to expand treatment to include additional tumor and cancer types.

PC4C member institutions are committed to streamlining research and precision medicine efforts. They include the division of Neurosurgery and Center for Data Driven Discovery at CHOP, Lewis Katz School of Medicine at Temple University, The Perelman School of Medicine at the University of Pennsylvania, Sidney Kimmel Medical College at Thomas Jefferson University, Cooper Medical School of Rowan University, Drexel Neurosciences Institute at Drexel University College of Medicine and The Hyundai Cancer Institute at The Children's Hospital of Orange County. They will work together and with commercial partners and payers to advance data-driven discovery through the rapid sharing and release of data to the entire research community through open science initiatives.

"Brain tumors are the leading cause of disease-related death in children and more than 20,000 adults are diagnosed each year," said Jay Storm, MD, chief of the division of Neurosurgery at CHOP. "Working with PC4C, we hope to define a new collaborative clinical and research ecosystem that harnesses partnerships among leading academic centers, commercial partners, and insurers to identify therapies and accelerate discovery."

PC4C is empowering data-driven discovery and improving treatments for brain tumors through treatments that are individually tailored and specific to the biology of each patient's tumor, young or old, with the aim of reducing toxic side effects and increasing the therapeutic effectiveness of targeted approaches. All patient-consented data for the PC4C will be accessible to the research community via Cavatica, a biomedical data analysis and storage platform that, for the first time, will integrate adult and pediatric brain tumor data.

"One of the mandates of the PC4C is that all the data has to be shared immediately, in real time," Dr. Storm said. "As soon as it's generated, it's going to be made available to the entire scientific community in a protected cloud environment that anyone can access. This kind of sharing is clearly a paradigm shift for academic medicine."

PUTTING RESEARCH IN MOTION: DRIVER LICENSURE FOR TEENS WITH AUTISM

Our paths to discovery intersect in unexpected ways, and exciting opportunities for research collaboration are around every corner. Two of the most highly regarded autism and pediatric injury research centers in the world are new neighbors at our Roberts Center for Pediatric Research building, and they worked together to study the driving safety of adolescents with autism spectrum disorder (ASD).

The Center for Autism Research (CAR) studies the causes and mechanisms of ASD and develops evidence-based clinical and behavioral interventions across the lifespan, while providing real-world support for individuals and families living with autism here and now.

As part of its mission, the Center for Injury Research and Prevention (CIRP) identifies causes of traffic-related injury and death, then works to translate the research into practical tools and guidelines for families, professionals, and policymakers.

These two premier centers put in motion a research project to begin to learn more about the proportion of adolescents with ASD who get licensed and the rate at which they progress through Graduated Driving Licensing. Their findings showed that as many as one in three teens with ASD without intellectual disability get licensed by age 21, and the results will lead to a new line of research about how to best support families in making that decision to have their children with ASD pursue a driver's license and to become safe drivers.

In addition to studying injury risk and interventions for individuals with ASD, CIRP is expanding its collaborative work with other CHOP research centers to learn how other developmental and intellectual conditions affect driving safety, such as attention-deficit/hyperactivity disorder, oppositional defiant disorder, and conduct disorder.

THIRSTY FOR ANSWERS: NEW URINARY STONE DISEASE RESEARCH NETWORK

A new Urinary Stone Disease Research Network (USDRN) that includes CHOP will perform the largest studies on urinary stone disease to date, and it has opened the Prevention of Urinary Stones with Hydration study (PUSH), a two-year randomized trial of a strategy to maintain high fluid intake to decrease stone recurrence among adolescents and adults.

The prevalence of kidney stones disease has nearly doubled in the last 15 years in both adults and children, affecting about one out of 11 Americans, according to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). It also is the most expensive non-malignant urologic condition in the U.S., costing about $10 billion annually. About 10 percent of visits to the emergency department for kidney stones are for repeat encounters.

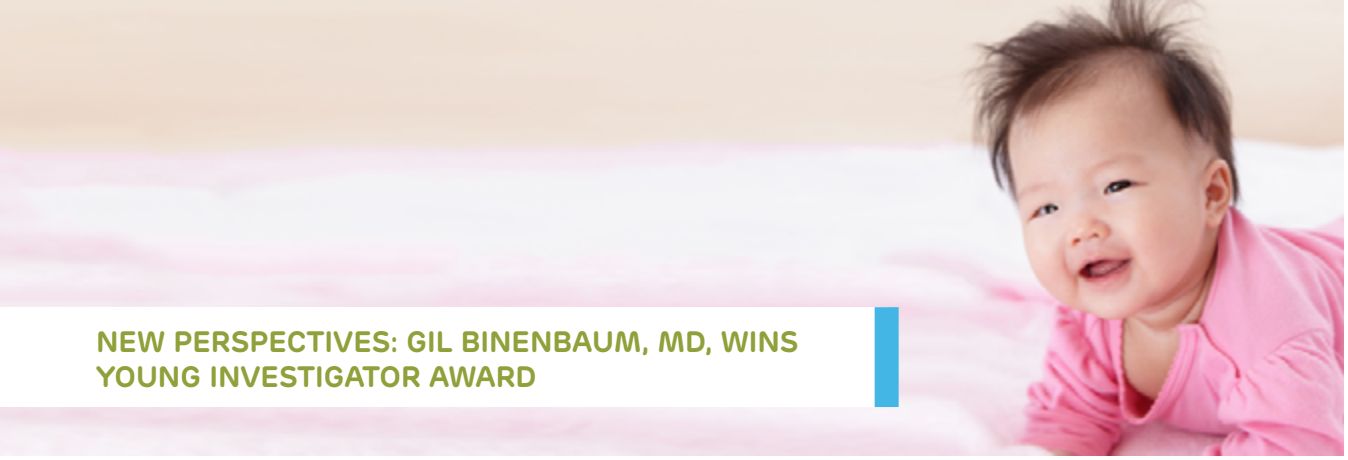
The PUSH study leaders at the CHOP-Penn Medicine site are principal investigators Gregory E. Tasian, MD, MSc, MSCE, a pediatric urologist and epidemiologist at CHOP; and Peter Reese, MD, MSCE, a nephrologist and epidemiologist at the Perelman School of Medicine at the University of Pennsylvania. They also are senior scholars with Penn's Center for Clinical Epidemiology and Biostatistics.

"As the largest children's hospital in the USDRN, CHOP and the Pediatric Kidney Stone Center will contribute substantially to this effort," Dr. Tasian said. "CHOP has long been a leader in advancing healthcare for children with rare and common diseases. CHOP's participation in the USDRN will allow us to be at the forefront of decreasing the morbidity of urinary stone disease, which now often begins during childhood."

The USDRN collaboration also includes the University of Washington, Washington University in St. Louis, University of Texas Southwestern Medical Center, and Duke University. It is supported by the NIDDK.

HONORS

VISIONARIES ›



NEW PERSPECTIVES: GIL BINENBAUM, MD, WINS YOUNG INVESTIGATOR AWARD

Inventive researchers like Gil Binenbaum, MD, MSCE, an attending surgeon in the Division of Ophthalmology at CHOP, look at children's health problems through different perspectives. His recent work has yielded new insights about retinopathy of prematurity (ROP), a blinding disease of the developing retinal blood vessels in premature babies, and also earned him recognition as recipient of the 2017 Young Investigator Award from the American Association for Pediatric Ophthalmology and Strabismus (AAPOS).

In 2012, Dr. Binenbaum became principal investigator of the Postnatal Growth and ROP (G-ROP) Study Group, a large-scale, multicenter project funded by the National Institutes of Health and headquartered at CHOP. The group, which now spans 41 institutions in the U.S. and Canada, has produced the largest detailed ROP dataset ever created.

G-ROP, which has published research findings in journals such as *JAMA Ophthalmology*, aims to address a large concern in current ROP screening: Many infants are examined, but only a small percentage actually require treatment.

"There are many babies getting exams; those exams can be stressful for the baby, and they are resource-intensive," said Dr. Binenbaum, who was named the Richard Shafritz Endowed Chair of Ophthalmology Research at CHOP and also is an associate professor of ophthalmology at the Perelman School of Medicine. "We're quite good at identifying who to treat, but less than 5 percent of those examined actually need to be treated. We're trying to come up with a better way to decide who to examine — a better way to screen."

The G-ROP study group developed new evidence-based birth weight, gestational age, and weight gain ROP screening criteria that can reduce the number of infants examined by one-third. Dr. Binenbaum presented these new screening criteria in 2017 at the AAPOS annual meeting where he received the Young Investigator Award.

INNOVATIVE THINKERS: BEVERLY DAVIDSON, PhD, JOINS PRESTIGIOUS HONORARY SOCIETY

Gene therapy expert Beverly Davidson, PhD, director of the Raymond G. Perelman Center for Cellular and Molecular Therapeutics and Chief Scientific Strategy Officer of CHOP Research Institute, joined today's most innovative thinkers as a newly elected member of the American Academy of Arts and Sciences. The Academy is one of the nation's oldest and most prestigious honorary societies that champions research and analysis in science and technology.

Dr. Davidson, who holds the Arthur V. Meigs Chair in Pediatrics at CHOP and also is a professor of Pathology and Laboratory Medicine at the University of Pennsylvania, studies the cell biology and biochemistry of inherited genetic diseases that attack the central nervous system (CNS), such as Batten disease and similar diseases called lysosomal storage disorders. In these disorders, the lack of an enzyme impairs lysosomes, proteins that perform crucial roles in removing unwanted byproducts of cellular metabolism. Toxic waste products then accumulate in the brain and cause progressively severe brain damage. Dr. Davidson's laboratory team has developed novel vector systems to reverse these neurological deficits and improve lifespan by delivering therapeutic genes to the CNS.

In addition to lysosomal storage disorders, Dr. Davidson focuses on other inherited neurological diseases such as Huntington's disease and spino-cerebellar ataxia. In these studies, she has delivered forms of RNA to animals' brains to silence the activity of disease-causing genes.

Dr. Davidson also wants to better understand how changes in the transcriptome — a collection of all the gene readouts (transcripts) present in a cell — influence neural development and neurodegenerative disease processes. This work is revealing new pathways of pathogenesis and novel targets for therapy.

ON TOP OF TECHNOLOGY: BIMAL DESAI, MD, RECEIVES HEALTHCARE INNOVATOR AWARD

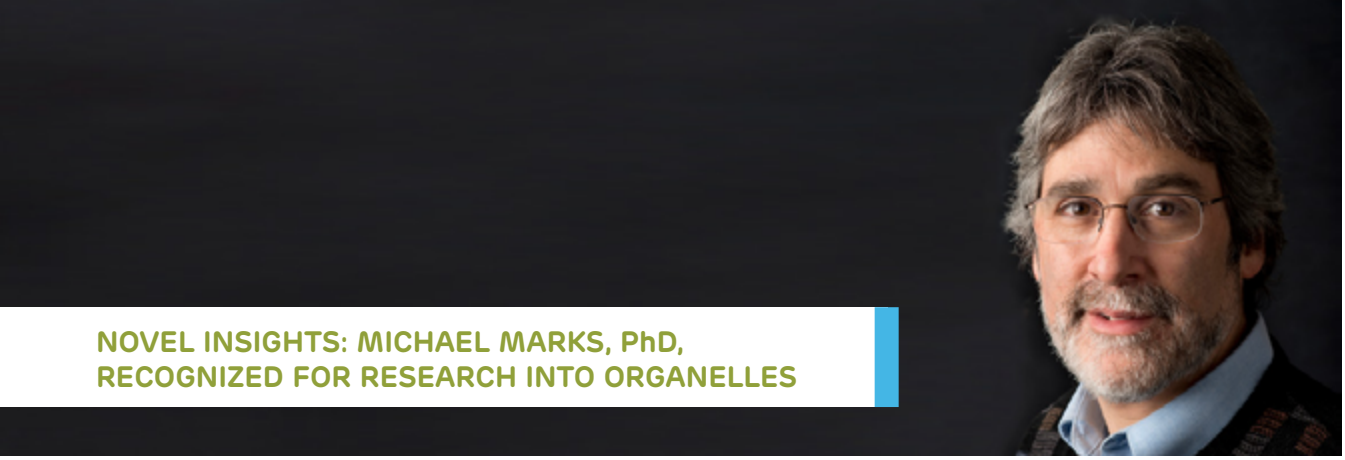
Advanced information technology is rebooting how patients, physicians, and researchers connect with each other, and Bimal Desai, MD, assistant vice president and chief of Health Informatics at CHOP, is always a few keystrokes ahead to ensure that our dynamic healthcare delivery environment is implemented effectively. That's why the Philadelphia Alliance for Capital and Technologies awarded Dr. Desai with the Healthcare Innovator Award, an honor that recognizes a company, researcher, or investor whose innovative solutions positively impact quality, cost, and access to healthcare.

Dr. Desai helped develop CHOP's new Digital Health Program, which leverages technology to transform and augment how pediatric healthcare is delivered. It's based on a four-pronged approach:

- Care Anywhere: Using the tools and modalities that patients and families prefer, in order to go beyond healthcare's traditional walls, such as telemedicine visits for routine care and remote monitoring of chronically ill children.
- Engage and Connect: Partnering with patients and families to identify ways that digital information can make the healthcare experience less cumbersome and confusing.
- Research Excellence: Extending the reach and impact of the world-class researchers at CHOP by improving cohort identification, enhancing research enrollment, and creating new methods for data collection.
- Enhanced Partnerships: Allowing clinicians to access patient information across organizations.

Dr. Desai also co-founded Haystack Informatics, a company that protects patient privacy by tracking patient's electronic health records along with healthcare employees' patterns of behavior. In our 2014 Research Institute Annual Report, we covered the company's early development of sophisticated algorithms to more rapidly identify patient data breaches.

Dr. Desai holds appointments on the faculties of both the Perelman School of Medicine and the Institute for Biomedical Informatics at the University of Pennsylvania.



NOVEL INSIGHTS: MICHAEL MARKS, PhD, RECOGNIZED FOR RESEARCH INTO ORGANELLES

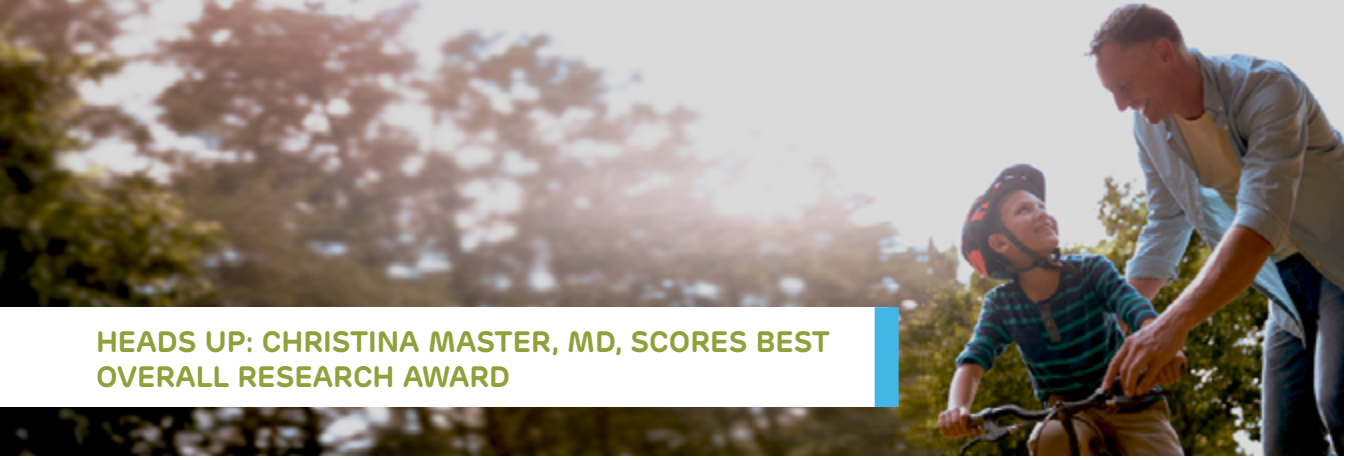
Cell biologist Michael Marks, PhD, is still curious about the biology of lysosome-related organelles, even after devoting two decades to establish how melanosomes are assembled within cells. His research has revealed how this building process goes awry in patients who have a rare genetic disease called Hermansky-Pudlak syndrome (HPS). Dr. Marks' perseverance and dedication earned him the esteemed recognition of Fellow by his peers in the American Association for the Advancement of Science, the world's largest general scientific society, including nearly 250 affiliated societies and academies of science.

People with HPS have problems with blood clotting and abnormally light coloring of skin, hair, and eyes, with consequent poor vision and susceptibility to skin cancer. Some forms of HPS also cause scar tissue formation in the lungs, called pulmonary fibrosis, which leads to breathing problems that can contribute to individuals' shortened lifespans of about 40 to 50 years.

The 10 genes that go awry in HPS encode subunits of four protein complexes that function in a loop between early endosomes and melanosomes to deliver cargo to and from these maturing organelles.

"Knowing more about how they actually function will perhaps allow us to generate some kind of drugs to fix the basic problems these kids have," Dr. Marks said. "It would be a big deal if we could find a way to prolong their lives."

Dr. Marks also is a professor in the department of Pathology and Lab Medicine, and the department of Physiology at the Perelman School of Medicine at the University of Pennsylvania.



HEADS UP: CHRISTINA MASTER, MD, SCORES BEST OVERALL RESEARCH AWARD

Christina Master, MD, a sports medicine pediatrician at CHOP, never stays in neutral when it comes to advancing brain injury research. At the 26th Annual Meeting of the American Medical Society of Sports Medicine, she received the "Best Overall Research Award" for her work, "The Use of Functional Near-Infrared Spectroscopy (fNIRS) for Assessing Cognitive Workload After Concussion."

Currently, physicians do not have reliable, objective biomarkers to identify the pathophysiologic changes associated with concussion. Dr. Master's studies provide preliminary evidence that suggests fNIRS, a noninvasive and portable neuroimaging modality that detects blood oxygenation changes in tissues using near-infrared light, can quantify changes in neuronal activity and cognitive workload after injury and during recovery.

Dr. Master is a world traveler, and her research program is always on the go as well. She helped to develop the Concussion Care for Kids: Minds Matter program at CHOP, a program designed to help parents, coaches, and school staff recognize the signs of concussion in children and teens. Dr. Master also recently presented at the Pediatric Academic Societies Meeting on policies that guide the participation of adolescents in organized sports. She leads several other research projects aimed at reducing the incidence and impact of concussions.

IMPROVING INFANT HEALTH: AWARD-WINNER BARBARA MEDOFF-COOPER, RN, PhD

Babies have a lot to tell researchers, and Barbara Medoff-Cooper, RN, PhD, a professor of Nursing at the University of Pennsylvania School of Nursing and Ruth M. Colket Professor in Pediatric Nursing (Emeritus) at CHOP, has been listening to their babbles, cries, and coos since the mid-1970s. For her novel insights into infant development, the Eastern Nursing Research Society awarded Dr. Medoff-Cooper its Distinguished Contributions to Nursing Research Award for 2017.

The award is in recognition of sustained and outstanding contributions to nursing research by a senior investigator. Dr. Medoff-Cooper studies infants' feeding behaviors, neurobehavioral development, and neonatal intensive care, among many other things. She is well-known for developing the globally used Early Infancy Temperament Questionnaire, an assessment that helps to treat difficult infants under 4 months old, and the NeoNur, a feeding device that allows physicians to detect developmental problems based on how an infant feeds. As part of her recent research, Dr. Medoff-Cooper reported that feeding issues in 3-month-old infants with congenital heart defects are associated with poor neurological development at 6 and 12 months.

"It is a great honor to be recognized by the Nursing research community," Dr. Medoff-Cooper stated in a press release. "My goal, and of course my passion, has always been to improve outcomes for vulnerable infants and their families."

A RIGOROUS APPROACH: BARBARA SCHMIDT, MD, PROMOTES EVIDENCE-BASED MEDICINE

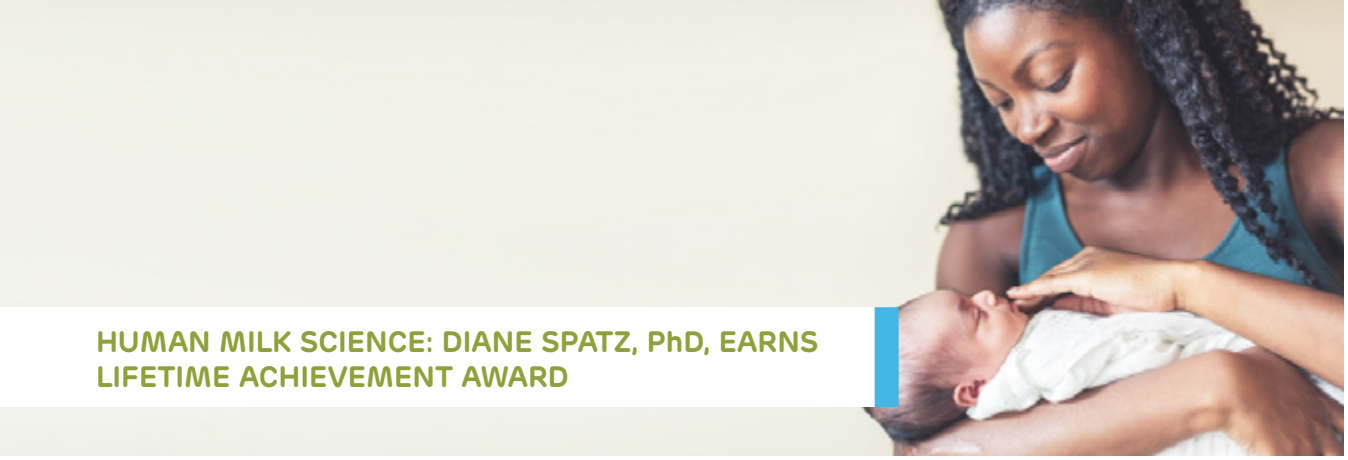
When it comes to treating sick infants, nothing but the most rigorous, evidence-based research should support every decision a clinician makes. In 2017, the American Academy of Pediatrics (AAP) Section on Perinatal Pediatrics honored Barbara Schmidt, MD, attending neonatologist at CHOP, and director of Clinical Research, Neonatology at Penn Medicine, with the William A. Silverman Lectureship Award for her contributions to evidence-based neonatal research.

Dr. Schmidt is the lead investigator of the International Trial of Caffeine for Apnea of Prematurity and a host of other collaborations and clinical trials in newborns. While all awards are an honor, Dr. Schmidt admits this one has a special significance to her.

"I was particularly happy about this [lectureship] because of my strong belief in evidence-based medicine, and my passion for trying to resolve uncertainty in our management of babies, slowly but surely," Dr. Schmidt said. "I also found it a major responsibility to do justice to Dr. Silverman."

As a postgraduate student at McMaster University in Canada, Dr. Schmidt met William A. Silverman, MD, for the first time. Known as the father of neonatal intensive care, Dr. Silverman had given a talk that inspired Dr. Schmidt in its rigorous and questioning approach to newborn research and care. Fast-forward to May 2017, and Dr. Schmidt's lecture titled "Progress in a Groove?" presented at the AAP Presidential Plenary Sessions during the annual Pediatric Academic Societies Meeting explored whether neonatal clinical research has improved since Dr. Silverman's critique of perinatal medicine.

Read a Q&A on Cornerstone about why the William A. Silverman Lectureship Award means so much to her and what she hopes to see in the future of both neonatology and neonatal research.



HUMAN MILK SCIENCE: DIANE SPATZ, PhD, EARNS LIFETIME ACHIEVEMENT AWARD

Better beginnings for babies and the mothers who care for them is the focus of the Breastfeeding and Lactation Program at CHOP led by Diane Spatz, PhD, an internationally known expert in the field who received the Lifetime Achievement in Neonatal Nursing Award from the National Association of Neonatal Nurses.

As a researcher and the Helen M. Shearer Term Chair in Nutrition and professor of Perinatal Nursing at the University of Pennsylvania's School of Nursing, Dr. Spatz over the last two decades has published numerous studies on breastfeeding and medically fragile infants. Her findings have contributed to CHOP's development of a state-of-the-art Human Milk Management Center and a new on-site human milk bank for hospitalized infants. She continues to pioneer studies of the largely unknown world of human milk science.

In 2017, Dr. Spatz also joined the Congressional Task Force on Research Specific to Pregnant and Lactating Women. One of the few nurses selected to participate on the Task Force, Dr. Spatz will help to fill the gaps in knowledge and research about safe therapies for pregnant and breastfeeding mothers. The Task Force is part of the 21st Century Cures Act and includes leaders from the National Institutes of Health, the Office of Women's Health, and the Centers for Disease Control and Prevention.

At the first task force meeting held at the NIH Aug. 21 and 22, Dr. Spatz highlighted the need for all women to have access to evidence-based information about medications during breastfeeding and pregnancy, as well as the important role nurses play in delivering accurate information to mothers.

"The lack of consistent evidence-based information on the safety of medications for pregnant women and mothers who are breastfeeding negatively impacts mothers every day," Dr. Spatz said. "This congressional task force is a historic opportunity to improve the care of women and infants in the United States as well as globally."

FAR-REACHING IMPACT: HUMANITARIAN AWARD HONORS DAVID SPIEGEL, MD

For over 20 years, David Spiegel, MD, a pediatric orthopaedic surgeon at CHOP, has been practicing humanitarian work in Nepal, Iraq and other underserved regions, bringing his expertise in pediatric orthopaedics to children around the world. He is a strong advocate for essential surgical services in low and middle-income countries. And he is a researcher who investigates how delayed diagnosis and treatment of childhood musculoskeletal disorders in countries with limited resources can complicate management options and decrease long-term quality of life.

In honor of Dr. Spiegel's far-reaching charitable work, the American Academy of Orthopaedic Surgeons recognized him with the 2017 AAOS Humanitarian Award.

Dr. Spiegel has visited Nepal 20 times, developing a very close relationship with Dr. Ashok Banskota and his team at the Hospital and Rehabilitation Centre for Disabled Children (HRDC), including a six-month visit in 2004 during the height of the Nepalese Civil War, when he introduced the Ponseti method for clubfoot treatment. The hospital has subsequently treated more than 4,000 feet throughout the years by using this technique. He also volunteered after the earthquake in April 2015. In addition to his work in Nepal, he served as an honorary professor at the University of Basra in Iraq, where he has made a two-week visit yearly since 2011. He is also working with colleagues in Pakistan to develop a pediatric musculoskeletal trauma course, and has worked with the World Health Organization (WHO) on their essential surgery program, mostly as a volunteer but also on several occasions as a consultant in Mongolia and Somalia.

"It has been a privilege to serve, and to continue to serve, those who desperately require assistance," Dr. Spiegel said. "I have always believed that the greatest value lies in the transfer of contextually relevant knowledge and skills. If I feel that if I'm able to teach and transfer even a granule of knowledge, then my efforts were a success."

In addition to his work abroad, Dr. Spiegel is an associate professor of Orthopaedic Surgery at the Perelman School of Medicine at the University of Pennsylvania.

EXPANDING SCIENCE: DOUGLAS WALLACE, PhD, HONORED FOR COURAGEOUS, CREATIVE CAREER

The accolades kept coming in 2017 for world-renowned mitochondrial medicine pioneer Douglas Wallace, PhD, founder and director of the Center for Mitochondrial and Epigenomic Medicine at CHOP. Dr. Wallace earned two highly esteemed international awards for the extraordinary innovation, courage, and creativity that he has dedicated throughout his career to introducing a new bioenergetics perspective to the biomedical community.

During the 1970s, Dr. Wallace defined the genetics of the DNA located in the mitochondria, the "power plants" of the cell, including demonstrating that human mitochondrial DNA is exclusively maternally inherited. Applying this fact to the study of human evolution, Dr. Wallace reconstructed the origins and ancient migrations of humans out of Africa and around the world.

Analysis of mitochondrial DNA genetics and application of its principles to an array of patients led Dr. Wallace to show that mitochondrial DNA variation contributes to a wide range of rare and common metabolic and degenerative diseases, as well as cancer and aging.

At an award ceremony and dinner held in May at The Franklin Institute in Philadelphia, Dr. Wallace received the 2017 Benjamin Franklin Medal in Life Science. In September, Dr. Wallace traveled to Belgium to receive another prestigious honor, the Dr. Paul Janssen Award for Biomedical Research, also in recognition of his unwavering commitment to bring forward new research.

"It is my hope that this validation will encourage innovative young physicians and scientists to apply the principles of mitochondrial genetics and bioenergetics to the pressing clinical problems that threaten global health," Dr. Wallace said. "Such efforts promise to have a profound effect on the well-being of all peoples."

Dr. Wallace also is a professor in the department of Pathology and Laboratory Medicine at the Hospital of the University of Pennsylvania. Read our Q&A with Dr. Wallace in Bench to Bedside.

EXCELLENCE IN MENTORING: DANIEL LICHT, MD, MATTHEW WEITZMAN, PhD, AND JOANNE WOOD, MD

The three winners of the Award for Excellence in Mentoring Research Trainees exemplify a unique mentoring style, an established history of guidance, and an influence that goes above and beyond just helping their mentee pick a research project. Former and current trainees nominated these outstanding faculty members for the 2017 award: Daniel Licht, MD, pediatric neurologist; Matthew Weitzman, PhD, associate professor of Pathology; and Joanne Wood, MD, attending physician and research director of Safe Space: the Center for Child Protection and Health at CHOP.

In their reactions to the award, the winners — as all great mentors do — turned their focus toward the research trainees who nominated them.

Dr. Licht shared his own enthusiasm as a mentor: "I have been ridiculously fortunate to have all these wonderful people find their way to my lab," he said. "I don't really know how it's all happened, but there has been almost a parade of really bright, inquisitive and hard-working students and fellows."

Dr. Weitzman called the Award a tremendous honor: "I have been very fortunate to attract a great group of enthusiastic and dedicated young scientists and clinicians to my lab," he said. "It has been a lot of fun to bring them together to form a collaborative group and watch them flourish. One of the most rewarding parts of my job is to engage and inspire trainees. We have formed a very interactive group, where everyone contributes to making new discoveries. Helping trainees grow scientifically and personally has been very fulfilling for me."

Dr. Wood credits her passion for mentoring to her own experience as a trainee: "During the past 15 years I have benefitted from the generosity of talented mentors who have selflessly shared their time, knowledge, and experiences with me," she said. "The incredible mentorship provided by senior faculty members is the reason I chose to come to CHOP for my training 15 years ago and the reason I have never left. Now as a junior faculty member I have the privilege and pleasure of working with talented trainees. I try to share some of what I learned from my mentors with my mentees. I am incredibly touched and humbled by this recognition."

CHANGING THE WAY: JOHN MARIS, MD, RECEIVES NCI OUTSTANDING INVESTIGATOR AWARD

In his more than 30 years of research and caring for hundreds of patients, today pediatric oncologist John M. Maris, MD, is known around the world for unearthing the genetic architecture of neuroblastoma and developing targeted treatments for children with cancer.

His unwavering dedication and innovation led the National Cancer Institute to honor him in October 2017 with their prestigious Outstanding Investigator Award, an accolade that supports accomplished leaders in oncology research who make significant contributions toward the understanding and treatment of cancer.

Over the last decade, the Maris Lab has pioneered discovery after discovery regarding the genetics that make an individual susceptible to neuroblastoma, as well as the mechanisms that lead to the formation of neuroblastoma tumors. Dr. Maris, who is also a professor of Pediatrics at the Perelman School of Medicine and holds the Giulio D'Angelo Chair in Neuroblastoma Research at CHOP, continues to lead innovative research addressing the most startling paradoxes about pediatric cancer.

"It is my career goal to fundamentally change the way that we cure childhood cancer," Dr. Maris said, and that is evident not only with the work in his laboratory but also with his leadership position with organizations such as Stand Up to Cancer (SU2C)-St. Baldrick's Foundation Pediatric Cancer Dream Team, a research effort focused on immunogenomics and developing new immunotherapies for high-risk childhood cancers.

With the support of the NCI Outstanding Investigator Award, Dr. Maris plans to carry out a multidisciplinary and collaborative research program with the goal of improving cure rates for pediatric patients with neuroblastoma. His lab will uncover the fundamental mechanisms that orchestrate the development of neuroblastoma and translate those discoveries into personalized, patient-specific therapies that are more effective and less toxic than current treatments.

RESEARCH, ACTION, IMPACT: FLAURA WINSTON, MD, PhD, JOINS NATIONAL ACADEMY OF MEDICINE

After decades of impactful work in the field of pediatric injury research, Flaura Winston, MD, PhD, is bringing her expertise to the National Academy of Medicine as one of 80 new physician members elected in 2017.

Founder and scientific director of the Center for Injury Research Prevention (CIRP) at CHOP, Dr. Winston is an inspirational pediatrician, engineer, and public health advocate whose research-action-impact approach to improving teen driving and child passenger safety has led to numerous breakthroughs and innovations. In 1997, Dr. Winston founded the Partners for Child Passenger Safety Program, a decade-long partnership with State Farm Insurance that reduced the number of car crash injuries in children.

Recently, Dr. Winston and her team of researchers developed Diagnostic Driving, a startup company that provides a virtual driving assessment to universities, corporate fleets, and driver licensing centers — a program already in use at centers in Ohio. Dr. Winston's expertise extends to her work as a professor of Pediatrics at the University of Pennsylvania, an associate editor of *Injury Prevention*, the director of the National Science Foundation's Center for Child Injury Prevention Studies, and more outlets that include U.S. federal advisory panels.

"I am deeply honored to be included among the members of the National Academy of Medicine and am humbled by the many partners who applied my team's research to innovations that achieved reductions in traffic crashes and injuries," Dr. Winston said. "I hope to bring this research-action-impact approach to deliberations at the National Academies to help accelerate benefit from research discoveries and technology, to narrow the chasm between discovery and value. I want to see scientific engineering breakthroughs, big and small, become life-saving discoveries, especially for children and youth."

TREMENDOUS STRIDES: DR. KATHLEEN SULLIVAN WINS BOYLE SCIENTIFIC ACHIEVEMENT AWARD

Immunodeficiency diseases include over 300 rare chronic disorders in which an individual's immune system does not function properly. Every year, the Immune Deficiency Foundation (IDF) recognizes members of the scientific medical community for their contributions toward diagnosis and care of patients with immunodeficiency diseases through the Boyle Scientific Achievement Award.

In October 2017, Kathleen Sullivan, MD, chief of the Division of Allergy and Immunology, was named one recipient of the 2017 Boyle Award. Dr. Sullivan, who also holds the Frank R. Wallace Endowed Chair in Infectious Diseases at CHOP, has made tremendous strides in immunodeficiency research with her investigations into common variable immunodeficiency, chromosome 22a11.2 deletion syndrome, and her work to define the role of epigenetics in inflammation.

"The Boyle Award is the highest honor in the field of primary immune deficiency, and I was thrilled to be recognized," Dr. Sullivan said.

NEXT-GENERATION RESUSCITATION CARE: DR. VINAY NADKARNI RECEIVES LIFETIME ACHIEVEMENT AWARD

The American Heart Association honored Vinay Nadkarni, MD, with their 2017 Award for Lifetime Achievement in Cardiac Resuscitation Science at its annual Resuscitation Science Symposium held in Anaheim, Calif. The AHA awards the honor every year to scientists who have made outstanding contributions in cardiac and trauma science.

A critical care physician at CHOP as well as medical and research director of our Center for Simulation, Advanced Education, and Innovation, Dr. Nadkarni's work in clinical, laboratory, and simulation-based research is paving the way for next-generation resuscitation care.

Dr. Nadkarni has worked extensively with the American Heart Association over the years, has conducted a number of collaborative multi-center National Institutes of Health research studies, and was the founding pediatric member of the AHA's National Registry of Cardiopulmonary Resuscitation. An initiative to collect resuscitation data from hospitals across the nation and create evidence-based guidelines for inpatient CPR, the registry formed the foundation for the AHA's collaborative "Get With the Guidelines-Resuscitation" program.

UNCHARTED AND EXCITING DIRECTIONS: DISTINGUISHED SCIENTIST AWARD BESTOWED ON DIMITRI MONOS, PhD

A passion for puzzles and problem solving fuels the devotion Dimitri Monos, PhD, has for tackling some of the greatest challenges in immunogenetics — a dynamic field of science and medicine that explores the connections between the immune system and genetics.

Those same qualities are among the many reasons why the American Society of Histocompatibility and Immunogenetics (ASHI) honored Dr. Monos in September 2017 with its prestigious 2017 Distinguished Scientist Award. The annual award recognizes those who have made extraordinary scientific contributions in their field, which may also have broad clinical applications to autoimmune diseases, cancer, vaccine development, and pharmacogenomics.

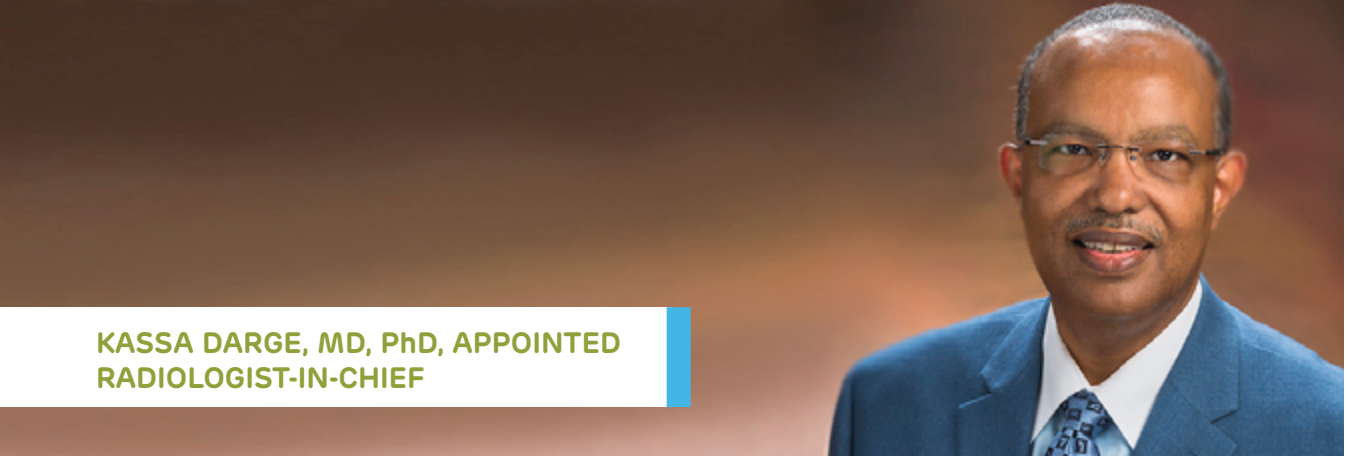
Dr. Monos was honored for his research and expertise on histocompatibility molecules called human leukocyte antigens (HLA) and the genes that encode them, known as the major histocompatibility complex (MHC). Identifying key HLA alleles is critical for the success of bone marrow, blood stem cell, and solid organ transplantation. To help prevent what could be a catastrophic immune response by a recipient's body to destroy foreign tissue, Dr. Monos' lab performs precise HLA typing to ensure that antigens between the donor and recipient are as similar as possible.

"For me, this work is another extension of having fun," said Dr. Monos, director of the Immunogenetics Laboratory in the department of Pathology and Laboratory Medicine that provides integral services to all of the transplantation programs at CHOP, along with supporting other clinical and research efforts.

During his Distinguished Scientist Award lecture at ASHI's annual meeting, Dr. Monos discussed how next-generation sequencing technology provides an advanced tool that reveals uncharted and exciting directions in MHC research.

VISIONARIES

DISCOVERY ›



KASSA DARGE, MD, PhD, APPOINTED RADIOLOGIST-IN-CHIEF

Children's Hospital named Kassa Darge, MD, PhD, the new chair of the Department of Radiology and Radiologist-in-Chief in December 2016. With an extensive research portfolio encompassing 28 years with more than 200 publications and multiple grants, Dr. Darge focuses his research on innovative and advanced body imaging methods, particularly magnetic resonance and ultrasound modalities.

Dr. Darge holds the John W. Hope Endowed Chair for Radiology Faculty Development at CHOP and has served as chief of the Division of Body Imaging in the Department of Radiology. He has been professor of Radiology at the Perelman School of Medicine at the University of Pennsylvania since 2006 while also serving as an honorary professor of Radiology in the Department of Radiology at Addis Ababa University in Ethiopia.

He has mentored dozens of trainees during his esteemed career and has received numerous awards for his research and educational work. Of note is his work to establish the CHOP Radiology International Education Outreach pediatric radiology fellowship program in Ethiopia. To further CHOP's mission of training the next generation of pediatric experts, Dr. Darge also started a mentoring program for junior faculty members in the Department of Radiology, for which he was awarded the CHOP mentor award.

"We are delighted to have Dr. Darge serve as our Radiologist-in-Chief," said Chad Hough, senior vice president, Support Services at CHOP, in announcing Dr. Darge's appointment. "Dr. Darge is a highly accomplished researcher, educator, and scholar in radiology who will help lead CHOP's strategy and future as we continue to find better ways to provide exceptional care and research discoveries for children."

ERIC EICHENWALD, MD, JOINS CHOP AS CHIEF OF THE DIVISION OF NEONATOLOGY

Following a nationwide search, Eric Eichenwald, MD, joined CHOP as its new chief of the Division of Neonatology at the end of 2016.

The neonatology program provides optimal care to more than 4,000 critically ill newborns and infants throughout the CHOP Care Network each year. Physicians and scientists from CHOP's Division of Neonatology conduct basic and clinical research on many conditions affecting newborns and infants.

"Dr. Eichenwald is a highly accomplished clinician, educator and scholar in neonatology who has outstanding leadership abilities and will undoubtedly guide the Division of Neonatology to an even higher level of excellence," said Joseph St. Geme, MD, physician-in-chief and chair of the Department of Pediatrics.

Dr. Eichenwald is also a Professor of Pediatrics at the Perelman School of Medicine at the University of Pennsylvania and holds the Thomas Frederick McNair Scott Endowed Chair at CHOP. He most recently served as chair of Pediatrics and chief of Neonatology at the University of Texas, Houston. In 2016, he received the Pediatric Education Award from the Southern Society for Pediatric Research.

STEPHAN GRUPP, MD, PhD, NAMED CHIEF OF CELLULAR THERAPY & TRANSPLANT SECTION

Pioneering pediatric oncologist Stephan Grupp, MD, PhD, accepted a new role at CHOP in June 2017 as chief of the Bone Marrow Transplant Section in the Hospital's Division of Oncology, renaming it the Section of Cellular Therapy and Transplant to reflect CHOP's global leadership role in engineered cell therapy for cancer and other diseases. He is already well known internationally for leading groundbreaking clinical trials of an innovative T cell therapy for children with acute lymphoblastic leukemia (ALL).

Notably, among his many achievements during his two decades at CHOP, Dr. Grupp served as the lead investigator in the development of a groundbreaking personalized cellular therapy for patients up to 25 years of age with ALL that is refractory or in second or later relapse. In August 2017, the U.S. Food and Drug Administration approved the therapy, a chimeric antigen receptor (CAR) T-cell therapy called Kymriah™, which was developed by CHOP, Penn, and Novartis. Kymriah is the first engineered cell therapy for any cancer, as well as the first-ever therapy based on gene transfer approved by the FDA.

Dr. Grupp has been an attending physician and oncology researcher at CHOP since 1996, when he also joined the University of Pennsylvania medical faculty. In addition to being chief of the Section of Cellular Therapy and Transplant, he is the director of the Cancer Immunotherapy Frontier Program at CHOP, director of Translational Research for the Center for Childhood Cancer Research, medical director of the Stem Cell Laboratory, and the Yetta Deitch Novotny Professor of Pediatrics at Penn's Perelman School of Medicine.

"Dr. Grupp was the top candidate for this crucial position, and will now expand an already outstanding program that is revolutionizing cell therapy for children with resistant relapsed or refractory ALL and pioneering new strategies for stem cell transplantation," said Stephen P. Hunger, MD, chief of Pediatric Oncology and director of the Center for Childhood Cancer Research at CHOP.

MICHELLE LEWIS TAKES HELM AS VP FOR RESEARCH ADMINISTRATION, OPERATIONS

While we talk a lot about discoveries that advance our understanding of pediatric diseases and conditions or that may lead to new treatments, we can't overlook the support investigators receive behind the scenes that allow them to focus on their areas of expertise. Administration is a critical component in the success of any research institution and often encompasses effectively managing myriad areas like grants, finances, training, and resources that investigators can tap into in their quest for discovery. Overseeing such a broad array of services and resources requires an insightful leader who is also a strategic thinker and problem solver.

The Research Institute found that kind of leader with Michelle A. Lewis, MS, CRA, who joined Children's Hospital in June 2017 as the new vice president for Research Administration & Operations. A seasoned academic medical center research administrator, Lewis has committed more than 18 years of her career serving in multiple positions of increasing responsibility, authority, and oversight in research administration.

A key member of the senior leadership team at the Research Institute, Lewis engages with leaders and groups across the entire CHOP enterprise to advance the Institute's strategic vision, build connections, and bolster collaboration that leads to research excellence. She is committed to leading with inspiration, directly overseeing several Research Administration departments that support investigators in their day-to-day needs, while looking for ways to enhance teamwork and support throughout CHOP Research Institute.

CLINICIAN-RESEARCHER JOSEPH ROSSANO, MD, NEW CHIEF, DIVISION OF CARDIOLOGY

Joseph Rossano, MD, was named chief of the Division of Cardiology at CHOP in May 2017. Since joining CHOP in 2011 to help manage its heart failure, transplant, and cardiac mechanical support program; train residents and fellows; and conduct research on the epidemiology and outcomes of heart disease in children, Dr. Rossano has also served as principal investigator or co-investigator on several ongoing research studies.

His research includes investigating the use of ventricular assist devices and artificial hearts in children; studying the effectiveness of post-transplant treatments for children who have received heart transplants; and studies of children with heart failure. Dr. Rossano has also worked on registries for pediatric ventricular assist devices and heart transplantation.

"Dr. Rossano has an impressive record of scholarship in heart failure and cardiac transplantation, including a number of important publications in the medical literature that have advanced the field and led to changes in care," said Joseph St. Geme, MD, physician-in-chief and chair of the Department of Pediatrics. "Given his leadership abilities and his talents as a clinician, an educator, and an investigator, he is poised to lead the Division of Cardiology to even greater excellence in the years ahead."

In addition to his new position, Dr. Rossano is the medical director of the Pediatric Heart Failure Program. He is also an attending physician in the Cardiac Center and an associate professor of pediatrics at the Perelman School of Medicine at the University of Pennsylvania. He is a core faculty member of the Center for Pediatric Clinical Effectiveness at CHOP, and a Senior Fellow of the Leonard Davis Institute of Health Care Economics at Penn.

ANDELINE VANDERVER, MD, PROGRAM DIRECTOR, LEUKODYSTROPHY CENTER OF EXCELLENCE

Adeline Vanderver, MD, has hit the ground running as the new program director of the Leukodystrophy Center of Excellence at CHOP. Since taking her new position at the end of 2016, Dr. Vanderver has been focused on creating new standards of care for children with leukodystrophies by advancing leukodystrophy gene discovery, creating new therapies, and supporting and advocating for patients and their families.

Leukodystrophies are caused by genetic defects that affect growth or formation of the myelin sheath, a protective coating that insulates surrounding nerve fibers. Without this protection, brain signals don't travel effectively, and children with leukodystrophies face a range of potentially devastating neurological problems. Currently, leukodystrophies comprise approximately 30 disorders, and scientists estimate they occur in one in 7,000 births.

Dr. Vanderver is leading two clinical studies with the goal of repurposing medications — one that is currently used to treat human immunodeficiency virus and another that targets interferon — for patients with Aicardi-Goutieres syndrome. Another clinical trial is assessing the efficacy and utility of whole genome sequencing as a first-line diagnostic test for leukodystrophies.

"We're hopeful that we'll be able to take that list of 30 disorders and check them off one by one to get them diagnosed earlier and eventually to deliver therapeutics," she said.

Dr. Vanderver holds the Kamens Endowed Chair in Neurological Disorders and Translational NeuroTherapeutics at CHOP. In addition to her clinical and research efforts, she also leads the Global Leukodystrophy Initiative, an advocacy group that includes parents, clinicians, and researchers, to raise disease awareness and ensure that patients receive appropriate social and medical support.

DISCOVERY

DEFECTS IN A CELL'S TRANSPORT SYSTEM CAUSE RARE GENETIC CRANIOFACIAL DISORDER

THE FINDING

An international research team led by a Children's Hospital of Philadelphia geneticist classified a new craniofacial disorder tied to disruptions in our cell's tiny protein transport systems. The researchers identified the genetic disorder, ARCN1-related syndrome, in three children and an adult who share similarities in clinically recognizable facial differences, small heads and limbs, and mild developmental delays. As the condition's name suggests, the four patients also share mutations in archain 1 (ARCN1) — a gene that encodes proteins in one of the body's delivery systems for transporting, or "trafficking," proteins between structures inside our cells: the COPI system. Previous research has linked the COPI system to neuronal functions, so the ARCN1 mutations may also affect brain development.

WHY IT MATTERS

Families of children with rare disorders often experience stress as they embark on a series of tests and unsuccessful treatments known as "diagnostic odysseys" with no clear explanation for their complex condition. Putting a definitive name to a rare set of symptoms — and learning that other individuals share the same diagnosis — offers relief for patients while also bringing researchers one step closer to developing effective treatments.

WHO CONDUCTED THE STUDY

Kosuke Izumi, MD, PhD, attending physician in the Roberts Individualized Medical Genetics Center and the Division of Human Genetics at CHOP, led the study with colleagues from the University of Tokyo, Nagano Children's Hospital, KK Women and Children's Hospital, Shinshu University Graduate School of Medicine, Hopital Robert Debre, Centre Hospitalier Universitaire et Université de Liège, St Thomas' Hospital, Genome Institute of Singapore, and SingHealth Duke-NUS Medical School.

HOW THEY DID IT

The researchers sequenced the exomes (the protein-coding portions of DNA) of the four patients and found loss-of-function mutations in the ARCN1 gene, which plays a role in the COPI system. COPI governs the transport of proteins between the cell's endoplasmic reticulum (ER) and the Golgi apparatus so that when a mutation in ARCN1 disrupts the cell's normal protein trafficking route, protein accumulates in the ER to cause a stress response that kills cells. ER stress can also impair the secretion of collagen — an important part of the connective tissue within bone and cartilage.

QUICK THOUGHTS

"This genetic syndrome represents a novel class of disorders," Dr. Izumi said. "We have reported only the second known disease associated with the COPI protein complex, one of the three key intracellular protein transport systems."

WHAT'S NEXT

Finding the cause of ACRN1-related syndrome is just the first step: The researchers will continue to identify more children and adults with similar symptoms, as well as conduct further studies to investigate COPI transport's role in bone formation. "In order to provide better care for children with ARCN1-related syndrome, we still need to understand the full clinical spectrum of this disorder," Dr. Izumi stated. "At the same time, we need to better understand the disease mechanism in order to discover therapies."

WHERE THE STUDY WAS PUBLISHED

The study was published in the *American Journal of Human Genetics*.

WHO HELPED FUND THE STUDY

Grants from the Japanese governmental agency MEXT, Core Research for Evolutional Science and Technology, the Japan Agency for Medical Research and Development, the Singapore Ministry of Health, and the French Ministry of Health supported this research.

WHERE TO LEARN MORE

You can learn more about this research in the press release and read the study abstract online. To find out about genetics research at CHOP, see the Roberts Individualized Medical Genetics Center and the division of Human Genetics.

ASTHMA AND ALLERGIC RHINITIS MORE COMMON IN CHILDREN WITH FOOD ALLERGIES

THE FINDING

Children with a history of food allergies might also have a high risk of developing the most common childhood medical conditions in the U.S.: asthma and allergic rhinitis (also known as hay fever). Thirty-five percent of pediatric patients with an established diagnosis of food allergy went on to develop asthma, with the risk increasing for children with multiple food allergies compared to those with just one, according to new research published this year. Peanuts, milk, and eggs emerged as the most significant food allergens for predisposing children to asthma and rhinitis.

WHY IT MATTERS

The disease rates of eczema, asthma, and rhinitis continue to fluctuate, with the current study finding higher asthma rates compared to previous reports. In Philadelphia, asthma affects one in five children— the highest rates in the nation. More surveillance and information about these conditions are necessary, and while previous research has already linked allergies to asthma, this is the largest study to date that examines the characteristics of primary healthcare provider-diagnosed eczema, asthma, allergic rhinitis, and food allergy in children.

WHO CONDUCTED THE STUDY

The research team included David Hill, MD, PhD, fellow in the division of Allergy and Immunology, Robert Grundmeier, MD, attending physician and director of clinical informatics in the department of Biomedical and Health Informatics, Gita Ram, MD, attending physician in the division of Allergy, and Jonathan M. Spergel, MD, chief of the Allergy Section, all at CHOP.

HOW THEY DID IT

The researchers conducted a retrospective analysis of electronic health records from over one million urban and suburban children in the CHOP Care Network between 2001 and 2015. They divided the records into a closed-birth cohort of 29,662 children followed continuously for their first five years of life, and a cross-sectional cohort of 333,200 children and adolescents, followed for at least 12 months.

QUICK THOUGHTS

"Using provider-based diagnosis data provided important information often lacking in existing studies," said Dr. Spergel, senior author of the study in a press release. "We found different disease rates than previously reported, and our research provides key data to shape future efforts aimed at prevention, diagnosis and management of these common pediatric conditions."

WHAT'S NEXT

Further studies should investigate whether the food allergy patterns identified in their paper are comparable to data from other geographical areas including those found in rural areas (as the study cohort primarily consisted of children residing in urban or suburban settings).

WHERE THE STUDY WAS PUBLISHED

The study was published in *BMC Pediatrics*.

WHO HELPED FUND THE STUDY

The American Academy of Pediatrics Resident Research Award, the Stuart Starr Chair of Pediatrics, the Children's Hospital of Philadelphia Food Allergy Research Fund, and Fare Education and Research Inc. supported the research.

WHERE TO LEARN MORE

You can read the full study online at *BMC Pediatrics* or learn more in the press release. To learn more about allergy research at CHOP, see the Division of Allergy.

GENE TIED TO TYPE 2 DIABETES MAY INFORM BETTER TREATMENTS

THE FINDING

Sophisticated scientific tools, including the gene editing tool CRISPR, allowed genomics researchers at Children's Hospital of Philadelphia and the University of Pennsylvania's Perelman School of Medicine to identify a new gene for Type 2 Diabetes (T2D) at a well-established genomic location. The gene in question, ACSL5, codes for a protein that regulates the body's recognition of insulin — a crucial function that is disrupted in patients with T2D. Without the ability to properly use or make enough insulin, the body cannot move glucose into its cells. Developing drugs to act on the protein in question might help patients with T2D by increasing their sensitivity to insulin.

WHY IT MATTERS

Type 2 Diabetes accounts for 90 to 95 percent of all diabetes cases, with an increase in cases for children and adolescents. Its exact cause, however, remains unknown. By learning more about the metabolic disorder's biological mechanisms and complex factors — as well as environmental influences — researchers can develop more effective treatments. The study also illustrates the complexity of unraveling a disease through gene discovery, since the current study builds on past findings about T2D's genetic underpinnings, including the role of another gene investigated in a previous study, TCF7L2.

WHO CONDUCTED THE STUDY

The research team included investigators from the divisions of Human Genetics and Endocrinology, the division of Hematology, the department of Pathology and Laboratory Medicine, and NAPCore at CHOP, as well as the department of Pediatrics, the Institute of Diabetes, Obesity, and Metabolism, and the Institute for Biomedical Informatics at the University of Pennsylvania's Perelman School of Medicine. Struan F.A. Grant, PhD, a genomics researcher at CHOP, led the study.

HOW THEY DID IT

Using CRISPR and a three-dimensional structural biology technique called circularized chromosome conformation capture (4C), Dr. Grant and his colleagues took a closer look at T2D from a molecular level — specifically, in cells derived from the colon. They used CRISPR to edit out precisely defined sequences around the TCF7L2 gene variant first reported by Dr. Grant in 2006 to be strongly associated with T2D in order to see how the deletion could change global gene expression. 4C also allowed them to examine the variant's interactions with other gene locations. The researchers discovered that the TCF7L2 variant strongly influenced the expression of ACSL5, another gene.

WHAT'S NEXT

"This well-known genomic location harbors an especially strong signal, and may control multiple other genes, yet to be identified," stated Dr. Grant in a press release. "In addition, we still don't know which specific tissue or tissues that these T2D-related signals operate in to affect patients — whether they act primarily in the gut, in the liver, in adipose tissue or on beta cells in the pancreas. As we continue to better understand the biological mechanisms functioning in type 2 diabetes, we expect to find better strategies for treatment."

WHERE THE STUDY WAS PUBLISHED

The study was published in *Diabetologia*.

WHO HELPED FUND THE STUDY

The Pennsylvania Department of Health, the Spatial and Functional Genomics Initiative at CHOP, and the Daniel B. Burke Endowed Chair for Diabetes Research supported this research.

WHERE TO LEARN MORE

Learn more in the press release. To learn more about genetics research at CHOP, see the Division of Human Genetics.

BIO-ENGINEERED MOLECULE COUNTERACTS EFFECTS OF NEWER BLOOD THINNERS

THE FINDING

A novel bio-engineered molecule developed by hematology researchers at Children's Hospital of Philadelphia and the University of Pennsylvania's Perelman School of Medicine has the ability to quickly control bleeding in animal models when infused. If the factor, called FXaI16L, also proves to be effective in humans, it gives physicians a rapid countermeasure for child and adult patients who bleed extensively as a result of taking newer types of blood-thinning drugs. These blood-thinners, known as anticoagulants, are taken to counteract blood clots.

WHY IT MATTERS

Blood clots play a role in heart attacks, strokes, and other serious conditions, killing one person every five minutes in the U.S. While anticoagulants can prevent these clots, they also increase the risk of bleeding. Thus, if a patient undergoes emergency surgery or suffers from a head bleed, doctors may need to reverse the anticoagulant's effect with a countermeasure. The problem, however, is that the newer variety of blood-thinners, which are also deemed safer and more convenient than older ones like warfarin, currently do not have any approved countermeasures. In this study of injured mice modeled to have excessive bleeding, FXaI16L was able to rapidly control bleeding.

WHO CONDUCTED THE STUDY

The study team involved researchers in the Division of Hematology, the Department of Pediatrics, and the Raymond G. Perelman Center for Cellular and Molecular Therapeutics at CHOP, and the department of Biostatistics and Epidemiology at the University of Pennsylvania's Perelman School of Medicine. Rodney Camire, PhD, a hematology researcher in the Raymond G. Perelman Center for Cellular and Molecular Therapeutics at CHOP, led the study.

HOW THEY DID IT

Newer blood thinners work by blocking a key molecule in blood clotting, called factor Xa (FXa). With this in mind, Dr. Camire and his team of researchers developed the novel molecule, FXaI16L, by modifying FXa into a variant that is more potent, longer-lasting, and safer than naturally occurring FXa. To test the variant's effectiveness, the researchers inhibited the expression of FXa in mice. When infused, the variant safely restored the mice's blood clotting ability and significantly reduced bleeding.

QUICK THOUGHTS

"This molecule holds the potential to fill an important unmet clinical need," stated Dr. Camire in a press release. "There are limited treatment options to stop uncontrolled bleeding in patients who are using the newer anticoagulant medications."

WHAT'S NEXT

The next step involves testing the approach in large animals to determine whether the variant is indeed safe and effective enough to progress to a clinical trial, according to Dr. Camire.

WHERE THE STUDY WAS PUBLISHED

This study appeared in *Nature Medicine*.

WHO HELPED FUND THE STUDY

Researchers received support from the National Institutes of Health, the Penn-CHOP Blood Center for Patient Care and Discovery, and Pfizer Inc. Dr. Camire and his colleagues have been collaborating with Pfizer to develop the FXa variant to control bleeding for specific conditions, like intracranial hemorrhage. The molecule is currently in phase I clinical trials and is being conducted by Pfizer.

WHERE TO LEARN MORE

You can read the study abstract online at *Nature Medicine* and learn more in the press release. To learn more about hematology research and care at CHOP, see the Division of Hematology.

RESEARCHERS IDENTIFY GENE REGION THAT RAISES THE RISK FOR EAR INFECTIONS

THE FINDING

Middle ear infections, also known as acute otitis media (AOM), might be caused by microbes, but genetics can also make a child more susceptible to developing the painful condition. In the largest genomics study to date, researchers at CHOP and Rotterdam's University Medical Center have discovered that a specific region in the human chromosome containing the gene FNDC1 raises a child's risk for a middle ear infection.

WHY IT MATTERS

Ear infections are among the most common childhood illnesses, causing discomfort and stress for both young children and their parents. Discovering more about the condition's biological mechanisms – including the interactions between genes and pathogens and who is most susceptible – gives researchers and clinicians a clue for developing more effective treatments. These treatments could include early medical interventions.

WHO CONDUCTED THE STUDY

The study was led by Hakon Hakonarson, MD, PhD, director of the Center for Applied Genomics (CAG) with Jin Li, PhD, statistician at CAG as the lead analyst, along with collaborators led by Gijs van Ingen from the University Medical Center Rotterdam.

HOW THEY DID IT

The researchers conducted a genome-wide association study (GWAS) on two cohorts with DNA samples from 11,000 children. After discovering an association between middle ear infections and a site on chromosome six that contains the gene FNDC1, they replicated the finding in a separate cohort with data from 2,000 additional children. Further studies showed that in mice, the gene that corresponds to FNDC1 was expressed in the middle ear.

QUICK THOUGHTS

"Parents and pediatricians are all too familiar with this painful childhood ear infection — it's the most frequent reason children receive antibiotics," stated Dr. Hakonarson in a press release. "Although microbes cause this condition, it's been well known that genetics also plays a role. This is the first and largest genetic study focused on risk susceptibility for acute otitis media."

WHAT'S NEXT

In their paper, the researchers noted that learning more about the complex polygenetic pathogenesis of middle ear infections will, in the future, help to develop more specific therapies.

WHERE THE STUDY WAS PUBLISHED

The study was published in *Nature Communications*.

WHO HELPED FUND THE STUDY

The National Institutes of Health, the EU 7th Framework Programme, and the Kubert Estate family supported this research.

WHERE TO LEARN MORE

Learn more in the press release and read the study's abstract online. To learn more about CHOP research into the genetic causes of rare and complex childhood diseases, see the Center for Applied Genomics.

PEDIATRIC HYPERTENSION OFTEN GOES UNDIAGNOSED AND UNTREATED

THE FINDING

This is the first study to show a widespread underdiagnosis of hypertension (high blood pressure) and prehypertension by pediatricians in U.S. children ages 3 to 18. The researchers found that only 23 percent of those who had blood pressures consistent with hypertension at multiple primary care visits were diagnosed with the disease, and only 10 percent of patients with symptoms of prehypertension were diagnosed. Of those children and adolescents with diagnoses of hypertension for at least a year, only 6 percent of those who needed anti-hypertension medication received a prescription.

WHY IT MATTERS

Hypertension is one of the 10 most common chronic diseases in childhood, but it is often overlooked because symptoms are usually silent. High blood pressure levels can carry over into adulthood, and if left untreated, can lead to cardiovascular disease and damage to the kidneys and brain. Catching the disease early can help families introduce strategies such as lifestyle changes and medications to lower these risks.

WHO CONDUCTED THE STUDY

Senior author Alexander Fiks, MD, MSCE, is a pediatrician at Children's Hospital of Philadelphia, a faculty member at CHOP's PolicyLab, and director of the Pediatric Research in Office Settings network at the American Academy of Pediatrics (AAP). He also is an associate professor of Pediatrics at the Perelman School of Medicine at the University of Pennsylvania. Lead author David Kaelber, MD, is a professor of pediatrics, internal medicine, epidemiology and biostatistics at Case Western Reserve University and chief medical informatics officer of The MetroHealth System.

HOW THEY DID IT

The researchers analyzed "big data" that combined the electronic health records of 400,000 children from nearly 200 pediatric primary care sites across the country, between 1999 and 2014. In addition, the study team relied on standard clinical (non-research), in-office blood pressure measurements, to help identify prescribing of antihypertensive medications.

QUICK THOUGHTS

"The new reality for pediatricians is that we're taking care of more and more children who are winding up with chronic conditions, such as hypertension, that were previously seen primarily in adults," Dr. Fiks said. "This study shows that many pediatricians are not responding to this new reality — not only are we underdiagnosing hypertension, but we're often not providing recommended treatment to children with the condition in order to minimize health risks."

WHAT'S NEXT

An American Academy of Pediatrics task force published new guidelines for diagnosis and initial medication management of abnormal blood pressure in pediatric patients. Future studies will be needed to determine if the new guidelines are implemented and routinely followed by pediatricians.

WHERE THE STUDY WAS PUBLISHED

The study appeared in the journal *Pediatrics*.

WHO HELPED FUND THE STUDY

The Health Resources and Services Administration and the Eunice Kennedy Shriver National Institute of Child Health and Human Development supported this research.

WHERE TO LEARN MORE

Find out more about the Comparative Effectiveness Research through Collaborative Electronic Reporting consortium, which is part of the Pediatric Research in Office Settings network at the AAP, that coordinated this research. Also, read about the AAP's new guidelines for high blood pressure in children.

RESEARCHERS MAP DYNAMIC ACTIVITIES IN IMMUNE CELLS' RESPONSE TO INFECTIONS

THE FINDING

Researchers revealed novel components and connections in the gene regulatory network underlying how CD8+ T cells mount an immune response. They identified a detailed map of the highly dynamic interactions between genetic regulatory regions called enhancers and promoters that put in motion the three stages of CD8+ T cell development. Those cells begin in a naïve pre-infected state, but after encountering an antigen, differentiate into large quantities of effector cells to clear an infection. After the infection, cell numbers diminish, but central memory T cells retain a long-term ability to defend against reinfection by microorganisms that carry the same antigen.

WHY IT MATTERS

While scientists know that CD8+ T cells play a pivotal role in immune response, their gene regulatory circuits are not well understood. In addition to enhancing their knowledge of cell biology, identifying these novel biological pathways may help uncover useful targets to advance vaccine development and cancer immunotherapy.

WHO CONDUCTED THE STUDY

Kai Tan, PhD, of the Center for Childhood Cancer Research and the departments of Pediatrics and Biomedical and Health Informatics at CHOP, co-led the study with a team from the Carver College of Medicine at the University of Iowa led by Hai-Hui Xue, MD, PhD. Dr. Tan also is an associate professor of Pediatrics at the Perelman School of Medicine at the University of Pennsylvania. The co-first authors are Bing He, PhD, from CHOP, and Shaojun Xing, PhD, from the University of Iowa.

HOW THEY DID IT

The scientists used genomics and systems biology tools that included sophisticated sequencing and computational techniques to map out molecular mechanisms and signaling circuits that come into play during each stage of the CD8+ T cells' responses that act against infections and cancer.

QUICK THOUGHTS

"Better understanding of these mechanisms is important because increasing the quantity and quality of memory CD8+ T cells is a key goal in developing more effective vaccines and immunotherapeutic strategies," Dr. Tan said. "In addition, although many shared properties exist between infection and cancer, future studies identifying distinct regulatory wiring in cancer-infiltrating T cells are essential for the continued progress of cancer immunotherapy."

WHAT'S NEXT

The researchers created a website to hold datasets resulting from this study, including a "roadmap" of methods for extracting useful clues for further study by other researchers. They anticipate that this resource will suggest novel targets for researchers in immunology and oncology. They also are performing experimental testing and refining of the circuit models from this study.

WHERE THE STUDY WAS PUBLISHED

The study appeared in the journal *Immunity*.

Who helped fund the study
Primary support for this study came from various National Institutes of Health grants to the co-authors.

WHERE TO LEARN MORE

Find out more about research being conducted by the Center for Childhood Cancer Research and the department of Biomedical and Health Informatics.

MENTAL HEALTH CONDITIONS ASSOCIATED WITH LONGER PEDIATRIC HOSPITAL STAYS

THE FINDING

Mental health conditions, such as anxiety, attention-deficit/hyperactivity disorder, and depression, can impact a child's length of stay in the hospital and are associated with higher hospital costs. The study team found that existing mental health conditions were present in one in seven medical and surgical hospitalizations of children ages 3 to 20. Children hospitalized for medical reasons commonly had depression and anxiety disorders, which added days to their hospital stay. Children hospitalized for surgical procedures commonly experienced substance abuse and anxiety disorders, which lengthened their time in the hospital. For nine types of medical hospitalizations, having one mental health condition added an extra day in the hospital for 28 percent of children. For nine types of surgical procedures, having one mental health condition increased 61 percent of children's hospital stays by one day. Adolescents had more than twice as many additional hospital days associated with an existing mental health condition compared to 3- to 12-year-old children.

WHY IT MATTERS

Mental health conditions are prevalent among children hospitalized for medical conditions and surgical procedures, and they add a layer of complexity to hospital care that influences pediatric hospital utilization and use additional resources. In this study, the additional resource utilization included nearly 32,000 additional hospital days nationwide in 2012, costing an additional $90 million. Extra days in the hospital disrupt family daily routines, including missed days from school and work. This research suggests healthcare policymakers and hospital administrators could do a better job addressing hospitalized children's mental health needs.

WHO CONDUCTED THE STUDY

Stephanie Doupnik, MD, MHSP, a researcher in PolicyLab at Children's Hospital of Philadelphia, was the lead author, and Jay Berry, MD, MPH, pediatrician and hospitalist with the Complex Care Service at Boston Children's Hospital, assistant professor of pediatrics at Harvard Medical School, was senior author of the study. Dr. Doupnik also is co-director of the inpatient Medical Behavioral Unit at CHOP, an instructor of Pediatrics at the Perelman School of Medicine at the University of Pennsylvania, and a practicing pediatric hospitalist.

HOW THEY DID IT

The study team analyzed 670,000 hospitalizations in a national database called the 2012 Kids' Inpatient Database. They conducted a retrospective, cross-sectional study of hospitalizations for 10 common medical and 10 common surgical conditions among 3- to 20-year-old patients. The investigators used adjusted generalized linear models to examine associations between mental health conditions and hospital length of stay. They used hospital cost-to-charge ratios to estimate costs of additional hospital days associated with mental health conditions. The researchers noted two limitation of the study: (1) documentation of mental health conditions during a patient's hospital stay can vary, and (2) unmeasured confounding factors not captured in hospital discharge data could help explain the relationship between child mental health conditions and hospital length of stay.

QUICK THOUGHTS

"My patients often tell me how difficult it is to get mental healthcare outside of the hospital, and they are grateful when clinicians can provide mental healthcare services in the hospital or help them get treatment after they go home," Dr. Doupnik said. "In order to ensure mental health conditions aren't adding unnecessary days to children's hospital stays that also use additional hospital resources, we need systems of care that provide efficient and convenient access to mental health clinicians for children who need mental health treatments."

WHAT'S NEXT

The researchers suggested potential explanations for the extended hospital stays — a lower ability to cope with pain and other symptoms of acute illness, lower adherence to treatment plans, and a lack of care coordination outside of the hospital — that could help to inform future approaches and policies aimed at improving systems to more efficiently provide mental healthcare to hospitalized children. For example, Dr. Doupnik is exploring collaborations between mental health clinicians and pediatricians, looking for ways to support children in positive coping, and working on how to help children and families connect with mental healthcare in the community after they leave the hospital

WHERE THE STUDY WAS PUBLISHED

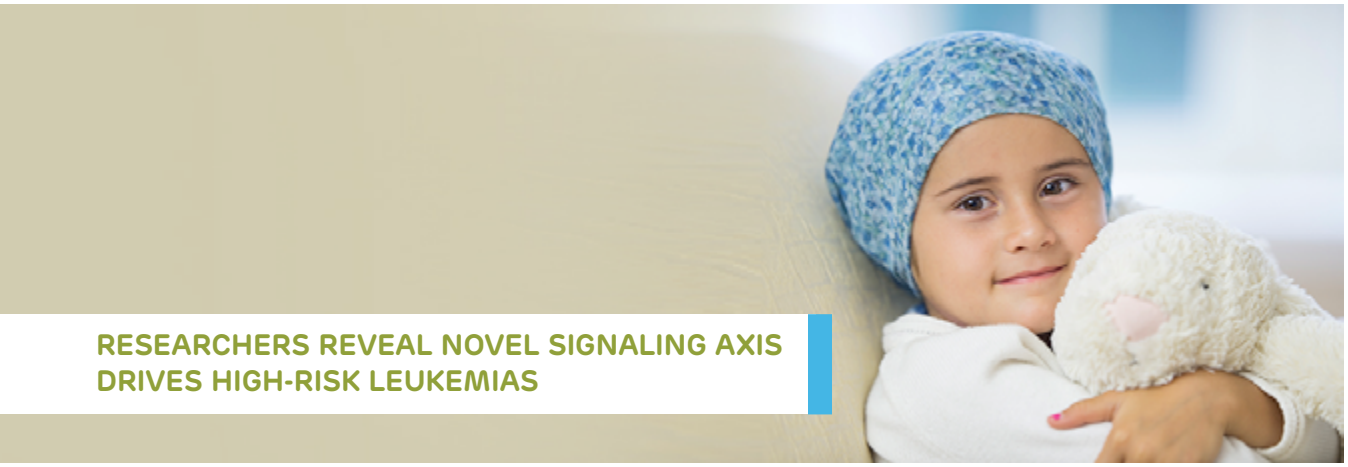
The study appeared in the journal Pediatrics.

WHO HELPED FUND THE STUDY

Various National Institutes of Health grants supported this research.

WHERE TO LEARN MORE

Read more about hospitalized children's mental health in a PolicyLab blog post written by Dr. Doupnik.



RESEARCHERS REVEAL NOVEL SIGNALING AXIS DRIVES HIGH-RISK LEUKEMIAS

THE FINDING

Researchers uncovered how mutations in a protein network drive chronic myelomonocytic leukemia (CMML) and juvenile myelomonocytic leukemia (JMML), both of which tend to have a poor prognosis as they progress to acute myeloid leukemia (AML). The scientists report that mutations in either of two proteins, CBL and LNK (also called SH2B3), form a complex with JAK2, which is a well-known signaling protein that plays a key role in the development of blood-forming cells in bone marrow, to disrupt JAK2 regulation. If something disrupts the normal regulation of JAK2 activity, JAK2 triggers the uncontrolled growth of marrow cells that give rise to a myeloid leukemia.

WHY IT MATTERS

Until now, the molecular events that regulate JAK2 were poorly established. Myeloid leukemias currently have few treatment options, so identifying the causative gene networks may lead researchers to develop novel leukemia drugs aimed at mutations in any of the three proteins — CBL-LNK-JAK2 — in a precision medicine approach. Also, an existing drug called ruxolitinib that inhibits JAK2 might be repurposed to treat these leukemias, based on scientists' new understanding of the molecular mechanisms at work in this signaling axis.

WHO CONDUCTED THE STUDY

A team led by Wei Tong, PhD, a hematology researcher at Children's Hospital of Philadelphia conducted the study. Dr. Tong also is an associate professor of Pediatrics at the Perelman School of Medicine at the University of Pennsylvania, and the co-director of the Hematopoietic Stem Cell program at the PENN institute for Regenerative Medicine. The lead author, Kaosheng Lyu, PhD, is a postdoctoral fellow in Dr. Tong's laboratory.

HOW THEY DID IT

Based on studies in animals and in primary human leukemia cells, the study team pinpointed the role of CBL proteins in JAK2 regulation via the adaptor protein LNK. They demonstrated that myeloid malignancies with CBL loss-of-function mutations exhibited elevated JAK2 protein levels.

QUICK THOUGHTS

"As we continue to discover that specific mutations may cause subtypes of cancer, learning the underlying molecular mechanisms provides opportunities to develop targeted treatments," Dr. Tong said.

WHAT'S NEXT

Clinical research will be needed to test whether the JAK inhibitor ruxolitinib can benefit patients with CMML and JMML, as well as AML patients who have CBL mutations.

WHERE THE STUDY WAS PUBLISHED

The research appeared in the journal *Genes and Development*.

WHO HELPED FUND THE STUDY

National Institutes of Health grants, the Gabrielle's Angel Foundation for Cancer Research, and Alex's Lemonade for Childhood Cancer Research supported this study. In addition, Dr. Tong is a Leukemia & Lymphoma Society Scholar.

WHERE TO LEARN MORE

Find out more about ongoing research in the Wei Tong Laboratory at CHOP.

HIGH COST OF HOSPITALIZATIONS FOR MITOCHONDRIAL DISEASES HIGHLIGHTED

THE FINDING

Estimated costs associated with a typical hospitalization were twice as high for a patient with mitochondrial disease compared to other patients. Patients with mitochondrial disease also had higher-than-typical rates of co-morbid diseases, as well as in-hospital mortality rates — 2.4 percent for children and 3 percent for adults. These mitochondrial disease mortality rates were 6 times higher than average in affected children and 3 times higher than average in affected adults.

WHY IT MATTERS

Few systematic investigations of the public health burden of mitochondrial disease have been completed, even as these disorders are being diagnosed more frequently than ever before. Mitochondrial diseases are a diverse group of disorders caused by mutated genes that impair energy production in a patient's cells, inflicting serious dysfunction in potentially any organ. This study's findings underscore the importance of developing preventive strategies and therapies for these complex energy-deficiency illnesses, as well as supportive care and improved therapies.

WHO CONDUCTED THE STUDY

Shana McCormack, MD, a pediatric researcher at Children's Hospital of Philadelphia, and study co-author, Marni Falk, MD, executive director of CHOP's Mitochondrial Medicine Frontier Program, conducted the analysis along with colleagues from multiple clinical areas at CHOP and the University of Pennsylvania. Dr. McCormack is an assistant professor in the division of Endocrinology, and Dr. Falk is an associate professor in the division of Human Genetics, within the department of Pediatrics at the Perelman School of Medicine at the University of Pennsylvania.

HOW THEY DID IT

The study team performed cross-sectional and longitudinal observational analyses that drew on national databases including medical records from patients hospitalized for mitochondrial disease. For the cross-sectional U.S. study (one year), this represented about 3,200 pediatric and 2,000 adult hospitalizations, and for the longitudinal study this captured data from 495 patients in California who were followed for five years. The study team noted that the actual costs and disease burden may well be higher than their estimates because hospital discharge records may fail to capture mitochondrial disease, which itself is often under-diagnosed.

QUICK THOUGHTS

"We hope that better knowledge of the economic burden of mitochondrial disease will lead to improved funding for research and drug development," Dr. Falk said. "In addition, understanding the true health burden may help healthcare providers and administrators to refocus efforts to prevent death and severe disability from mitochondrial disorders."

WHAT'S NEXT

The researchers suggest that future studies should focus on investigating better strategies for supportive care, preventing hospitalizations, and minimizing the burden of hospitalizations on patients and families living with mitochondrial disease.

WHERE THE STUDY WAS PUBLISHED

This research appeared in the journal *Molecular Genetics and Metabolism*. Dr. Falk presented a summary of the work on Capitol Hill to congressional leaders in the Congressional Mitochondrial Disease Caucus in October.

WHO HELPED FUND THE STUDY

National Institutes of Health grants supported this research.

WHERE TO LEARN MORE

Find out more about research led by the Mitochondrial Medicine Frontier Program at CHOP.

INSPIRATION

FACTS & FIGURES ›

FDA-APPROVED CANCER IMMUNOTHERAPY BRINGS MORE CHANCES AT CHILDHOOD

A Cub Scout in the Webelo Rank, a collector of rocks and gems, and an inquisitive explorer, 10-year-old Austin Schuetz is fascinated by the wonder and workings of everyday objects. And although he doesn't grasp all of the complex details just yet, Austin knows a little bit about his own special molecular machinery, too: "Super killer" T-cells act as a living drug to find and fight any potential cancer growth inside his body.

In October of 2013, scientists at Children's Hospital of Philadelphia and the University of Pennsylvania genetically modified Austin's T-cells as part of an experimental clinical trial for a novel type of cancer immunotherapy. The innovative treatment, known as chimeric antigen receptor T-cell therapy, or CTL019, captivated the attention of both scientific communities and the mainstream media. As the first-ever gene therapy for cancer, the one-time treatment trains a patient's own immune system to target and destroy leukemia cells.

In 2017, the treatment broke new ground for pediatric cancer treatment when the U.S. Food and Drug Administration approved its use for the treatment of B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse in patients up to 25 years old. The move was historic and unprecedented: In an FDA advisory panel this past July, one expert called the therapy "the most exciting thing I've seen in my lifetime." With FDA approval, Novartis Pharmaceuticals will market CTL019 under the name Kymriah™ (tisagenlecleucel), and it is anticipated to reach pediatric patients through a network of certified treatment centers throughout the U.S.

The approval arrived after decades of intensive lab work and clinical trials conducted in collaboration with a team of scientists from CHOP, the University of Pennsylvania, and Novartis, along with the courage of young patients like Austin facing refractory and relapsed forms of ALL— for many of whom, as Kim puts it, the clinical trial was their "last roll of dice."

"I look at him every day and thank God, science, and research that we have [Austin] with us," Kim said.

HOW IT'S MADE: THE SCIENCE OF CTL019

One of the most common cancers in children, ALL is also one of the most aggressive. It occurs when immature white blood cells called lymphocytes crowd out normal, healthy cells in the bone marrow. About 20 percent of the 3,500 pediatric and young adult patients diagnosed with ALL each year relapse or fail to respond to conventional treatments.

Over the last 30 years, Carl June, MD, director of the Center for Cellular Immunotherapies at Penn, and his colleagues had been genetically altering a type of immune cell called a T-cell so that it could detect and destroy lymphocytes. After showing CTL019 successfully eradicated cancer cells in mice, Dr. June's team tested the therapy in adult patients with advanced chronic lymphocytic leukemia (CLL) in 2010. As the evidence supporting immunotherapy began to build, Stephan Grupp, MD, PhD, director of the Cancer Immunotherapy Program at CHOP, was preparing to lead pioneering clinical trials for CTL019 in pediatric patients with an advanced form of ALL.

Years before her son's diagnosis, Kim, an oncology nurse in Wisconsin, watched the remarkable story of Emily Whitehead, who was 6-years-old when her leukemia stopped responding to conventional treatment, on the news. Looking for a last chance, Emily's family met with Dr. Grupp and made the brave decision in April 2012 for her to become the first child in

the world to be treated with engineered T-cell therapy. The new treatment differs from any pediatric cancer treatment seen before.

First, patients have a small percentage of their T-cells extracted from their body through a process called leukaphresis. While the patient returns home, scientists get to work: Using a modified version of the HIV virus, they reprogram the cells with the ability to target a specific protein called CD19, found on the surface of cancerous B-cells. The bulked-up new T-cells can now recognize and attack quickly-dividing cancerous B-cells in a similar way that immune cells typically fight viruses or bacteria.

When infused back into the patient, the T-cells multiply into a brigade of hunter cells that dispatch throughout the body, binding to and killing B-cells. Tests show that an army of infused T-cells can grow to more than 100,000 new cells for each single engineered cell that a patient receives. The bioengineered cells then survive in the body for years, controlling any new cancer cells. Because they also kill off healthy B-cells, patients must come in for routine follow-ups to receive IV immunoglobulin, which provides them with the antibodies they lose during the treatment.

PIONEERS: CAR-T CELL THERAPY'S EARLIEST PATIENTS

Emily is now 13, and her cancer remains in remission. For the pediatric patients like her who enrolled in the earliest trials, the treatment was a high-risk but high-impact gamble. Most had reached a critical moment in their disease progress.

When a biopsy revealed that it was only a matter of time before Austin suffered a full-blown relapse despite bouts of chemotherapy and a bone marrow transplant, Kim moved fast, packing the family's bags and arranging to have Austin's information sent to CHOP for qualification, and his cells collected by one of her colleagues in the oncology department at the hospital where she worked.

Arriving in Philadelphia, Austin became participant number 21 — a number that Kim recalls brought to earth just how investigational the treatment was.

"He ended up being No. 21, and you think, 'Oh, my gosh, that's not a lot of kids at all.' We really just had to roll the dice and pray that it worked. Nothing in this path is a guarantee," Kim said. "So I just held onto hope. We had to go for it, and just hope and pray along the way that it would work."

After meeting Dr. Grupp and the tireless team of providers conducting the trial including Shannon Maude, MD, attending physician in the Cancer Center at CHOP, Austin received his T-cell infusion in two doses on Oct. 1 and 2, 2013. His family remained watchful for the appearance of the cytokine release syndrome (CRS) that they had been warned of: a side effect in the form of a hurricane of flu-like symptoms. Six days after his infusion, Austin began to show signs of CRS, including severe headaches and low-grade fevers. He was admitted to the hospital for three nights.

As Austin recovered, the Schuetz's waited. News of the results from a bone marrow biopsy taken about four weeks after Austin's infusion arrived on Halloween night, which also happened to be Kim's birthday. The family was trick-or-treating in a Philadelphia suburb when Austin (dressed as one of the Ghostbusters) reached for a doorbell, and the phone rang. It was Dr. Maude, and her message was short and sweet: The CTL019 therapy was working.

The family returned to home Wisconsin, joining the growing number of cancer immunotherapy patients who, like Austin and Emily, now had hope for healthy, normal childhoods ahead of them. In the early stage clinical trials of CTL019, more than 90 percent of patients achieved a complete remission one month after the therapy. In a subsequent global registration trial in 2015, 83 percent of patients with advanced ALL who received a single dose achieved a complete remission.

NEXT STEPS

As Kymriah™ enters the market over the next few years, research into more cellular therapies continues to drive forward at CHOP. Dr. Maude is leading a pilot study to evaluate humanized CART19 cells (or huCART19 cells) for patients with relapsed or refractory CD19+ leukemia and lymphoma who were previously treated with a B-cell directed engineered cell therapy product. The hope for this product is to extend the time that cells stick around and help more patients avoid the risks of bone marrow transplant.

Meanwhile, CHOP's Immunotherapy team is also leading the development of a trial that tests Kymriah as part of first-line therapy to prevent relapse or the subsequent need for bone marrow transplant in children with treatment-resistant ALL. Investigators are also developing trials to identify other ALL populations who might benefit from immunotherapy, including patients with Down syndrome and those with central nervous system ALL.

As for Kim, her life feels full of gratitude, purpose, and very welcome cuddles from 9-year-old Austin.

"I don't think that I could ever repay [the CHOP team] for the work that they've done," Kim said. "I'm just thankful that they are dedicated to kids like mine; that they are just as invested as I am in my son's life because they want to see this happen."

The treatment at age 5 that allowed Austin to be so many wonderful things at age 9 — from Cub Scout to collector to cancer survivor — now gives Kim yet another thing that she happily adds to the list: Pioneer.

FACTS & FIGURES

FINANCIAL/STATS INFO - FY 17

$383,865,187

TOTAL RESEARCH OPERATING EXPENSES

$229,558,823

EXTERNAL GRANTS AND CONTRACTS

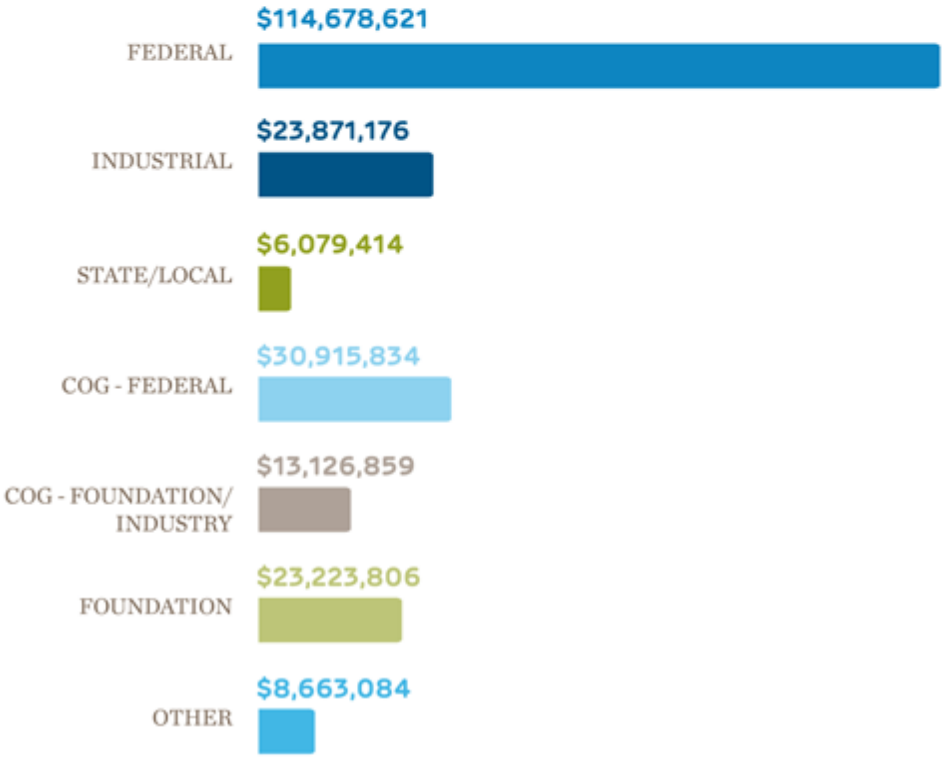
$115,384,124

684 AWARDS

2322

PUBLICATIONS


$229,558,823
EXTERNAL FUNDING
GRANTS & CONTRACTS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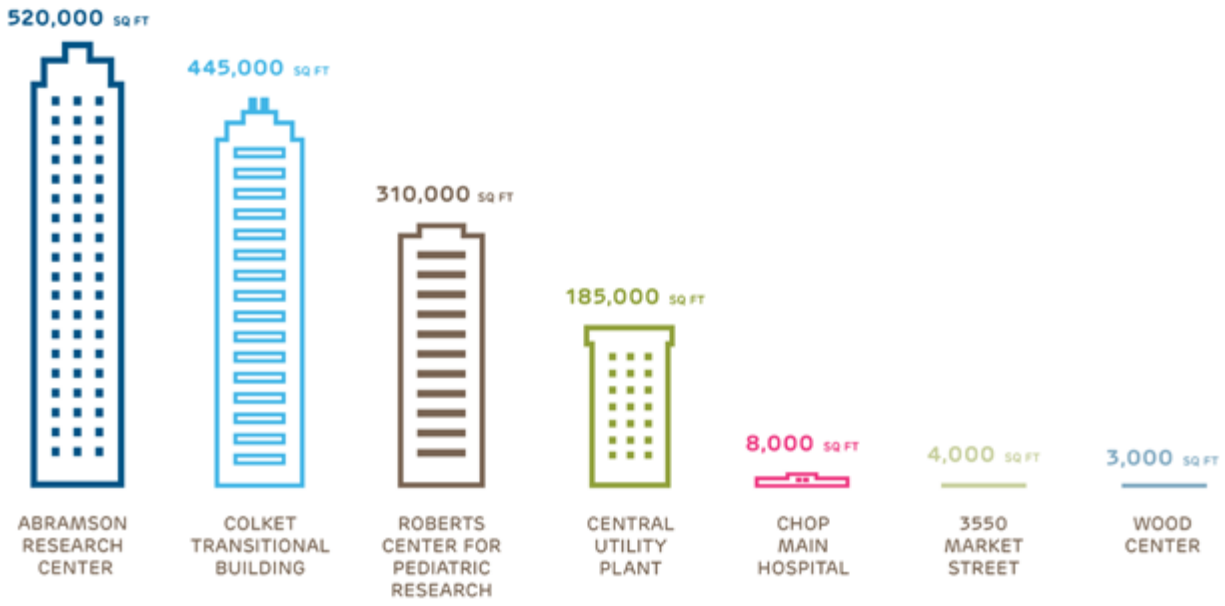
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ABRAMSON RESEARCH CENTER
445,000 SQ FT
COLKET TRANSITIONAL BUILDING
310,000 SQ FT
ROBERTS CENTER FOR PEDIATRIC RESEARCH
185,000 SQ FT
CENTRAL UTILITY PLANT
8,000 SQ FT
CHOP MAIN HOSPITAL
4,000 SQ FT
3550 MARKET STREET
3,000 SQ FT
WOOD CENTER

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- **Beverly L. Davidson, PhD**
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- **Richard Aplenc, MD, PhD, MSCE**
  Assistant Vice President and Chief Clinical Research Officer
- **Michelle Lewis, MS, CRA**
  Vice President, Research Administration and Operations
- **Zev Sunleaf**
  Vice President, Office of Technology Transfer, Commercialization and Innovation
- **Matthew Hodgson**
  Assistant Vice President, Research Compliance and Regulatory Affairs

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- Center for Autism Research
  Director: Robert Schultz, PhD
- Center for Childhood Cancer Research
  Director: Stephen P. Hunger, MD
- Center for Clinical Pharmacology
  Director: Athena F. Zuppa, MD, MSCE
- Center for Injury Research and Prevention
  Directors: Flaura Winston, MD, PhD, and Kristy Arbogast, PhD
- Center for Mitochondrial and Epigenomic Medicine
  Director: Douglas Wallace, PhD

- Center for Pediatric Clinical Effectiveness
  Director: Theoklis Zaoutis, MD, MSCE

- PolicyLab
  Director: David Rubin, MD, MSCE

- Raymond G. Perelman Center for Cellular and Molecular Therapeutics
  Director: Beverly Davidson, PhD

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- **Neuroscience**
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- **Normal and Malignant Hematopoiesis**
  Leader: Carolyn Felix, MD

- **Proteins**
  Leader: Yair Argon, PhD

- **Protective Immunity and Immunopathology**
  Leaders: Edward Behrens, MD, and Paula Oliver, PhD

- **Qualitative Methods**
  Leader: Cynthia Mollen, MD, MSCE

› **Spatial and Functional Genomics**
Leaders: Struan Grant, PhD, Andrew Wells, PhD, and Gerd Blobel, MD, PhD

› **Stem Cells and Benign Hematopoiesis**
Leaders: Mortimer Poncz, MD and Deborah French, PhD

ENDOWED CHAIRS

› **Leonard and Madlyn Abramson Endowed Chair in Pediatrics**
Holder: Joseph W. St. Geme III, MD

› **Leonard and Madlyn Abramson Endowed Chair in Pediatric Urology**
Holder: Douglas A. Canning, MD

› **Frederick H. Allen Endowed Chair in Child Psychiatry**
Holder: Tami D. Benton, MD

› **Gisela and Dennis Alter Endowed Chair in Pediatric Neonatology**
Holder: Haralambos Ischiropoulos, PhD

› **Mary D. Ames Endowed Chair in Child Advocacy**
Holder: David Rubin, MD, MSCE

› **Richard M. Armstrong Jr. Endowed Chair in Pediatric Orthopaedic Surgery**
Holder: John M. Flynn, MD

› **T. Hewson Bache Endowed Chair in Pediatrics**
Holder: Robert W. Doms, MD, PhD

› **Lester Baker Endowed Chair in Pediatric Diabetes**
Holder: Michael A. Levine, MD

› **Michael and Charles Barnett Endowed Chair in Pediatric Mitochondrial Medicine and Metabolic Diseases**
Holder: Douglas Wallace, PhD

› **James Battaglia Endowed Chair in Pediatric Pain Management**
Holder: Gordon Barr, PhD

› **Fred and Suzanne Biesecker Endowed Chair in Pediatric Liver Disease**
Holder: David A. Piccoli, MD

› **Patricia Borns Endowed Chair in Radiology Education**
Holder: Janet R. Reid, MD

› **Irma and Norman Braman Endowed Chair for Research in GI Motility Disorders**
Holder: Robert O. Heuckeroth, MD, PhD

› **Evelyn Willing Bromley Endowed Chair in Clinical Laboratories and Pathology**
Holder: Michael Bennett, PhD

› **Evelyn Willing Bromley Endowed Chair in Pathology and Clinical Laboratories**
Holder: Nancy B. Spinner, PhD, FACMG

- **Catherine D. Brown Endowed Chair in Pediatric Epilepsy**
  Holder: Dennis Dlugos, MD

- **Buck Family Endowed Chair in Hematology Research**
  Holder: Pending Appointment

- **Mortimer J. Buckley Jr., MD Endowed Chair in Cardiac Surgery**
  Holder: Thomas L. Spray, MD

- **Daniel B. Burke Endowed Chair for Diabetes Research**
  Holder: Struan Grant, PhD

- **Louis and Amelia Canuso Family Endowed Chair for Clinical Research in Oncology**
  Holder: Frank M. Balis, MD

- **Henry S. Cecil, MD Endowed Chair in Rehabilitative Medicine at Children's Seashore House**
  Holder: Susan E. Levy, MD

- **Children's Hospital of Philadelphia Endowed Chair in Anesthesiology and Critical Care Quality and Patient Safety**
  Holder: Pending Appointment

- **Children's Hospital of Philadelphia Endowed Chair in Biomedical Informatics and Entrepreneurial Science**
  Holder: Pending Appintment

- **Children's Hospital of Philadelphia Endowed Chair in Cardiac Critical Care Medicine**
  Holder: Andrew T. Costarino, MD

- **Children's Hospital of Philadelphia Endowed Chair in Critical Care Medicine**
  Holder: Vinay Nadkarni, MD

- **Children's Hospital of Philadelphia Endowed Chair in Fetal Imaging**
  Holder: Beverly Gilbert Coleman, MD

- **Children's Hospital of Philadelphia Endowed Chair in Pediatric Hematology**
  Holder: Rodney Camire, PhD

- **Children's Hospital of Philadelphia Endowed Chair in Pediatric Neuroradiology**
  Holder: Robert Zimmerman, MD

- **Children's Hospital of Philadelphia Endowed Chair in Pediatric Orthopaedic Surgery**
  Holder: Pending Appointment

- **Children's Hospital of Philadelphia Endowed Chair in Pediatric Otolaryngology**
  Holder: Ken Kazahaya, MD

- **Children's Hospital of Philadelphia Endowed Chair in Pediatric Otolaryngology and Pediatric Airway Disorders**
  Holder: Ian N. Jacobs, MD

- **Alan R. Cohen Endowed Chair in Pediatrics**
  Holder: Peter Adamson, MD

› **Ruth M. Colket Endowed Chair in Pediatric Nursing**
Holder: Pending Appointment

› **Ruth M. and Tristram C. Colket, Jr. Endowed Chair in Pediatric Surgery**
Holder: Alan W. Flake, MD

› **Tristram C. Colket, Jr. Endowed Chair in Pediatric Neurology**
Holder: Robert R. Clancy, MD

› **Colman Family Endowed Chair in Pediatric Inflammatory Bowel Disease**
Holder: Robert N. Baldassano, MD

› **David Cornfeld Endowed Chair in Pediatrics**
Holder: Richard Rutstein, MD

› **Jean Cortner Endowed Chair in Pediatric Gastroenterology**
Holder: Virginia A. Stallings, MD

› **Nicholas Crognale Endowed Chair in Pediatric Emergency Medicine**
Holder: Kathy N. Shaw, MD

› **Giulio D'Angio Endowed Chair in Neuroblastoma Research**
Holder: John Maris, MD

› **Distinguished Chair in the Department of Pediatrics**
Holder: Phillip Bryant, DO

› **Distinguished Chair in the Department of Pediatrics**
Holder: Susan Coffin, MD

› **Distinguished Chair in the Department of Pediatrics**
Holder: Alex Fiks, MD, MSCE

› **Distinguished Chair in the Department of Pediatrics**
Holder: Ian Krantz, MD

› **Distinguished Chair in the Department of Pediatrics**
Holder: Jonathan Rome, MD

› **Distinguished Chair in the Department of Pediatrics**
Holder: Gail Slap, MD

› **Distinguished Chair in the Department of Pediatrics**
Holder: Flaura Winston, MD, PhD

› **Distinguished Chair in the Department of Pediatrics**
Holder: Pending Appointment

› **John J. Downes, MD Endowed Chair in Pediatric Anesthesiology and Critical Care Medicine**
Holder: C. Dean Kurth, MD

› **Mary Downs Endowed Chair in Pediatric Craniofacial Treatment and Research**
Holder: Jesse A. Taylor, MD

- **John W. Duckett, Jr. Endowed Chair in Pediatric Urology**
  Holder: Stephen A. Zderic, MD

- **Audrey E. Evans Endowed Chair in Pediatric Oncology**
  Holder: Garrett M. Brodeur, MD

- **Kenneth E. Fellows Endowed Chair in Radiology Quality and Patient Safety**
  Holder: Raymond Sze, MD, MAMS

- **Mark Fishman Endowed Chair in Genomics and Computational Science**
  Holder: Joseph Zorc, MD, MSCE

- **Ann and Richard Frankel Chair in Gastroenterology Research**
  Holder: Pending Appointment

- **Friends of Brian Endowed Chair in Pediatric Plastic and Reconstructive Surgery**
  Holder: Pending Appointment

- **William T. Grant Endowed Chair in Child Development and Rehabilitation**
  Holder: Marc Yudkoff, MD

- **William J. Greeley Endowed Chair in Pediatric Anesthesiology and Critical Care Research**
  Holder: Francis McGowan, MD

- **Jane Fishman Grinberg Endowed Chair in Stem Cell Research**
  Holder: Mortimer Poncz, MD

- **Steven D. Handler Endowed Chair in Medical Ethics**
  Holder: Christopher Feudtner, MD, PhD, MPH

- **Robert and Dolores Harrington Endowed Chair in Pediatric Cardiology**
  Holder: Jack Rychik, MD

- **George Leib Harrison Endowed Chair in Fetal Therapy**
  Holder: Mark Paul Johnson, MD

- **Werner and Gertrude Henle Endowed Chair**
  Holder: Theoklis Zaoutis, MD, MSCE

- **Maurice R. Hilleman Endowed Chair in Vaccinology**
  Holder: Paul Offit, MD

- **Joseph Lee Hollander Endowed Chair in Pediatric Rheumatology**
  Holder: Edward Behrens, MD

- **John Westgate Hope Endowed Chair in Radiology Faculty Development**
  Holder: Pending Appointment

- **Justin Michael Ingerman Endowed Chair for Palliative Care**
  Holder: Wynne Morrison, MD

- **Orton P. Jackson Endowed Chair in Adolescent Medicine**
  Holder: Carol Ford, MD

› **John H. and Hortense Cassell Jensen Endowed Chair in Pediatric Development and Teaching**
Holder: Stephen Ludwig, MD

› **Richard B. Johnston, Jr. Endowed Chair in Pediatrics**
Holder: Ronald Rubenstein, MD, PhD

› **Joshua Kahan Endowed Chair in Pediatric Leukemia Research**
Holder: Carolyn Felix, MD

› **Jacob A. Kamens Endowed Chair in Neurological Disorders and Translational NeuroTherapeutics**
Holder: Adeline Vanderver, MD

› **John M. Keating Endowed Chair in Pediatrics**
Holder: Pending Appointment

› **C. Everett Koop Endowed Chair in Pediatric Surgery**
Holder: N. Scott Adzick, MD

› **Laffey-Connolly Endowed Chair in Pediatric Nephrology**
Holder: Susan Furth, MD

› **Harriet and Ronald Lassin Endowed Chair in Pediatric Neonatology**
Holder: Scott Lorch, MD

› **Anthony A. Latini Endowed Chair in the Prevention of Child Abuse and Neglect**
Holder: Cindy Christian, MD

› **Dr. Bong S. Lee Endowed Chair in Pediatric Orthopaedics**
Holder: Maurizio Pacifici, PhD

› **Mabel E. Leslie Endowed Chair in Pediatric Ophthalmology**
Holder: Monte D. Mills, MD

› **Grace R. Loeb Endowed Chair in Neurosciences**
Holder: Brenda Banwell, MD

› **Stephen Ludwig Endowed Chair in Medical Education**
Holder: Lisa Zaoutis, MD

› **Suzi and Scott Lustgarten Endowed Chair for Clinical Care of GI Motility Disorders**
Holder: Ritu Verma, MBChB

› **Soroosh Mahboubi Endowed Chair in Body Imaging at Children's Hospital of Philadelphia**
Holder: Pending Appointment

› **Thomas Frederick McNair Scott Endowed Chair in Pediatrics**
Holder: Eric Eichenwald, MD

› **Arthur Vincent Meigs Endowed Chair in Pediatrics**
Holder: Beverly Davidson, PhD

› **Minimally Invasive Surgery Endowed Chair in Pediatric Urology**
Holder: Pending Appointment

› **Jeffrey Modell Endowed Chair in Pediatric Immunology Research**
Holder: Neil Romberg, MD

› **Robert Gerard Morse Endowed Chair in Pediatric Pulmonary Medicine**
Holder: Julian Allen, MD

› **Thomas Moshang Endowed Chair in Endocrinology**
Holder: Craig Alter, MD

› **E. Mortimer Newlin Endowed Chair in Pediatric Otolaryngology and Human Communication**
Holder: Ralph Wetmore, MD

› **Edmond F. Notebaert Endowed Chair in Pediatric Research**
Holder: Bryan Wolf, MD, PhD

› **Yetta Deitch Novotny Endowed Chair in Pediatric Oncology**
Holder: Stephan Grupp, MD, PhD

› **Oberkircher Family Endowed Chair in Pediatric Radiology**
Holder: Timothy Roberts, PhD

› **Kwame Ohene-Frempong Endowed Chair in Pediatric Hematology**
Holder: Stefano Rivella, MD

› **Patrick S. Pasquariello Jr. Endowed Chair in General Pediatrics**
Holder: Louis M. Bell, MD

› **R.A.F. Penrose Endowed Chair in Pediatrics**
Holder: Stewart A. Anderson, MD

› **Jeffrey E. Perelman Distinguished Chair in the Department of Pediatrics**
Holder: Stephen Hunger, MD

› **Perelman Scholars**
Holders: Pending Appointment

› **Raymond G. Perelman Endowed Chair in Pediatric Neuro-Ophthalmology**
Holder: Grant T. Liu, MD

› **R. Anderson Pew Distinguished Chair in the Department of Pediatrics**
Holder: Carole Marcus, MBBCh

› **Stanley Plotkin Endowed Chair in Pediatric Infectious Diseases**
Holder: Jeffrey M. Bergelson, MD

› **William Potsic Endowed Chair in Pediatric Otolaryngology and Childhood Communication**
Holder: Pending Appointment

› **Gerald D. Quill Distinguished Chair in the Department of Pediatrics**
Holder: Ron Keren, MD, MPH

› **Peter Randall Endowed Chair in Plastic and Reconstructive Surgery**
Holder: Scott P. Bartlett, MD

› **Russell C. Raphaely Endowed Chair in Critical Care Medicine**
Holder: Robert A. Berg, MD

› **William J. Rashkind Endowed Chair in Pediatric Cardiology**
Holder: Robert J. Levy, MD

› **Regional Autism Center Endowed Chair**
Holder: Robert T. Schultz, PhD

› **Mildred L. Roeckle Endowed Chair at Children's Hospital of Philadelphia**
Holder: Andrei Thomas-Tikhonenko, PhD

› **Lucy Balian Rorke-Adams Endowed Chair in Neuropathology**
Holder: Pending Appointment

› **Richard and Sheila Sanford Endowed Chair in Pediatric Oncology**
Holder: Alex Seif, MD, MPH

› **Louise Schnaufer Endowed Chair in Pediatric Surgery**
Holder: Holly L. Hedrick, MD

› **Hubert J.P. and Anne Faulkner Schoemaker Endowed Chair in Pediatric Neuro-Oncology**
Holder: Peter C. Phillips, MD

› **Elias Schwartz, MD Endowed Chair in Hematology**
Holder: Kim Smith-Whitley, MD

› **Letitia B. and Alice Scott Endowed Chair in Human Genetics and Molecular Biology**
Holder: Elaine H. Zackai, MD

› **Thomas Frederick McNair Scott Endowed Chair in Pediatrics**
Holder: Eric Eichenwald, MD

› **Richard Shafritz Endowed Chair in Pediatric Ophthalmology Research in the Division of Ophthalmology**
Holder: Gil Binenbaum, MD, MSCE

› **William Wikoff Smith Endowed Chair in Pediatric Genomic Research**
Holder: Pending Appointment

› **Howard M. Snyder III Endowed Chair in Pediatric Urology**
Holder: Thomas F. Kolon, MD

› **Louis Starr Endowed Chair in Pediatrics**
Holder: Pending Appointment

› **Stuart E. Starr Endowed Chair in Pediatrics**
Holder: Jonathan Spergel, MD, PhD

› **Leslie N. Sutton Endowed Chair in Pediatric Neurosurgery**
Holder: Phillip B. Storm Jr., MD

› **Daniel M. Tabas Endowed Chair in Pediatric Cardiothoracic Surgery**
Holder: J. William Gaynor, MD

- **Evelyn Rome Tabas Endowed Chair in Pediatric Cardiology**
  Holder: Victoria L. Vetter, MD

- **Josephine J. Templeton Endowed Chair in Pediatric Anesthesiology Clinical Education**
  Holder: Susan C. Nicolson, MD

- **Josephine J. and John M. Templeton Jr. Endowed Chair in Pediatric Trauma**
  Holder: Michael L. Nance, MD, FAAP, FACS

- **Jennifer Terker Endowed Chair in Pediatric Cardiology**
  Holder: Joseph Rossano, MD

- **Charles E.H. Upham Endowed Chair in Pediatric Medicine**
  Holder: Beverly S. Emanuel, PhD

- **William L. Van Alen Endowed Chair in Pediatric Radiology**
  Holder: Kassa Darge, MD, PhD

- **Frank R. Wallace Endowed Chair in Infectious Diseases**
  Holder: Kathleen Sullivan, MD, PhD

- **Alice Langdon Warner Endowed Chair in Pediatric Cardiothoracic Surgery**
  Holder: Pending Appointment

- **Wawa Endowed Chair in International Adoption**
  Holder: Susan Friedman, MD

- **Frank E. Weise III Endowed Chair in Pediatric Hematology**
  Holder: Gerd Blobel, MD, PhD

- **Mai and Harry F. West Endowed Chair in Pediatric Research**
  Holder: Pending Appointment

- **Alexander B. Wheeler Endowed Chair in Neurosurgical Research**
  Holder: Adam Resnick, PhD

- **Evelyn and George Willing Endowed Chair in Pathology Research**
  Holder: Janis Burkhardt, PhD

- **Nancy Abramson Wolfson Endowed Chair in Health Services Research**
  Holder: Jeffrey H. Silber, MD, PhD

- **Richard D. Wood Jr. and Jeanette A. Wood Endowed Chair in Pediatric Diagnostic Medicine**
  Holder: Pending Appointment

ADMINISTRATIVE UNITS

- **Clinical Research Support Office**
  Jennifer Goldfarb, Director
  Michele Toms, Assistant Director

- **Center for Human Phenomic Science**
  Richard Aplenc, MD, PhD, MSCE

Clinical Trials Financial Management
Veronica Kain, Director
Tiana Dingle, Assistant Director

Core Facilities Administration
Lisa MacDowell, Administrative Director

Faculty Development
Virginia Stallings, MD, Director
Mary Blitzer Field, PhD, Assistant Director

Postdoctoral Affairs
Wendy Williams, PhD, Director
David Taylor, PhD, Assistant Director

Research Communications
Jennifer Long, Director

Research Compliance and Regulatory Affairs
Matthew Hodgson, Assistant Vice President

Research Finance
Steven Wiley, Director
Luz Arrison, Assistant Director
Bethann Kurek, Assistant Director

Research Information Systems
Michael Schultz, Director

Research Resources
Howard Eck, Director

Research Safety
Raymond Colliton, Director
Denise Melvin, Assistant Director

Responsible Research Training
Wendy Williams, PhD, Director
Jodi Leckrone, Assistant Director

Sponsored Projects and Research Business Management
Sara Dubberly, Director
Brigid Czyszczin, Assistant Director
Robert Denight, Assistant Director

Technology Transfer, Commercialization and Innovation
Zev Sunleaf, Director
Camille Jolly-Tornetta, Assistant Director, Intellectual Property & Licensing

CREDITS

- **Madeline Bell**
  Chief Executive Officer
- **Bryan A. Wolf, MD, PhD**
  Chief Scientific Officer & Executive Vice President
- **Michelle A. Lewis**
  Vice President, Research Administration and Operations
- **Jennifer Long**
  Director, Research Communications
- **Sharlene George**
  Senior Medical/Science Writer
- **Jillian Lim**
  Medical/Science Writer
- **Angela Knott**
  Art Director
- **Juliet Kilcoyne**
  Creative Designer & Developer
- **Melissa LaVigne**
  Graphic Designer
- **Alexis Arvanitides**
  Graphic Designer

LINKS OF INTEREST

- Children's Hospital of Philadelphia Research Institute Website
- Cornerstone, CHOP Research Institute's blog
- CHOP Research Institute Press Releases
- *Bench to Bedside*, CHOP Research's Monthly Online Newsmagazine
- CHOP Research Institute's Facebook Page
- CHOP Research Institute's Twitter Feed
- CHOP Research Institute's LinkedIn Page
- CHOP Research Institute's YouTube Channel
- Children's Hospital of Philadelphia Website
- Children's Hospital of Philadelphia YouTube Channel
- Children's Hospital of Philadelphia Foundation Website

CHOP Research Institute's Department of Research Communications produced the 2017 Research Annual Report.