2021
ANNUAL RESEARCH REPORT

Children's Hospital of Philadelphia®
RESEARCH INSTITUTE

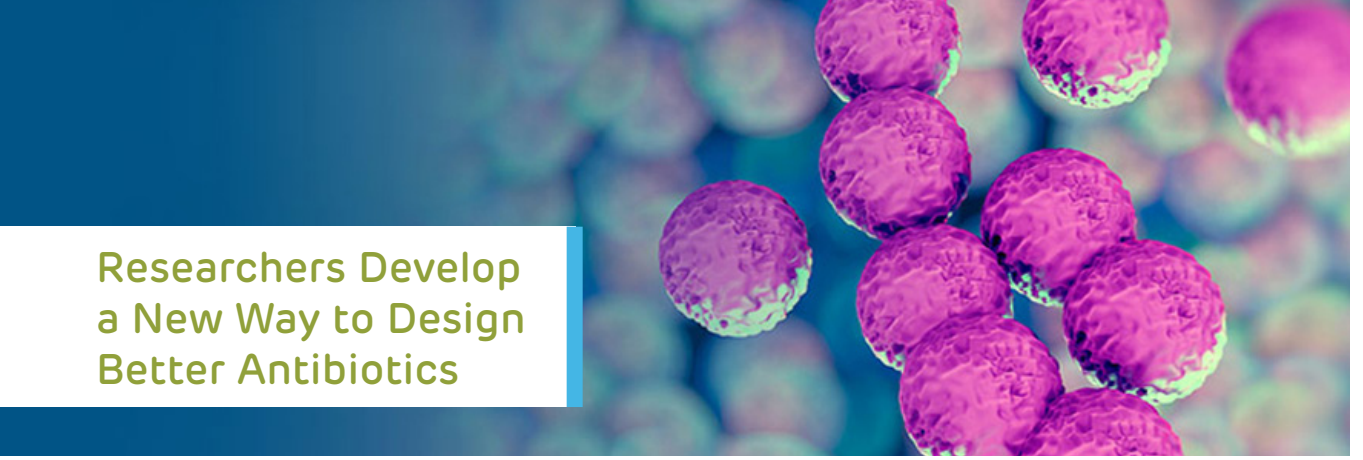
Shaping the Future

The 2021 Research Annual Report focuses on our patient-driven research that broadens the world of possibility for more children. At the same time, the Research Institute is developing a diverse and inclusive culture where investigators and staff at all levels and from all backgrounds feel welcome and respected. In our Inspiration story, learn more about our long-standing commitment to increasing diversity in the STEM-M pipeline, celebrate our accomplishments, and see what programs are in the works.

CONTENTS

Novel Approaches, Therapeutics, and Devices Accelerate Breakthroughs

New vaccine approaches and an FDA-approved non-surgical heart valve replacement device are among the many novel therapeutics and devices developed by our researchers, who are committed to collaboration and excellence on their quest for pediatric science discovery.



Researchers Develop a New Way to Design Better Antibiotics

IMPORTANT STEP FORWARD

"We've created a sort of 'Trojan horse' that would allow antibiotics to reach desired tissues undisturbed."

By using structure-guided design, researchers in the John Laboratory at Children's Hospital of Philadelphia developed a novel approach for developing new antibiotics that are able to reach resistant bacteria.

This newly established method reported in *eLife* takes a cue from the Trojan horse strategy in Homer's epic poem, *The Odyssey*, by creating prodrugs, or blocking agents, that conceal the antibiotics and then allow them to be revealed and released — by the bacteria themselves — once the antibiotics arrive at the site of infection. By learning how the mechanism by which the bacteria remove the prodrug, the research team designed a better way of delivering the effective compound without releasing the prodrug early and missing the intended target, which has been a major challenge in the effort to develop effective antibiotics.

"We've created a sort of 'Trojan horse' that would allow antibiotics to reach desired tissues undisturbed, until the bacteria itself activates the drug, effectively releasing an 'army' of antibiotics," said senior author Audrey Odom John, MD, PhD, chief of the Division of Infectious Diseases. "Using structure-guided design, we have developed a new way to design better antibiotics. Given the growing concern over antimicrobial resistance, we think this is an important step forward."

Managing Mitochondrial Disease With Effective Combination of Therapies

OPTIMIZED THERAPY REGIMEN

"We've gotten a lot smarter about the genetics of mitochondrial disease ..."

Mitochondrial disease comprises a group of energy deficiency disorders that impair mitochondrial respiratory chain function — a function necessary to make energy to power cells in the body. Healthcare providers often recommend vitamins and supplements to patients but do so with no definitive knowledge about how much to recommend, or what formulation to recommend, or if there is any value to combining several types of vitamins or supplements.

In a preclinical study, led by Marni Falk, MD, executive director of CHOP's Mitochondrial Medicine Frontier Program, the researchers identified a group of three drugs that may be a potential effective treatment for mitochondrial disease. The findings showed that a combination of glucose, nicotinic acid, and N-acetylcysteine — all vitamins or supplements that are available over the counter — appears to be beneficial for patients with mitochondrial respiratory chain disorders.

"The variable combinations of therapies used to manage mitochondrial disease patients tend to include empirically-based 'cocktails' of vitamins and nutrients whose safety and efficacy are difficult to objectively evaluate and compare," Dr. Falk said. "Our preclinical study demonstrates that identifying the right combination of therapies that is rationally designed based on addressing the unique cellular deficiencies of major mitochondrial disease classes can provide clear, measurable survival benefits over individual therapies that each address only part of the cellular problem."

Drug for Rare Form of Pediatric Cancer Approved by FDA

A PIVOTAL ROLE

"This is a big step forward and one that will give hope to many patients and families."

The Food and Drug Administration approved crizotinib, also known by its brand name Xalkori, a first generation ALK inhibitor, for the treatment of pediatric patients witha rare form of non-Hodgkin's lymphoma known as ALK-fusion positive relapsed/refractory anaplastic large cell lymphoma (ALCL). Approximately 90 percent of pediatric ALCL cases are ALK-positive. The approval was based on a pivotal study led by CHOP researchers through the Children's Oncology Group.

Yael Mossé, MD, an oncologist in CHOP's Cancer Center and co-leader of the Genes, Genomics, and Pediatric Disease Research Affinity Group, has researched ALK alterations in the context of several cancers and was the principal investigator for several studies that led to the FDA approval of this cancer treatment drug.

"The approval of Xalkori marks an important moment for pediatric patients with ALK-positive ALCL who suffer a relapse during or after standard upfront chemotherapy, and who now have another treatment option that may one day prove to be an integral component of curative therapy," Dr. Mossé said "This is a big step forward and one that will give hope to many patients and families."

Food and Drug Administration Approves Non-surgical Heart Valve Replacement Drive

A LESS INVASIVE APPROACH

"Researchers in the Cardiac Center at CHOP are committed to bringing our expertise to the development of cutting-edge treatments."

Approximately 40,000 infants each year are affected by congenital heart disease, the most common birth defect in the United States. These tiny patients face several open-heart surgeries over their lifetimes to correct issues related to their dysfunctional pulmonary valves. However, with a new non-surgical device approved by the FDA, less invasive procedures can now reduce the many risks associated with open heart surgery.

CHOP was the lead enrolling site in the clinical trial that led to the FDA approval of the Harmony™ Transcatheter Pulmonary Valve. This medical technology advancement allows for pulmonary valve replacement via a minimally invasive catheter-based procedure. The device consists of a self-expanding metal frame combined with valve leaflets that can be implanted inside a patient's heart and will require less anesthesia, reduce the risk of infection, and lead to a faster recovery, than open heart surgery.

"The approval of this device will allow us to provide a non-surgical option to patients with congestive heart disease, reducing or eliminating the need for multiple open heart surgeries over the course of a patient's lifetime," said CHOP site PI, Matthew Gillespie, MD, interventional cardiologist in the Cardiac Center, director of CHOP's Cardiac Catheterization Laboratory, and co-director of its Center for Pediatric Heart Valve Disorders. "Researchers in the Cardiac Center at CHOP are committed to bringing our expertise to the development of cutting-edge treatments, which will improve the lives of our patients and their families."

Image courtesy of Medtronic.

Study Shows New Standard of Care for High-risk Relapse B-ALL

LESS TOXIC, BETTER OUTCOMES

"This study shows that blinatumomab can replace chemotherapy in certain subsets of B-ALL because it is less toxic and leads to better outcomes."

Researchers with CHOP's Cancer Center, in collaboration with 154 other hospitals in the Children's Oncology Group, revealed that the drug blinatumomab, a bispecific T-cell engaging antibody, is less toxic than chemotherapy for high-risk relapsed B-cell acute lymphoblastic leukemia (B-ALL). The findings reported in *JAMA* suggest blinatumomab as the standard of care for patients with the high-risk, difficult-to-treat cancer.

Blinatumomab links a patient's CD3+ T cells to CD19+ leukemia cells, inducing an immune response that destroys the cancer cells. The Food and Drug Administration approved this targeted treatment for patients — adults and children — with relapsed/refractory B-ALL and minimal residual disease (MRD)- positive B-ALL.

"When it comes to high-risk cancers like relapsed B-ALL, we have reached a plateau in what we can accomplish with more intense chemotherapy, which comes with numerous toxic side effects," said co-senior author Stephen Hunger, MD, chief of the Division of Oncology, and director of the Center for Childhood Cancer Research. "This study shows that blinatumomab can replace chemotherapy in certain subsets of B-ALL because it is less toxic and leads to better outcomes. Additional studies will examine this therapy in other disease stages of B-ALL to see if it has a similar benefit."

Researchers Advance Vaccine Approach for Nontypeable Haemophilus Influenzae

VACCINE POTENTIAL AGAINST DIVERSE NTHI STRAINS

"Taken together, the findings in this study highlight the vaccine potential of the HMW1 and HMW2 proteins."

CHOP researchers, including Joseph St. Geme, MD, physician-in-chief and chair of the Department of Pediatrics at CHOP, have identified two proteins that could be used for a potential vaccine against nontypeable *Haemophilus influenzae* (NTHi). The most common cause of bacterial respiratory tract infections, NTHi can cause middle ear infections, sinus infections, and exacerbations of chronic obstructive pulmonary disease (COPD) and other underlying lung disease, resulting in significant morbidity in both children and adults.

The scientists focused their research on two proteins — HMW1 and HMW2 — involved in NTHi colonization of the nasopharynx (upper part of throat, behind nose), the first step in the pathogenesis of NTHi disease. These proteins help the bacteria adhere to respiratory cells and are present in approximately 75 to 80 percent of NTHi strains.

The study findings reported in the *Proceedings of the National Academy of Sciences of the United States of America* showed that administering these two adhesive proteins stimulated protective immunity against not only the parent strain of NTHi from which the adhesive proteins were derived, but also other diverse NTHi strains, highlighting the vaccine potential.

"Currently there are no vaccines or other approaches to protect against infection due to this organism," said senior author Dr. St. Geme. "Our study has identified two proteins that stimulate both an antibody response and a broader cell-mediated immune response that protect against diverse strains of NTHi *influenzae* and thus may be valuable for inclusion in a vaccine to protect against a full range of NTHi disease."

Curiosity and Technology Help to Find Drivers of Rare and Complex Diseases

Learn about advances that offer hope for healthier, happier lives: a new disease discovery, a unique partnership to study links between mitochondrial disease and pediatric cancer, and identification of the underlying genetic causes for several rare and complex pediatric diseases.

New Disease Called PU.MA Prevents Antibody Formation

NEW IMMUNODEFICIENCY DISEASE

"We think just like PU.MA taught us all about B-cell development, these patients can teach us a lot about more common disorders including autoimmune diseases and cancer."

Researchers at CHOP discovered a new immunodeficiency disease, which they named PU.1 Mutated Agammaglobulinemia (PU.MA), that prevents the formation of infection-fighting B cells and antibodies. They performed whole exome sequencing on 30 patients born without B lymphocytes and discovered that six patients had a mutation in the *SPI1* gene. This gene encodes the PU.1 protein, and because of the mutation, there was less PU.1, and B cells were unable to form. The findings appeared in the *Journal of Experimental Medicine*.

The paper's senior author, Neil Romberg, MD, investigator in the Department of Pediatrics, and the first author, Carole Le Coz, PhD, collaborated with numerous CHOP departments, including the Roberts Individualized Medical Genetics Center, the Center for Spatial and Functional Genomics, and the Cancer Center, as well as institutions worldwide.

"Identifying rare genetic variants in patients is now faster, cheaper, and more readily available using next-generation sequencing," Dr. Romberg said. "Proving variant causality still requires multiple orthogonal scientific approaches and big collaborative teams that ideally include patients/patient families."

Clinical Traits Identified for Major Gene Linked to Epilepsy and Autism

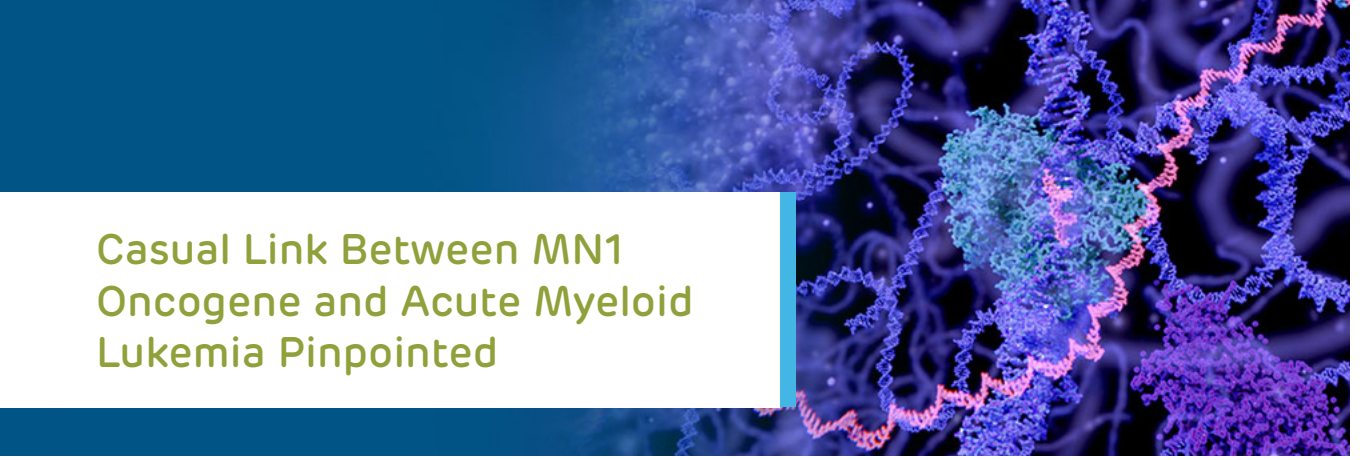
FULL PHENOTYPIC LANDSCAPE

"Our findings help define subclasses within SCN2A-related disorders that could pave the way for future precision medicine approaches to help these individuals."

CHOP researchers affiliated with the Epilepsy Neurogenetics Initiative (ENGIN) compiled a genetic and clinical analysis of more than 400 individuals with SCN2A-related disorder, which is linked to various neurodevelopmental disorders, including epilepsy and autism. Linking the clinical features to genetic abnormalities in a standardized format may help improve identification of the disorder and clinical intervention.

Researchers led by Ingo Helbig, MD, director of the genomic and data science core of ENGIN, used Human Phenotype Ontology (HPO), a method that standardizes patients clinical features and allows that data to be translated like genetic data. They extracted phenotypic information from SCN2A-related disorders published over nearly two decades. Across 413 unrelated individuals, the study team derived more than 10,000 clinical annotations in HPO terms, with a total of 562 unique terms, allowing the researchers to link clinical features with specific gene variants. The findings appeared in *Genetics in Medicine*.

“This work, built upon our previous studies, now provides a framework on how HPO terminology can map complex clinical data in a variety of rare disorders to get to answers about clinical features, natural history, and outcomes that we do not have yet,” Dr. Helbig said.



Casual Link Between MN1 Oncogene and Acute Myeloid Lukemia Pinpointed

NOVEL MECHANISTIC LINK

"What's exciting about this research is its potentially broad implications."

Researchers in the CHOP Cancer Center discovered that the oncogene meningioma-1 (MN1) is linked to acute myeloid leukemia (AML) through its effect on the BAF complex, a site crucial for the regulation and differentiation that is mutated in about 20 percent of cancers. They found that overexpression of MN1 strengthens the BAF complex's interaction with DNA, which has consequences on blood cell production.

In addition, researchers found that MN1's ability to stabilize the BAF complex is dependent on an MN1 protein structure called the polyQ-stretch. PolyQ-stretches are best known for their role in neurodegenerative diseases. Researchers found that deleting the polyQ-stretch impairs MN1's ability to over-stabilize the BAF complex binding to DNA, thus allowing blood cells to differentiate normally. The study appears in *Molecular Cell*.

"What's exciting about this research is its potentially broad implications," said Kathrin Bernt, MD, a physician-scientist in the Leukemia and Lymphoma Program, and senior author of the paper. "This is a look at how cancer can happen beyond the classic mechanisms of overactive signaling and DNA damage."

Researchers Implicate New Genetic Variants in Neurodevelopmental Disease

SMARCA5 VARIANTS ASSOCIATED WITH DEVELOPMENTAL CHANGES

"Our findings expand the spectrum of neurodevelopmental disorders linked to chromatin remodeling genes."

Researchers in the Center for Applied Genomics (CAG) identified how variants of a gene responsible for packing and condensing genetic material cause certain neurodevelopmental disorders. The gene, *SMARCA5*, is responsible for encoding a chromatin remodeling complex. Preclinical evidence suggests that variants of this gene were associated with developmental changes, but a specific disorder was never described.

The study, which appeared in *Science Advances*, reports on 12 patients across 10 unrelated families. The patients had similar clinical features, including mild developmental delay, short stature, and microcephaly.

"Our study is the first to describe how certain germline mutations in SMARCA5 are responsible for a spectrum of neurodevelopmental delays," said study leader Dong Li, PhD, a research scientist in CAG. "Apart from identifying patients with such germline variants for the first time, our extended translational modeling study efforts to determine the underlying functions for these variants further elucidated their clinical relevance."

Dr. Li collaborated with Yuanquan Song, PhD, of the Department of Pathology and Laboratory Medicine at CHOP. Hakon Hakonarson, MD, PhD, director of CAG, was the senior author of the study.

Gene Linked to Imapired Stem Cell Regeneration in Ribosomopathies

PAVING THE WAY FOR POTENTIAL THERAPIES

"We found a mechanism that prevents ribosomes from assembling properly in mammals, leading to stem cell defects, which could potentially be exploited in future therapeutic interventions."

Researchers led by Wei Tong, PhD, investigator in the Division of Hematology at CHOP, identified a protein coding gene, *HectD1*, that appears to be responsible for hematopoietic stem cell (HSC) regeneration via ribosome assembly. The discovery paves the way for potential therapies for children with ribosomopathies, a group of inherited bone marrow failure disorders that result from impaired ribosome function.

The findings, which appear in *Cell Stem Cell*, found that the ribosomal assembly factor ZNF622 mediates the function of the E3 ubiquitin ligase *HectD1* in HSC regeneration. Knocking out the *Znf622* gene in HSCs that lack the *HectD1* gene restores protein synthesis and HSC production.

"These findings not only highlight the connection between protein degradation, ribosome assembly, and stem cell production, but they also reveal the potential for knocking down *Znf622* to restore proper bone marrow function, which is critical for child development," Dr. Tong said. "Future research should look at this mechanism as a potential target for patients with these disorders."

MC2 Program Connects Mitochondrial Disease and Pediatric Cancer Research

YIN AND YANG: MITOCHONDRIAL DISEASE VS CANCER

"Our basic goal is to learn from the survival strengths and weaknesses of one disease, to shed light on precision treatment strategies for the other."

The Mitochondrial Medicine Frontier Program and the Center for Data-Driven Discovery in Biomedicine (D3b) at CHOP joined forces to form the Mitochondria and Cancer Connections (MC^2) Research Program. Under the new program, researchers led by Marni Falk, MD, director of the Mitochondrial Medicine Frontier Program, and Adam Resnick, PhD, director of D3b, aim to leverage their existing centers and knowledge to establish a research initiative to find new insight into disease processes and therapeutics, at the intersection of mitochondrial disease and cancer. They will harness a data analysis and sharing platform developed by D3b called CAVATICA to analyze multi-omics data.

"Ultimately, we aim to steal strategies from cancer to help mitochondrial disease cells grow and function better, while at the same time stealing strategies from mitochondrial disease to slow down cancer," Dr. Falk said. "In other words, our basic goal is to learn from the survival strengths and weaknesses of one disease, to shed light on precision treatment strategies for the other. If we're lucky, we'll find therapies for both classes of diseases."

Precision Medicine Supports New Therapeutic Perspectives

Targeted therapeutic interventions from the fields of cell and gene therapy, infectious disease, computational and genomic medicine, image-based medicine, and data analysis are changing the way we think about disease intervention and treatment.

Scientists Engineer 'Dimmer Switch' to Fine-Tune Gene Therapy Expression Levels

FINE CONTROL OF GENE THERAPY PRODUCTS

"We're taking the field of gene therapy to an entirely new level ..."

Today's gene therapies allow scientists to revise the script of a patient's DNA to correct defective or deficient gene expression responsible for disease development. But once a therapy is delivered into a patient's tissue, regulating levels of expression presents a challenge: Too much can have detrimental effects, while too little can fail to yield a result.

Children's Hospital of Philadelphia researchers led by Beverly Davidson, PhD, director of the Raymond G. Perelman Center for Cellular and Molecular Therapeutics and chief scientific strategy officer at CHOP, engineered a delivery system — called the Xon system — to fine-tune levels of gene therapy expression, essentially a "dimmer switch" that advances precision medicine for common, rare, and complex conditions.

Together with collaborators from the Novartis Institutes for BioMedical Research (NIBR), Dr. Davidson and her team published the first research describing this innovation in *Nature*.

They showed that by using a small molecule drug in combination with gene therapy vectors, they could control dosing of protein expressed to achieve the maximum therapeutic benefit.

CHOP and NIBR are collaborating to develop next-generation small molecule splicing modulators and the Xon system to achieve fine-tuned gene regulation across multiple clinical applications.

Photomicrograph courtesy of Luis Tecedor

A-to-I RNA Editing Affects Gene Expression and Phenotype

COMPUTATIONAL MINING OF BIG DATA

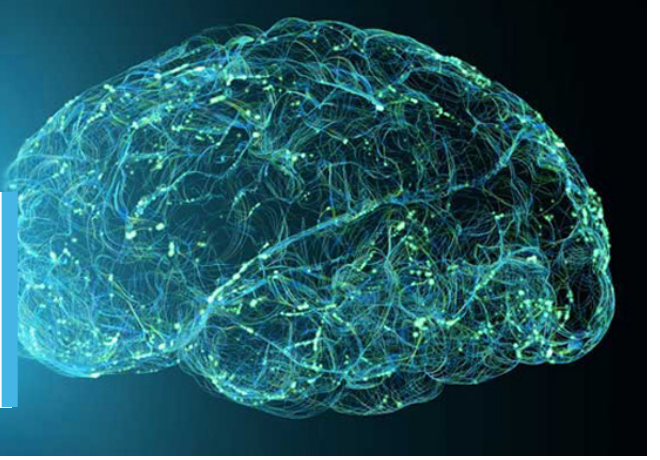
"Understanding how RNA editing affects gene expression and phenotype could help us unravel the genetic basis to many human conditions."

Combining computational mining of big data with experimental testing in the lab, researchers at Children's Hospital of Philadelphia have identified RNA editing events that influence gene expression and, in turn, the phenotypic manifestation of that expression. In analyzing so-called A-to-I RNA editing, in which the adenosine of an RNA molecule is chemically modified into an inosine, the researchers describe how a single nucleotide change by RNA editing can have large downstream effects. The findings were published in *Genome Biology*.

Yi Xing, PhD, director of the Center for Computational and Genomic Medicine at CHOP and senior author of the study, worked with his team to study the functions of RNA editing through the lens of human genetic variation, or the differences that occur among people in approximately 1 in 1,000 DNA base pairs, affecting not only how genes are expressed but also how messenger RNAs are processed.

"What is so useful about this approach is that it is disease agnostic," Dr. Xing said. "Future research can use this strategy to study specific diseases and look at the impact of RNA editing events from a disease perspective."

Researchers Explore Focal Gene Therapy Approach to Mental Illness Intervention



REBALANCING CIRCUITRIES

"Our goal is to return disrupted or diseased brain circuitry to its optimal tuning range."

A collaborative research team at Children's Hospital of Philadelphia and the University of Pennsylvania found that a focal, molecular approach that targets circuit excitability may prove to be an effective intervention for treatment-resistant symptoms of mental illness.

Stewart Anderson, MD, associate chair of research, Department of Child and Adolescent Psychiatry and Behavioral Services, and associate director of the Lifespan Brain Institute at CHOP and the University of Pennsylvania, and Douglas Coulter, PhD, CHOP investigator and professor of Pediatrics at the Perelman School of Medicine at Penn, and colleagues published findings from their cross-disciplinary project in *Biological Psychiatry*.

The team identified circuits that normally underlie critical brain functions and compared them to instances of abnormal brain function in neurologic and psychiatric disease models to see if circuit disruptions could account for behavioral manifestations associated with the conditions. Then, they focally introduced "designer" receptors to correct the deficit.

The scientists identified hyperactive brain circuitry that affects social and spatial memory functions in a laboratory model of 22q11.2 deletion syndrome (22q11DS). They used focal gene therapy to correct the circuit hyperactivity and resolve the functional problem, thereby improving social and spatial memory. While translating this work from the lab to the clinic is a future goal, these findings are uniquely relevant to the 22q and You Center at CHOP for children who have hyperexcitability of the same hippocampal circuit.

GNU-based Identification Sheds Light on Viral Diversity

FASCINATING INSIGHTS INTO SARS-COV-2

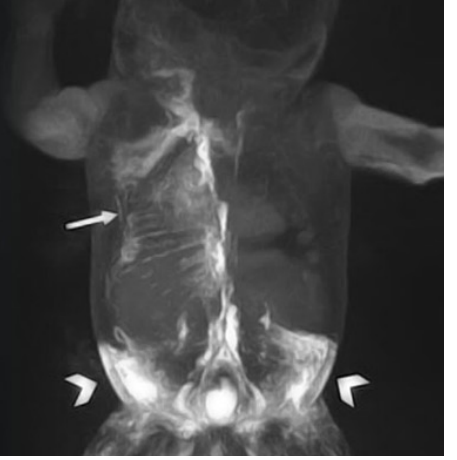
"It's kind of like the ultimate contact tracing because you can actually distinguish different viruses really rapidly to see where they were transmitted from."

Children's Hospital of Philadelphia researchers Paul Planet, MD, PhD, and Ahmed Moustafa, PhD, created a novel technology that traces the evolution of SARS CoV-2, called GNU-based Virus Identification (GNUVID). Drs. Planet and Moustafa gathered new findings that shed light on the importance of mask mandate policies and the effect of human immunity on viral diversity. With enhanced understanding of viral diversity, scientists are better positioned to detect concerning mutations and develop effective approaches to treatment and prevention.

GNUVID is an automatic tool that can take all currently available data and systematically name different viruses in the data bank, then sequence and deposit them in a database called GISAID that enables researchers to see where each virus comes from, where was it seen last, and, perhaps in the future, will allow them to learn which person it came from as the virus mutates. Noted by the scientists as the ultimate contact tracing, this tool can distinguish different viruses rapidly to see where they were transmitted from.

Dr. Moustafa, lead scientist in the Microbial Archive and Cryo-collection unit under the PennCHOP Microbiome Program, identified the dates in which mask mandates were put into place for 16 states in the United States to learn about the circulating diversity in those states over the period of the pandemic. Using GNUVID, Drs. Planet and Moustafa can categorize and follow new mutants as they arise, and then track those pathogens back to their closest relatives and to others circulating around the world and in the Philadelphia community.

Novel Imaging Methods Improve Neonatal Outcomes



CLEARER PICTURE OF LYMPHATIC SYSTEM AT WORK

"It's imaging that allows us to find out where all the problems are."

Novel imaging methods developed by Children's Hospital of Philadelphia researchers help clinicians have a clearer picture of the lymphatic system at work — an innovation that has led to improved outcomes for infants with severe neonatal lymphatic disorders.

Researchers in the Jill and Mark Fishman Center for Lymphatic Disorders described the impact of these novel, minimally invasive imaging methods on two complex neonatal lymphatic disorders: neonatal chylothorax (NCTx) and central lymphatic flow disorder (CLFD) in a paper that appeared in the *Journal of Perinatology*. With high mortality and morbidity rates, detecting and diagnosing these disorders early is critical, in order to direct the best treatment strategies.

"NCTx and CLFD have been historically challenging to diagnose because there really wasn't a way to image the system," said Erin Pinto, MSN, RN, CCRN, first author of the paper and a nurse practitioner in the Center for Lymphatic Disorders.

Yoav Dori, MD, PhD, director of Pediatric Lymphatic Imaging and Interventions and Lymphatic Research, developed a method of accessing different compartments of the lymphatic system called dynamic contrast MR lymphangiography (DCMRL) that essentially "maps" the anatomy of a patient's lymphatic system.

MAUS Open-Drug Development Possibilities

HIGH-RESOLUTION 3D STRUCTURAL INFORMATION FOR PROTEINS

"Our method really helps overcome these barriers and addresses a critical need."

Data generated using nuclear magnetic resonance (NMR) spectroscopy holds great promise, but researchers are often frustrated by how laborious it can be to perform the analysis before they can begin to derive meaningful results.

Nikolaos Sgourakis, PhD, lead principal investigator in the Mechanistic Molecular Immunology Lab at Children's Hospital of Philadelphia, with colleagues from the University of California Santa Cruz and Universidade Federal do Rio de Janeiro, developed a new procedure for recording and analyzing NMR data, methyl assignments using satisfiability (MAUS), that effectively tackles these challenges. Now, solving a problem that would normally take weeks of NMR machine and expert time can be accomplished in just a few days.

MAUS allows biomedical researchers to visualize protein molecules with atomic-detail accuracy, opening new possibilities in drug development. With MAUS, researchers can apply the analysis method to larger, more complex proteins to understand their interactions with other molecules and induced structural changes — both aspects that are critical for targeting proteins often deemed undruggable because their predominant structures offer limited surfaces for interactions with antibodies and small molecules.

Their paper in *Nature Communications* demonstrates the effectiveness of MAUS on a range of important protein molecules, including a common form of the human leucocyte antigen, the therapeutic cytokine interleukin 2, and the Cas9 nuclease.

Scientists Make Big Strides in Research that Spans a Lifetime

Our scientists make big strides in children's health research that span a lifetime — from longitudinal studies for identifying genetic markers associated with bone growth to a big data center for Down syndrome, from the long-term complications of type 2 diabetes to preventing white matter loss in HIV.

Bystander Rescue-breathing CPR Improves Outcomes for Children in Cardiac Arrest

BYSTANDER ALERT

"We really need to do a better job emphasizing rescue-breathing CPR in children ..."

The best CPR approaches for children are not necessarily identical to those for adults. This year, CHOP researchers published findings in the *Journal of the American College of Cardiology* that support the use of bystander CPR with rescue breathing in children experiencing cardiac arrest. The finding is a departure from the compression-only CPR recommended for adults by the American Heart Association (AHA) and the European Resuscitation Council (ERC).

While compression-only CPR has shown to be as effective as CPR with rescue breathing in adults, pediatric cardiac arrest often stems from breathing problems. Thus researchers at CHOP hypothesized the former approach might actually prove less effective in children.

"At the moment, most lay people are trained in compression-only CPR because that is the standard of care in adults," said Maryam Y. Naim, MD, MSCE, a pediatric cardiac intensive care physician in the Division of Cardiac Critical Care Medicine and first author of the study. "However, children are not simply small adults, and our study shows there is a tremendous need for education in all communities about the benefits of CPR with rescue breathing in the pediatric population."

Using data from the Cardiac Arrest Registry to Enhance Survival (CARES) database, Dr. Naim and her team analyzed more than 10,000 out-of-hospital cardiac arrests in patients between 0 and 18 years of age. They found that less than half of those who experienced pediatric cardiac arrest outside of the hospital received bystander CPR and of those who did, the majority received compression-only CPR. Compared to those who received compression-only CPR, children who received CPR with rescue breathing were nearly 1.5 times as likely to have better neurological outcomes. Further supporting the use of rescue breathing, the researchers found that infants who received compression-only CPR had the same outcomes as infants who received no CPR at all.

The results carry critical implications for bystander CPR education and training, including the need to emphasize and teach lay rescuers how to perform rescue breathing, according to Dr. Naim.

Genetic Markers Associated With Lifetime Bone Growth Help Early ID of Osteoporosis

CRITICAL PERIOD OF BONE GROWTH

"Our findings may help us better tailor lifestyle interventions ..."

The discovery of dozens of new genetic markers associated with bone mineral accrual has set the stage for using genetic testing to identify the causes of eventual osteoporosis.

Publishing their findings in *Genome Biology*, the multidisciplinary team of genetics and bone biology experts at CHOP used data from the Bone Mineral Density in Childhood Study (BMDCS) to follow a group of children over several years.

"We wanted to do a GWAS study that measured bone mineral accrual at multiple time points to provide us with proper longitudinal data at ages when the skeleton is growing and developing," said Struan F.A. Grant, PhD, director of the Center for Spatial and Functional Genomics and lead author of the study. "By doing a longitudinal study, we had much greater power in a relatively small cohort of patients."

Accruing bone density in childhood is critical for achieving optimal bone mass as an adult. Until now, however, few studies have looked at genetic markers for bone health during this important period of growth. In the study, Dr. Grant and his team identified 40 distinct loci, or genetic markers, associated with bone accrual, several of which are associated with later fracture risk. The team also identified two novel, potentially causative effector genes, as well as multiple genetic pathways involved in bone accrual variation that help determine whether cells eventually become osteoblasts (bone cells) or adipocytes (fat cells).

According to Babette Zemel, PhD, the study's first author and associate program director of CHOP's Center for Human Phenomic Science, the findings demonstrate how such genetic markers manifest themselves earlier in life than previously thought. "In this case, our findings may help us better tailor lifestyle interventions, such as exercise and dietary changes, that will help patients later in life, and they may also lead to novel therapeutic interventions," Dr. Zemel said.

New Wood Center for Fetal Diagnosis and Treatment Boosts Fetal Medicine Research Initiatives

NEXT GENERATION OF FETAL MEDICINE BREAKTHROUGHS

"Their generous philanthropic support will allow for a major expansion of infrastructure, patient services, research, and recruitment ..."

A transformational gift of $25 million from Richard Wood Jr., the chairperson emeritus of Wawa, allows Children's Hospital of Philadelphia scientists to continue advancing fetal medicine research and treatment for the next generation of tiny patients. In recognition of the donation, which was gifted in the spring of FY2020, CHOP re-named the Center for Fetal Diagnosis and Treatment (CFDT) the Richard D. Wood Center for Fetal Diagnosis and Treatment.

First opened in 1995, the internationally recognized CFDT is home to groundbreaking scientific breakthroughs, most notably the research, development, and accomplishment of the first successful fetal surgical repair of spina bifida. The Center's director, N. Scott Adzick, MD, and its leaders are considered founders of modern fetal medicine for providing life-changing surgical options for unborn patients with spina bifida, congenital diaphragmatic hernia, Twin-Twin Transfusion Syndrome, lung lesions, sacrococcygeal teratoma, and lower urinary tract obstruction.

The new donation will allow Dr. Adzick and his team to expand their clinical, educational, and research efforts even further, including the construction of a new clinical space for the Garbose Family Special Delivery Unit, the creation of a birth defects biorepository, and the establishment of endowments for a Distinguished Chair in Pediatric Surgical Science as well as fellowships in Pediatric Surgical Science.

"It's a great privilege and honor to name the hospital's Center for Fetal Diagnosis and Treatment after Richard D. Wood Jr.," said Dr. Adzick, who is also Surgeon-in-Chief of CHOP's Department of Surgery. "On behalf of our entire team, I would like to express my gratitude to the Wood family on this historic gift, which will fuel a new era of breakthroughs in fetal medicine and surgery. Their generous philanthropic support will allow for a major expansion of infrastructure, patient services, research, and recruitment that will categorically be pivotal to our hospital and the patients and families we serve worldwide."

CHOP Co-Leads Data Coordinating Center for Down Syndrome Research

CREATING A WORLD-CLASS RESOURCEREATING A WORLD-CLASS RESOURCE

"The scientific community is demonstrating the power of platforms to connect different communities with diverse areas of expertise and datasets ..."

A new data coordinating center (DCC) co-led by CHOP scientists seeks to improve the lives of individuals with Down syndrome by accelerating research and advancing medical care.

Supported by a five-year $19.5 million grant from the National Institutes of Health's Investigation of Co-occurring conditions across the Lifespan to Understand Down syndrome (INCLUDE) project, our Center for Data Driven Discovery in Biomedicine (D3b) is developing the DCC in partnership with Sage Bionetworks and the Linda Crnic Institute for Down Syndrome at the University of Colorado Anschutz Medical Campus.

The project's leaders, including our own Adam Resnick, PhD, envision the INCLUDE DCC as a world-class resource for data sharing, data access, and integrative analysis in Down syndrome. Three specialized cores — the Data Portal, Data Management, and Administration and Outreach — will work together to advance scientists' understanding of Down syndrome, including the biology behind why individuals living with the condition have an increased risk for some medical conditions (such as hearing loss) but not others (such as heart disease).

"More and more, the scientific community is demonstrating the power of platforms to connect different communities with diverse areas of expertise and datasets to drive surprising discoveries and accelerated impact across a broad number of conditions in both children and adults," said Dr. Resnick, who is D3b's director. "The DCC Project will build on these efforts through the implementation of new technologies and platforms that will empower large-scale, diverse INCLUDE datasets on behalf of individuals with Down syndrome and other associated medical conditions and diseases."

Youth Onset Type 2 Diabetes Research Reveals Long-Term Complications

CULMINATION OF TODAY2 STUDY

"We need to treat the disease aggressively at an earlier point on the timeline ..."

Treating type 2 diabetes in youth at an earlier point in time is critical, according to novel findings from CHOP and Penn researchers. In a landmark study published in the *New England Journal of Medicine*, the researchers reported that young people diagnosed with type 2 diabetes during childhood and adolescence have a high risk of developing serious complications by early adulthood. The complications, which can include high blood pressure, kidney disease, and others, accumulate rapidly: 60 percent of study participants developed at least one condition by early adulthood. Nearly a third of participants had two or more complications.

The Treatment Options for Type 2 Diabetes in Adolescents and Youth (TODAY) follow-up study (TODAY2) monitored 500 patients from the original TODAY study every year for signs of diabetes complications, from heart disease to kidney disease to diabetic foot complications, and more. When the participants enrolled, they ranged between the ages of 10 and 17, and had been diagnosed with type 2 diabetes for fewer than two years. The TODAY2 study found that 67 percent of participants developed high blood pressure, nearly 55 percent had kidney disease, and 51 percent had eye disease. Almost a third of patients showed signs of nerve disease.

"The results of this important study show that type 2 diabetes in children is a severe disease — more severe than in adults — and so we need to treat the disease aggressively at an earlier point on the timeline, ideally at the pre-diabetes stage," said Lorraine Katz, MD, director of the Center for Human Phenomic Science at CHOP and PI of the study's CHOP site. "We also must explore better therapeutic options for young people with type 2 diabetes to prevent the disease from worsening and leading to serious complications."

Researchers Elucidate How HIV Infections Affect the Brain's White Matter

MYELINATION'S KEY ROLES IN LIFE STAGES

"The more we find out about this biology, the more we can do to prevent white matter loss and the harms that can cause."

While it's well known that individuals living with HIV experience a loss of white matter in the brain, not much is known about how exactly the virus contributes to such reduction. This year, researchers at CHOP and Penn described in *Glia* the mechanism by which HIV infection blocks the maturation process of the brain cells that produce myelin, the substance white matter is made of that provides neurons with a protective coat.

"When people think about the brain, they think of neurons, but they often don't think about white matter, as important as it is," said Judith B. Grinspan, PhD, a research scientist at CHOP. "But it's clear that myelination is playing key roles in various stages of life: in infancy, in adolescence, and likely during learning in adulthood too. The more we find out about this biology, the more we can do to prevent white matter loss and the harms that can cause."

By looking at both human and animal cells for the study, Dr. Grinspan and her team were able to detail how HIV hinders the maturation of oligodendrocytes, the brain cells that make myelin, and thus reduce the production of white matter. Testing the finding further, the team applied a compound that blocks this process and found that oligodendrocytes could once again mature. The findings are key for discerning how much of the white matter loss experienced by patients with HIV can be attributed to the virus itself, and how much can be attributed to antiretroviral therapy (ART), drugs used to treat HIV that have been shown by the team to also cause myelin reduction.

"When we put people on ART, especially kids or adolescents, it's important to understand the implications of doing that," said Kelly Jordan-Sciutto, PhD, Dr. Grinspan's collaborator and a professor in Penn's School of Dental Medicine, in *Penn Today*. "Antiretrovirals may prevent the establishment of a viral reservoir in the central nervous system, which would be wonderful, but we also know that the drugs can cause harm, particularly to white matter.

Image courtesy of Raj Putatunda.

Research Institute Creates Opportunities for Dynamic Connections

CHOP Research Institute empowers change that leads to success. Under the new leadership of Executive Vice President and Chief Scientific Officer Susan Furth, MD, PhD, we're working toward a streamlined, world-class research infrastructure and state-of-the-art future campus expansion.

CHOP Research Institute Welcomes New Chief Scientific Offer

Children's Hospital of Philadelphia Research Institute's commitment to science that translates into innovation and improvement in children's health is under the new leadership of Susan L. Furth, MD, PhD, who assumed the role of Chief Scientific Officer in June 2021.

"Using research findings to develop and improve interventions promoting the health and well-being of children is at the heart of everything we do at the Research Institute," Dr. Furth said.

In her CSO role, Dr. Furth brings a distinguished background in research to guide the Research Institute as its investigators tackle the most pressing issues in pediatric research. A tenured professor in the Departments of Pediatrics and Epidemiology at the University of Pennsylvania's Perelman School of Medicine, Dr. Furth has had continuous National Institute of Health (NIH) funding for more than 25 years. She has authored more than 200 papers in peer-reviewed journals related to the epidemiology and health outcomes for children with kidney disease and has led the design and implementation of pediatric observational studies and clinical trials.

Dr. Furth has been recognized nationally for her work, receiving honors and awards that include election to the Johns Hopkins Society of Scholars, the 2020 Maureen Andrew Mentor Award from the Society of Pediatric Research, and the 2020 FOCUS Award for the Advancement of Women in Medicine from Penn Medicine. She is an elected member of the Association of American Physicians and served as President of the Society for Pediatric Research. Dr. Furth is currently a Councilor for the International Pediatric Nephrology Association.

With a passion for mentoring junior researchers, Dr. Furth held a NIH Mid-Career Mentoring Award for 10 years, developed the Carole Marcus Mid-Career Award to Promote Career Development and Mentoring in Pediatric Research at CHOP, and won the Faculty Mentor Award at CHOP in 2016.

"In addition to her impressive scientific achievements, which have been recognized globally, she is also an outstanding mentor who has helped younger researchers develop their careers," said Madeline Bell, President and CEO of CHOP. "Combined, these skills will be invaluable in supporting the Research Institute fulfill CHOP's mission of delivering exceptional clinical care, research, and education."

Maximizing Success With Genomics, Other Omics, and Big Data Strategy

The Board of Directors for Children's Hospital of Philadelphia approved in March a living strategy and framework to synergize individual strengths and support a community of "omics" experts across laboratories and research programs. The overarching vision is two-fold:

- Lead in developing new omics-based diagnostics and therapeutics for children.
- Be the destination of choice for the diagnosis and treatment of complex diseases which result from our collective expertise in "omics" technology.

By leveraging the wealth of data available from our investments in research, CHOP and its Research Institute has the opportunity to use "multiomics" technologies — genomics, transcriptomics, proteomics, and metabolomics — and emerging approaches to data science to drive faster, more accurate diagnoses and treatments for children with both rare and complex childhood diseases.

To this end, the Research Institute will accelerate the development of an industry-leading data platform and sharing model so that individuals who collect, manage, or use institutional data have maximal opportunities to make insights that may impact child health. Two committees — the CHOP Data Use Committee led by Marilyn Li, MD, and Ingo Helbig, MD, and the CHOP Data Science Strategy Committee led by Yi Xing, PhD — are meeting frequently with a concerted focus on active institutional data management with uniform governance, policy, sharing, and accountability.

The 'omics and big data strategy promotes the use of Arcus, an informatics platform for CHOP's research community, to manage genomic data and streamline the generation, archival, and research use of 'omic and other research data. Initial goals include building the CHOP 'Omics Data Warehouse to host genomic data linked to clinical phenotype data. This repository will grow to incorporate other types of 'omic data representing intermediate molecular phenotypes.

Three more workgroups are ramping up to focus on basic and translational research, external partnerships, and training and career development:

- The Omics and Big Data Basic and Translational Research Workgroup is charged with engaging stakeholders across the institution to bring back key information to build a complete picture of current omics work and opportunities. This workgroup will envision opportunities to expand and accelerate omics research and CHOP-sponsored clinical trials in the near- and long-term.
- The Omics and Big Data External Partnerships Workgroup will improve CHOP's efficiency and effectiveness at pursuing omics and big data-focused strategic partnerships with industry and academic institutions to accelerate clinical and research efforts.
- The Omics and Big Data Training and Career Development Workgroup will introduce new programs to attract and retain the best talent.

Working collaboratively to implement the strategy, CHOP and the Research Institute will create a faster and more efficient operating model to improve diagnosis and treatment, provide a more coordinated and patient-centered experience, and seamlessly integrate clinical care models and research.

Meet the Research Institutes' New Fronteir Programs

Frontier Programs differentiate Children's Hospital of Philadelphia because of their unique combination of translational research and exceptional clinical care of children with highly complex conditions. By investing in initiatives like our Frontier Programs, we are accelerating the transformation of high-potential ideas into life-changing advances for patients.

Two new Frontier Programs were selected in 2021:

Rare Lung Diseases Center

Historically, achieving a specific pulmonary diagnosis has been challenging, as children with disparate types of lung disease present with overlapping clinical symptoms and nonspecific radiologic findings of diffuse lung disease. The Rare Lung Diseases Center Frontier Program seeks to change the diagnostic pathway by expanding genetic and pathologic testing for their patient population.

The Frontier Program will build upon its basic science platform and seek to identify novel genetic targets, develop biomarkers, and model the molecular mechanisms in rare lung diseases to allow for enhanced outcomes for all patients. Its leaders are Lisa Young, MD, and Sharon McGrath-Morrow, MD, MBA.

Center for Precision Diagnosis and Therapy for Pediatric Motility Disorders

Despite the high prevalence of gastrointestinal motility disorders in the pediatric population, there are only a few centers in the world that can address the complex needs of children with severe motility diseases. This Center for Precision Diagnosis and Therapy for Pediatric Motility Disorders Frontier Program will expand on the outstanding clinical reputation of the Suzi and Scott Lustgarten Motility Center and position CHOP as the top research institution for treating and curing gastrointestinal motility disorders.

This Frontier Program will seek to expand the clinical pathways, translate precision diagnostics to the clinic by developing novel therapies and treatment strategies, and ultimately improve outcomes. Its leaders are Hayat Mousa, MD, and Robert O. Heuckeroth, MD, PhD.

Diversity, Equity, and Inclusion Council Committed to Change

A new Research Institute Diversity, Equity, and Inclusion (DEI Council) formed this year to take accountability for the RI's Diversity Action Steps, to serve as a guiding body for the working groups engaged in accomplishing the Action Step-related tasks, and to communicate transparently and bidirectionally with the Senior Leadership team, research faculty, and staff.

Co-chairing the Council is Lamia Barakat, PhD, professor of Clinical Psychology in Pediatrics and Psychiatry, Director of Behavioral Oncology, and co-Division Chief for Integrated Psychiatry, Psychology, and Behavioral Health; and Wendy Reed Williams, PhD, senior director, Academic Training and Outreach Programs (ATOP). Paulette McRae, PhD, is the DEI Council's Strategy and Logistics Deputy, and she is assistant director, Specialty Programs and Diversity, in ATOP.

Ensuring different roles and viewpoints are at the table, the Council is a minimum of nine voting members from across Children's Hospital of Philadelphia and its Research Institute. Along with faculty, including Department and Division leaders, and ATOP representation, the Council includes members from the offices of Human Resources, Faculty Development, and Immigration and Visa Services, as well as postdoctoral fellows. Gilbert Davis, MHA, CHOP's vice president and chief Diversity Officer rounds out the group, ensuring that our DEI Council's work synergizes with the hospital's DEI efforts.

The Council is establishing four Working Groups whose members will actively work on our strategic priorities related to DEI across the research community:

- DEI of research participants in CHOP studies.
- Assessing and enhancing the RI DEI landscape.
- Promoting a welcoming and inclusive environment.
- Building a diverse workforce.

Having strategic priorities and Council members who are working to ensure we follow through with them reinforces our commitment to providing a more diverse, equitable, and inclusive environment here at the Research Institute.

New Groups Representing Researchers Communicate From the Inside Out

When information is openly shared between employees and across levels of the organization, it encourages communication and innovation that aligns with the Research Institute's goals to promote the health and well-being of children, adolescents, and young adults.

With this perspective in mind, two new groups were launched in 2021 to help researchers stay collectively informed and increase the sharing of ideas. The Vice Chairs of Research for Departments represent Anesthesiology and Critical Care Medicine, Biomedical and Health Informatics, Pathology, Psychiatry, Radiology, and Surgery. The Department of Pediatrics Research Council includes directors of research from each of the department's 18 divisions.

At an early stage of formation this fall, these two groups have begun meeting on a regular basis to share success stories, best practices, problem-solve, and increase awareness of potential multidisciplinary collaboration on research projects. They aim to cascade this information to the principal investigators within their related areas of expertise, as well as upwardly communicate with the Research Institute's senior leadership.

Inquiries regarding either of these collaborative groups can be directed to Brian Fisher, DO, MPH, MSCE, associate chair of research for the Department of Pediatrics.

Future Research Institute Campus Expansion Planning Underway

Construction plans are underway for the Schuylkill Avenue Research Building (SARB1), anticipated to be completed in November 2024. Research staff and administrators from all levels across the Research Institute are contributing insights to develop dedicated space for wet labs, vivarium floors, core facilities, genome sequencing, mechanical infrastructure, and more.

At 14-stories tall and a variety of outdoor spaces, SARB1 will elevate the Research Institute's commitment to excellence in research, creativity, innovation, and community engagement. It will be designed for maximum flexibility to incorporate new technologies as they emerge. The dynamic work environment will include collaboration zones and comprehensive breakout spaces that will facilitate interaction among our communities of science.

The new building will help to recruit and retain the best scientists dedicated to improving children's healthcare and instill a culture of support for personal and professional development within a world-class pediatric research destination.

Conceptual Rendering: Schuylkill Avenue Research Building as of December 2021

Building on a Decade of Commitment to Diversity in STEM-M Pipeline

It's thrilling to see the moment when "the lightbulb goes on" in students and they can picture themselves working in translational medicine and doing research that has the potential to transform children's health.

That moment came for Chitra Mosarla, MD, as one of the first undergraduate interns of CHOP's Research Institute Summer Scholar Program (CRISSP), which celebrated its 10-year anniversary in 2021.

"It was a really phenomenal experience for me, and it definitely helped shaped my career," said Dr. Mosarla, who is now a cardiology fellow at New York University. "You need the right people who give you the resources and encouragement."

Children's Hospital of Philadelphia Research Institute works tirelessly to nurture diverse students, from high schoolers to postdoctoral fellows, who have an interest in careers in science, technology, engineering, math, and medicine (STEM-M), with a goal to increase the pipeline of future scientists and physicians.

In addition to CRISSP, the CHOP Research Internship for Scholars and Emerging Scientists (CHOP-RISES) program is a two-summer STEM-M program for high school students from under-represented groups. The Postdoctoral Research Fellowship for Academic Diversity at CHOP partners with Penn's Provost Fellowship Program to increase diversity of the scholar community. New programs also are underway to reach even more groups at various levels throughout the Research Institute.

> "THE REASON THAT WE ARE ABLE TO DO THESE PROGRAMS IS THE COMMITMENT THE RESEARCH INSTITUTE HAS TO BUILDING THE PIPELINE AND THEIR COMMITMENT TO DIVERSIFYING STEM-M," SAID PAULETTE MCRAE, PHD, ASSISTANT DIRECTOR OF SPECIALTY PROGRAMS AND DIVERSITY IN THE OFFICE OF ACADEMIC TRAINING AND OUTREACH PROGRAMS (ATOP) IN THE CHOP RESEARCH INSTITUTE.

"There are amazing people at CHOP who are truly committed to building that pipeline, but if the institution doesn't commit to it, those ideas go nowhere. CHOP has that commitment and has continued to invest in diversity-focused pipeline programs over the years."

Building a diverse workforce and investing in student/trainee programs are two of the main goals being implemented as part of the Research Institute's Diversity, Equity, and Inclusion Action Steps formalized in 2020. The CRISSP and CHOP-RISES programs for underrepresented minorities will add more slots for students, and more funding will be available for additional awards for the Postdoctoral Research Fellowship for Academic Diversity.

Former program participants are helping students along the way. The CHOP Student Advisory board established in 2021 includes nine alumni from the CRISSP and CHOP-RISES programs.

"The members of the Student Advisory Board were elected to advise on programming and recruitment efforts with a goal of promoting an equitable environment within the context of diversity and inclusion," said Michelle E. Marshall, MEd, senior outreach programs officer in ATOP. "The board will support CHOP Research Institute's commitment to creating an enduring community of belonging, in which all students can take pride and realize their potential."

Student Advisory Board member Maia Cone, currently a junior at Xavier University in Louisiana where she majors is biochemistry, participated in the 2018 pilot CHOP-RISES class. She credits her experience at CHOP-RISES for solidifying her goal of a STEM career, which is to attend Philadelphia School of Osteopathic Medicine and become a pediatric orthopedic surgeon.

"The program introduced me to other professions in medicine besides physician, and it showed me what I could potentially specialize in," Cone said. "Hearing other professionals' stories about how they achieved their goals empowered me and gave me the confidence and courage I needed to pursue mine."

The Research Institute is offering new ways to ensure each employee can flourish, feel valued, and contribute to culturally sensitive, compassionate care and more accurate, inclusive medical research. For example, the Advancing Representation in Research Administration is an internship opportunity for undergraduate students of historically underrepresented groups that is dedicated to learning about research administration.

Beyond the undergraduate level is the CHOP Gap Year program, which is designed for recent graduates of undergraduate programs who may be taking some time for scientific exploration before going on to pursue graduate or medical school.

"This program is dedicated to giving underrepresented students the opportunity to hone their research skills at CHOP and support them as they prepare for medical school or graduate school," McRae said.

At the graduate level, a new program that launched in 2021 was the Gateway to Pediatric Research program, which is an opportunity for graduate students to learn more about CHOP and what it has to offer for postdoctoral researchers.

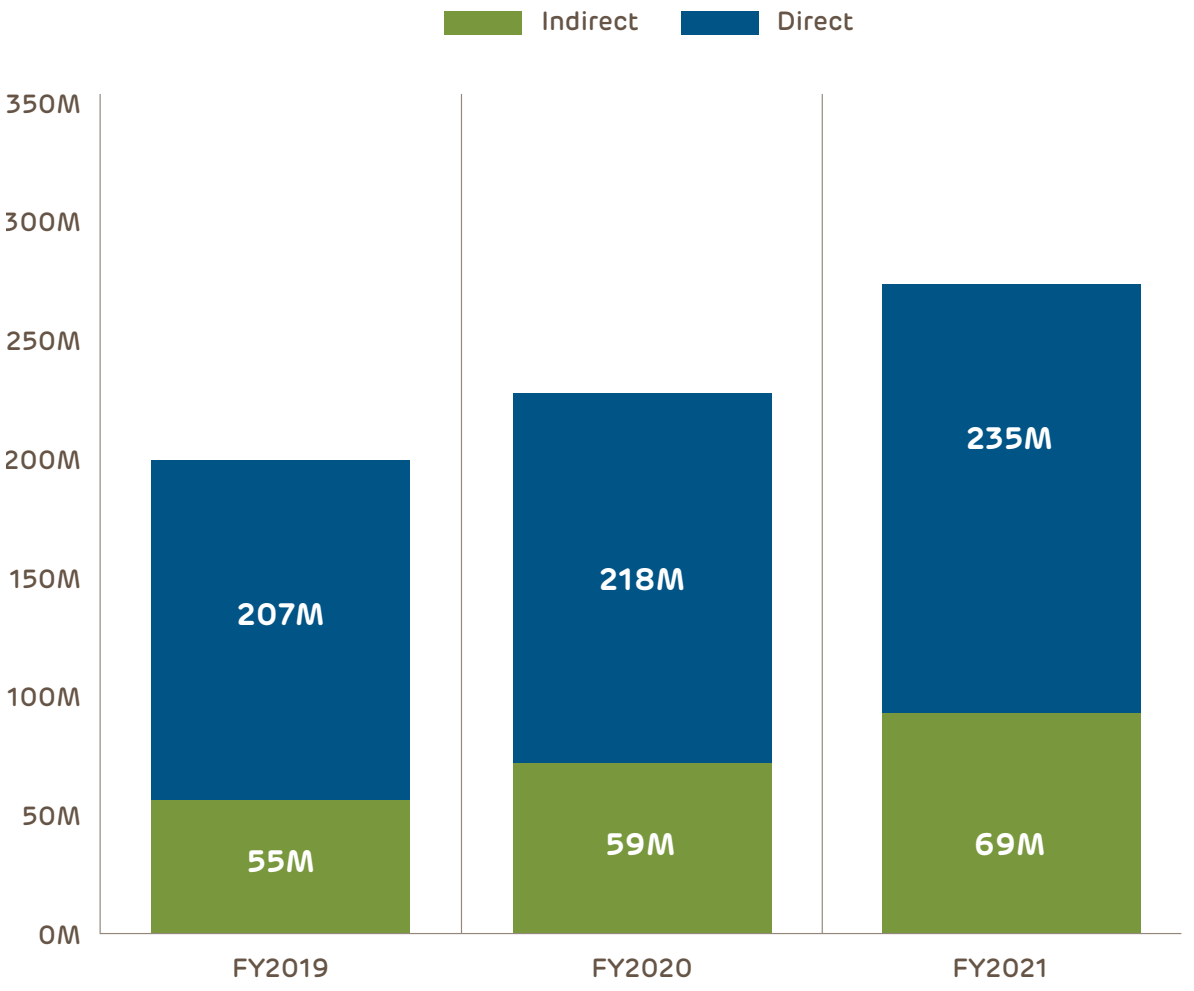
Senior postdoctoral researchers with diverse representation who are transitioning into faculty roles will soon gain more support through the Bridge to Faculty program designed to help acclimate them to their new responsibilities.

“It’s pretty clear that there’s still a massive discrepancy in representation in STEM-M, and there certainly have been efforts focused on diversifying the STEM-M pipeline,” Dr. McRae said. “We need to be working on increasing that pipeline, but we also need to ensure that the people already in our space — our physicians, scientists, and faculty — are also diverse so that the students in the pipeline see themselves represented.”

2021 RI Annual Report
Facts and Figures

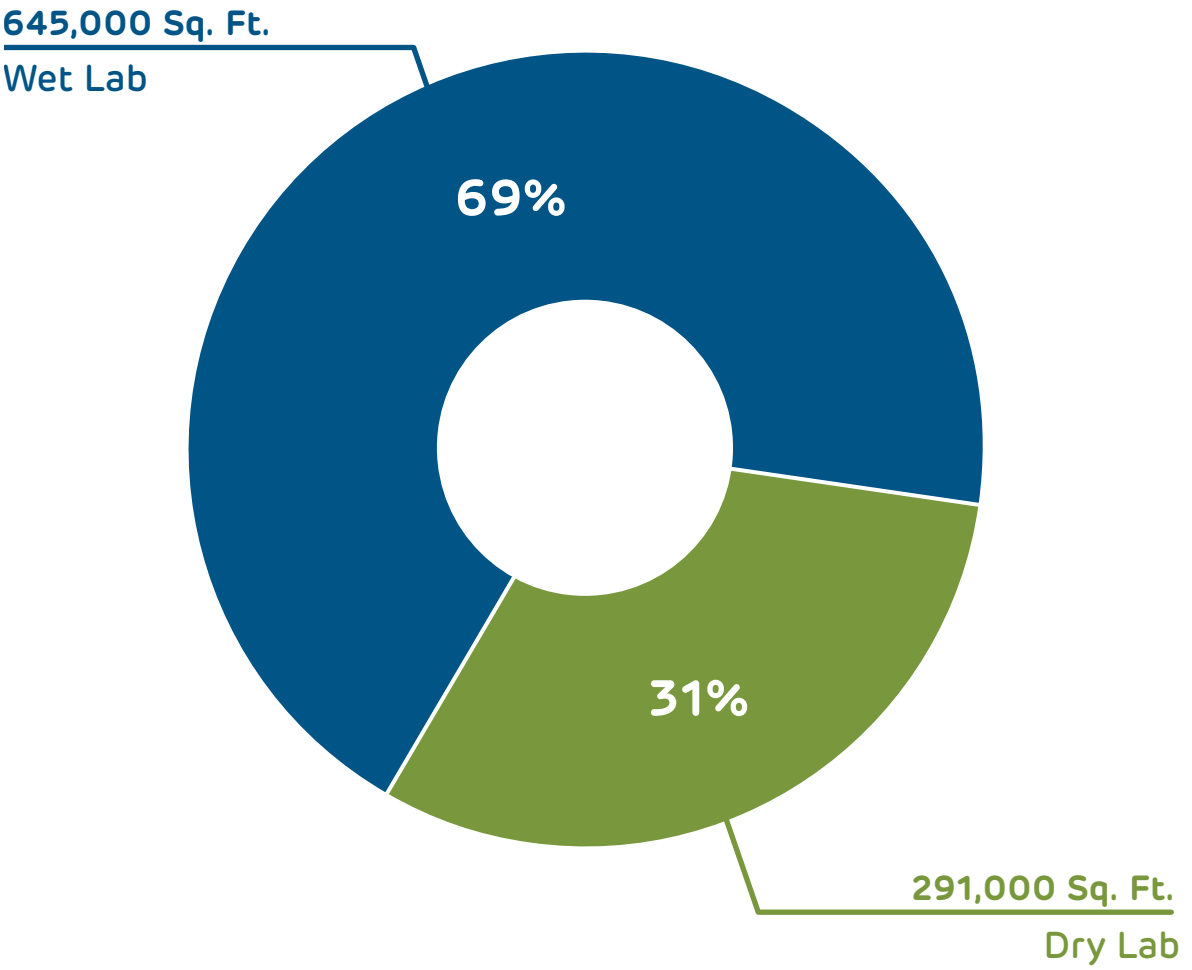
Key Metrics

Total Grant Funding

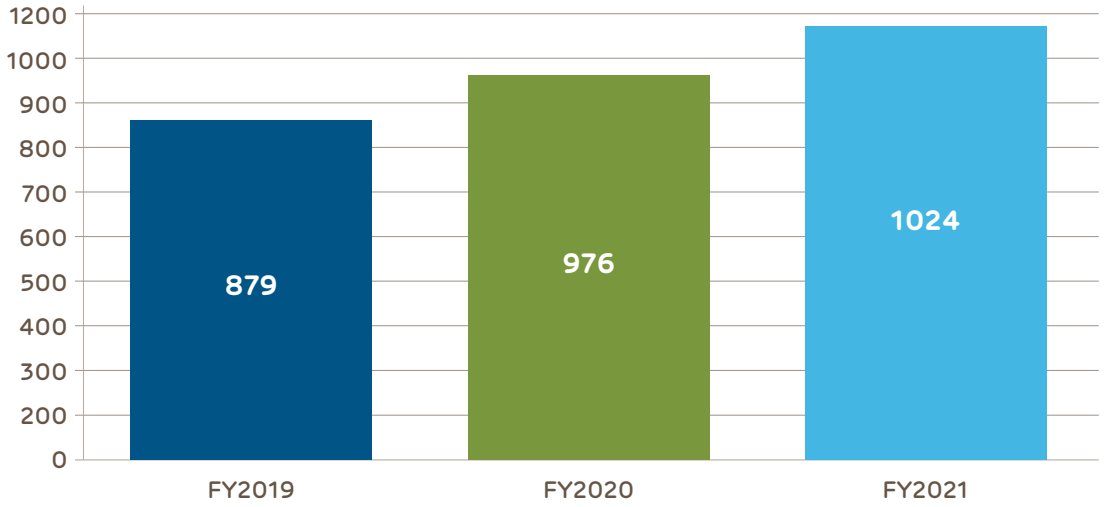


FY20 Research Space (Sq. Ft.)

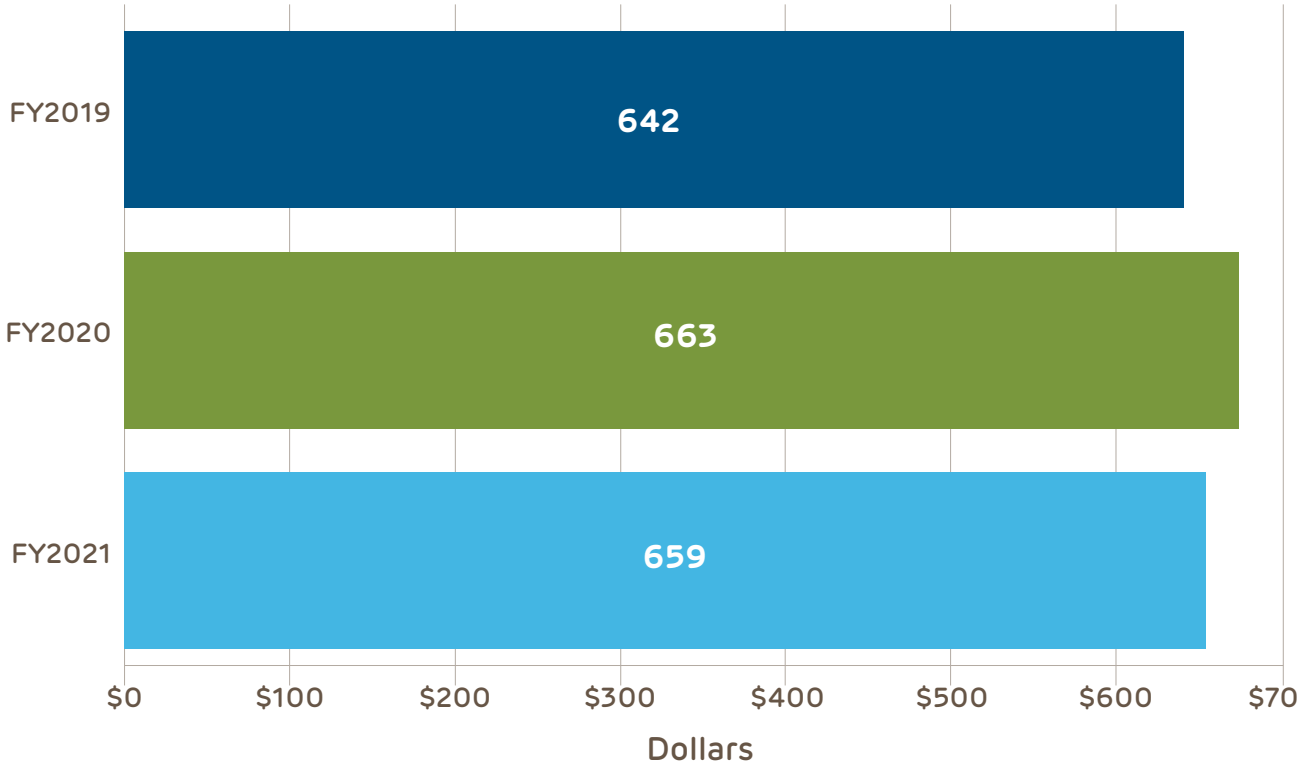
Total: 936K



Number of PI (With Active Grants/Protocols)

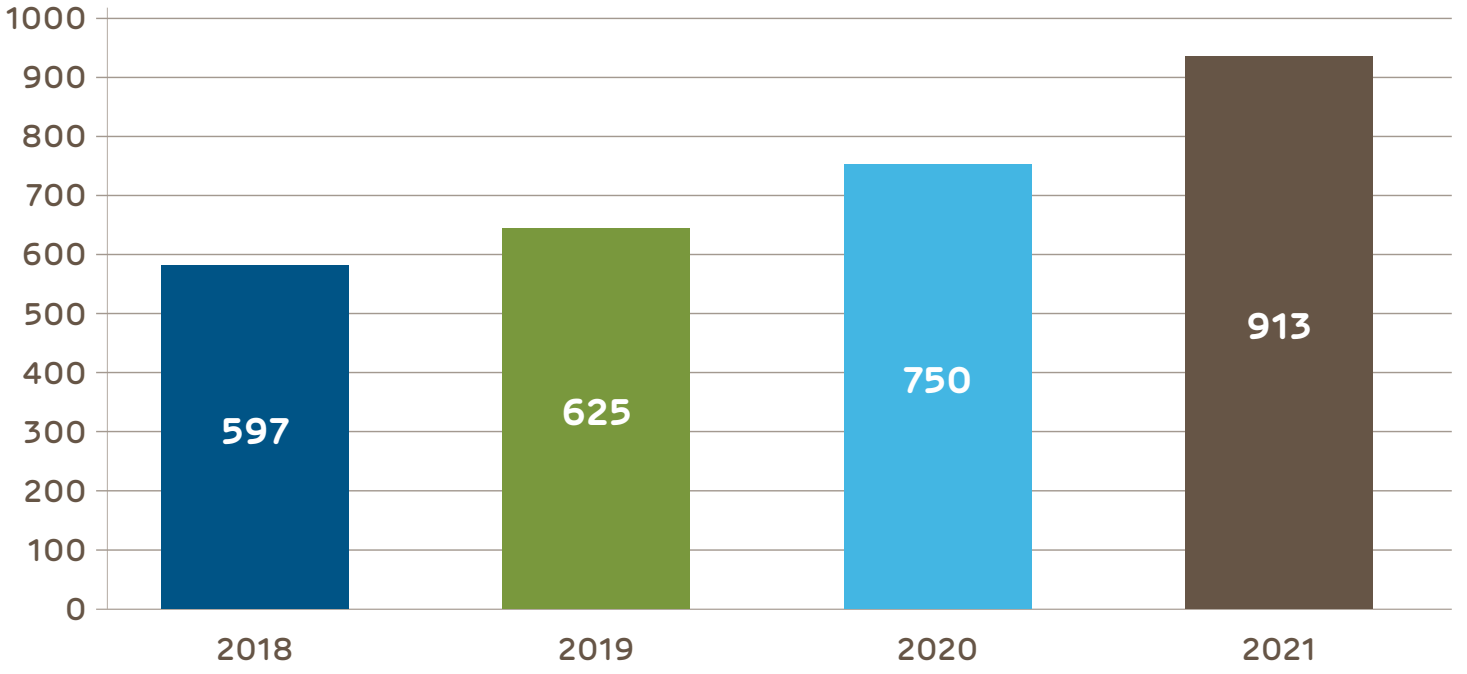


Wet Lab - Average $/Sq. Ft.

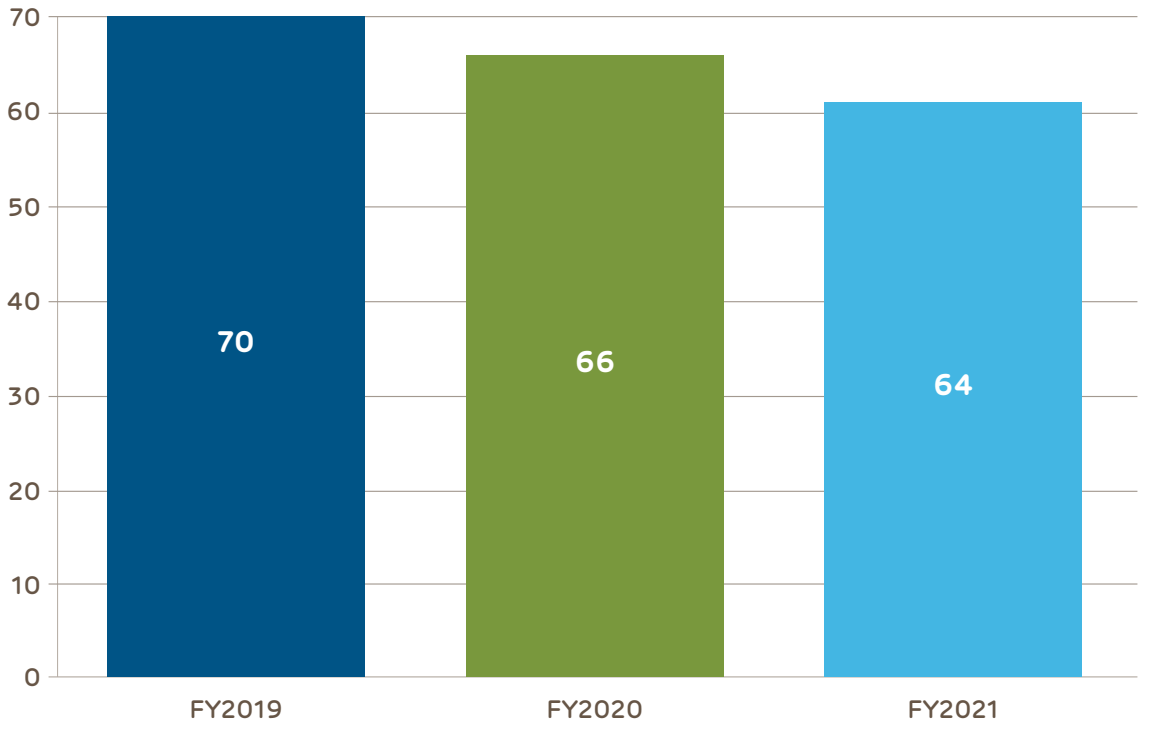


Strategic Impact & Innovation

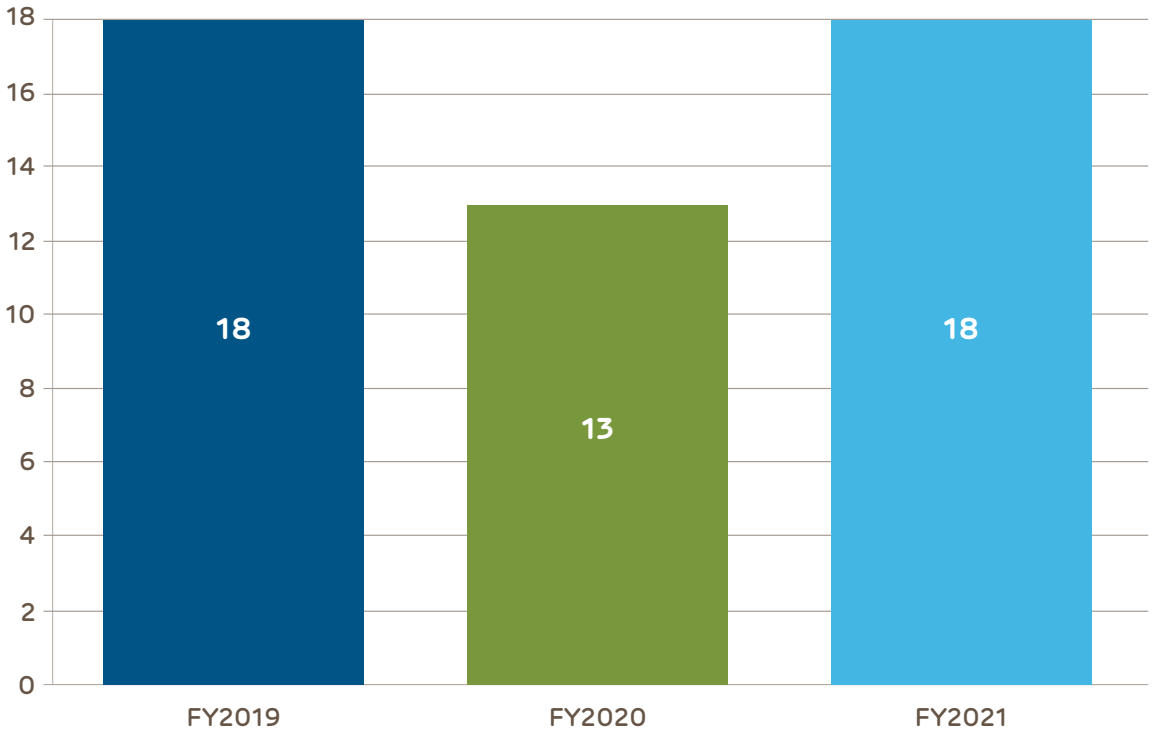
Number of High-Impact Publications
(Calendar Year)



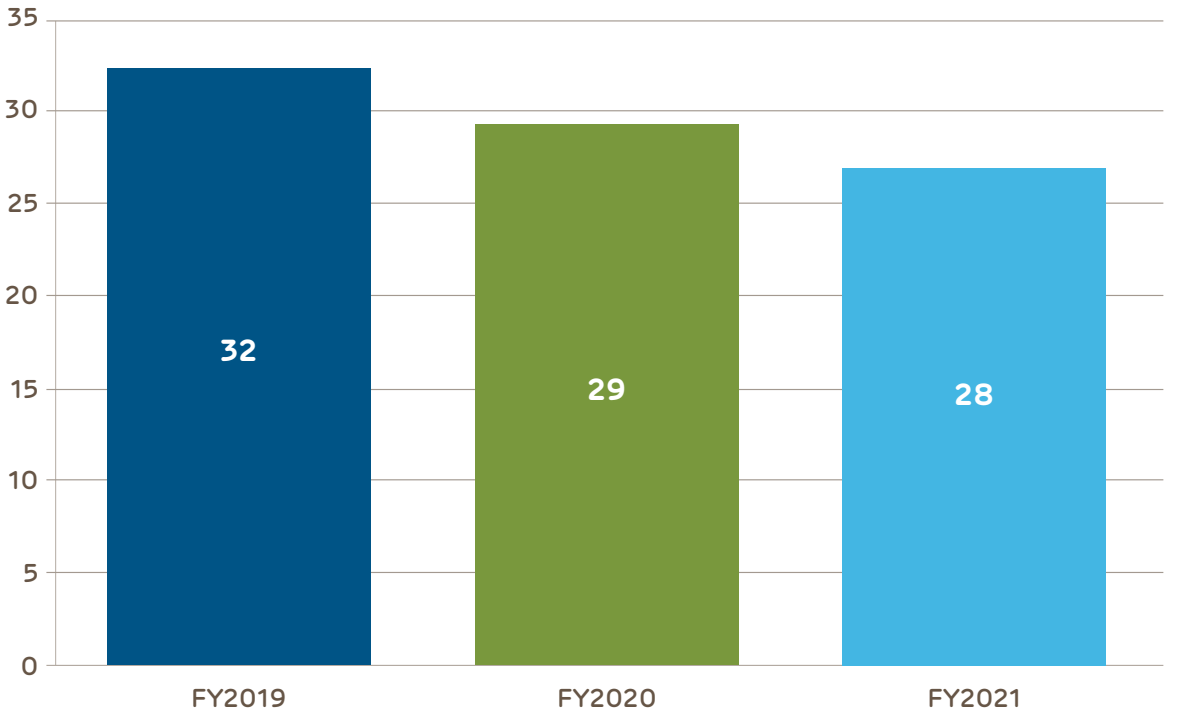
Number of New Patent Applications



Number of Patents Issued



Number of Licenses & Options



Key Strategic Initiatives & Growth

2.16M
OF PATIENTS WITH DATA IN ARCUS

31
OF TRAINING GRANTS

5,310
OF PATIENTS WITH GENOMIC DATA IN ARCUS