2019
RESEARCH ANNUAL REPORT

Children's Hospital of Philadelphia
RESEARCH IN STITUTE

2019 RESEARCH ANNUAL REPORT

MILESTONES ›

MILESTONES

INITIATIVES ›

NEW CLINICAL MANUFACTURING FACILITY LAUNCHES TO DEVELOP NOVEL GENE THERAPY TOOLS

The Raymond G. Perelman Center for Cellular and Molecular Therapeutics (CCMT) at Children's Hospital of Philadelphia unveiled the Clinical Vector Core's new manufacturing facility to produce biotechnology tools that will deliver cell and gene therapy for difficult-to-treat diseases.

CHOP partnered with the CEO Council for Growth of the Chamber of Commerce for Greater Philadelphia to officially open the facility in October 2018 and highlighted the city's position as an important hub of scientific and medical innovation.

"Philadelphia is a city of breakthroughs," said Madeline Bell, CHOP President and CEO, during the event. "In this facility, we make the tools — the vectors — that scientists use to deliver cell and gene therapies, bringing dramatic precision medicine treatments to patients."

CHOP researchers developed two vectors that are the among the first gene therapies approved by the U.S. Food and Drug Administration: CAR T-cell therapy (Kymriah®) to combat an aggressive form of pediatric acute lymphoblastic leukemia and voretigene neparvovec (Luxturna™) to treat a form of inherited blindness.

The Clinical Vector Core focuses on tapping into how viruses efficiently infect and transfer their genes to host cells. Core Director Johannes van der Loo, PhD, leads a team dedicated to producing high-quality viral vectors for numerous preclinical and clinical trials at CHOP and other facilities.

The Clinical Vector Core was established as a Core facility within the CCMT more than a decade ago, and it began at a time when treatment of patients through gene therapy at CHOP was just getting underway, Dr. van der Loo noted.

At first, the Clinical Vector Core developed one clinical product a year, but it now works on approximately 10 each year, according to Director of Quality Olga Zelenaia, PhD. It has also expanded from delivering products primarily for CHOP and the University of Pennsylvania to national and international clients.

CONGENITAL HYPERINSULINISM CENTER CELEBRATES 20TH ANNIVERSARY AND 500 SURGERIES

The Congenital Hyperinsulinism Center at Children's Hospital of Philadelphia celebrated its 20th anniversary in October 2018 and marked its 500th surgery, which saved the life of a baby girl named Alaya from North Carolina.

Congenital HI is a life-threatening, genetic disorder in which the insulin cells of the pancreas secrete too much insulin. Fortunately for Alaya, doctors discovered her low blood sugar just moments after she was born. She was later diagnosed with HI and brought to CHOP, where the HI team determined Alaya had focal disease, and a PET scan found a legion on the head of her pancreas. It took two surgeries for Surgeon-in-Chief N. Scott Adzick, MD, to remove the entire lesion.

Established in 1998, CHOP's HI Center was the first of its kind in the United States. Today, it is the largest and most active HI Center in the world and has evaluated, diagnosed, and treated more than 1,000 children with congenital HI from around the nation and the globe. The 500 pancreatectomies performed at CHOP far exceeds the number performed by any other hospital.

Building on the momentum of the clinical program, Diva De León-Crutchlow, MD, MSCE, director of the Congenital Hyperinsulinism Center, saw an opportunity to expand and integrate the combined scope of the clinical and research programs under the auspices of the new Frontier Program for the Advancement of Hyperinsulinism Care and Research.

Co-principal investigator Dr. Adzick and a multidisciplinary team of collaborators are working toward a future where novel ways to treat, monitor, and support young patients with HI throughout their lifespan will improve long-term outcomes. They anticipate that Frontier Program support will give rise to the discovery of new genetic forms of hyperinsulinism and broaden scientists' understanding of disease mechanisms that will help to develop effective targeted therapies.

KARABOTS PEDIATRIC CARE CENTER IN WEST PHILADELPHIA MARKS FIFTH ANNIVERSARY

The Nicholas and Athena Karabots Pediatric Care Center in West Philadelphia celebrated five years of providing innovative community healthcare and programs for thousands of children and their families.

The Karabots Center opened in 2013, funded by a gift from philanthropists Nicholas and Athena Karabots to provide primary care services and programs for West Philadelphia families. The 52,000-square-foot environmentally sustainable building contains 56 child-friendly exam rooms and dedicated space for radiology, hearing and vision testing, and a phlebotomy laboratory.

The center works closely with West Philadelphia community leaders to best meet the needs of families in the area. Over the past five years, it has served 32,000 patients, with 85 percent enrolled in medical assistance, and held more than 700 community events on site.

The Karabots Center additionally serves as a base of operations and research initiatives for 16 diverse community programs, including the Center for Grieving Children, Community Asthma Prevention Program, Homeless Health Initiative, Keystone First Cares Program, Kids Smiles, Lutheran Settlement House-Domestic Violence, Pediatric Research Consortium, PriCARE Parenting Program, Reach Out and Read, Refugee Health Program, and Violence Prevention Initiative.

One of the center's most unique outreach efforts, the Karabots Garden, brings together more than 1,300 corporate and community volunteers to cultivate a wide variety of fruits and vegetables, which are then distributed to local families through the Early Head Start and Healthy Weight programs. The Karabots Garden has grown 4.2 tons of fresh produce in the past five years to share with the community.

PARENTS MAGAZINE HONORS CHOP AS ONE OF THE MOST INNOVATIVE CHILDREN'S HOSPITALS

Parents magazine named Children's Hospital of Philadelphia one of the 20 most innovative children's hospitals in the nation in 2018.

The magazine surveyed members of the Children's Hospital Association who identified hospitals with a proven track record of innovations that lead to medical advances. The survey also asked members about children's hospitals that have adopted the latest technologies and led the way in sharing its innovations with other pediatric centers.

Parents specifically recognized CHOP for its significant contributions to the development of a groundbreaking treatment for advanced acute lymphoblastic leukemia (ALL) and its efforts to help other hospitals offer the new therapy to patients. CHOP researchers helped develop the first national and international clinical trials for an immunotherapy known as chimeric antigen receptor (CAR) T-cell therapy for children, a first-of-its-kind treatment approved by the U.S. Food and Drug Administration.

Parents magazine focuses on helping mothers and fathers navigate parenthood from pregnancy to school, including children's health, safety, nutrition, and behavior issues, and is read by 11.8 million subscribers.

CHOP-BASED PEDIATRIC DEVICE CONSORTIUM EXPANDS WITH NEW PARTNERSHIPS

The Pennsylvania Pediatric Medical Device Consortium (PPDC), which is based at Children's Hospital of Philadelphia, now spans from Philadelphia to Pittsburgh.

The PPDC announced a new partnership with two programs at the University of Pittsburgh to continue supporting the development of promising medical devices that address unmet clinical needs in children. The expansion follows the award of a five-year, $5 million grant renewal from the PPDC's funder, the U.S. Food and Drug Administration. It is one of only five consortia in the nation funded by the FDA through the Pediatric Device Grants Consortia Program.

"With genetic diseases and congenital malformations, there are many circumstances where off the shelf products just don't work," said Robert Levy, MD, William J. Rashkind Endowed Chair in Pediatric Cardiology and PPDC principal investigator. "The opportunity for us to set up a model to show how you can create personalized pediatric medical devices on a routine basis is one of the main goals I would like to accomplish over the next five years."

Formerly known as the Philadelphia Pediatric Medical Device Consortium, the PPDC's recent name change reflects its new, statewide scope. The PPDC's new University of Pittsburgh partners are the McGowan Institute for Regenerative Medicine and sciVelo, which advances the university's translational research in brain health, cell therapy, and digital health to create market-ready solutions.

The PPDC has assisted more than 150 innovative projects over the past six years and awarded more than 20 seed grants of up to $50,000 each to companies through a competitive application process. It has provided both funding and guidance for pediatric products including an airway clearance system, a powered arm brace, a speech-generating communication system, and a vision acuity test for preverbal children.

In addition to awarding grants to support pediatric device advancement and regulatory approval, the PPDC has launched a new early-stage development program in partnership with the Philadelphia-area medical device design company, Archimedic, to develop innovative pediatric medical device ideas.

The PPDC guides applicants through every step of the process, from building partnerships within the business community, matching inventors with funding, and introducing them to a medical device developer, to assisting inventors through the FDA submission process.

CHOP RECEIVES RECOGNITION AS CENTER OF EXCELLENCE FOR RARE BLADDER DISORDER

The Association for the Bladder Exstrophy Community (A-BE-C) named Children's Hospital of Philadelphia one of eight Centers of Excellence in the United States that provides complete, effective care for children born with bladder or cloacal exstrophy.

Bladder or cloacal exstrophy is a rare disorder that occurs while a fetus is developing. The condition results in the abdominal wall not fully forming, leaving the pubic bones separated and the bladder exposed to the outside skin surface through an opening in the lower abdominal wall.

A-BE-C determined that CHOP and seven other hospitals meet the organization's rigorous criteria for the treatment of bladder or cloacal exstrophy in infants and children. The criteria includes that the program is led by a physician/medical director who has at least five years post-fellowship training in pediatric urology/surgery; the hospital follows a sufficient number of patients with diverse manifestations of bladder and cloacal exstrophy to offer wide array of treatment options; and the hospital engages in single or multicenter research to share their patient information and program results.

The criteria also requires that the care team includes a pelvic floor physical therapist, and inpatient nursing and outpatient staff who have received specialized training. The care team must additionally collaborate with orthopedic surgeons, pediatric anesthesiologists, radiologists, plastic surgeons, and when necessary, neurosurgeons and gastroenterologists who have expertise in bladder and cloacal exstrophy.

Additional requirements are that board-certified behavioral health specialists are included in the care team to provide support to patients and families throughout treatment, and offer resource interventions, education, and individual, family and group therapy.

A-BE-C will bring all Centers of Excellence together at least once a year to share updates on care activities and research initiatives. Each Center must re-apply every three years to renew the designation.

INITIATIVES

INNOVATION ›

COMMITTED TO SCIENCE, TECH, ENGINEERING, MATHEMATICS IN OUR WORKPLACE AND COMMUNITY

The Research Institute expanded its awareness and support of Science, Technology, Engineering, and Mathematics (STEM) initiatives. Efforts from the Office of Academic Training and Outreach Programs (ATOP) and iSTEM, an employee resource group, have made significant impacts internally and externally. Together, they support STEM education and programming across Children's Hospital of Philadelphia and beyond.

"When we all have a voice in STEM, there are no limits to what we can achieve," said Paulette McRae, PhD, assistant director, Specialty Programs and Diversity.

ATOP's backing of trainee populations within the Research Institute spans the educational spectrum including high school, undergraduate, and graduate students; and postdoctoral and physician fellows. CHOP-RISES, CRISSP, Discovery Day, and Young Men and Women in Charge Job Shadowing programs, are just a few of many STEM-focused programs administered through ATOP focused on our trainee populations and community engagement.

iSTEM seeks to promote breakthroughs in child health by improving the cultural competency of the STEM professional community at CHOP, by creating avenues for our patients and families to be exposed to STEM, and by providing educational opportunities to underrepresented youth in our community. iSTEM volunteers serve CHOP employees and the future scientific pipeline by addressing gaps and disparities in the biomedical science, technology, engineering, and math workforce. This group also partners with the Office of Diversity and Inclusion and the Office of Immigration and Visa Services.

"ATOP and iSTEM are fully committed to enhancing diversity and supporting inclusion for our employees, trainees, patients, families, and community members," McRae said. "Generating excitement and engagement in STEM areas lays the foundation for building a representative STEM workforce."

INNOVATION DRIVES SIX NEW FRONTIER PROGRAMS

The addition of six new centers as Frontier Programs made 2019 a banner year for Children's Hospital of Philadelphia. Frontier Programs are a trailblazing group of initiatives conducting visionary research that translates to cutting-edge clinical care. They offer answers often not available anywhere else in the world.

Meet the six new Frontier Programs:

Advancement of Hyperinsulinism Care and Research: Primary investigators Diva DeLeón-Crutchlow, MD, and N. Scott Adzick, MD, are building on CHOP's status and experience as the world's leading hyperinsulinism center. This program seeks to further innovate by using personalized medicine to treat patients with the condition in which insulin regulation fails, resulting in dangerously low blood sugar levels that can damage the brain.

Biomedical Optical Devices to Monitor Cerebral Health: With Daniel Licht, MD; Todd Kilbaugh, MD; and Wesley Baker, PhD; at the helm, this frontier program is developing and testing a first-of-its-kind optical device that could revolutionize cardiac resuscitation.

Complex Vascular Anomalies Program: Primary investigators Jean Belasco, MD, and Hakon Hakonarson, MD, PhD, are establishing a national leading center to care for complex vascular anomalies. They are creating an expert, multidisciplinary team to provide evidence-based care for patients with complex vascular anomalies and researching the genetic basis for these cases to help inform new therapeutic approaches.

Comprehensive Center for the Cure of Sickle Cell Disease and Other Red Blood Cell Disorders (CuRED): Scientific director, Stefano Rivella, PhD; clinical director, Janet Kwiatkowski, MD; and the rest of the CuRED team will be advancing CHOP's position as a global leader in cell and gene therapies. The program will develop and deliver novel gene therapies and stem cell transplants to patients with red blood cell disorders in a family-centered clinic.

Congenital Diaphragmatic Hernia (CDH): Lead investigators Holly Hedrick, MD, and Emily Partridge, MD, PhD, are leveraging CHOP's standing as the largest CDH treatment center in the country. This program aims to become the international hub for the care of CDH and to eliminate morbidity and mortality through new research and the development of novel devices.

Epilepsy NeuroGenetics Initiative (ENGIN): Under the leadership of Ethan Goldberg, MD, PhD; Ingo Helbig, MD; Dennis Dlugos, MD; Eric Marsh, MD; Benjamin Kennedy, MD; and Sudha Kessler, MD; this program seeks to diagnose, treat, and cure epilepsy by expanding genetic testing to all children with epilepsy. Ultimately, the program aims to optimize medical and surgical care and drive development of precision therapies.

CHOP champions these programs and ensures they receive critical support to accelerate their progress. By investing in Frontier Programs that bring the best minds to the most challenging conditions, CHOP is once again redefining what's possible.

LEARNING HEALTH SYSTEM TRAINING FOR JUNIOR FACULTY MADE POSSIBLE WITH AHRQ GRANT

With a five-year grant from the Agency for Healthcare Research and Quality (ARHQ) and the Patient-Centered Outcomes Research Institute, Christopher Forrest, MD, PhD, pediatrician and member of the Department of Biomedical and Health Informatics at Children's Hospital of Philadelphia, is enriching and expanding the efforts of PEDSnet, a multi-institute, national consortium of which he is principal investigator.

"This faculty development award allows us to develop the next generation of researchers who will advance our knowledge on the best ways to deliver healthcare to children and youth," Dr. Forrest said.

By harnessing the learning health system (LHS) framework, PEDSnet uses collaboration, big data, and patient-centered outcomes research to improve the health and quality of care for children. Across its eight founding institutions, PEDSnet has created a 10-year, analysis-ready database for more than 6.2 million children. As one of 11 recipients of the $40 million award, CHOP, along with the other founding PEDSnet collaborating institutions, is using the funds to support faculty development.

The PEDSnet Scholars career development program, under the guidance of Dr. Forrest, prepares promising junior faculty to conduct LHS research that will improve both care delivery and outcomes for children. It builds upon prior efforts of a multidisciplinary faculty with decades of experience in research mentorship as well as the resources of the eight nationally renowned founding pediatric academic medical centers. The first batch of junior faculty scholars began training in January.

These scholars will use new methods that leverage modern data systems and test interventions in pragmatic child/family-centered outcomes research studies, embedded in diverse delivery systems and communities. Their work will provide the evidence base for shared clinical decisions and effective delivery system interventions that will bring us closer to the goal of improved health for individual children and populations.

FIRST-OF-ITS-KIND BIOENGINEERING LABORATORY

Research-scientist Ricardo Gottardi, PhD, joined Children's Hospital of Philadelphia in January to lead the new Bioengineering and Biomaterials Laboratory (Bio^2 Lab) dedicated to pediatric laryngology.

"I'm excited to be part of CHOP's mission that drives the work in the Bio^2 Lab to engineer solutions for airway disorders so that discoveries in the lab reach patients and make a difference in children's lives," said Dr. Gottardi, assistant professor of Pediatrics at the Perelman School of Medicine in the University of Pennsylvania.

His multidisciplinary team includes talented researchers from materials science, bioengineering, microbiology, genomics, and laryngology. Collaborating on clinical and research efforts, they offer engineering solutions for treatments of airway disorders.

Bio^2 Lab, the first-of-its-kind, is part of the Center for Pediatric Airway Disorders, a Frontier Program and one of the few centers in the country specializing in tracheal reconstruction, recurrent laryngeal nerve reinnervation, and a variety of other specialized airway procedures.

The lab takes a multiscale, multipronged approach to find optimal ways to regenerate organs, repair tissue, and prevent disease. While collaborating on tissue engineering and controlled drug delivery across CHOP, Bio^2 Lab is especially focused on novel drug delivery approaches to the upper airway, biomaterials for laryngotracheal cartilage engineering, and approaches to prevent and repair damage to the vocal folds.

THE GROWING RANKS OF NURSE RESEARCHERS INTEGRAL PART OF RESEARCH INSTITUTE

The Research Institute is well on the way of growing its ranks of nurse scientists. In step with Children's Hospital of Philadelphia's vision of leading a new era of pediatric research and innovation where we can all work together to solve the most challenging problems in child health, the Institute has created opportunities for researchers to situate their research within interprofessional teams, including nurse scientists.

"The increasing numbers of clinically based nurse researchers stem from our desire to provide nursing care that is second to none based on best available evidence," said Martha Curley, RN, PhD, FAAN, who holds the Ruth M. Colket Endowed Chair in Pediatric Nursing at CHOP, and is a professor at the University of Pennsylvania School of Nursing.

Through a new Colket Lecture Series, stellar nurse scientists who have impacted pediatric care are being showcased. This enables the Institute to recruit and encourage the best new nurse scientists to launch their programs of research at CHOP.

"Nursing science supports our disciplinary perspective in keeping people healthy, in avoiding iatrogenesis, in creating healing environments, and in helping the most vulnerable to feel well-cared-for," Dr. Curley said.

Next year, 2020, marks Florence Nightingale's 200th birthday — our first nursing scientist who said: "The purpose of nursing is to put the patient in the best condition for nature to act," Dr. Curley noted.

STREAMLINING OPERATIONS WITH NEW RESEARCH ADMINISTRATION OFFICES

A restructuring of the Research Administration Offices occurred in 2019 with Michelle A. Lewis, Vice President, Research Administration and Operations, appointing visionary leaders to oversee several areas of the Research Institute: Pre-Award Research Administration, Post-Award Research Administration and Research Portfolio Management, Program Management, and Research Business Operations.

The goal of the reorganization is to ensure Research Administration is best serving the needs of Children's Hospital of Philadelphia researchers by increasing efficiencies, streamlining operations, and ensuring objectives align with the Institute's strategic goals.

Brent Bell, CRA, Director, Pre-Award Research Administration: This office provides principal investigators and the CHOP research community with key resources to plan, develop, and prepare grant proposals, subawards, and other internally funded projects for successful implementation.

Liza Craig, MS, CRA, Director, Post-Award Research Administration and Research Portfolio Management: This area provides principal investigators and the CHOP research community with key resources to prepare budgets for new and existing research proposals, manage complex multi-million dollar research portfolios comprised of internally and externally funded research projects, and ensures all financial requirements are compliant with sponsor and institutional guidelines.

Anne Geary, Senior Program Manager, Program Management Office: This unit provides an approach to identify, prioritize, and successfully execute program and project initiatives that align with Research Administration's strategic goals.

Robert DeNight, Assistant Director, Research Business Operations: This Research Administration office will lead, manage, and support the optimization of key operational business activities required to effectively administer and manage internally and externally sponsored research at CHOP.

The leaders in these four areas are partnering closely with Lewis and Institute senior leadership to ensure grant support services and all process improvement initiatives result in optimizing business operations.

"Together, we will ensure a partnership between faculty and administration is achieved and the objectives outlined in the strategic plan are fulfilled," Lewis said. "Ultimately, all staff are committed to ensuring that our work is a source of optimism and ease for CHOP's current and future researchers."

INNOVATION

COLLABORATION ›

IMPACT OF INNOVATION

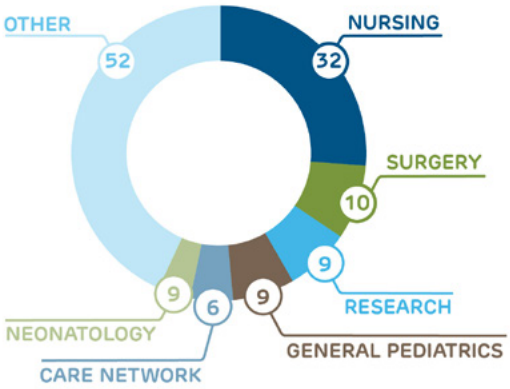
OFFICE OF TECHNOLOGY TRANSFER	FY 2018	FY 2019
Licensing Deals	20	32
Inter-Institutional Agreements	7	7
Other Agreements	6	44
Invention Disclosures Received from Inventors	101	83
U.S. Patent Applications Filed	61	70
U.S. Patents Awarded to CHOP	16	18
International Patent Applications Filed (PCT and Foreign)	136	92
International Patents Awarded to CHOP	33	132

OFFICE OF COLLABORATIVE AND CORPORATE RESEARCH CONTRACTS	FY 2018	FY 2019	6-YEAR CHANGE
Material Transfer Agreements (MTAs)	445	604	+63.2%
Confidential Disclosure Agreements (CDAs)	297	411	+43.7%
Data Use & Data Transfer Agreements (DUAs & DTAs)	250	372	+167.6%
Consulting Agreements	154	254	+76.4%
Other Agreements	438	572	+20.9%
TOTAL AGREEMENTS FULLY EXECUTED	**1584**	**2213**	**+56.7%**

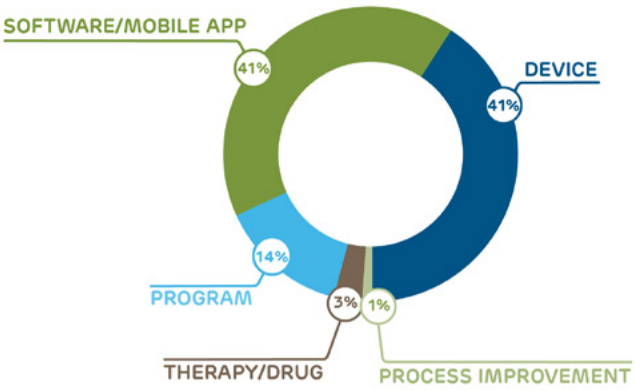
FY19: SPRINT PROGRAM MOVES TO TWICE A YEAR

THE NEW BI-ANNUAL SPRINT PROGRAM DRIVES SIGNIFICANT INCREASE IN INNOVATION DEVELOPMENT

APPLICATIONS PER DEPARTMENT



IDEA BREAKDOWN

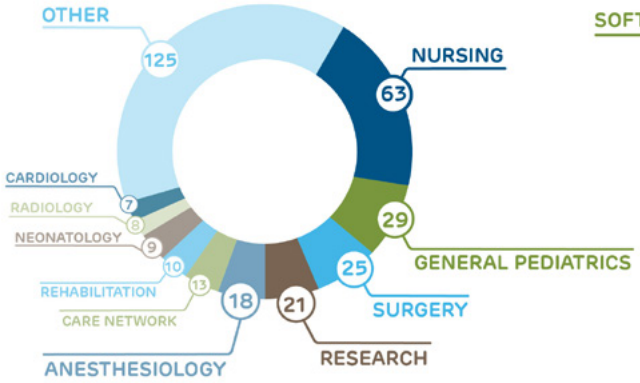


OEI-SPRINT HAS BROAD AND DIVERSE IMPACT ACROSS CHOP

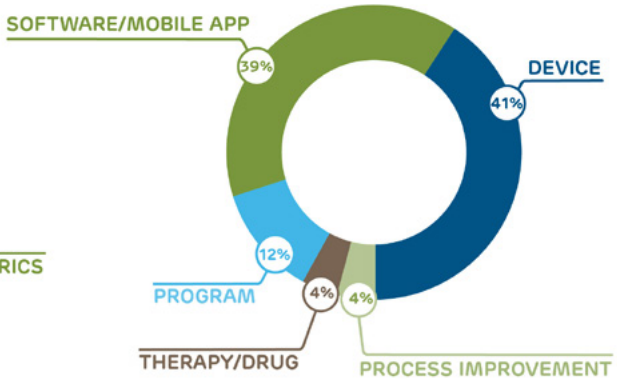
NURSING LEADS, BUT OVER 67 DEPARTMENTS HAVE PARTICIPATED IN THE SPRINT PROGRAM

OEI SPRINT PROGRAM: 2015-PRESENT

APPLICATIONS PER DEPARTMENT



IDEA BREAKDOWN



AUTOMATED DATA TOOL IMPROVES EARLY ALERTS FOR SEPSIS

A precise and early diagnosis of sepsis is critical in premature infants, whose rates of sepsis are 200 times higher than full-term infants, to prompt rapid intervention and prevent future long-term problems such as lung disease or disability. Despite this urgency, ambiguous clinical signs and inaccuracies in screening tests can make a quick diagnosis difficult.

Researchers at Children's Hospital of Philadelphia developed a machine-learning model that recognizes sepsis in hospitalized infants in the Neonatal Intensive Care Unit (NICU) hours before clinicians spot the life-threatening condition. In the study published in the journal *PLOS One*, physician-scientists and data researchers evaluated how well eight machine-learning models predicted sepsis by analyzing patient data in the electronic health record.

Because the data was retrospective, the team could compare each model's predictions to whether or not an infant indeed developed sepsis. Six of the eight models accurately predicted sepsis up to four hours before clinical recognition of the condition. The findings are a step toward developing a real-time clinical tool that physicians can utilize in hospitals, according to first author Aaron J. Masino, PhD, an assistant professor in the Department of Anesthesiology and Critical Care and a member of the Department of Biomedical and Health Informatics at CHOP.

"Because early detection and rapid intervention are essential in cases of sepsis, machine-learning tools like this offer the potential to improve clinical outcomes in these infants," Dr. Masino said. "Follow-up clinical studies will allow researchers to evaluate how well such systems perform in a hospital setting."

DIGITAL INNOVATION HELPS QUANTIFY AUTISM SPECTRUM DISORDER ASSESSMENTS

With the help of a new invention from the Center for Autism Research (CAR), a simple three-minute chat can provide a powerful window of insight that can augment psychological assessment and improve doctors' ability to measure and predict the effectiveness of interventions for complex conditions such as autism spectrum disorder (ASD). A team of scientists at the CAR Technology and Innovation Lab at Children's Hospital of Philadelphia invented and tested the unique and fully automated method to capture, digitize, and analyze social communication between two individuals engaged in a conversation.

The portable biometric sensor system, nicknamed the Sensor Tree, is only about the size of a coffee cup, but this powerful device uses markerless motion capture technology to record and digitize all outward expressions of human behavior, including tone of voice, facial expression, motion and gestures. When combined with heart rate, temperature, and brain waves, these precision measurements can paint a highly detailed digital portrait of each person's behavior and biology — called a "digital phenotype."

Because social synchrony is diminished in ASD, clinician-researchers have much to gain in objectively assessing ASD by tracking behaviors like atypical eye contact or reduced nonverbal communication with exquisite precision. As machine-learning algorithms turn these granular behaviors into time-synced and objective data, the digitized method allows clinicians to move beyond a diagnostic process that, thus far, has mainly relied on human judgments.

"The Sensor Tree lets us track the coordinated facial and body movements between social partners and statistically quantifies the amount of alignment between the individuals' movements with one another over time," said Robert Schultz, PhD, director of CAR. "None of our current evaluations does that."

In preliminary studies, the Sensor Tree detected with 90 percent accuracy whether a person has autism by analyzing the degree of coordination in people's facial expressions during a three-minute conversation.

The Sensor Tree is currently being used with adults and children as young as 6 years old, and the CAR team recently received funding from the National Institutes of Health to test the device in trials with infants as an early screening tool for autism and developmental delays.

RESEARCHERS USE CUTTING-EDGE IMAGING TO BETTER UNDERSTAND BABY BRAIN DEVELOPMENT

The third trimester of life is a time of abundance and awe, as soon-to-be newborns establish complex neuronal connections in the cerebral cortex, laying down the wiring that will enable them to think, remember, and navigate the outside world. In 2019, scientists at Children's Hospital of Philadelphia and collaborating institutions developed a novel, noninvasive method for peeking into this key window of brain development.

With immense detail, 20-minute magnetic resonance imaging (MRI) scans allow researchers to not just map how the microstructure of brain regions develops in early infancy, but identify imaging markers that will help to better understand typical and atypical brain development. The diffusion MRI scans work by detecting clues to anatomical structure based on the diffusion properties of water molecules in brain tissue, since the presence of neurons, dendrites, and other structures in the cerebral cortex are barriers to the water molecules' movement.

"We can use quick, noninvasive brain scans as a cutting-edge way to measure microstructural maturation at critical periods of development, and then analyze those measurements in longitudinal studies that could yield new insights into the cellular processes that may go awry in neurodevelopment," said Hao Huang, PhD, a principal investigator of Radiology Research at CHOP. "This could lead to novel screening methods that would facilitate age-appropriate interventions as soon as possible."

Previous methods for studying the formation of neural circuits relied on time-consuming and less-detailed histological methods. Through the new method, researchers can identify the nuances of microstructural differences that may be early biomarkers for conditions such as over-connectivity, which emerges later and may be associated with autism spectrum disorder.

Publishing their findings in the *Proceedings of the National Academy of Sciences*, the team of researchers studied 89 preterm infants, mapping out the changes across the entire cerebral cortex. They used two types of measurements – mean kurtosis (MK) to measure microstructural complexity, and fractional anisotropy (FA) to quantify microstructural organization. Using data-driven clustering analysis of the MK and FA measurements, the researchers then identified patterns of cortical differentiation during typical brain development.

With further research underway, Dr. Huang and his colleagues plan to compile a 4-D atlas of the infant brain, which illustrates three spatial dimensions plus changes over time. Ultimately, they would like to produce a Brain Chart, or a baseline standard that outlines typical measurements of brain development much like a pediatrician's growth chart for standard measures of height and weight.

SCIENTISTS DEVELOP SOFTWARE TO STREAMLINE AND SUPPORT GENETIC DIAGNOSES

Thanks to a growing mass of genomic data, physicians and researchers discover and diagnose thousands of rare disease cases in children every day. By connecting genetic mutations in patients to hereditary conditions, they help patients and families receive answers to symptoms once deemed puzzling.

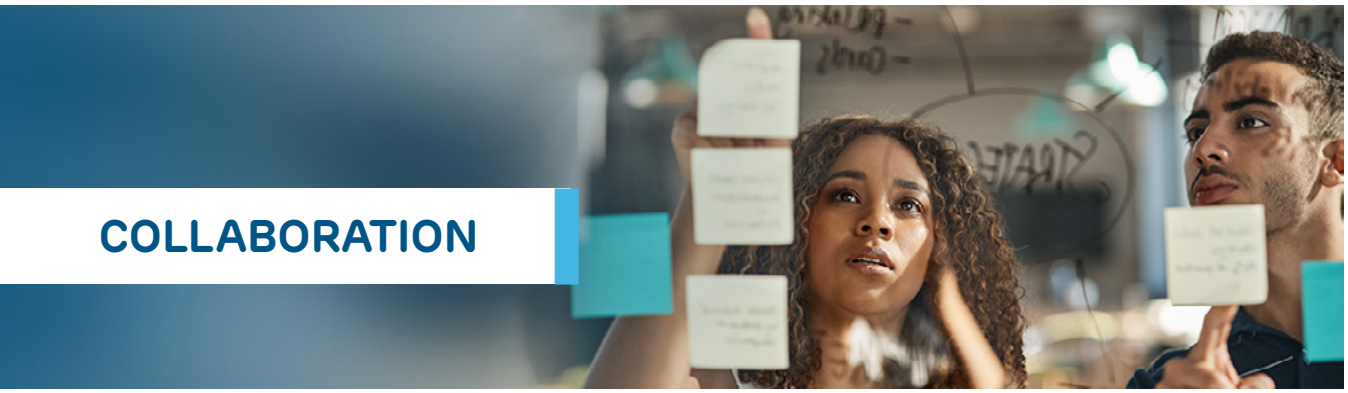
In 2019, a Children's Hospital of Philadelphia data scientist developed a novel tool to make this process of discovery more efficient. The automated software, named EHR-Phenolyzer after its use of electronic health records (EHR), draws on information from a patient's medical history to match potential phenotypes with gene mutations in the software's system.

"This tool is especially relevant to a large pediatric hospital like ours, which sees many children with undiagnosed hereditary diseases," said Kai Wang, PhD, a data scientist in the Department of Pathology and Department of Biomedical and Health Informatics who developed EHR-Phenolyzer alongside colleagues at Columbia University. "Our goal is to reduce the duration, uncertainty, and costs of the 'diagnostic odyssey' experienced by many affected children and their families, and to help guide them more quickly to the most appropriate clinical care."

Dr. Wang first developed the tool's predecessor, Phenolyzer, while at the University of Southern California. But while Phenolyzer requires clinical experts to manually input data about phenotypes, or the observable physical manifestations of a disease, EHR-Phenolyzer automates the process.

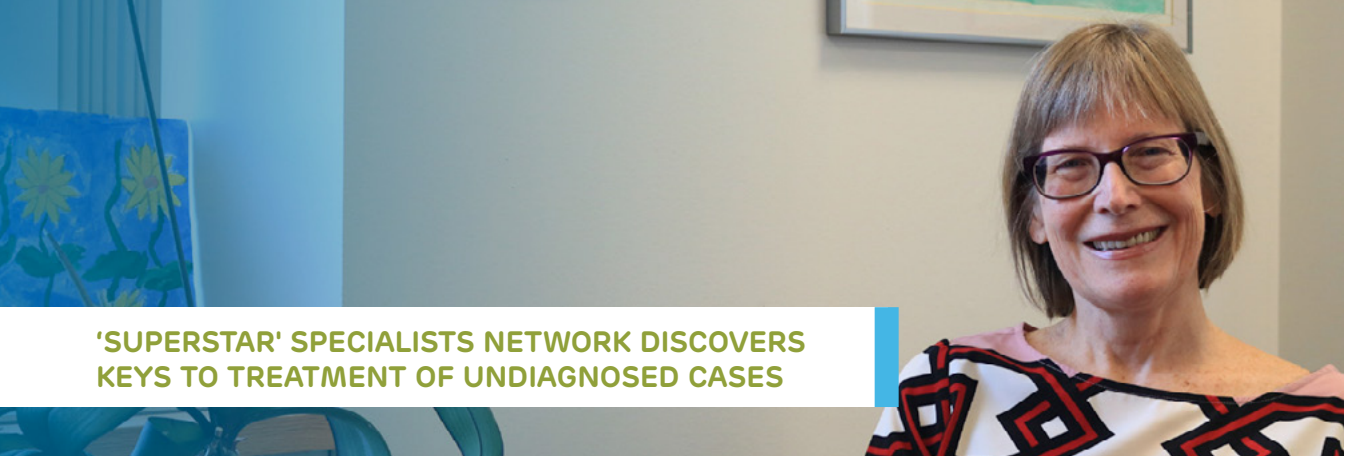
First, the software extracts clinically relevant information from the text of a narrative patient history, such as that written by a genetic counselor or clinical geneticist. The program then translates the extracted descriptors into a common language called Human Phenotype Ontology, and then matches those terms to candidate causal genes. The software prioritizes the genes by how strongly they correlate with a patient's phenotype.

In a paper published in the *American Journal of Human Genetics*, Dr. Wang and his team assessed the EHR-Phenolyzer's performance in four separate cohorts of adults and children with suspected or diagnosed genetic diseases across two centers. In more than half of the individuals, the disease-causing mutations appeared in EHR-Phenolyzer's top 100 candidate genes; in some cases, the top 10.



COLLABORATION

HONORS ›



'SUPERSTAR' SPECIALISTS NETWORK DISCOVERS KEYS TO TREATMENT OF UNDIAGNOSED CASES

Families struggling to find a diagnosis can turn to a team of super sleuths from Children's Hospital of Philadelphia and the Hospital of the University of Pennsylvania who are ready to unravel these perplexing diseases. A core group of expert clinician-scientists will leverage their collective brainpower to tackle these tough cases and consult with ad hoc members — "superstars" of their specialties — when needed to shed light on each patient's condition from multidisciplinary perspectives.

The two institutions received $2.5 million in research grants from the National Institutes of Health as a newly designated Undiagnosed Diseases Network (UDN) site. Kathleen Sullivan, MD, PhD, chief of the Division of Allergy Immunology at CHOP and Reed Pyeritz, MD, PhD, the William Smilow Professor of Medicine and professor of Genetics at Penn, are co-directors for the joint CHOP/Penn site.

The UDN research study was developed to improve and accelerate the diagnosis of conditions that are rarely seen, have not previously been described, or are unrecognized forms of more common diseases. Since its launch in 2015, the UDN has diagnosed more than 200 cases that had long confounded the medical community, yet many more remain unexplained.

Arriving at an accurate diagnosis is like finding a key to that could unlock treatment possibilities; however, the National Human Genome Institute reports that about 95 percent of rare disorders do not even have one treatment approved by the Food and Drug Administration. If an effective treatment doesn't already exist, CHOP Research Institute has an ideal bench-to-bedside infrastructure to expedite the UDN team's ability to successfully engage with basic science researchers who are eager to participate in projects that eventually could change children's lives.

"It's humbling and exciting that we're at the forefront of learning about different types of diseases and what the diseases look like in different patients," Dr. Sullivan said. "I hope we can help in some way all of the families who come to us through the network and are desperate for the right answer."

CANCER MOONSHOT GRANT CATALYZES RESEARCH FOR IMMUNOTHERAPY IN CHILDHOOD CANCER

New grants awarded by the National Cancer Institute Moonshot Initiative through a multi-institutional, collaborative group — the Pediatric Immunotherapy Discovery and Development Network (PI-DDN) — aim to fundamentally change our understanding of how to harness the power of the immune system to treat childhood cancers.

"Cancer is sinister and, generally, when you think you have a leg up on cancer, it figures out a way to outsmart you," said John M. Maris, MD, pediatric oncologist and Giulio D'Angio Chair in Neuroblastoma Research at Children's Hospital of Philadelphia, whose research team received funding to lead a pediatric immuno-oncology Center for Discovery and Development of Optimal Immunotherapeutic Strategies for Childhood Cancers. "We are trying to develop breakthrough therapies to fundamentally change the paradigm of how we treat childhood cancers."

The Center is a collaboration led out of CHOP with Stanford University, the University of Wisconsin, Texas Children's Hospital, and the British Columbia Cancer Agency in Vancouver.

A key part of this success, Dr. Maris said, will be to discover immunotherapeutic strategies for childhood cancer that not only improve cure rates, but also are less toxic than current therapies.

The Center includes three highly integrated multicomponent projects that will occur in parallel and inform each other.

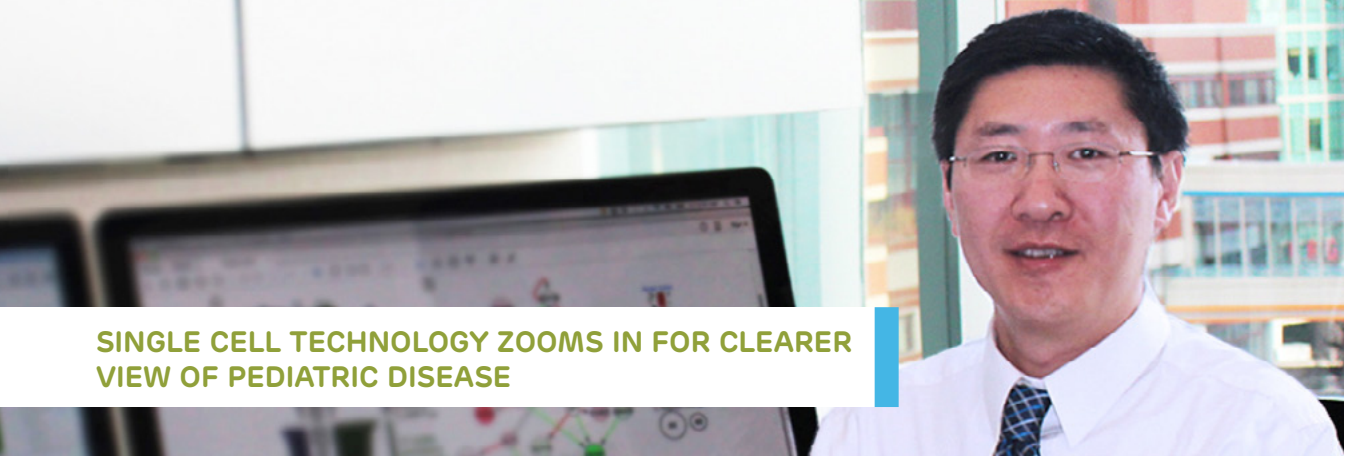
In project one by the Discovery and Development of Optimal Immunotherapeutic Strategies for Childhood Cancers team, the researchers aim to discover lineage-specific cell surface molecules that have project-defined optimal attributes for synthetic immunotherapeutic-based targeting. They will use their findings to create and credential new therapeutics based upon preclinical efficacy in high-risk childhood cancer models.

The second project will focus on major mechanisms of immunotherapy resistance by developing approaches to circumvent the fundamental issues of intra- and inter-tumoral heterogeneity and T cell dysfunction due to both intrinsic and extrinsic factors.

Project three will probe the major difference between pediatric and many adult malignancies: Pediatric cancers typically elicit little adaptive immunity. Scientists' goal will be to develop approaches to enhance adaptive immune responses against pediatric cancer-specific antigenic targets.

With the underpinnings of state-of-the-art technology and interdisciplinary teamwork, the Center is poised to extend the early accomplishments of CD19-directed immunotherapies in a limited number of highly refractory cases of pediatric leukemia and neuroblastoma. They will use these insights to improve scientists' understanding of the fundamental mechanisms in other high-risk or difficult-to-treat childhood cancer phenotypes, including how these malignancies evolve to evade the immune system and resist modern therapies. Beyond the stated goals of the grant, researchers are working to identify opportunities for collaboration.

"The idea is for this to be greater than individual projects, that there will be a network of expertise with the mark of the Moonshot behind it along with some significant resources to help us with our research goals," Dr. Maris said.



SINGLE CELL TECHNOLOGY ZOOMS IN FOR CLEARER VIEW OF PEDIATRIC DISEASE

Two cutting-edge, cooperative biomedical research projects — the Center for Pediatric Tumor Cell Atlas and the Pediatric Cell Atlas (PCA) — are exploring the potential of single cell technology to zero in on pathogenesis of cancer and other diseases.

Novel technologies have become available in recent years that combine next-generation sequencing and massively parallel processing, such as RNA sequencing, of single cells. These single cell studies, said Deanne Taylor, PhD, director of Bioinformatics in the Department of Biomedical and Health Informatics at Children's Hospital of Philadelphia and a research assistant professor of Pediatrics in the Perelman School of Medicine at the University of Pennsylvania, open up a high-definition view of cell physiology and functioning that will expand scientific knowledge of health and disease — particularly during the dynamic childhood period, when growth and development are underway.

The PCA will compile age-matched trajectories of tissue and organ development in healthy children, referencing key data patterns in cell differentiation and cell signaling. Those trajectories will offer a standard for researchers to better understand when and how childhood illnesses diverge from those patterns, because of genetic influences, environmental factors, or both. Enabled by dramatic advances in single-cell technology, the PCA will offer an unprecedented window into the unique biology of children by benchmarking healthy and abnormal tissues at the molecular level.

"Ultimately, researchers would leverage knowledge from single-cell data into a deeper understanding of organ development and function, to better inform precision treatments to advance children's health," said Dr. Taylor, who is co-author of an open-access perspective article on the PCA in the journal Developmental Cell.

The PCA is a cornerstone of the Human Cell Atlas (HCA), a global effort into understanding human single-cell biology. As part of the broader international consortium represented in the HCA, the PCA will share data among members and with other researchers worldwide. It will also store data in the HCA's repository with associated biobanking and data repositories in different centers available to biological researchers. As the PCA moves forward, it will develop its overall organization, protocols, data systems, and multiple projects, including pilot studies of specific organs and diseases.

In addition, the PCA will compare atlas data from healthy tissues with data from diseased tissue, such as those generated by the Center for Pediatric Tumor Atlas. Awarded a five-year research grant totaling $12.5 million, Kai Tan, PhD, an investigator in the Center for Childhood Cancer Research (CCCR) at CHOP, and co-principal investigator Stephen Hunger, MD, chief of the Division of Oncology and director of the CCCR, created the Center as part of a 10-center national consortium.

Drs. Tan and Hunger will work closely with other key investigators in the CCCR at CHOP including Kristina Cole, MD, PhD; Kathrin Bernt, MD; David Barrett, MD, PhD; John Maris, MD; Kristopher Bosse, MD; and Sharon Diskin, PhD. Additional off-site key investigators are Hao Wu, PhD, assistant professor of genetics, and Nancy Zhang, associate professor of statistics, both at University of Pennsylvania, and Kun Zhang, PhD, professor of bioengineering at University of California at San Diego.

Their project is under the umbrella of the larger Moonshot Human Tumor Atlas Network (HTAN) that aims to generate atlases of a diverse cancer patient population and high-risk cancers. The CHOP team is the only pediatric cancer group recipient on account of its world-class pediatric cancer researchers, large volume of patients, and unique ability to acquire biosamples of pediatric cancer.

HTAN will generate a large volume of genomic data, imaging data, and clinical data with a three-pronged goal: an easily searchable, publicly available database; research community access to the computational tools utilized in the project; and access to biospecimens including tissue sections, viably frozen specimens, and patient-derived xenograft models.

“I’m very excited about the kind of promise that can deliver, and that excitement is shared by all the researchers,” Dr. Tan said. “Single cell technologies is revolutionizing biomedical research, not only cancer but other diseases as well.”

BIG DATA COLLABORATION UNDERWAY TO UNCOVER PATHWAYS BETWEEN CANCER AND BIRTH DEFECTS

As a single-cell zygote proliferates into a 37 trillion-cell being, something happens in the course of its development — a dysfunction, a deviance, a DNA-driven decision — that underpins not just the development of life-changing birth defects, but a potential vulnerability to childhood cancer as well.

Adam Resnick, PhD, co-founder and co-director of the Center for Data-Driven Discovery and Biomedicine (D3b) at Children's Hospital of Philadelphia, thinks that to unravel the inextricable link between childhood cancer and other rare conditions, we must visualize pediatric cancer as a process. A unique and pioneering endeavor launched in September 2018, fueled by technology and funded by the National Institutes of Health (NIH) Common Fund, is providing investigators with a powerful tool for piecing together the science behind Dr. Resnick's vision: a comprehensive discovery platform for data — and volumes of it.

The Gabriella Miller Kids First Data Resource Center (Kids First DRC) is a multi-institute collaboration that aims to advance our knowledge of cancer and birth defects through large-scale sharing of genomic, phenotypic, and clinical information. Investigators, clinicians, data scientists, and patients are working together to continuously improve the Kids First DRC's chief outward-facing tool: a centralized, cloud-based database and discovery portal containing well-curated clinical and genetic sequence data.

The data contained within the Kids First DRC is being generated from tens of thousands of sequenced biosamples to determine if mutations or genetic changes exist for each disease type. Users worldwide can access the genetic disease data at one central location, share their findings, or collaborate in real time.

The Kids First DRC is part of the broader Gabriella Miller Kids First Pediatric Research Program, launched in 2015 by the NIH Common Fund to help researchers better understand the role of genetics in childhood cancer and structural birth defects, and the genetic pathways underlying these conditions. The Kids First DRC combines efforts between CHOP, CHU Sainte-Justine Research Center, the Ontario Institute for Cancer Research, the University of Chicago, Children's National Health System, Oregon Health and Science University, and Seven Bridges.

In addition, the Kids First DRC supports collaborations within CHOP, including the partnership between the Craniofacial Program and the D3b Center. Although statistics show that children with a cleft palate or birth defect of the central nervous system are two to four times more likely to have a cancer, scientists have yet to understand the potential genetic pathways and links underlying both conditions.

"By learning more about brain tumors, we may help ourselves to learn more about other congenital anomalies," said Jesse Taylor, MD, attending surgeon in the Division of Plastic and Reconstructive Surgery at CHOP and a co-investigator of the Kids First DRC. "And by learning about the congenital anomalies like craniosynostosis, we may learn more about how to treat brain tumors."

FIRST-OF-ITS-KIND DATA RELEASE ENABLES TARGETED TRIALS FOR PEDIATRIC CANCER

The Pediatric Preclinical Testing Consortium (PPTC) announced their new pediatric cancer model datasets are now available to any qualified academic petitioner, putting information about both patients' genetic data and their response to various drugs at scientists' fingertips. This is the first time that an academic consortium has teamed up to generate data to guide drug development.

With the release of more than 244 genomic tumor models spanning 27 different types of childhood cancer, researchers may now have the ability to skip lengthy preclinical work in their development of novel treatments. The traditional process was to test a drug, learn that some tumors responded and some didn't, and then researchers would need to go through the exercise of trying to figure out why. Finding that "why" could take months or even years.

"Now, the explanation may be right in front of us because it was either the exact hypothesis we were testing there that had the mutation or not, or even if our hypothesis was wrong, we have this enormous amount of data at our disposal to ask: Why did some respond, and why did some not?" said John M. Maris, MD, oncologist at Children's Hospital of Philadelphia Cancer Center and principal investigator of the PPTC's CHOP site. "I think that we've streamlined significantly."

With funding from Alex's Lemonade Stand Foundation, the project will enable more precise clinical trials by not only allowing scientists to draw on previous analyses (so as to identify the most impactful drugs to take to clinical trials and avoid repeating failed experiments), but also by providing researchers with a wealth of data on genetic targets rather than broad disease types.

"This really is about moving toward treating pediatric cancer not as diseases, but as molecular entities," Dr. Maris said. "Five patients who have neuroblastoma and their tumors look identical under the microscope, may actually be genetically very distinct."

The PPTC is a National Cancer Institute-funded academic collaboration between CHOP, Greehey Children's Cancer Research Institute in San Antonio, Ann & Robert H. Lurie Children's Hospital of Chicago, MD Anderson Cancer Center in Houston, the Children's Cancer Institute in Sydney, and the Research Triangle International coordinating center in Research Triangle Park, North Carolina.

As the only release of childhood cancer data where multiple types of different cancers are all analyzed together, the PPTC offers a unique resource of genetic data as well as response data to different drugs.

"Making that available broadly will allow other researchers to either not repeat experiments that are doomed to fail or extend experiments that look very interesting," Dr. Maris said.

SYNERGISTIC PARTNERSHIP EXAMINES INTERPLAY BETWEEN NUTRITION AND MEDICINE

The Penn Center for Nutritional Science and Medicine (PenNSAM) brings researchers from the University of Pennsylvania and Children's Hospital of Philadelphia together to investigate nutritional biology in the prevention and treatment of disease.

Under the direction of Gary Wu, MD, academic investigator in childhood obesity research at CHOP and a member of the Division of Gastroenterology at Penn, PenNSAM will focus on integrating human clinical metadata, traditional dietary assessments, and standard nutritional biomarkers with data generated by high-throughput molecular profiling technologies and analyzed through advanced biostatistical and computational algorithms. These capabilities enable the PenNSAM team to employ a holistic approach using genomics, proteomics, and metabolomics, combined with immune profiling, to further understanding of the impact of nutrition on human health.

Drawing on the knowledge of Penn and CHOP experts in disciplines ranging from psychiatry, neuroscience, and medicine, to immunology, biochemistry, and bioinformatics, PenNSAM is a uniquely resourced center for the advanced study of human nutrition. This multidisciplinary approach also bridges the divide between human subject and wet bench research, enabling investigators to develop model systems designed to more precisely identify and characterize molecular mechanisms that drive the human response to diet and nutrition.

Advanced analytic technologies available through the support of the Human Subject Research Core, Biobanking Core, Computation and Biostatistics Core, Quantitative Proteomics Resource Core (QPRC), PennCHOP Microbiome Program, and the Human Immunology Core at Penn allow a systems approach to human nutritional biology.

Projects currently under development at PenNSAM include studies focused on the impact of diet on brain function through the consumption of a ketogenic diet, the characterization of molecular markers that distinguish a healthy Mediterranean diet from an unhealthy "convenience diet," and a study focused pancreatic insufficiency.

"The close collaborative relationship between CHOP and Penn will facilitate the implementation of projects such as the ketogenic diet study, where studies will be performed at both institutions," Dr. Wu noted.

PenNSAM researchers envision their holistic approach will lead to reducing the risk for disease by identifying new biomarkers that predict human responses to diet and nutrition, optimizing currently available nutritional interventions for hospitalized patients, and developing novel diet-based interventions to treat disease.

HONORS

VISIONARIES ›

AND THE SERVICE AWARD GOES TO … FETAL IMAGING DIRECTOR, BEVERLY G. COLEMAN, MD

The Society of Radiologists in Ultrasound (SRU) honored Children's Hospital of Philadelphia radiologist, Beverly G. Coleman, MD, for her outstanding service to the society and the field of radiology. Dr. Coleman received the 2018 Distinguished Service Award at the SRU annual meeting in San Diego. Radiologists Edward Oliver, MD, PhD, and Steven Horiim, MD; and Lori Howell, DNP, executive director of the Center for Fetal Diagnosis and Treatment, travelled from CHOP to attend the reception and dinner honoring Dr. Coleman.

"Ultrasound is my passion," Dr. Colelman enthused. "Throughout my career, I have tried to use this very unique imaging modality to serve patients and in so doing, I have had the pleasure and opportunity to serve many others."

SRU is the only medical society in North America representing radiologists in the field of ultrasound. The society promotes the advancement of the science, practice, and teaching of the ultrasound specialization in patient care.

Dr. Coleman is the director of Fetal Imaging at CHOP's Center for Fetal Diagnosis and Treatment, which provides highly specialized care to mothers carrying fetuses with known birth defects. The Center is recognized as an international leader in fetal diagnosis and care, and it is one of the few locations in the world that performs fetal surgery for life-threatening conditions. Dr. Coleman holds CHOP's Endowed Chair in Fetal Imaging. She is currently the ultrasound commission chair for the American College of Radiology and served as president of the SRU from 2003 to 2005.

BEVERLY DAVIDSON, PhD, ELECTED VP FOR AMERICAN SOCIETY OF GENE AND CELL THERAPY

Chief Scientific Strategy Officer Beverly Davidson, PhD, was elected vice president for the American Society of Gene and Cell Therapy (ASGCT) for a three year term — positioning her for the presidency in 2021.

"I'm excited to provide support to the ASGCT membership and the broader gene and cell therapy community," Dr. Davidson said, "and I'm looking forward to the continued advancement and implementation of these life changing medicines."

Dr. Davidson, a leading investigator in gene therapy, has been an active member in ASGCT, the nation's largest association of individuals in gene and cell therapy research, since its founding in 1995. ASGCT seeks to advance research, education, and clinical application in gene and cell therapies to treat disease. Its membership includes more than 2,500 scientists, physicians, and patient advocates.

Dr. Davidson is also the Director of the Raymond G. Perelman Center for Cellular and Molecular Therapeutics (CCMT), where, in 2018, she oversaw the opening of Children's Hospital of Philadelphia's new Clinical Vector Core facilities that produce clinical-grade viral vectors to deliver cell and gene therapy for difficult-to-treat diseases. She holds the Arthur V. Meigs Chair in Pediatrics and is a professor in the Department of Pathology and Laboratory Medicine at the Perelman School of Medicine at the University of Pennsylvania.

LONGTIME HIV/AIDS RESEARCHER STEVEN DOUGLAS, MD, GIVES PRESTIGIOUS LECTURE

Steven Douglas, MD, chief of the Immunology Section in the Division of Allergy-Immunology at Children's Hospital of Philadelphia, was recognized for his significant contributions in the field of pediatric HIV/AIDS with the 25th Herman and Gertrude Silver Lecture Award.

In his lecture entitled, "HIV/AIDS Virology and Immunology: Toward Durable Success," Dr. Douglas drew on his 50-year career in immunology to review major milestones in pediatric HIV/AIDS research and shared his optimism that paradigm shifts and new discoveries are ahead.

"We have made great strides over this period of 35 to 40 years," said Dr. Douglas, who also is a professor of Pediatrics in the Perelman School of Medicine at the University of Pennsylvania. "We know a great deal about the pathogenesis. We have a strong pharmacopeia of antiviral drugs. We have exciting ideas with new ones emerging. It's a remarkable story that I'm thrilled to have been a part of in my career and to have watched this evolve."

The Silvers established a fund for the award in 1990, in memory of their children who were treated at CHOP. The award has recognized physicians and researchers from leading academic institutions including the National Institutes of Health, the Centers for Disease Control and Prevention, Oxford University, and past recipients of The Nobel Prize.

Throughout the decades, Dr. Douglas' research has led to important advancements in the pediatric HIV/AIDS field. In the late 1970s, he established laboratory methods for investigating two types of immune cells —monocyte-macrophages and lymphocytes — which facilitated laboratory research around the world. He further discovered that an important neuropeptide plays a key role in the neurological manifestations of AIDS.

Dr. Douglas also lends his talents to the Philadelphia International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Unit, which includes a clinical research site at CHOP. The Douglas Lab is the central immunology laboratory for the IMPAACT Network.

LINDSEY GEORGE, MD, RECEIVED 2019 CLINICAL RESEARCH ACHIEVEMENT AWARD

Congratulations went out this year to Lindsey George, MD, hematologist at Children's Hospital of Philadelphia and assistant professor of Pediatrics in the Perelman School of Medicine at the University of Pennsylvania, a recipient of the 2019 Clinical Research Achievement Award from the Clinical Research Forum. Dr. George was recognized for her promising research of the first gene therapy clinical trial to report a phenotypic cure for hemophilia B patients.

Hemophilia B is a hereditary bleeding disorder caused by a lack of the blood clotting factor IX — without it, the blood cannot clot properly to control bleeding. Dr. George served as the lead investigator for the clinical trial, which involved a single intravenous administration of a bioengineered, gene therapy vector that then allows patients to produce their own clotting factor IX to safely and effectively stop bleeding in hemophilia B patients.

"The ultimate goal of gene therapy is to have a one-time, disease altering or curative treatment," Dr. George said. "We're thrilled that we've made significant progress toward that goal and are cautiously optimistic."

YOUNG INVESTIGATOR AWARD GOES TO ONCOLOGY RESEARCHER ALLISON BARZ LEAHY

The 2019 Conquer Cancer Foundation/Anna Braglia Endowed Young Investigator Award in Cancer Supportive Care was awarded to Allison Barz Leahy, MD, attending physician with the Cancer Center at Children's Hospital of Philadelphia.

As the foundation of the American Society of Clinical Oncology, Conquer Cancer funds research and education across every facet of cancer. The award is a one-year $50,000 grant supported by Helsinn, a Swiss pharmaceutical group focused on building quality cancer products. The award is given to a physician in the final years of training, to assist with the transition from a fellowship program to a faculty appointment promoting quality research in clinical oncology.

Dr. Leahy's current research focuses on the benefits and drawbacks of using patient-reported symptom monitoring for children with cancer in order to examine the impact of such monitoring on the quality of life, hospitalization rate, and illness severity in childhood cancer.

"I am greatly honored to receive the Anna Braglia Endowed Young Investigator Award in Cancer Supportive Care," Dr. Leahy said. "This award will provide invaluable resources for the investigation of the use of patient-reported symptom monitoring in pediatric oncology care. Determining how best to incorporate the child's voice into their medical care is essential — and we are hopeful that this work lay the necessary groundwork to enhance communication with the treating team, increase patient and family engagement in care, and ultimately lead to better clinical outcomes for children undergoing treatment for cancer."

BONE AND MINERAL RESEARCH SOCIETY PAYS TRIBUTE TO MICHAEL A. LEVINE, MD

Michael A. Levine, MD, received the 2018 Frederic C. Bartter Award honoring his work, spanning nearly four decades, to advance the understanding of inherited bone and mineral disorders. The award is given each year to an American Society of Bone and Mineral Research (ASBMR) member for his/her outstanding clinical investigation in disorders of bone and mineral metabolism.

"It is particularly gratifying to receive this award acknowledging the impact of my research from the ASBMR, which I consider my 'home' society," Dr. Levine said. "Given that I have focused on uncommon or orphan diseases over my career, I could not have pursued these studies without the support of the outstanding resources and talented colleagues of the CHOP-Penn scientific community."

A pediatric endocrinologist, Dr. Levine is the medical director of the Center for Bone Health at Children's Hospital of Philadelphia, and chief emeritus of CHOP's Division of Endocrinology and Diabetes. He holds the Lester Baker Endowed Chair in Pediatric Diabetes at CHOP.

Throughout his distinguished career, Dr. Levine achieved scientific breakthroughs by identifying the molecular basis of several inherited disorders of mineral metabolism, including the role of the GNAS gene and associated mutations in patients with pseudohypoparathyroidism and McCune Albright syndrome, and the role of the GCM2 gene as the basis of isolated hypoparathyroidism. His work has advanced the understanding of the parathyroid gland function.

Dr. Levine also studied the molecular pathogenesis of unusual metabolic bone disorders to provide insights into the basis of more common bone diseases. This research demystified the causes of various forms of rickets along with the revelation that genetic variation in some of these genes contributes to vitamin D insufficiency in North America and Europe.

LIFETIME ACHIEVEMENT AWARD CELEBRATES CAREER OF BARBARA SCHMIDT, MD

The Society for Pediatric Research awarded Barbara Schmidt, MD, a neonatologist recently retired from Children's Hospital of Philadelphia's Division of Neonatology and its former director of Clinical Research, with the Douglas K. Richardson Award for her contributions to children's health as a perinatal researcher.

Among her career accomplishments and contributions, Dr. Schmidt directed a study entitled "Trial of Indomethacin Prophylaxis in Preterms," in which researchers followed 1,202 extremely low birth weight infants from five countries through the end of their second year of life. The study found that the high rate of mental and motor deficits in these children is not improved by prophylactic treatment with indomethacin, a nonsteroidal anti-inflammatory drug.

In other work, Dr. Schmidt, professor emeritus of Pediatrics in the Perelman School of Medicine at the University of Pennsylvania, served as the principal investigator of the "Caffeine for Apnea of Prematurity" trial, which enrolled more than 2,000 very low birth weight infants in North America, Europe, Israel, and Australia. The study revealed caffeine therapy for apnea of prematurity improves the rate of survival without any neurodevelopmental disability up to two years after birth.

BREASTFEEDING EXPERT DIANE SPATZ, PhD, HONORED WITH EXCELLENCE IN RESEARCH AWARD

The Association of Women's Health, Obstetrics, and Neonatal Nurses (AWHONN) honored Diane Spatz, PhD, RN-BC, FAAN, with an Excellence in Research Award which recognizes members who exemplify the highest standards of service in nursing. Dr. Spatz, nurse scientist and founder of the Lactation Program at Children's Hospital of Philadelphia, is internationally recognized for her research and education initiatives on the use of human milk and breastfeeding that are making a difference in the lives of mothers and infants in vulnerable populations around the world.

"Receiving this award was so meaningful to me because it recognizes the contributions that my research has made to improve the lives of children and families globally," Dr. Spatz said. "Human milk is a life-saving medical intervention, and all families deserve evidence-based lactation care and support so that they can reach their personal breastfeeding goals."

Dr. Spatz is also the founder of the CHOP Mothers' Milk Bank and serves as the Clinical Director. At CHOP, Dr. Spatz developed the Breastfeeding Resource Nurse (BRN) course, a training program that enables nurses to provide families with evidence-based lactation support and care. More than 1,400 CHOP nurses have taken the course.

Dr. Spatz's 10-Step Model to Promote and Protect Human Milk and Breastfeeding in Vulnerable Infants helps clinicians and mothers make informed choices about why human milk is a medical intervention and provides comprehensive breastfeeding support to mothers who choose to breastfeed. The model has been implemented in neonatal intensive care units in the United States and countries including Thailand, India, China, Mexico, and Japan.

With having all nurses in the Newborn Infant Intensive Care Unit trained as BRNs and by using her 10-step model at CHOP, the number of infants discharged on human milk has significantly increased over the past 18 years, with human milk rates at discharge being well above 75 percent. Some of her research with surgical infants has demonstrated rates of human milk/breastfeeding at over 86 percent.

SPOTLIGHT SHINES ON JONATHAN SPERGEL, MD, PhD, FOR EOSINOPHILIC ESOPHAGITIS RESEARCH

Life Sciences Pennsylvania honored Jonathan Spergel, MD, PhD, Chief of the Allergy Program at Children's Hospital of Philadelphia, with a Patient Impact Award for his work with CHOP's Food Allergy Frontier Program. The award honors significant contributions to the quality of healthcare or length of life of patients.

Dr. Spergel was recognized for leading research on eosinophilic esophagitis (EoE), a rare chronic allergic inflammatory disease of the esophagus, the muscular tube that carries food from the throat to the stomach. EoE causes certain food allergens to trigger adverse reactions in children, including vomiting, heartburn sensations, and failure to thrive. Eliminating a suspected allergen from a patient's diet can prove to be difficult, because individuals with EoE are often sensitive to several foods, making it unclear which food triggers a reaction.

His work with families at the Food Allergy Center — the only pediatric program nationally recognized for its expertise in diagnosing and treating all types of food allergies — is answering questions about the nature of EoE. Recently, Dr. Spergel and his team discovered that children enrolled in a clinical trial had outgrown their EoE, indicating that EoE was not a lifelong condition as previously believed.

"I am very honored about the award and it is truly the work of multiple people," Dr. Spergel said. "But, most importantly, it gives hope to the families for a better treatment, which is the true goal of medicine."

Photo by Jordan Brian Photography

RADIOLOGIST LISA STATES, MD, ENJOYS 'BE MY SUGAR' AWARD FOR MEDICAL EXCELLENCE

What — or should we say — who is sweeter than sugar? Answer: Lisa States, MD, pediatric radiologist at Children's Hospital of Philadelphia with an expertise in nuclear medicine. Dr. States received the 2018 Congenital Hyperinsulinism International "Be My Sugar" Award for Medical Excellence, in recognition of her life-saving work on the FDOPA PET/CT study — an integral component to finding an effective treatment for congenital hyperinsulinism (HI).

HI is a rare genetic disorder in which the insulin cells of the pancreas secrete too much insulin. The excess insulin causes low blood sugar, also known as hypoglycemia, which can lead to seizures, brain damage, and even death if left untreated. The Congenital Hyperinsulinism Center at CHOP cares for approximately 80 percent of children in the United States who require surgery for HI.

Dr. States has played a key role in studying the effectiveness of F-DOPA, a radioactive tracer drug that is used in PET scans to capture images of the pancreas. By highlighting areas of the pancreas that overproduce insulin, researchers are able to use F-DOPA to diagnose HI in newborns and detect and localize the focal form of the disease.

"One of the most rewarding aspects of my research is my collaboration with Congenital Hyperinsulinism International," Dr. States said. "This group unites clinicians and families from across the globe to support patients and families, educate clinicians, and share research ideas."

HEALTHCARE HERO AWARD HONORS PHILLIP B. STORM, MD, FOR BRAIN TUMOR RESEARCH

Chief of the Division of Neurosurgery Phillip (Jay) Storm, MD, received an inaugural Healthcare Hero Award for his work at Children's Hospital of Philadelphia in the research and treatment of pediatric brain tumors, the leading cause of cancer-related death in children. With these awards, TEVA Pharmaceuticals recognizes leaders in healthcare research and treatment whose accomplishments have benefitted their patients, their field, and the global community.

"It is a great honor for our team, families, supporters, and collaborators to be the first recipient of this prestigious award," Dr. Storm said. "I know that our efforts will continue to accelerate discovery, foster innovation, and lead to cures for our patients."

In 2009, Dr. Storm partnered with fellow surgeons, oncologists, pathologists, foundations, and patients and their families to launch the Children's Brain Tumor Tissue Consortium (CBTTC) at CHOP, a multi-institutional research program dedicated to the study and treatment of pediatric brain tumors. CBTTC provides free and open-access data to find a cure for pediatric brain cancer, with 6,400 samples provided to researchers to date, including data from 1,446 patients. It is the world's largest pediatric brain tumor repository of information.

Building on the CBTTC model, Dr. Storm led the 2017 launch of the Philadelphia Coalition for a Cure (PC4C), a first-of-its-kind collaborative program that bridges discoveries between adult and pediatric cancer care. PC4C assesses, promotes, and facilitates the diagnosis and treatment of both adult and pediatric patients with brain tumors and other cancers, with the goal of streamlining research and precision medicine efforts.

ENDOCRINE SOCIETY RECOGNIZES MARY ELLEN VAJRAVELU, MD, MSHP, AS EARLY INVESTIGATOR

Mary Ellen Vajravelu, MD, MSHP, pediatric endocrinologist at Children's Hospital of Philadelphia, earned the Endocrine Society's Early Investigators Award for her fellowship research on congenital hyperinsulinism and type 1 diabetes.

The Early Investigators Awards were established to promote the development of early-career investigators and recognize their accomplishments in endocrine-related research. Recipients receive a monetary award to assist in their development and public recognition of their research accomplishments.

"I'm continuously inspired by the innovative research going on throughout CHOP," Dr. Vajravelu said, "and I'm grateful to have the opportunity to continue to learn from and collaborate with researchers across the institution."

Dr. Vajravelu's work focuses on improving clinical effectiveness of therapies for children with endocrine-related diseases by combining her experience in epidemiology, biostatistics, and qualitative research with her advanced training in quality improvement and patient safety. Her current research centers on the use of innovative healthcare delivery strategies, such as mobile health applications, to facilitate behavior change in adolescents with prediabetes and type 2 diabetes.

OUTSTANDING MITOCHONDRIAL RESEARCH AWARD GOES TO DOUGLAS WALLACE, PhD

Douglas Wallace, PhD, was honored with the 2019 Charles L. Hoppel, MD, Award for Outstanding Contributions in Mitochondrial Research from Case Western Reserve University School of Medicine.

A pioneer and internationally renowned scientist in human mitochondrial genetics, Dr. Wallace is the director of the Center for Mitochondrial and Epigenomic Medicine (CMEM) and the Michael and Charles Barnett Endowed chair in Pediatric Mitochondrial Medicine and Metabolic Diseases at Children's Hospital of Philadelphia.

More than 35 years ago, Dr. Wallace and colleagues founded the field of human mitochondrial genetics. He's dedicated his career to the understanding of, and potential treatments for, a variety of disorders and diseases by focusing on mitochondria, tiny structures within human cells that produce 90 percent of the body's energy.

"A revolution is occurring in medical genetics," Dr. Wallace said. "With the elucidation of the rules of mitochondrial genetics, not only has a new class of genetic diseases been identified, but a totally new perspective is emerging on the etiology of the common metabolic and degenerative diseases. Thanks to the support provided by CHOP for the Center for Mitochondrial and Epigenomic Medicine and the Mitochondrial Medicine Frontier Program, CHOP is taking the leadership in this exciting new branch of medicine."

Dr. Wallace discovered that the mitochondria's own DNA (mtDNA), which encodes the blueprint for the cell's power generators, is inherited exclusively from the mother. Dr. Wallace's findings on mtDNA revealed women left Africa about 65,000 years ago to colonize Eurasia, and from Siberia, they crossed the Bering land bridge to populate the Americas.

He also proved that genetic alterations in the mtDNA can result is a wide range of metabolic and degenerative diseases, and he continues to study the communication between the mitochondria and nuclear DNA. This communication is mediated by the epigenome, inherited modifications in gene expression caused by tags or proteins that bind to DNA.

Under his leadership, CMEM researchers are investigating mitochondrial and epigenomic dysfunction in a wide range of medical conditions such as autism, epilepsy, heart disease, diabetes and obesity, forms of blindness, Alzheimer disease, Parkinson disease, cancer, and aging.

FACULTY MENTOR AWARD IS 'ULTIMATE RECOGNITION'

Children's Hospital of Philadelphia Research Institute recognized Babette Zemel, PhD, professor in the Division of Gastroenterology, Hepatology, and Nutrition, with the 2019 Faculty Mentor Award. On top of Dr. Zemel's impactful contributions to the field of bone health and growth research, she has supported many mentees in their journey to make their own scientific contributions, achieve funding, and carve out career paths by securing academic appointments.

The award is a special honor given to faculty investigators whose mentorship has helped their colleagues become the next generation of brilliant researchers at CHOP. Dr. Zemel received the award at the annual Scientific Symposium, an event which celebrates the Research Institute's remarkable scientific community: a diverse group of thought leaders, innovators, experts, and early career scientists committed to advancing children's health.

"Mentoring is, by far, the most enriching and fulfilling thing that I do," Dr. Zemel enthused. "I have the most extraordinary, talented, dedicated people to mentor here at CHOP, coming from diverse disciplines within pediatrics, as well as nursing, and anthropology. As I work with them to establish their research programs, I am also learning and expanding my knowledge and experience. It's a journey that we take together. The Faculty Mentor Award is the ultimate recognition of all of those things, and I am deeply, deeply honored."

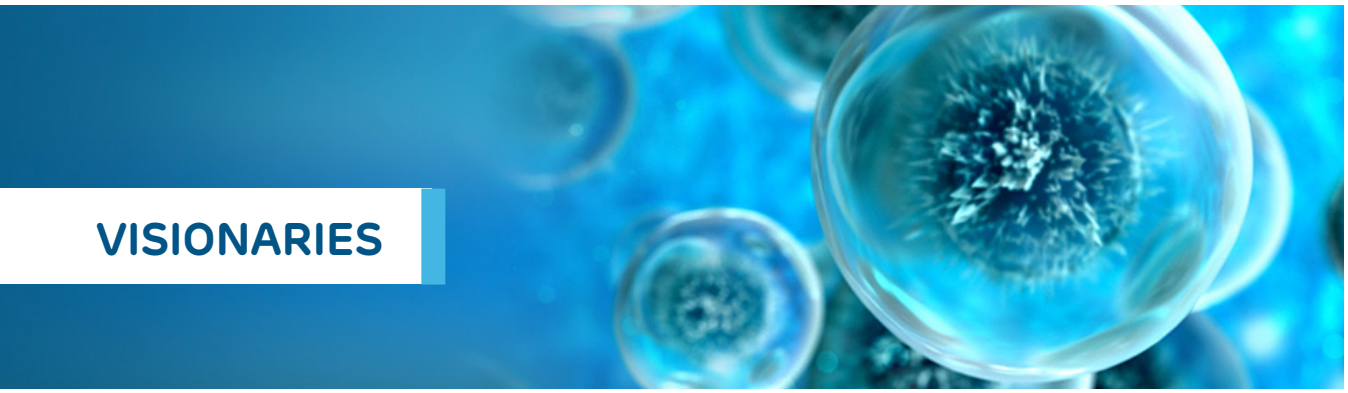
22Q11.2 SOCIETY INAUGURAL SPECIAL SERVICE AWARD HONORS CHOP-PENN CENTER

Special recognition went out to the 22q and You Center at Children's Hospital of Philadelphia and the Perelman School of Medicine at University of Pennsylvania for its outstanding, longstanding, exemplary, and unwavering commitment and contributions to the chromosome 22q11.2 community. Donna McDonald-McGinn, MS, CGC, director of the Center, and colleagues were in British Columbia at the 22q11.2 Society's international conference to accept the inaugural Special Service Award.

Individuals with 22q11.2 deletion are missing a small piece of chromosome 22. This genetic condition is the most common cause of DiGeorge syndrome. Until CHOP identified the chromosomal etiology, it had also gone by other names such as velocardiofacial syndrome, among others. It may cause a wide variety of health problems, ranging from heart defects and cleft palate, to feeding difficulties, immune problems, speech delay, a unique pattern of learning disabilities and behavioral differences such as ADHD and autism.

The condition is difficult to diagnose because it affects each child differently, can display varying symptoms, and manifests in features associated with many other conditions. But the internationally recognized 22q and You Center continues to lead in supporting early detection, basic science research, and improved care toward better outcomes for all patients.

"The 22q and You Center was launched in the early 1990's at the behest of families desperate for condition specific, experienced, coordinated multidisciplinary care following the longstanding clinical and basic science research efforts of Drs. Elaine Zackai and Beverly Emanuel," McDonald-McGinn said. "The success of the Center can only be credited to the dedication of healthcare providers, coordinators, laboratory technicians, researchers, and students both within the Division of Human Genetics and across the entire institution. Although the physical plaques were presented to the Center leads, the award was accepted collectively as each and every breakthrough is the result of this singular focus — to help our patients and families in whatever way we can by working as a team."



VISIONARIES

ACCOMPLISHED PHYSICIAN-RESEARCHER NAMED CHIEF OF DIVISION OF CARDIOTHORACIC SURGERY

Jonathan Chen, MD, joined Children's Hospital of Philadelphia as chief of the Division of Cardiothoracic Surgery in September 2018, bringing his noteworthy track record of promoting collaborative, multidisciplinary care in pediatric cardiovascular cases. Dr. Chen's clinical research is focused on surgical issues in complex congenital heart care, cardiac transplantation, and development of mechanical ventricular assist devices for children.

He holds the Mortimer J. Buckley Jr., MD, Endowed Chair in Pediatric Cardiothoracic Surgery and is co-director of the Cardiac Center with Joseph Rossano, MD, chief of the Division of Cardiology. The Cardiac Center team performs more than 1,000 cardiothoracic surgeries each year, including 600 open-heart procedures in children and adolescents with complex heart conditions.

"We want the Cardiac Center to be the destination where you come to have the highest level of expertise across the entire spectrum of congenital heart care — where you have access to novel therapies, devices, investigative trials that represent the vanguard of our field," Dr. Chen shared when he joined CHOP. "There are a lot of great cardiac centers in the world, but there are very few places like CHOP that have the individual intellect, the drive, and the desire to solve unanswered questions. Only a place like CHOP can hope to find those answers and, in fact, change the game."

Dr. Chen most recently served as chief of Congenital Cardiac Surgery at Seattle Children's Hospital, co-director of the Heart Center, and professor of Surgery at the University of Washington School of Medicine and held the Sam and Althea Stroum Endowed Chair in Pediatric Cardiovascular Surgery. Over the past decade, he has led humanitarian trips with several volunteer organizations to provide cardiovascular care to developing countries including Cambodia, Senegal, China, India, and Brazil. Committed to continuing education, Dr. Chen serves on the editorial board of the *Journal of Thoracic and Cardiovascular Surgery*.

RARE DISORDER EXPERT NAMED DIRECTOR OF COMPREHENSIVE BONE MARROW FAILURE CENTER

Peter Kurre, MD, joined Children's Hospital of Philadelphia as director of the Comprehensive Bone Marrow Failure Center (CBMFC) in August 2018 to lead the development of new therapies for bone marrow failure (BMF) syndromes in children. The Center, which has an international reputation of excellence in the treatment of BMF disorders, currently follows more than 200 patients.

Established in 2010, the CBMFC provides world-class clinical care for patients and families with inherited and acquired forms of BMF and conducts groundbreaking basic, translational, and clinical research to improve diagnosis and treatment for patients with BMF disorders. Dr. Kurre leads collaborative efforts to leverage molecular technologies to improve diagnostic approaches to BMF; develop clinical trials for patients and investigate their heightened risk for developing cancer; and facilitate development of stem-cell-directed gene therapy.

Designed with an integrative approach to patient care and translational research in mind, the Center supports several research labs investigating clonal evolutions in severe aplastic anemia, human leukocyte antigen risk allele definition, niche contributions to haematopoietic stem cell deficits in inherited BMF disorders, stem cell gene therapy, and developmental origins of BMF. One of the largest repositories of samples from patients with BMF disorders supports CBMFC research activities and a range of collaborative projects with centers elsewhere in the United States and abroad.

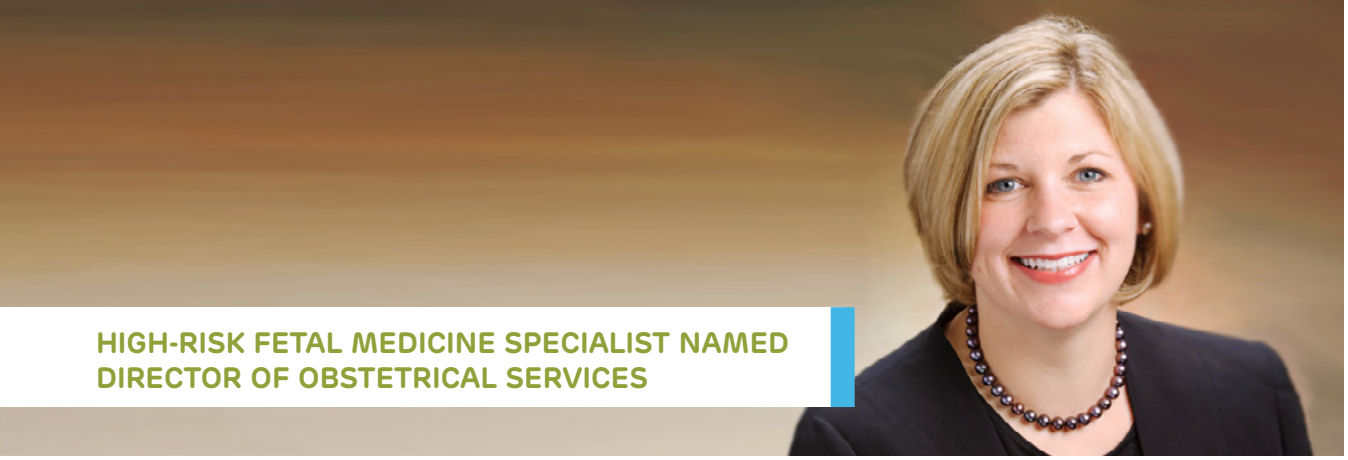
In addition his directorship, Dr. Kurre is a professor of Pediatrics at the Perelman School of Medicine at the University of Pennsylvania and holds the Buck Family Chair in Hematology Research, which supports research in BMF syndromes.

CHOP CARDIOLOGIST GUIDES PEDIATRIC MEDICAL DEVICE INNOVATION IN EXPANDED CONSORTIUM

In January 2019, Robert Levy, MD, took the leading role as director and principal investigator of the Pennsylvania Pediatric Medical Device Consortium (PPDC) at Children's Hospital of Philadelphia, which is focused solely on developing pediatric medical device concepts. Formerly known as the Philadelphia Pediatric Medical Device Consortium, the new name reflects a new partnership with the University of Pittsburgh, and statewide expansion.

One of five consortia currently funded through the U.S. Food and Drug Administration's Pediatric Device Grants Consortia Program, the recent renewal of the PPDC's five-year grant created a fortuitous time to solidify a partnership with colleagues and collaborators with the University of Pittsburgh-based McGowan Institute for Regenerative Medicine and Pitt's innovation center, sciVelo.

In addition to awarding its own extramural grants, the PPDC has a new early stage development program in partnership with the Philadelphia-area medical device design company, Archimedic, with the goal of taking pediatric medical device ideas from concept to feasibility with expert engineering assistance. Dr. Levy looks forward to guiding the future of the consortium by continuing the project he and founding director Matthew Maltese, PhD, initiated.



HIGH-RISK FETAL MEDICINE SPECIALIST NAMED DIRECTOR OF OBSTETRICAL SERVICES

As the new director of Obstetrical Services at Children's Hospital of Philadelphia's Center for Fetal Diagnosis and Treatment (CFDT), Julie Moldenhauer, MD, FACOG, FACMG, oversees highly specialized, comprehensive obstetrical care in the multidisciplinary fetal medicine program while continuing as medical director of the Garbose Family Special Delivery Unit, the world's first birth facility in a pediatric hospital specifically designed for healthy mothers who will deliver babies with known birth defects or genetic conditions.

An internationally recognized leader in fetal diagnosis, fetal surgery and fetal care, the CFDT has cared for more than 22,775 expectant women or mothers from all 50 states and from more than 70 countries, and it has performed more than 1,691 fetal surgeries, including those to treat spina bifida, congenital diaphragmatic hernia, and twin-twin transfusion syndrome before birth.

Among Dr. Moldenhauer's translational research interests are improvements to the prenatal and obstetrical management of pregnancies complicated by fetal birth defects, the impact of fetal therapy on maternal outcomes, and postpartum depression in mothers carrying babies with fetal anomalies.

In addition to her appointments within the CFDT, Dr. Moldenhauer serves as an associate professor of Clinical Obstetrics and Gynecology in Surgery at the Perelman School of Medicine at the University of Pennsylvania, holds the George Leib Harrison Endowed Chair in Fetal Therapy, and is the immediate past chair of the Board of Directors of the North American Fetal Therapy Network.

INNOVATOR AND SCIENTIST HOLDS FIRST ENDOWED CHAIR IN NEUROBLASTOMA RESEARCH

Pediatric oncologist and researcher Yael Mossé, MD, is the inaugural holder of Children's Hospital of Philadelphia's Patricia Brophy Endowed Chair in Neuroblastoma Research.

As director of the Neuroblastoma Development Therapeutics Program at CHOP and an attending physician at its Cancer Center, Dr. Mossé treats patients with high-risk neuroblastoma. Among her patients was 8-year-old Alex Scott, who founded the Alex's Lemonade Stand Foundation before succumbing to neuroblastoma in 2004.

The endowed chair is named for Patricia "Pat" Brophy, one of Alex's nurses at CHOP as well as a dear friend, colleague, and mentor of Dr. Mossé. Ms. Brophy passed away in 2008 after her own cancer illness. The Brophy Endowed Chair was established to support the development of new therapies for neuroblastoma patients, and first announced in June 2018, during the foundation's 15th annual "Lemonade Stand" fundraiser at CHOP to benefit pediatric cancer research.

"It's simply wonderful to know that Pat's memory is still very present," Dr. Mossé said. "I know she would be really amazed by the progress we've made, but she was always one to want to do more for these kids. Her memory, her grit, and her passion for these kids is always with me. And now to be able to carry her with me as I move forward in a new phase of my career is humbling."

Neuroblastoma is a formidable cancer that starts in the nerve tissues of infants and young children and is one of the more common childhood cancers. Unfortunately, cure rates have improved only slightly in the last 20 years. Dr. Mossé and her research team discovered gene mutations that are the primary cause of inherited neuroblastoma and that also play a significant role in the more common, non-inherited form of the disease.

Dr. Mossé led the breakthrough discovery that identified the most common neuroblastoma-specific cancer-causing mutation in the anaplastic lymphoma kinase (ALK) gene and is leading efforts to translate this discovery to the therapeutic use of ALK-inhibiting drugs.

DIVISION OF PLASTIC AND RECONSTRUCTIVE SURGERY NAMES CRANIOFACIAL SURGEON AS CHIEF

In his new position as chief of the Division of Plastic and Reconstructive Surgery at Children's Hospital of Philadelphia, Jesse Taylor, MD, oversees one of the largest children's plastic surgery centers in the United States.

Dr. Taylor holds the Peter Randall Chair in Plastic and Reconstructive Surgery at CHOP and is the co-director of the Cleft Lip and Palate Program. Each year, CHOP performs more than 1,000 surgical procedures related to cleft lip and palate repair and provides ongoing care for more than 700 patients with cleft defects.

In treating children and adolescents with congenital and acquired differences of the face and skull, Dr. Taylor specializes in craniosynostosis surgery, jaw surgery, surgery for facial asymmetries, cleft lip and palate repair, rhinoplasty, otoplasty, cranial reconstruction, cranio-maxillo-facial distraction osteogenesis, and complex facial reconstruction. He also shares his expertise by providing for children who may otherwise go untreated on international surgical mission trips, and he contributes to the care of international cleft and craniofacial patients through visiting professor appointments throughout Central and South America, Europe, and Asia.

In 2017, Dr. Taylor successfully co-led a 30-member clinical team to complete the surgical separation of 10-month-old twins. While the procedure marked the 24th time CHOP surgeons have separated conjoined twins, it was the first time the twins were joined at the head.

Dr. Taylor also is a professor of surgery at the Perelman School of Medicine at the University of Pennsylvania and director of the Penn Craniofacial Fellowship Program.

LUNG DISEASE EXPERT JOINS CHOP AS CHIEF OF DIVISION OF PULMONARY MEDICINE

Children's Hospital of Philadelphia welcomed Lisa R. Young, MD, as chief of the Division of Pulmonary Medicine and the John M. Keating Endowed Chair in Pediatrics – President's Scholar in June 2019. An international expert in rare and genetic lung diseases in children, Dr. Young has received multiple awards for her research, including the American Thoracic Society Robert B. Mellins Outstanding Achievement Award, the American Thoracic Society Public Advisory Roundtable Excellence Award, and the LAM Foundation Scientific Advancement Award. She will use her expertise to further CHOP's leadership in training and career development for young investigators focused on pulmonary research.

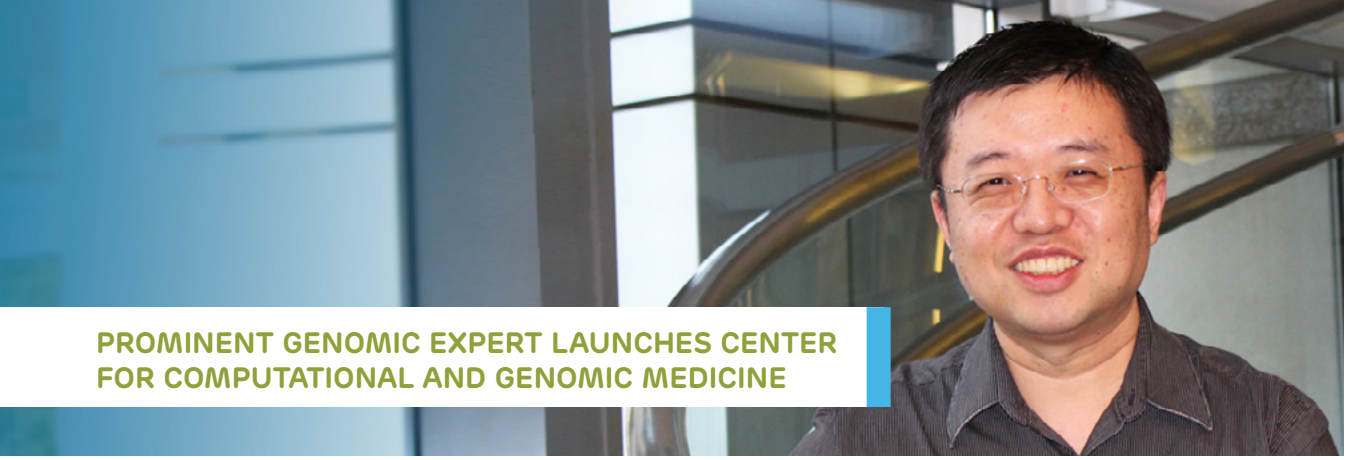
"A growing body of evidence demonstrates that lung development is ongoing in childhood, and many lung diseases start early in life, resulting in long-term health consequences," Dr. Young said. "We now have unprecedented opportunity to advance our understanding of rare and common diseases across the lifespan and translate these findings to improve lung health and patient outcomes."

Respiratory illnesses are responsible for the majority of visits to pediatricians, the emergency department, and hospital admissions, and the Division of Pulmonary Medicine has high quality, large volume inpatient and outpatient clinical programs to address the spectrum of childhood lung diseases.

A renowned physician-scientist, Dr. Young has received numerous grant awards for laboratory and clinical research on a variety of lung diseases, and is the principal investigator on multiple National Institutes of Health-funded projects including a Midcareer Award in Mentoring in Patient-Oriented Research. She is especially interested in interstitial and other rare lung diseases including Hermansky-Pudlak syndrome, neuroendocrine cell hyperplasia of infancy, bronchopulmonary dysplasia, and lymphangioleiomyomatosis.

Dr. Young is a professor of Pediatrics at the Perelman School of Medicine at the University of Pennsylvania and an associate director in the recently established Penn-CHOP Lung Biology Institute (LBI). With founding director Edward Morrissey, PhD and Jason Christie, MD, she joins the LBI leadership team in its mission to integrate the outstanding expertise in translational pulmonary research and patient care at both CHOP and Penn with fundamental discovery research across campus.

She most recently was a faculty member in the Departments of Pediatrics, Medicine, and Cell and Developmental Biology at Vanderbilt University, and was the director of the Pediatric Rare Lung Diseases Program for Monroe Carell Jr. Children's Hospital at Vanderbilt in Nashville, Tennessee.



PROMINENT GENOMIC EXPERT LAUNCHES CENTER FOR COMPUTATIONAL AND GENOMIC MEDICINE

Yi Xing, PhD, arrived at Children's Hospital of Philadelphia in September 2018 to launch the Center for Computational and Genomic Medicine, which harnesses computing, big data, and genomic technologies to facilitate biological discoveries and medical innovations.

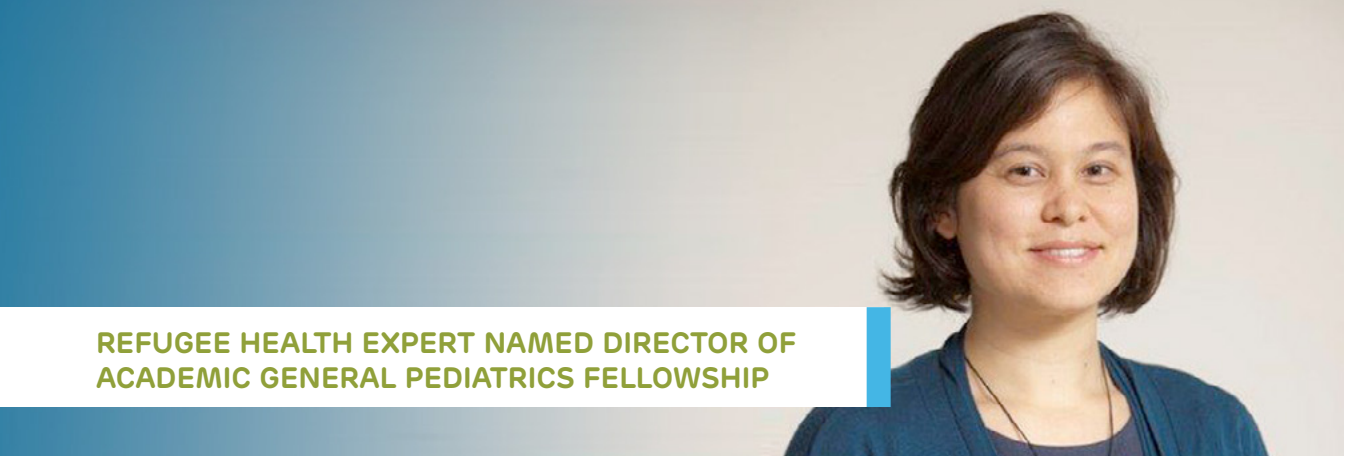
As founding director, Dr. Xing brings his expertise in synthesizing vast and diverse data sets to generate novel insights into how the human genome works and create new opportunities for pediatric medicine. The Center leverages the Research Institute's strength in recognizing the underlying genetics of pediatric disorders and developing molecular and cellular therapeutics, while drawing on resources such as CHOP's biorepositories and electronic health record.

Dr. Xing relocated his hybrid computational/experimental lab and team of 20 investigators from the University of California at Los Angeles to CHOP's research campus. Up to 60 percent of the mutations that cause human disease disrupt ribonucleic acid (RNA) processing. Among the team's research priorities is to focus on how gene regulation is controlled at the level of RNA molecules, specifically messenger RNA processing. Understanding how RNA-level complexities are generated and how they function will lead to new diagnostic approaches and therapies.

The Xing Lab team has developed transformative technologies that are already used by the genomic research community. These include a computational tool, called DARTS, which uses deep learning to harness the wealth of information available in large-scale public RNA sequencing datasets.

Dr. Xing holds the new Francis West Lewis Chair in Computational and Genomic Medicine at CHOP, and is a professor of Pathology and Laboratory Medicine at the Perelman School of Medicine at the University of Pennsylvania. He has published extensively on bioinformatics, genomics, and RNA biology, receiving numerous awards for his work.

The Center will recruit new faculty members, focusing on experts who can develop new genomic technologies or computational tools for use by the broader scientific community. Dr. Xing's vision is to make the Center an engine for technological and biomedical innovation.



REFUGEE HEALTH EXPERT NAMED DIRECTOR OF ACADEMIC GENERAL PEDIATRICS FELLOWSHIP

Katherine Yun, MD, MHS, a researcher at PolicyLab and pediatrician with CHOP's Refugee Health Program, was named director of the Academic General Pediatrics (AGP) Fellowship.

The AGP fellowship addresses key clinical, health services, and policy issues in primary care pediatrics, and offers research training and mentorship. The fellowship is intended to prepare trainees to improve healthcare for underserved children through primary care research and leadership.

Dr. Yun's research focuses on access and quality of care for refugee and immigrant children, with a particular emphasis on equitable care for families who have recently arrived in the United States and English language learners. As part of her work with the Refugee Health Program, she provides high-quality healthcare for refugee, asylee, and other immigrant children who have recently arrived in the United States.

Dr. Yun is assistant professor of Pediatrics at the University of Pennsylvania's Perelman School of Medicine and an attending physician in CHOP's Division of General Pediatrics. She previously served as supervising physician at the award-winning Pediatric Refugee Clinic at Yale-New Haven Children's Hospital in Connecticut and as a coordinator for pediatric care at Puentes de Salud.

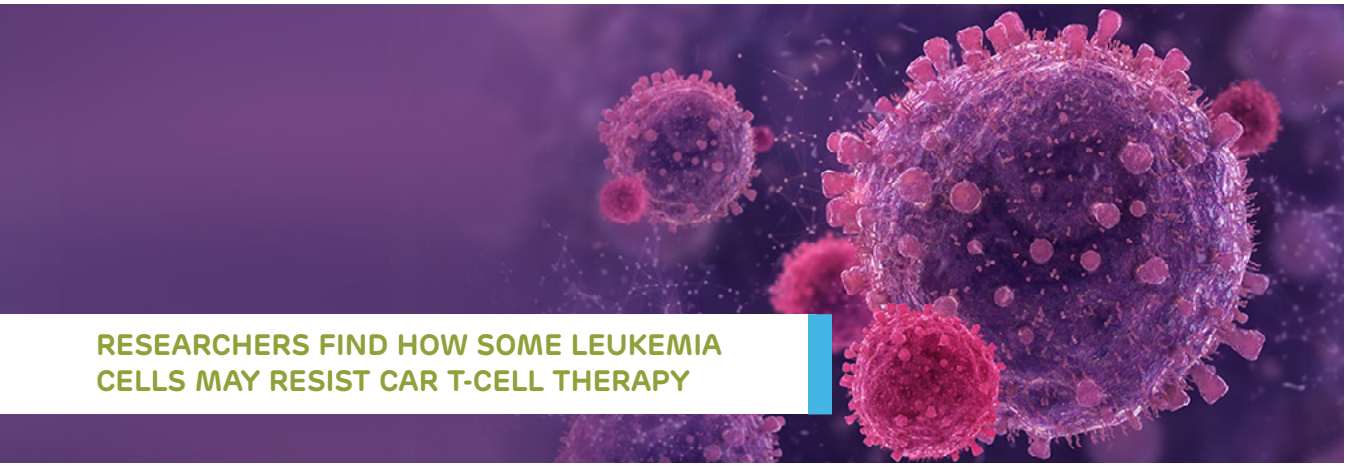
TRANSLATIONAL PHYSICIAN-SCIENTIST NAMED ASSOCIATE CHIEF CLINICAL RESEARCH OFFICER

Elizabeth Goldmuntz, MD, FAAP, FACC, assumed the newly created leadership role of associate chief clinical research officer at Children's Hospital of Philadelphia Research Institute in July 2019. Working closely with Richard Aplenc, MD, PhD, MSCE, chief clinical research officer, she will devise and implement improved communication practices and processes for principal investigators through the Research Institute.

A professor of Pediatrics at the Perelman School of Medicine at the University of Pennsylvania and an attending cardiologist in CHOP's Cardiac Center, Dr. Goldmuntz has directed a translational research program on the genetic basis of congenital heart disease and the relationship of genotype to clinical outcomes, with a focus on conotruncal cardiac defects. Through her research, Dr. Goldmuntz has banked samples from more than 6,000 case-parent trios in conjunction with relevant family and medical histories, and engaged in collaborative, genomic analyses and outcome studies.

In the Cardiac Center, Dr. Goldmuntz specializes in echocardiography and the care of cardiac patients with the 22q11.2 deletion and other genetic syndromes. She has been at CHOP for more than 30 years, having completed all of her pediatric and specialized clinical training here before joining the faculty.

DISCOVERY



RESEARCHERS FIND HOW SOME LEUKEMIA CELLS MAY RESIST CAR T-CELL THERAPY

THE FINDING

Children's Hospital of Philadelphia investigators revealed the biological events by which some cancer cells develop resistance to a groundbreaking cellular therapy, called CAR T-cell therapy, that has successfully treated many patients with particular forms of leukemia. They also found clues to a possible method to overcome the cancer's resistance.

WHY IT MATTERS

Chimeric antigen receptor (CAR) T-cell therapy, also called CAR T-cell therapy, represents a landmark achievement in personalized cancer immunotherapy — harnessing the body's immune cells to treat cancer. The therapy has dramatically improved survival in children and young adults who relapsed or never responded to their initial chemotherapy. However, some 20 to 30 percent of patients with acute lymphoblastic leukemia (ALL) receiving CAR T-cell treatment either never respond or develop resistance within a few weeks.

WHO CONDUCTED THE STUDY

Andrei Thomas-Tikhonenko, PhD, chief of the Division of Cancer Pathobiology and a professor with the Departments of Pathology and Laboratory Medicine and Pediatrics at CHOP, led the study.

HOW THEY DID IT

The researchers built upon their previous study showing that mutations in the leukemia cell hamper a protein, called CD19 antigen, that is essential for CAR T-cell therapy to succeed. The CD19 antigen needs to be produced in sufficient quantities to be recognized by CAR T cells. Some of the originally discovered mutations prevent CD19 from ever being produced. Yet other seemingly innocuous mutations would simply insert a few extra elements into the protein's amino acid chain. How such insertional mutations could cause resistance to therapy was not clear.

THE RECENT STUDY FOCUSED ON THE BIOLOGICAL MECHANISMS AT WORK.

For CD19 to be recognized by CAR T cells, it first needs to reach the surface of the leukemia cell. The researchers found that the insertional mutations cause the CD 19 antigen to misfold within the cell so that it can't be carried to the cell surface intact, and is instead retained in the structure called the endoplasmic reticulum. However, they also found that misfolded CD19 proteins are tightly bound to the machinery that breaks down full-length proteins into short peptides and transports them to the cell surface for immune recognition.

QUICK THOUGHTS

"Experimental science is capricious and utterly unpredictable," said Dr. Thomas-Tikhonenko, regarding the study. "It doesn't care about gaps in your education, and more often than not takes you in directions you would rather avoid. Before we embarked on this project, my knowledge of protein folding and intracellular transport had been limited to undergraduate-level cell biology textbooks written one millennium ago. Talk about on the job training!"

WHAT'S NEXT

The team's next steps are to investigate whether mutant CD19 peptides indeed reach the leukemia cell's surface, and then to generate T cells that recognize and attack that peptide.

WHERE THE STUDY WAS PUBLISHED

The study appeared in the journal *Molecular and Cellular Biology*.

WHO HELPED FUND THE STUDY

A variety of public and private sponsors. National Institutes of Health, William Lawrence and Blanche Hughes Foundation, Alex's Lemonade Stand Foundation, and St. Baldrick's-Stand Up To Cancer Pediatric Cancer Dream Team.

WHERE TO LEARN MORE

Learn more about this study in this CHOP press release.

NOVEL GENES TIED TO OSTEOPOROSIS MAY POINT TO FUTURE TREATMENT FOR OTHER DISEASES

THE FINDING

Using data analysis tools and three-dimensional studies of genomic geography, researchers found new risk genes for osteoporosis, opening the door to potentially more effective treatments.

WHY IT MATTERS

The research team identified two novel genes that affect bone-forming cells relevant to fractures and osteoporosis. As a potential added benefit, the analytical methods the researchers used could be applied more broadly to other diseases with a genetic component, including certain pediatric cancers, diabetes, and lupus.

WHO CONDUCTED THE STUDY

Struan F.A. Grant, PhD, and Andrew D. Wells, PhD, directors of the Center for Spatial and Functional Genomics (CSFG) at Children's Hospital of Philadelphia, co-led the study.

HOW THEY DID IT

Dr. Grant and his colleagues investigated genetic loci, or DNA regions, previously established to be associated with bone mineral density in genome-wide association studies (GWAS), both in adults and children. They used state-of-the-art massively parallel, high-resolution tools to analyze genome-wide interactions in human osteoblasts — bone-forming cells derived from mesenchymal stem cells. Their analytical tools used a "multi-omic" approach, integrating data from the genome sequence and details of chromatin structure to map interactions between potential bone mineral density (BMD)-related gene promoters and regions harboring genetic variants related to BMD biology. The study pinpointed two novel genes, *ING3* and *EPDR1*, which in turn revealed strong effects on human osteoblasts.

QUICK THOUGHTS

"The geography of the genome is not linear," Dr. Grant said. "Because DNA is folded into chromosomes, parts of the genome may come into physical contact, enabling key biological interactions that affect how a gene is expressed. That's why we study the three-dimensional structure of the genome."

WHAT'S NEXT

Follow-up studies investigating the biological pathways affected by one of the genes, *ING3*, identified in the study may present targets for therapies to strengthen bone mineral density and ultimately prevent fractures.

WHERE THE STUDY WAS PUBLISHED

The study appeared in the journal *Nature Communications*.

WHO HELPED FUND THE STUDY

The National Institutes of Health supported this research study.

WHERE TO LEARN MORE

Learn more about the study in this CHOP press release.

INTERNATIONAL TEAM HONES IN ON NEW GENETIC CAUSE OF SEVERE CHILDHOOD EPILEPSY

THE FINDING

A large international research team discovered a new genetic cause for a severe, difficult-to-treat childhood form of epilepsy, identifying spontaneous mutations in a brain-expressed calcium channel that result in epileptic overactivity. The team's research in patients also found clues to potential medical treatments for the rare condition.

WHY IT MATTERS

The study focused on disease-causing changes in the *CACNA1E* gene. This gene was long suspected to play a key role in regulating electrical activity in brain cells, but it was not yet known as a cause for a human disorder. Their study was the first to link this gene to human epilepsy and to demonstrate that overactivity of the ion channel encoded by *CACNA1E* leads to severe early-onset epilepsy.

WHO CONDUCTED THE STUDY

Katherine L. Helbig, MS, CGC, co-director of the Epilepsy NeuroGenetics Initiative (ENGIN) and senior genetic counselor in the Division of Neurology at Children's Hospital of Philadelphia, served as first author on the study. The full research team included nearly 100 scientists, from Europe, Canada, China, Australia, New Zealand, and the United States.

HOW THEY DID IT

The study team performed next-generation sequencing, including whole exome sequencing, in 30 infants and young children with severe epilepsy, and identified disease-causing variants in *CACNA1E*. In most cases, the gene variants were de novo — present in the affected children, but not found in their parents. De novo variants are being increasingly found in severe childhood epilepsies.

QUICK THOUGHTS

"The fact that we were able to identify 30 patients at this stage of research indicates that we could be looking at a more common cause of genetic epilepsy than we would have initially assumed," Helbig said. "This research enables us to give some families an answer as to why their child has severe epilepsy. It also offers the potential that we can build on this knowledge to find new strategies for treatment."

WHAT'S NEXT

Most of the 30 patients did not respond to any anti-epileptic medications, except for a few who responded to the medication topiramate, known to target the *CACNA1E* channel. Further studies will focus on this finding and other aspects of the team's research, with the aim of translating their knowledge into targeted precision therapies for children with severe genetic epilepsy.

WHERE THE STUDY WAS PUBLISHED

The study appeared in the *American Journal of Human Genetics.*

WHO HELPED FUND THE STUDY

The study was supported by multiple sources worldwide, including national medical institutes of various countries, the U.S. National Institutes of Health (grant NS069605), and the Deciphering Developmental Disorders study, sponsored by the Wellcome Trust.

WHERE TO LEARN MORE

Learn more about this study in this *Cornerstone blog story* or this CHOP press release.

GIRLS AND BOYS ON AUTISM SPECTRUM TELL STORIES DIFFERENTLY

THE FINDING

Researchers at Children's Hospital of Philadelphia examined differences in the way girls and boys on the autism spectrum use certain types of words during storytelling. The investigators found that autistic girls used significantly more "cognitive process" words such as "think" and "know" than autistic boys, despite comparable autism symptom severity. Identifying differences like these can open the door to ensuring that girls with autism spectrum disorder (ASD) receive the diagnosis and support they need to achieve the best possible quality of life.

WHY IT MATTERS

Boys are four times more likely than girls to be diagnosed with ASD, yet a growing body of research shows that the condition is more common in girls than previously thought, strongly suggesting that new methods are required to diagnose the disorder at younger ages.

WHO CONDUCTED THE STUDY

Julia Parish-Morris, PhD, a scientist in the Center for Autism Research and faculty member in the Departments of Child Psychiatry and Biomedical & Health Informatics at CHOP, led the study.

HOW THEY DID IT

Dr. Parish-Morris and her co-authors studied 102 verbally fluent school-aged children who either had a diagnosis of ASD (21 girls and 41 boys) or were typically developing (19 girls and 21 boys), and were matched on age, IQ, and maternal education. Children viewed a sequence of pictures involving a fisherman, a cat, and a bird, and then told a story based on what they saw.

Results revealed that autistic girls used significantly more cognitive process words than autistic boys did, even when they had similar levels of autism severity. Girls with ASD and typical girls used comparable numbers of cognitive process words. Autistic boys and girls both used more nouns than typically developing children, demonstrating object-focused storytelling. Autistic girls therefore showed a unique narrative profile that overlapped with typical children as well as with autistic boys.

QUICK THOUGHTS

"In order to place these findings in context, it's important to understand that because girls tend to exhibit different traits than autistic boys do, they are often incorrectly diagnosed or missed entirely by standard diagnostic tools. That discrepancy also skews the research literature," Dr. Parish-Morris said. "Autism studies have historically included three to six times as many males as females. This means that we don't yet know enough about gender differences in autism, and so we miss girls whose traits differ from those of boys."

WHAT'S NEXT

Sex-informed screening and diagnostic methods may help physicians identify autism in verbal girls at an earlier age, which should spur efforts to develop appropriate, personalized early interventions resulting in improved support for girls and women with ASD.

WHERE THE STUDY WAS PUBLISHED

The study appeared online in the journal *Molecular Autism*.

WHO HELPED FUND THE STUDY

The Autism Science Foundation, the Eagles Charitable Trust, the McMorris Family Foundation, the Allerton Foundation, and a National Institutes of Child Health and Human Development supported the study.

WHERE TO LEARN MORE

Learn more about this research by reading this CHOP press release.

STUDY LINKS TEENS WITH ADHD WITH INCREASED CAR CRASHES AND VIOLATIONS

THE FINDING

Teen drivers diagnosed with attention-deficit/hyperactivity disorder (ADHD) are significantly more likely to crash, be issued traffic and moving violations, and engage in risky driving behaviors than their peers without ADHD.

WHY IT MATTERS

By highlighting the specific types of crashes and traffic violations, the study identified risky driving behaviors that those with ADHD may be more likely to engage in — such as driving while intoxicated, not wearing a seat belt, and speeding.

WHO CONDUCTED THE STUDY

Allison E. Curry, PhD, MPH, a senior scientist and director of Epidemiology and Biostatistics at the Center for Injury Research and Prevention at Children's Hospital of Philadelphia and an assistant professor of Pediatrics at the Perelman School of Medicine at the University of Pennsylvania, led the study.

HOW THEY DID IT

The multidisciplinary team of researchers from CHOP's Center for Injury Research and Prevention and Center for Management of ADHD analyzed detailed crash and traffic violation records for newly licensed drivers to conduct the first large-scale longitudinal study. They reviewed the records of 14,936 adolescents and linked the adolescents' electronic health data with New Jersey driver licensing records, traffic violations, and police-reported crash data. Within this group, the researchers identified 1,769 adolescents with childhood-diagnosed ADHD who obtained an intermediate driver's license during the study period, and compared their crash outcomes with those of the drivers without ADHD.

The study team found the crash rate was 62 percent higher for those with ADHD the first month after getting licensed, and 37 percent higher during the first four years after licensure, regardless of their age when licensed. They also found the rates of traffic and moving violations were significantly higher among young drivers with ADHD as compared to those without ADHD. Among these drivers, nearly 37 percent were issued a traffic violation, and nearly 27 percent a moving violation within their first year of driving, compared to 25 percent and 18 percent respectively among their peers without ADHD. Drivers with ADHD had higher rates of alcohol or drug violations and moving violations (including speeding, nonuse of seat belts, and electronic equipment use).

QUICK THOUGHTS

"What this study suggests is that we have to go beyond current recommendations of medication and delaying the age of getting licensed to decrease crash risk for teens with ADHD," Dr. Curry said. "Their higher rate of citations suggest that risky driving behaviors may account for why they crash more. More research is needed to objectively measure if and how these behaviors specifically contribute to crash risk."

WHAT'S NEXT

Additional research is needed to understand the specific mechanisms by which ADHD symptoms influence crash risk so that researchers can develop skills training and behavioral interventions to reduce the risk for newly licensed drivers with ADHD. Because the behaviors identified in the study are amenable to change, clinicians and families can ultimately work with this at-risk group of teens to practice safe driving behaviors and potentially reduce their crash risk.

WHERE THE STUDY WAS PUBLISHED

The study appeared online in the journal *Pediatrics*.

WHO HELPED FUND THE STUDY

The Eunice Kennedy Shriver National Institute of Child Health and Human Development at the National Institutes of Health supported the research.

NURSE-RESEARCHER PRESENTS NATIONAL MODEL FOR BREASTFEEDING VULNERABLE BABIES

THE FINDING

New research presents an alternative model for healthcare providers that focuses on serving the needs of vulnerable infants who are hospitalized and separated from their mothers. The resource is called the Spatz 10-Step and Breastfeeding Resources Nurse Model to Improve Human Milk and Breastfeeding Outcomes.

WHY IT MATTERS

Mothers of critically ill infants may not receive necessary breastfeeding support because their babies may be taken directly to a newborn intensive care unit or to surgery. The 10-Step Model consists of informed decision, establishment and maintenance of milk supply, human milk management, oral care and feeding of human milk, skin-to-skin care, non-nutritive sucking, transition to breast, measuring milk transfer, preparation for discharge, and appropriate follow-up.

WHO CONDUCTED THE STUDY

Diane Spatz, PhD, RN-BC, FAAN, nurse-researcher and founder of the Breastfeeding and Lactation Program at Children's Hospital of Philadelphia developed these models.

HOW THEY DID IT

Dr. Spatz drew upon her own extensive clinical experience and on her NIH funding research studies to create the Spatz 10-Step and Breastfeeding Resources Nurse Model to Improve Human Milk and Breastfeeding Outcomes.

QUICK THOUGHTS

"Because nurses are the largest health profession globally and in the U.S., nurses should play a critical role in providing evidence-based lactation care and support," Dr. Spatz said. "At CHOP, we developed a specialized educational and training program so that nurses across the institution could implement the 10-step model effectively."

WHERE THE STUDY WAS PUBLISHED

The study appeared in the *Journal of Perinatal Neonatal Nursing*.

WHERE TO LEARN MORE

Learn more about this study in this CHOP press release.

GREATER INSIGHT TO CARDIAC DISEASE PROVIDED BY SEQUENCING OF 20,000 HEART CELLS

THE FINDING

Scientists using a powerful new technology that sequences RNA in 20,000 individual cell nuclei uncovered new insights into biological events in heart disease. The researchers worked with animal studies to identify a broad variety of cell types in both healthy and diseased hearts, and they investigated in rich detail the "transcriptional landscape" in which DNA transfers genetic information into RNA and proteins.

WHY IT MATTERS

While the heart is a complex organ, with a multitude of cell types, much still remains to be understood about mammalian heart development and heart disease, especially during the postnatal period. This research provided key insights into normal heart development, heart disease, and gene regulatory mechanisms of a heart hormone called GDF15. The findings lay the groundwork for a greater understanding of cardiac biology and may ultimately lead to targeted therapies aimed at key gene networks that could offer better treatments for heart patients.

WHO CONDUCTED THE STUDY

Liming Pei, PhD, a molecular biologist in the Center for Mitochondrial and Epigenomic Medicine (CMEM) at Children's Hospital of Philadelphia and an associate professor in the Department of Pathology and Laboratory Medicine in the Perelman School of Medicine at the University of Pennsylvania, and Hao Wu, PhD, an assistant professor of Genetics at Penn Medicine co-led the study.

HOW THEY DID IT

The research team was the first to adapt massively parallel single-nucleus sequencing (snRNA-seq) technology for use in postnatal heart tissue. They used the snRNA-Seq method termed sNucDrop-seq to analyze nearly 20,000 nuclei in heart tissue from normal and diseased mice, focusing on cardiomyopathy.

The sequencing tool identified major types of heart cells, such as cardiomyocytes, fibroblasts, and endothelial cells, as well as more rare cardiac cell types. The study team found great variety among each cell type, as well as indications of functional changes in the heart cells during both normal development and diseased conditions.

Another finding concerned gene networks that regulate production of cardiac hormones in heart disease — specifically GDF15. The cardiac synthesis and secretion of GDF15 is increased in heart disease, which slows overall body growth by inhibiting liver growth hormone action and helps reduce the energetic demands on a damaged heart. Such signaling could reveal more about the biological mechanisms that underlie the growth restriction commonly seen in children with congenital heart disease.

QUICK THOUGHTS

"This is the first time to our knowledge that massively parallel single-nucleus RNA sequencing has been applied to postnatal mouse hearts, and it provides a wealth of detail about biological events in both normal heart development and heart disease," Dr. Pei said. "Ultimately, our goal is to use this knowledge to discover new targeted treatments for heart disease. In addition, this type of large-scale sequencing may be broadly applied in many other fields of medicine."

WHAT'S NEXT

Future work by the research team will center on investigating how heart disease progresses over a longer timespan than the early postnatal period. The research tool may also offer opportunities to investigate diseases in organs and systems beyond the heart. Indeed, Dr. Pei's lab is working together with other investigators at CHOP and elsewhere using such single-cell genomics methods to advance our understanding of pediatric biology and disease, including the ambitious goal of a Pediatric Cell Atlas to define the growth phase of human development at single-cell resolution.

WHERE THE STUDY WAS PUBLISHED

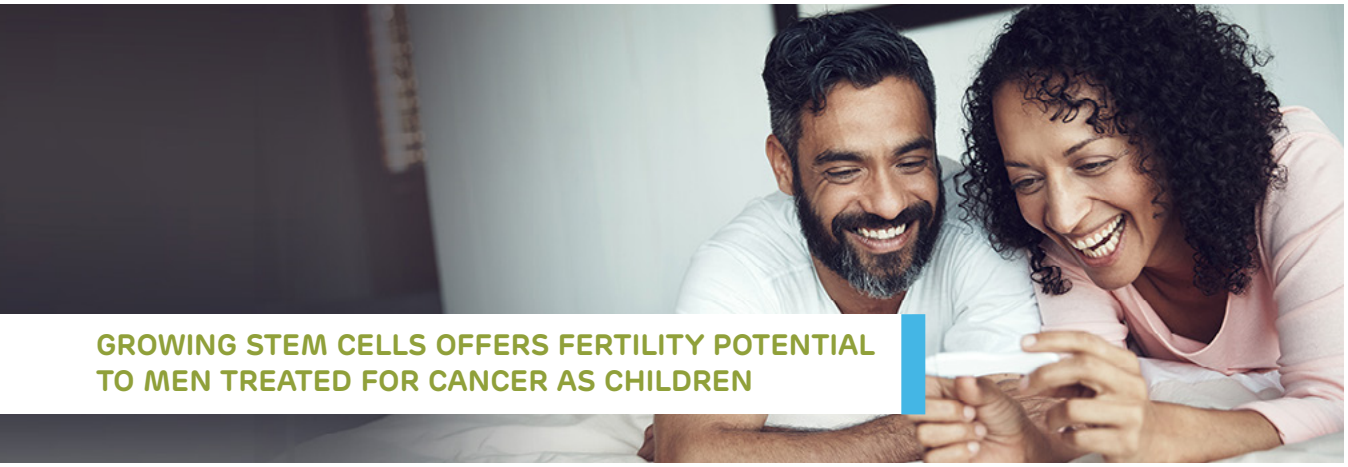
The study appeared in the journal *Genes & Development*.

WHO HELPED FUND THE STUDY

The National Institutes of Health, the Department of Defense, and the W.W. Smith Charitable Trust provided funding for the study.

WHERE TO LEARN MORE

Learn more about this study in this CHOP press release.



GROWING STEM CELLS OFFERS FERTILITY POTENTIAL TO MEN TREATED FOR CANCER AS CHILDREN

THE FINDING

Researchers discovered a way to grow human stem cells destined to become mature sperm, in an effort to provide fertility options later in life to males who are diagnosed with cancer and undergo chemotherapy and radiation as children.

WHY IT MATTERS

According to the American Cancer Society, about one in 530 young adults between the ages of 20 and 39 years is a survivor of childhood cancer. Cancer treatments leave many boys infertile, as chemotherapy and radiation often kill spermatogonial stem cells (SSCs). While there are ways to preserve fertility for boys diagnosed with cancer after puberty, no such options exist for prepubescent boys.

WHO CONDUCTED THE STUDY

Sandra Rveom, PhD, of the Perelman School of Medicine at the University of Pennsylvania; Jill Ginsberg, MD, a pediatric oncologist and director of the Cancer Survivorship Program at Children's Hospital of Philadelphia; and Thomas Kolon, MD, attending pediatric urologist in the Division of Urology at CHOP, co-led the study.

HOW THEY DID IT

Researchers have known that the production of sperm could be restored in mice that were sterilized after chemotherapy by injecting spermatogonial stem cells into their seminiferous tubules in the testes. From this, oncologists suggested that SSCs might be harvested from boys before the start of chemotherapy and reintroduced into their testes when treatment was complete. However, the testes of prepubescent boys contain such a small number of SSCs that, in order for this approach to be successful, the cells would need to be grown and multiplied in the lab prior to subsequent reinjection.

Given these challenges, the investigators identified testicular endothelial cells as a critical niche population for the maintenance and expansion of human SSCs in the lab. Additionally, they also identified five growth factors produced by testicular endothelial cells needed to keep human and mouse SSC cultures alive over the long term. Mouse cells in long-term culture restored the ability to produce sperm after chemotherapy-induced infertility. Researchers are hopeful that eventually patient samples containing the human SSCs could be expanded and used similarly when needed.

QUICK THOUGHTS

"We have never had any fertility preservation options for prepubescent boys," Dr. Ginsberg said. "The findings in this work are a great first step forward for our youngest patients."

WHAT'S NEXT

The next step in the research is to determine whether it is possible to re-inject or engraft the expanded SSCs into patients after they are cancer free.

WHERE THE STUDY WAS PUBLISHED

The study appeared in the journal *Nature Communications*.

SKIN PATCH HELPS PATIENTS WITH 3MILK-INDUCED EOSINOPHILIC ESOPHAGITIS

THE FINDING:

A skin patch measuring just over an inch long containing trace amounts of milk protein may be useful in treating children with a painful, chronic condition called eosinophilic esophagitis (EoE) triggered by milk.

WHY IT MATTERS:

This is the first study to examine how this treatment, called epicutaneous immunotherapy, may help children with milk-induced EoE, a food-based disease that is not helped by traditional allergy testing. If left untreated, EoE may lead to a narrowing of the esophagus due to scarring.

WHO CONDUCTED THE STUDY:

Jonathan Spergel, MD, PhD, chief of the Allergy Program at Children's Hospital of Philadelphia, led the study.

HOW THEY DID IT:

The pilot study followed 20 children ages 4 to 17 with EoE. The patients followed a milk-free diet for nine months, then re-introduced milk into their diet for the next two months. At the end of the study, almost half of those wearing the patch had fewer EoE symptoms, including less inflammation down to the normal range when they underwent an endoscopy compared to none in the placebo group.

QUICK THOUGHTS:

"This study shows great promise for an immunotherapy that aims to desensitize children to milk," Dr. Spergel said.

WHAT'S NEXT:

Dr. Spergel's next step in this line of research is to launch a much larger study to confirm their results. Since there is no cure for EoE, the larger study would be the first strategy to treat the underlying cause of the disease.

WHERE THE STUDY WAS PUBLISHED:

The study appeared online in the journal *Clinical Gastroenterology and Hepatology*.

WHO HELPED FUND THE STUDY:

DBV Technologies funded the study but had no role in analysis or interpretation of data.

WHERE TO LEARN MORE:

Learn more about this study in this CHOP press release.

CLOTTING FACTOR USED TO CONTROL HEMOPHILIA MAY WORK AS PREVENTIVE TREATMENT

THE FINDING

A team of researchers in the Division of Hematology at Children's Hospital of Philadelphia further refined how a treatment currently used on an urgent basis to control bleeding in hemophilia patients holds promise as a preventive treatment as well. Their animal study may set the stage for a new therapy for a subset of patients with hemophilia who develop antibodies to the standard maintenance treatment and then require on-demand "bypass" therapy.

WHY IT MATTERS

"Patients who develop antibodies to the coagulation factors usually prescribed for hemophilia have a complicated treatment," said study leader Paris Margaritis, DPhil. "A different factor, called coagulation factor VIIa, restores blood clotting when given after a bleed occurs, but we don't know the target level of circulating factor VIIa that would prevent bleeds before they start. Our new preclinical results are the first to show target levels that could act prophylactically."

WHO CONDUCTED THE STUDY

Dr. Margaritis, a hematology researcher in the Raymond G. Perelman Center for Cellular and Molecular Therapeutics at CHOP, led the study.

HOW THEY DID IT

Dr. Margaritis and his team have extensively investigated gene transfer in animal models, finding that delivering corrective DNA carrying the coded instructions produced factor VIIa and reduced bleeding episodes. Building upon those studies, the study team worked with a hemophilia A rat model and used adeno-associated virus as a vector to deliver a rat factor VIIa gene, which expressed steadily in the bloodstream, simulating prophylaxis. Hemophilia A rats that had a specific level of factor VIIa in their bloodstream experienced reduced bleeding, and those with a higher level, had no bleeds whatsoever.

QUICK THOUGHTS

"For the first time, we have threshold levels of factor VIIa for prophylactic use," Dr. Margaritis said. "Because factor VIIa bypasses the need for factor VIII or IX, it should work in both hemophilia A and hemophilia B. Furthermore, it works whether or not inhibitors are present in the blood."

WHAT'S NEXT

The next steps are to translate threshold levels in rats to levels in humans and then leverage that information to test the approach in clinical trials.

WHERE THE STUDY WAS PUBLISHED

The study appeared in the journal *Blood Advances*.

WHO HELPED FUND THE STUDY

Novo Nordisk A/S and the National Institutes of Health provided funding for the study.

WHERE TO LEARN MORE

Learn more about this research in this CHOP press release.

KIDNEY DISORDER DRUG MAY BENEFIT PRIMARY MITOCHONDRIAL ENERGY PRODUCTION DISORDERS

THE FINDING

New pre-clinical findings from extensive cell and animal studies suggest that a drug already approved by the U.S. Food and Drug Administration for a rare kidney disease could potentially benefit patients with some primary mitochondrial disorders — complex, multi-system conditions with severe energy deficiency for which no proven effective treatments exist.

WHY IT MATTERS

Because pathogenic variants in over 350 different genes across both nuclear and mitochondrial DNA genomes are now recognized to cause mitochondrial diseases, these disorders are collectively common and highly complex. They typically cause 16 or more major symptoms in each patient, affecting multiple organs and body systems. The current study found therapeutic potential for this repurposed drug in primary mitochondrial disease, based on evidence for neuroprotection in two different animal model species as well as studies in human patient cells.

WHO CONDUCTED THE STUDY

Marni J. Falk, MD, who serves as executive director of the Mitochondrial Medicine Frontier Program at Children's Hospital of Philadelphia, led the study.

HOW THEY DID IT

Dr. Falk and her colleagues have been evaluating a variety of drug candidates for use as possible treatments for mitochondrial RC diseases. For example, they recently found that an antioxidant called NAC (short for N-acetylcysteine) that crosses into the brain showed encouraging pre-clinical results in animal studies. Because cysteamine bitartrate, which is currently approved by the FDA to treat a rare kidney disorder called nephropathic cystinosis, was thought to possibly act similarly to NAC on some biochemical pathways, Dr. Falk's team performed their current pre-clinical research study.

They specifically tested the hypothesis that cysteamine bitartrate would increase synthesis of glutathione, a potent antioxidant enzyme that humans and animals naturally produce from amino acids including cysteine — which can be generated from cysteamine bitartrate to scavenge free radicals. The team learned that cysteamine bitartrate did not, in fact, increase total glutathione levels in their experiments. Nonetheless, Dr. Falk and her team found it had beneficial health effects that appear to result from different mechanisms than they had anticipated.

They found therapeutic potential for cysteamine bitartrate in mitochondrial disease, based on evidence for significant neuroprotection in two different zebrafish vertebrate animal models, improved mitochondrial function and reduced mitochondrial oxidative stress in *C. elegans* worm in vertebrate animal models, and improved survival of mitochondrial disease patient cells when stressed. However, they also showed that the drug has a narrow therapeutic window — even relatively small increases in dosage could dramatically increase free radical production and were toxic in diverse laboratory animals and human cells, implying that dosages would need to be very carefully controlled if cysteamine bitartrate eventually were to become a precision medicine treatment option for mitochondrial disease patients.

QUICK THOUGHTS

"A better understanding of each mitochondrial disease patient's level of oxidative stress and defenses, tested in carefully designed clinical trials to determine the health benefits or risks of candidate therapies from preclinical animal studies, will enable a precision mitochondrial medicine approach to select optimal therapies including antioxidants, and their specific doses, to use to improve health resiliency and outcomes for each patient," Dr. Falk said.

WHAT'S NEXT

Future clinical research is needed to explore whether the drug, cysteamine bitartrate, will meaningfully benefit patients. New clinical diagnostic tests, outcome measure assessments, and advanced data integration and visualization systems to facilitate this process are under development in CHOP's Mitochondrial Medicine Frontier Program.

WHERE THE STUDY WAS PUBLISHED

The study appeared in advance online and in print in the journal *Human Molecular Genetics*.

WHO HELPED FUND THE STUDY

The National Institutes of Health, Raptor Pharmaceuticals, the Juliet's Cure Mitochondrial Disease Research Fund, and the Will Woleben Research Fund funded this research study.

WHERE TO LEARN MORE

Learn more about this study in this CHOP press release.

SIGNALING PATHWAYS IN DEVELOPING LUNGS MAY SHED LIGHT ON FUTURE TREATMENTS

THE FINDING

A team of Children's Hospital of Philadelphia researchers found that specialized lung cells appear in the developing fetus much earlier than scientists previously thought. Their study reported how cells that become alveoli begin their specialized roles very early in prenatal life.

WHY IT MATTERS

Investigating the fetal signaling pathways active in this biological event may offer future opportunities to treat lung damage caused by prematurity and other lung injuries.

WHO CONDUCTED THE STUDY

David B. Frank, MD, PhD, a pediatric cardiologist at CHOP and a member of the Penn Center for Pulmonary Biology and the Penn Cardiovascular Institute, co-led the study with colleagues from the University of Pennsylvania.

HOW THEY DID IT

The research team focused on the basic function of respiration — the exchange of oxygen and carbon dioxide within alveolar type 1 and type 2 cells. They used single-cell RNA sequencing analysis, protein expression studies, and a new lineage-tracing tool to reveal details of early lung formation in a fetal mouse model.

They found that the specification of alveolar cells begins simultaneously with early lung formation, as cells in the developing embryo begin to move apart and branch out into specialized structures such as airways and alveoli. Many lung cells commit themselves to "cell fates," their specialized roles, during branching morphogenesis, which occurs before the formation of the sac-shaped structure that becomes the lung alveolus.

QUICK THOUGHTS

"This cell specification begins remarkably early in lung development, and it progressively seeds the premature lung alveolus throughout the fetus's gestation," Dr. Frank said. "The early presence of these specialized alveolar cells may account for the fact that a minority of extremely premature human babies survive even with underdeveloped lungs."

WHAT'S NEXT

The research team plans to further explore how their findings could eventually contribute to future treatments. A better understanding of lung development could lead to potential tools in regenerative medicine, perhaps by manipulating key signaling pathways or novel progenitor cell targets to grow new lung tissue after injury from prematurity or from acquired lung disease.

WHERE THE STUDY WAS PUBLISHED

The study appeared in the journal *Proceedings of the National Academy of Sciences*.

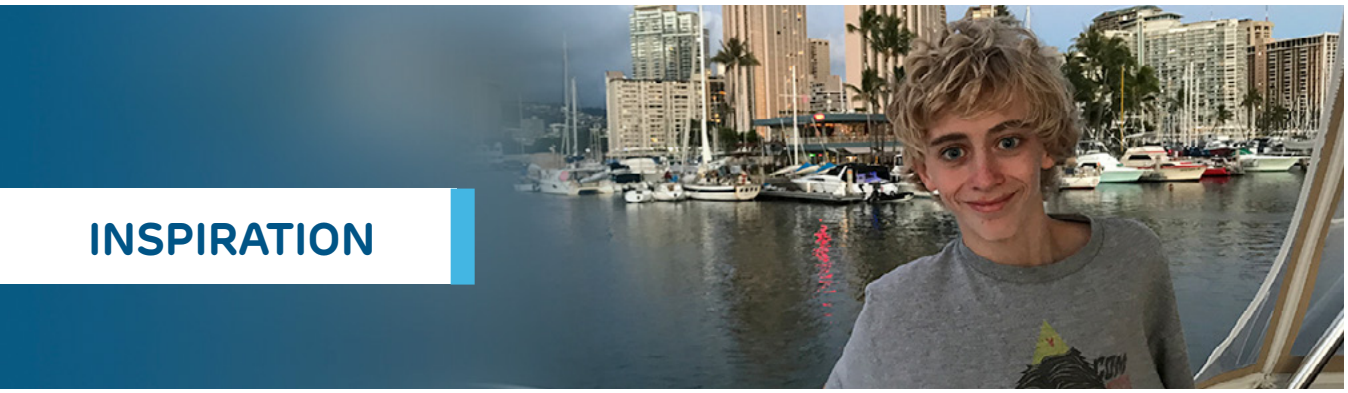
WHO HELPED FUND THE STUDY

The National Institutes of Health, the Parker B. Francis Foundation, the Pulmonary Hypertension Association, Burroughs Wellcome, the National Science Foundation, and the Gilead Research Scholars Foundation provided funding for the study.

WHERE TO LEARN MORE

Learn more about this study in this CHOP press release.

INSPIRATION



FACTS & FIGURES ›

GENETIC DISCOVERY LEADS TO PRECISE TREATMENT FOR CHILD WITH SEVERE LYMPHATIC DISORDER

Daniel, an athletic preteen who played sports and had recently run a 5k, suddenly was in pain and struggling to breathe, with swelling in his lower body. Visits to his primary care doctor revealed no answers, and he was referred to a rheumatologist. When the specialist examined Daniel, there was so much fluid around Daniel's heart, it blocked the sound of his heartbeat.

His family learned lymphatic fluid was leaking into his pericardium, the outer layer of the heart. Cardiologists inserted a drain to remove the fluid, but the area kept filling back up, causing swelling throughout his body. It was at this point that Daniel transferred to Children's Hospital of Philadelphia for evaluation by experts in the Center for Lymphatic Imaging and Interventions, world renowned for its expertise in diagnosing and treating lymphatic system disorders. The team uses an innovative procedure to image and close lymphatic leaks, and they diagnosed Daniel with a severe and rare lymphatic condition.

In a breakthrough discovery, a team of researchers, co-led by Yoav Dori, MD, PhD, a cardiologist and director of the Center for Lymphatic Imaging and Interventions, and Hakon Hakonarson, MD, PhD, director of the Center for Applied Genomics, developed an innovative, precision medicine therapy that would lead Daniel back to health.

MOVING SCIENCE FORWARD

At CHOP, researchers worked to isolate the genetic root of Daniel's disease so they could target therapy to correct his abnormal lymphatic system. Dr. Hakonarson's team performed whole-exome sequencing on Daniel's DNA and that of an adult patient from another center who also had a severe lymphatic condition. The sequencing identified a previously undiscovered gain-of-function mutation in the *ARAF* gene. This gene mutation was driving uncontrolled proliferation of abnormal lymphatic vessels, causing the leak of lymphatic fluid, edema, and respiratory difficulties that Daniel was experiencing.

The researchers explored the function of the *ARAF* mutation by inserting it into the embryos of zebrafish, which are frequently used to model genetic diseases; the zebrafish developed similar abnormal lymphatic channels. The next step was to use a drug called an MEK inhibitor, typically approved for use in patients with melanoma and known to act on biological pathways affected by *ARAF*. Then came some great news: The drug "rescued" the structural defect in the zebrafish, causing them to develop normal lymphatic vessels.

The physician-scientists had saved the fish – and they were determined to save Daniel, too.

With no time to waste, Drs. Dori and Hakonarson consulted with Jean Belasco, MD, from the CHOP Oncology team, who helped obtain compassionate permission from the U.S. Food and Drug Administration to treat Daniel with an MEK inhibitor called trametinib.

Within two months after starting the experimental treatment in March 2017, Daniel's breathing improved. Three months after starting the treatment, he had reduced fluid retention and was able to cut back on supplemental oxygen, start breathing room air, and begin more physical activity. An MRI showed that his lymphatic vessels were remodeling themselves, with no signs of leaks. The heavy swelling in Daniel's legs gradually disappeared.

SETTING A NEW COURSE

"This case is a dramatic example of implementing a precision medicine treatment for a life-threatening rare disease," Dr. Hakonarson said. "We discovered a causative gene mutation in two patients, identified an existing drug that acts on that gene's pathway, showed that the drug relieves the condition in lab animals, and then successfully treated the original patient."

What Dr. Hakonarson summarizes here was, of course, a years' long journey through pain, uncertainty, surgical procedures, treatment, and perseverance that ultimately led to discovery.

The result may form the basis of a new therapy for this type of defective lymphatic circulation. Drs. Dori and Hakonarson said this research is the first real evidence for complete remodeling of an entire organ system by a drug, and it offers potential new research pathways to explore for many patients with similar lymphatic flow disorders. The discovery appeared in *Nature Medicine* in July 2019.

As a result of Daniel's case, all lymphatics patients are now also seen by the genomics team, and CHOP is expanding a Frontier program in complex vascular anomalies that investigates underlying genetic mutations that impair normal development of blood or lymphatic vessels.

"As difficult as this process of discovery, experimentation and treatment has been, we are so grateful for the perseverance and skill of his medical team, in addition to Daniel's resilience and optimism," said Daniel's mother, Anna. "The fact that Daniel's case has the potential to help countless other patients is a silver lining for sure."

BACK TO BEING A TEEN

Now 15-years-old, Daniel has been able to resume many normal activities, such as riding his bicycle, playing basketball, weight training, and helping to coach soccer camps. As he prepared to begin his freshman year of high school, his mother couldn't help but recall the long way he's come in a relatively short time.

"Just over two years ago, Daniel was getting measured for a wheelchair and had to be tutored at home," she said. "Now he's back at school full time and is able to be active with his friends."

FACTS & FIGURES

FINANCIAL/STATS INFO

$472,014,095

TOTAL RESEARCH OPERATING EXPENSES

$261,338,746

EXTERNAL GRANTS AND CONTRACTS

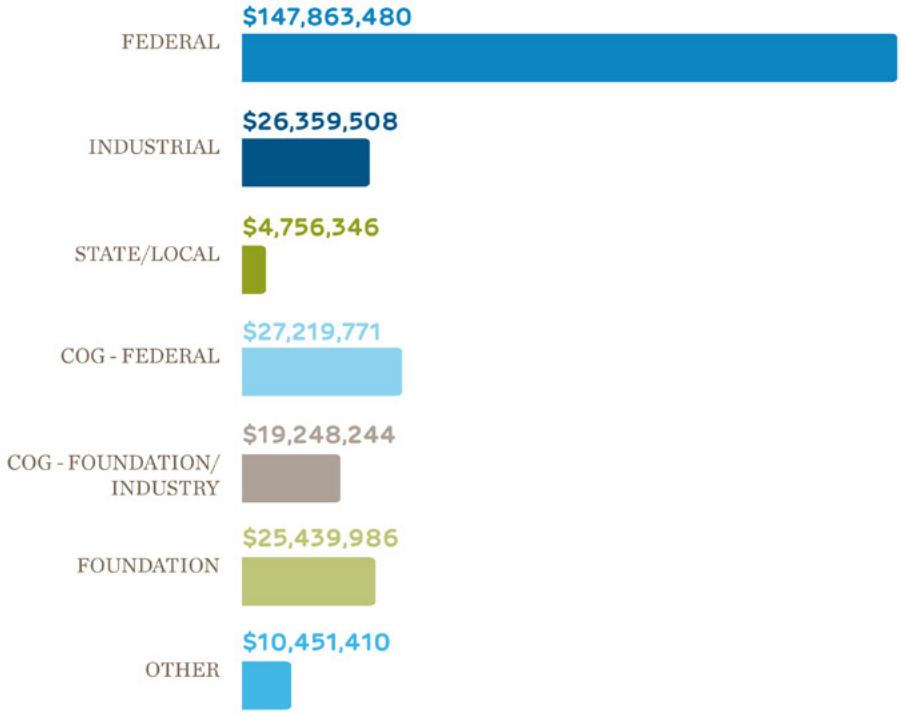
$169,556,684

693 AWARDS

2,779

PUBLICATIONS


$261,338,746
EXTERNAL FUNDING
GRANTS & CONTRACTS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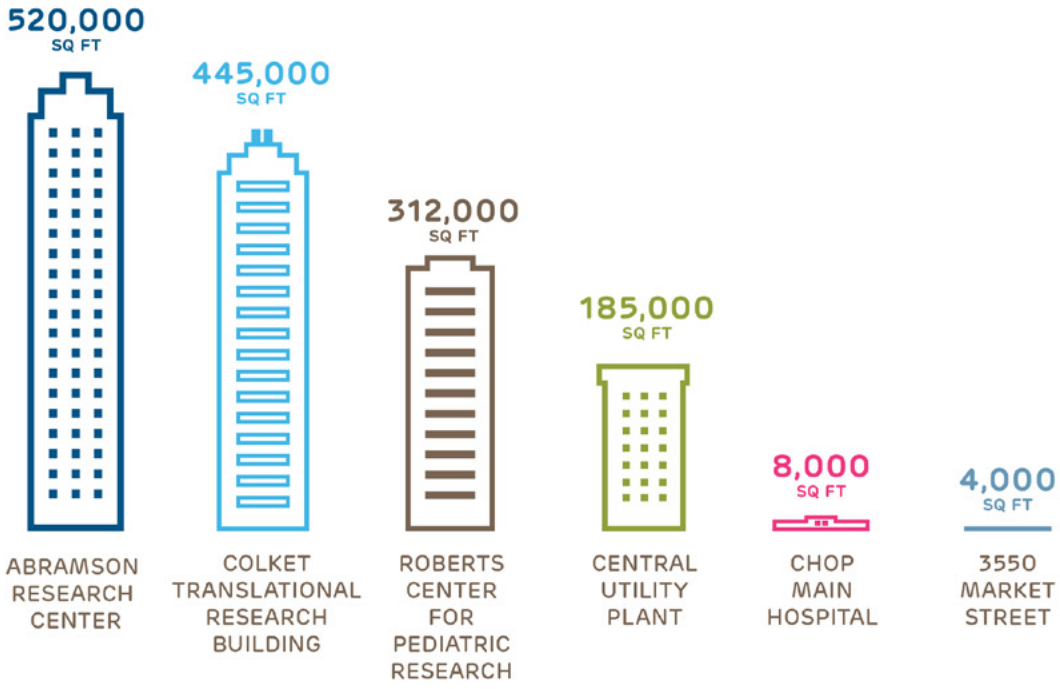
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185,000
SQ FT
CENTRAL UTILITY PLANT
8,000
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CHOP MAIN HOSPITAL
4,000
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3550 MARKET STREET

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- Center for Childhood Cancer Research
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- Center for Clinical Pharmacology
  Director: Athena F. Zuppa, MD, MSCE
- Center for Computational and Genomic Medicine
  Director: Yi Xing, PhD

- Center for Data-Driven Discovery in Biomedicine (D3b)
  Directors: Jay Storm, MD, Adam C. Resnick, PhD, and Jena Lilly

- 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
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- PolicyLab
  Director: David Rubin, MD, MSCE

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

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RESEARCH AFFINITY GROUPS

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  Leader: Yair Argon, PhD, and Janis K. Burkhardt, PhD

- Clinical Trials
  Leader: Pamela Weiss, MD, MSCE

- Developmental Biology
  Leaders: Stewart Anderson, MD, and Judy Grinspan, PhD

- Fetal Biology and Therapy
  Leader: Alan Flake, MD

- Genes, Genomics, and Pediatric Disease
  Leaders: Yael P. Mossé, MD, and Marcella Devoto, PhD

- Global Health
  Leaders: Elizabeth Lowenthal, MD, MSCE

- Health and Behavior
  Leaders: Stephen Leff, PhD, and Joel Fein, MD, MPH

- Metabolism, Nutrition, and Physical Development
  Leader: Babette Zemel, PhD

- MetaCHOP
  Leader: Helen Loeb, PhD

- mHealth
  Leaders: Nadia L. Dowshen, MD, MSHP, Linda Fleisher, PhD, MPH, and Lisa Schwartz, PhD

- Mitochondria
  Leader: Marni Falk, MD, and Eiko Nakamara-Ogiso, PhD

- Neuroscience
  Leader: Michael Robinson, PhD

- Normal and Malignant Hematopoiesis
  Leader: Carolyn Felix, MD

- 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 F.A. Grant, PhD, Andrew D. Wells, PhD, and Gerd Blobel, MD, PhD

ENDOWED CHAIRS

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

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  Holder: Adam C. Resnick, PhD

- **Alice Langdon Warner Endowed Chair in Pediatric Cardiothoracic Surgery**
  Holder: Christopher E. Mascio, MD

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

- **Arthur Vincent Meigs President's Scholars Endowed Chair**
  Holder: Beverly L. Davidson, PhD

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

- **Buck Family Endowed Chair in Hematology Research**
  Holder: Peter Kurre, MD

- **C. Everett Koop Endowed Chair in Pediatric Surgery**
  Holder: N. Scott Adzick, MD, MMM, FACS, FAAP

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

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  Holder: Daniela H. Davis, MD, MSCE

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  Holder: Beverly S. Emanuel, PhD

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  Holder: Audrey O. John, MD, PhD

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  Holder: Sarah Evans

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

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

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

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  Holder: Pending Appointment

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

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

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

› **Department of Radiology Endowed Chair in Molecular Imaging**
Holder: Lisa J. States, MD

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Holder: Ian D. Krantz, MD

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

› **Distinguished Chair in the Department of Pediatrics**
Holder: Daniel C. West, MD

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

› **Distinguished Chair in the Department of Pediatrics**
Holder: Maully Shah, MBBS, FACC, FHRS, CCDS, CEPS

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Holder: Alexander G. Fiks, MD, MSCE

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- **Distinguished Chair in the Department of Pediatrics**
  Holder: Diva D. DeLeón-Crutchlow, MD, MSCE

- **Distinguished Chair in the Department of Pediatrics**
  Holder: Sandra Amaral, MD, MHS

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  Holder: Maurizio Pacifici, PhD

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

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

- **Elias Schwartz, M.D. Endowed Chair in Hematology**
  Holder: Kim Smith-Whitley, MD

- **Elizabeth B. Weller Endowed Chair in Psychiatry**
  Holder: Pending Appointment

- **Elizabeth Paige Lavin Endowed Chair in Research in Clinical Care and Immunology**
  Holder: Jennifer R. Heimall, MD

- **Endowed Chair in Pediatric Interventional Radiology**
  Holder: Anne Marie Cahill, MBBch, BAO

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

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

- **Evelyn Willing Bromley Endowed Chair in Clinical Laboratories and Pathology**
  Holder: Dimitrios S. Monos, PhD

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

- **Francis West Lewis Endowed Chair in Computational and Genomic Medicine**
  Holder: Yi Xing, PhD

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

- **Frank R. Wallace Endowed Chair in Infectious Diseases**
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- **Fred and Suzanne Biesecker Endowed Chair in Pediatric Liver Disease**
  Holder: David A. Piccoli, MD

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

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Holder: Julie S. Moldenhauer, MD

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› **Giulio D'Angio Chair in Neuroblastoma Research**
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Holder: Brenda L. Banwell, MD

› **Harriete and Ronald Lassin Endowed Chair in Pediatric Neonatology**
Holder: Scott A. Lorch, MD, MSCE

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

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

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

› **Irma and Norman Braman Endowed Chair for Research in GI Motility Disorders**
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› **Jacob A. Kamens Endowed Chair in Neurological Disorders and Translational NeuroTherapeutics**
Holder: Adeline Vanderver, MD

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Holder: Gordon Barr, PhD

› **Jane Fishman Grinberg Endowed Chair in Stem Cell Research**
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Holder: Virginia A. Stallings, MD

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Holder: Stephen P. Hunger, MD

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› **Jennifer Terker Endowed Chair in Pediatric Cardiology**
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› **John W. Duckett, Jr. Endowed Chair in Pediatric Urology**
Holder: Stephen A. Zderic, MD

› **John Westgate Hope Endowed Chair in Radiology Faculty Development**
Holder: Savvas Andronikou, MBBch (Wits), PhD, FCRad (Diag)

› **Joseph Lee Hollander Endowed Chair in Pediatric Rheumatology**
Holder: Edward M. Behrens, MD

› **Josephine J. And John M. Templeton Jr. Endowed Chair In Pediatric Trauma**
Holder: Michael L. Nance, MD

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

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

› **Justin Michael Ingerman Endowed Chair in Palliative Care**
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Holder: Susan L Furth, MD, PhD

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Holder: Douglas A. Canning, MD

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

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

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

› **Lisa Zaoutis Endowed Chair in Pediatric Education**
Holder: Jeanine Ronan, MD

› **Louis and Amelia Canuso Family Endowed Chair for Clinical Research in Oncology**
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› **Louis Starr Endowed Chair in Pediatrics**
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› **Louise Schnaufer Endowed Chair in Pediatric Surgery**
Holder: Holly L. Hedrick, MD

› **Lucy Balian Rorke-Adams Endowed Chair in Neuropathology**
Holder: Angela Viaene, MD, PhD

› **Lynne L. Garbose Endowed Chair in Fetal Family Care**
Holder: Lori J. Howell, DNP, MS, RN

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

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

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

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

› **Mary Downs Endowed Chair in Craniofacial Surgery and Research**
Holder: Scott P. Bartlett, MD

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

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

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

› **Minimally Invasive Surgery Endowed Chair in Pediatric Urology**
Holder: Aseem R. Shukla, MD

› **Morgan Family Endowed Chair in Pediatric Surgery**
Holder: Peter Mattei, MD

› **Mortimer J. Buckley Jr. M.D. Endowed Chair in Cardiac Surgery**
Holder: Jonathan M. Chen, MD

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

› **Nicholas Crognale Chair in Pediatric Emergency Medicine**
Holder: Kathy Shaw, MD, MSCE

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

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

› **Patricia "Pat" Brophy Endowed Chair in Neuroblastoma Research**
Holder: Yael P. Mossé, MD

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

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

› **Peter Randall Chair in Plastic and Reconstructive Surgery**
Holder: Jesse A. Taylor, MD

› **President's Scholars Endowed Holding Fund**
Holder: Pending Appointment

› **R. Anderson Pew Distinguished Chair in the Department of Pediatrics**
Holder: Kristy B. Arbogast, PhD

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

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

› **Richard and Sheila Sanford Endowed Chair in Pediatric Oncology**
Holder: Sogol Mostoufi-Moab, MD, MSCE

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

› **Richard D. Wood Jr. and Jeanette A. Wood Endowed Chair in Pediatric Diagnostic Medicine**
Holder: Louis M. Bell, MD

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

› **Richard Shafritz Endowed Chair in Pediatric Opthalmology Research**
Holder: Gil Binenbaum, MD, MSCE

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

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

› **Robert M. Campbell Jr. Endowed Chair in Thoracic Insufficiency Syndrome**
Holder: John M. Flynn, MD

› **Robert Zimmerman Endowed Chair in Pediatric Neuroradiology**
Holder: Larissa T. Bilaniuk, MD

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

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

› **Ruth M. Colket Endowed Chair in Pediatric Nursing**
Holder: Martha A.Q. Curley, PhD, RN, FAAN

› **Soroosh Mahboubi Endowed Chair in Body Imaging at Children's Hospital of Philadelphia**
Holder: Sudha A. Anupindi, MD, FSAR

› **Stanley Plotkin Chair in Pediatric Infectious Disease**
Holder: Jeffrey M Bergelson, MD

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

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

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

› **Surgical Technology and Technique Endowed Chair in Pediatric Surgery**
Holder: Thane A. Blinman, MD, FACS

› **Suzi and Scott Lustgarten Endowed Chair for Clinical Care of GI Motility Disorders**
Holder: David A. Piccoli, MD

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

› **The Children's Hospital of Philadelphia Endowed Chair in Fetal Imaging**
Holder: Beverly G. Coleman, MD, FACR

› **The Children's Hospital Endowed Chair in Cardiac Critical Care Medicine**
Holder: Andrew T. Costarino, Jr., MD, MSCE

› **The Children's Hospital of Philadelphia Endowed Chair in Biomedical Informatics and Entrepreneurial Science**
Holder: Fuchiang (Rich) Tsui, PhD

› **Thomas Frederick McNair Scott Endowed Chair in Pediatrics**
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› **Thomas L. Spray, MD Endowed Chair in Pediatric Cardiothoracic Surgery**
Holder: Stephanie Fuller, MD

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

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  Holder: Robert R. Clancy, MD

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

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

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

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

- **William L. Van Alen Endowed Chair in Pediatric Radiology**
  Holder: Kassa Darge, MD, PhD, DTM&P, FSAR, FESUR

- **William Potsic Endowed Chair in Pediatric Otolaryngology and Childhood Communication**
  Holder: Ralph F. Wetmore, MD

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

- **William Wikoff Smith Endowed Chair in Pediatric Genomic Research**
  Holder: Fanxin Long, PhD

- **Yetta Deitch Novotny Chair in Pediatric Oncology**
  Holder: Stephan A. Grupp, MD, PhD

ADMINISTRATIVE UNITS

- Academic Training and Outreach Programs
  Wendy Williams, PhD, Director
  Paulette McRae, PhD, Assistant Director, Specialty Programs and Diversity
  David Taylor, PhD, Associate Director, Academic Training
  Jodi Leckrone, Associate Director, Outreach Programs

- Business Operations
  Pending Appointment

- Clinical Research Support Office
  Richard Aplenc, MD, PhD, MSCE, Assistant Vice President and Chief Clinical Research Officer
  Elizabeth "Betsy" Goldmuntz, MD, Associate Chief Clinical Research Officer
  Jeffrey Gerber, MD, PhD, Associate Chief Clinical Research Officer
  Kristina Harr, JD, Director, Clinical Trial Support
  Veronica Kain, Director, Clinical Trial Financial Management
  Michele Toms, BSN, RN, CCRC, Administrative Director, Clinical Research Staffing Core

- Core Facilities Administration
  Lisa MacDowell, Director

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Beverly Davidson, PhD, Chief Scientific Strategy Officer

› Institutional Review Board
Amy Schwarzhoff, MS, MBA, CIP, Director, Human Subjects Research

› Non-Traditional Research Personnel
Kaila Gammon, Business Manager

› Pre-Award Research Administration
Brent Bell, Director

› Post-Award Research Administration
Liza Craig, Director

› Project Management Office
Anne Geary, Senior Program Manager

› Research Creative Services
Pending Appointment

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Denise Ancharski-Stutler, Administrative Director, IACUC Administration
Neil Patel, Manager, Investigational Drug Service

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Bethann Kurek, Assistant Director

› Research Information Systems
John Knab, Senior Director

› Research Resources
Howard Eck, Director

› Research Safety
Denise Melvin, Director

› Office of Technology Transfer, Innovation and Research Contracts
Zev Sunleaf, Vice President, Technology Transfer, Innovation, and Research Contracts
Camille Jolly-Tornetta, Director, Technology Transfer
Thomas Privette, Head, Global Business Development and External Partnering
Charles Bartunek, Director, Collaborative and Corporate Research Contracts

› Veterinary Resources
Laike Stewart, VM, DACLAM, Senior Director

CREDITS

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  Chief Executive Officer
- Bryan A. Wolf, MD, PhD
  Chief Scientific Officer & Executive Vice President
- Michelle A. Lewis
  Vice President, Research Administration and Operations
- **Angela Knott**
  Interim Director, Creative Services
- **Jennifer Long**
  Director (former), Research Communications
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  Content and Creative Manager
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- **Barbara Drosey**
  Medical/Science Writer
- **Nancy McCann**
  Medical/Science Writer
- **Juliet Kilcoyne**
  Interim Art Director
- **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 Instagram 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 Creative Services produced the 2019 Research Annual Report.