RESEARCH BREAKTHROUGHS:

DELIVERING BEST OUTCOMES FOR KIDS AND COLUMBUS

NATIONWIDE CHILDREN'S®

When your child needs a hospital, everything matters.

WORLD-CLASS RESEARCH BENEFITS CHILDREN IN CENTRAL OHIO AND BEYOND

Dennis Durbin, MD, MSCE, is president of the Abigail Wexner Research Institute at Nationwide Children's Hospital, a professor of Pediatrics at The Ohio State University College of Medicine and vice chair for Research in the Department of Pediatrics.

Gideon Griffiths is the young boy pictured on the cover. He's also the first child at Nationwide Children's Hospital to receive a new gene therapy for Duchenne muscular dystrophy following approval by the FDA earlier this year.

But the full story begins 50 years ago.

As one of the earliest innovators of gene therapy, Dr. Jerry Mendell, a neurologist and renowned researcher at Nationwide Children's, has the unique perspective of a scientist working on the pioneering edge of discovery. As a physician, he sees the perseverance required of families affected by rare diseases.

He was 27 years old when he met his first Duchenne muscular dystrophy patient in 1969: a 7-year-old boy on the threshold of losing his ability to walk. No treatments existed at that time, but Dr. Mendell was firmly committed to finding one.

Fast forwarding to today, Dr. Mendell and his fellow innovators at Nationwide Children's have made the hospital an epicenter for gene therapy. Two of the first eight gene therapies approved by the FDA—Zolgensma® for spinal muscular atrophy and Elevidys® for Duchenne muscular dystrophy—were developed at Nationwide Children's.

We are passionate about making a difference in the lives of children not only here in Columbus, but across the country and around the world. Bold investments in our research have produced significant advances that are vastly improving child health.

Read on to meet some of our most recognized scientists and hear the inspiring stories of the patients who have benefited from our research — research that also benefits Columbus.

Dennis R. Durbin, MD, MSCE
President of the Abigail Wexner Research Institute at Nationwide Children's Hospital

Of the first eight gene therapies approved by the FDA, two were discovered and developed right here in Columbus, at Nationwide Children's Hospital.

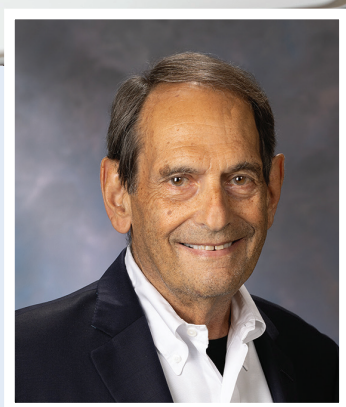
Thanks to Dr. Jerry Mendell and his fellow gene therapy pioneers at Nationwide Children's, children who would have died by age 2 from spinal muscular atrophy are in elementary school and looking forward to recess. Young boys who would have lost their ability to walk and breathe because of Duchenne muscular dystrophy now are riding bikes and playing with friends.

See more about these innovations here:

Dr. Jerry Mendell with Gideon and his mom.

"It is thrilling to arrive at this moment of getting treatment to a patient population that has waited so long for more hope."

– Jerry Mendell, MD, principal investigator in the Center for Gene Therapy at the Abigail Wexner Research Institute at Nationwide Children's Hospital



Gideon's Story:

A LIFE-CHANGING GENE THERAPY

Five-year-old Gideon Griffiths and other children like him who were born with a rare and severe genetic disorder involving progressive muscle degeneration and mobility loss have a brighter future now. In June, after decades of research and testing in the Center for Gene Therapy at Nationwide Children's Hospital, the FDA issued an accelerated approval for a gene therapy treatment for Gideon and others with Duchenne muscular dystrophy (DMD).

Gideon was the first patient in the state to receive a life-altering dose of Elevidys, outside of the approximately 200 participants in the Nationwide Children's-based clinical trial. In early August, Gideon visited Nationwide Children's to receive the injection with the help of a team involving the treatment's co-inventor Jerry Mendell, MD, who is a principal investigator for the Center for Gene Therapy.

"It is thrilling to arrive at this moment of getting treatment to a patient population that has waited so long for more hope," says Mendell, who saw his first patient with Duchenne in 1969. He has spent his career working to understand and develop viable treatments for DMD and other neuromuscular diseases, conducting years of research and hundreds of clinical trials.

Mendell and Louise Rodino-Klapac, PhD, co-developed the therapy to treat DMD. Rodino-Klapac, formerly based at Nationwide Children's, is the executive vice president, head of Research and Development and chief scientific officer at Sarepta Therapeutics, which now holds the license for Elevidys.

Children battling DMD, a disease primarily diagnosed in boys, develop problems with walking, breathing and heart function, leading to a shortened life expectancy. In the past, children with DMD usually did not survive past their teens.

Gene therapy treatment provides an opportunity to deliver missing or corrected genes to cells. "Gene therapy is better than any drug therapy because it's one-time delivery," says Mendell. "If we treat patients very early, we can get to the disease before it wipes out all of the muscle or nerve."

Now families like Gideon's who feared their children would slowly succumb to the disease have hope for a longer, healthier future. "It's life-changing to be able to experience this, to be able to give Gideon a better quality of life," says Erin Griffiths, Gideon's mother. "We feel hopeful and thankful, and we're excited to watch our little boy run around, play and just be a boy."

This is the second gene therapy developed at Nationwide Children's Hospital to receive FDA approval. In 2019, the FDA approved a treatment for spinal muscular atrophy type 1 (SMA1), the most severe form of SMA. Of the first eight gene therapies now approved by the FDA, two have been developed by researchers at Nationwide Children's Hospital.

"This is what I've devoted my life to; since I began investigating gene therapy as a potential treatment for children with neuromuscular disorders, it's been my dream to develop a gene therapy for DMD," says Mendell. "The FDA's decision means we can save more function and save the quality of life for these children and their families."

See more about Gideon's treatment here.

Avery at age 6

Avery's Story:

A YOUNG PIONEER GETS HOPE FROM A TISSUE ENGINEERED VASCULAR GRAFT

"We're ever learning, ever refining, always striving to provide better outcomes for our patients."

– Christopher Breuer, MD, pediatric surgeon, and Nationwide Endowed Chair in Surgical Research who serves as director of the Nationwide Children's Center for Regenerative Medicine

Many children born with congenital heart disease require the need for one or more reconstructive operations, often beginning with surgery in their earliest days of life. Such was the case with Avery, a now thriving tween who underwent her first surgery when she was a tiny 2-day-old infant.

Avery was born with "half a heart." The medical term for this condition is hypoplastic left heart syndrome —a life-threatening congenital heart disease in which the left ventricle is underdeveloped and cannot properly pump blood to the body. After a series of operations necessary to repair the condition, Avery underwent the final surgery known as the Fontan procedure when she was 3 years old.

Fontan surgery previously involved the implantation of manufactured materials, such as vascular grafts, vascular patches or replacement heart valves—all of which can cause challenges as the child grows and the materials do not.

To solve these challenges, researchers led by Chris Breuer, MD – Nationwide Children's pediatric surgeon, director of the Center for Regenerative Medicine and Nationwide Endowed Chair in Surgical Research – developed a method for using biomaterials in which an individual's own cells can be used to develop tissues that can then be used to repair the heart. Avery was among the first children in a clinical trial to receive a tissue engineered vascular graft (TEVG) made from her own cells that should continue to grow with her.

While Avery continues to grow and thrive with her TEVG, the researchers are using what they've learned from the first clinical trials to continue improving TEVGs of the future.

"Moving what we've learned in the clinical trial back to the laboratory and bringing it back to the patients is the heart of what we do. We're ever learning, ever refining, always striving to provide better outcomes for our patients," says Dr. Breuer.

"We've recently begun evaluating the use of tissue engineering in fetal surgery, so we're able to correct small structural defects during the developmental period, and this can really expand or augment our ability to care for patients," he says.

"Participating in research means hope. Not just for our family, but for those that follow us," says Avery's mom. "We are fortunate to have such an amazing facility right here in Columbus that has a vision of always searching for a better way to help children."


June
September
October
Jack

Jack's Story:

A TINY BABY TRANSCENDS MANY OBSTACLES WITH THE HELP OF A SPECIALIZED NATIONWIDE CHILDREN'S HOSPITAL TEAM

"You're much more likely to find patients playing on a mat on the floor than you are in a bed, laying there getting ventilator therapy."

– Leif Nelin, MD, chief, Division of Neonatology and Dean Jeffers Endowed Chair in Neonatology at Nationwide Children's

The energy to breathe is something most of us don't think about. But for a baby who develops bronchopulmonary dysplasia (BPD), every breath is a miracle due to very fragile lungs. Most newborns with BPD arrive 10 weeks or more before their due dates, and many weigh 2 pounds, or less. The Nationwide Children's Hospital BPD unit allows babies the opportunity to not just breathe, but also get additional developmental help so that they can grow and play.

This is a process that Jack Shields — now a T-ball playing, action-oriented 5-year-old — and his family understand well. Jack and his twin brother were born 14 weeks earlier than expected. Jack's brother progressed and left the hospital after five months, but Jack continued using a mechanical ventilator and had a tracheostomy. He was assigned to the BPD unit for additional help. It was a challenging launch to life, but Jack had quickly declared himself a fighter, according to his dad, Joe.

The benefits of Jack's tracheostomy began to emerge over time as he received care in the BPD unit. The work of breathing became a bit easier for him. He was able to gain weight and, as babies do, he eventually found his hands, his nose and his mouth. He began playing, too, enjoying time on an activity mat on the floor. Jack gradually learned to sit up, roll over and, at five months, he started learning sign language.

"We think of our BPD unit not so much as a pulmonary unit, but more of a neurodevelopmental unit," says Leif Nelin, MD, division chief of Neonatology at Nationwide Children's Hospital. "We've found that when we give the right mechanical ventilation setting, we can really focus on their neurodevelopment, and that's one of the things we do very differently here."

Rather than sedating patients, ventilator settings that deliver more oxygen with slower breaths allow babies to interact with the world around them and participate in guided therapy and play. This not only prevents developmental delays and helps babies reach normal milestones, but it also results in better medical outcomes.

After more than a year in Nationwide Children's BPD unit, Jack left the hospital with a ventilator, a tracheostomy and a gastrostomy tube for feedings. With the support of his dedicated parents, a home care team of nearly 24-hour nursing service and scheduled sessions for physical, occupational and speech therapy, Jack began to catch up on his childhood milestones. He learned to walk and build on his extensive sign language vocabulary.

Jack's dad describes life as even more of a blur now that medical care has been replaced by the activities of a little boy ready to explore. At about 3 years old, Jack's tracheostomy was removed and he no longer needed a ventilator. In fact, Jack started playing T-ball and entered preschool.

This fall, Jack has started kindergarten and his days are filled with activities and adventures. "He's going to have a great life," Joe recently proclaimed.

AN ECOSYSTEM FOR INNOVATION

Nationwide Children's focuses on ensuring that research can be translated into the pediatric care that advances child health. This is a distinguishing feature among children's hospitals.

Nationwide Children's has effectively built an internal biotech company within the hospital with its Office of Technology Commercialization. This office facilitates the transfer of new technologies, research and innovations to outside partners, benefitting patients, the local community and children around the world.

A portfolio of over 130 technologies developed by Nationwide Children's researchers and clinicians is diverse and ever-growing.

Supporting the commercialization of discoveries promotes a cycle of progressive growth and innovation, which attracts world-class researchers, inventors and bold thinkers who make further discoveries. Thanks to this commercialization infrastructure, established players have been drawn to the Central Ohio region with increasing frequency.

By bringing impactful innovations to market, we ensure novel technologies find their way beyond our walls, and this commercialization helps drive economic development.

The Abigail Wexner Research Institute

The integration of research and clinical care is at the heart of Nationwide Children's Hospital's strategic priorities. The Abigail Wexner Research Institute at Nationwide Children's is a dynamic state-of-the-art environment for world-class research. Four dedicated buildings are full of the brightest minds in their fields, with more than 200 researchers and physician-scientists along with 1,500+ employees working together. AWRI has been a top-10 National Institutes of Health-funded freestanding pediatric research institute for more than a decade. NIH funding has doubled over the past 5 years.

TYPES OF INNOVATIONS

Biomarkers: Detect and measure normal biological processes, pathogenic processes or responses to interventions.

End User Innovations: Improve clinical or business practices and patient outcomes with improved/ novel medical devices and software.

Gene Therapies: Deliver new genetic material to replace impaired or harmful genetic material to treat various conditions.

Therapeutics: Prevent or treat diseases.

Tissue Engineering Innovations: Combine scaffolding, seeded cells and biologically active molecules into functional tissues, allowing a patient's own cells to be used to grow new tissue or organs for repair.

Research and Clinical Tools: Enhance therapeutic or research activities.

A DECADE OF GROWTH (2012 - 2022)

900%
GROWTH IN OUT-LICENSING OF TECHNOLOGIES

over 70%
OF THE HOSPITAL'S PATENT PORTFOLIO IS LICENSED

28
LICENSED TECHNOLOGIES CURRENTLY IN CLINICAL TRIALS

7
ACTIVE DEALS IN 2012

87
ACTIVE DEALS AT END OF 2022

18 startups

Q&A with Clinical Research Expert Cynthia Gerhardt, PhD

You were recently named Chief Clinical Research Officer. What does your role entail?

I am responsible for clinical research operations across the institution and the full life cycle of the clinical research process. I oversee the expansion and oversight of a variety of clinical research resources, such as our clinical trial support, biostatistics core and human research protections program. As part of the strategic plan, we are creating state-of-the-art, centralized laboratory space—which will provide infrastructure for our investigational pharmacy—and clinical trials for new pediatric drugs and devices, as well as social and behavioral science. Our goal is to increase quality and efficiency, while promoting a culture of excellence among investigators and clinical research staff.

A key component of Nationwide Children's strategic plan is the integration of research and clinical care. Why is that important?

Our goal is to lead the journey to best outcomes for children everywhere. Clinical research allows for advances in the treatment, diagnosis and prevention of diseases and/or conditions. Cultivating an organization where clinical care drives research and research drives clinical care ensures that children receive the most advanced therapies possible. It also brings together bright minds from every corner of the organization dedicated to solving the most challenging problems affecting pediatric health. Everyone at the hospital has a role in the discoveries that will transform children's health care.

Why should children participate in clinical research?

Children are often left out of clinical trials, resulting in fewer drugs and devices that are developed and proven safe specifically for pediatric use. This leaves health care providers and families with fewer options for treatment. It is critically important that children and their families are provided with opportunities to participate in research that can advance our understanding and care of both common and rare pediatric conditions. Families often know that their child can benefit from treatments that were developed because another family participated in research. Involvement in clinical research gives families the chance to help scientists discover the cures and best care for the most pressing challenges in children's health.

What are the most important factors parents should consider when enrolling their child in a clinical study?

Parents can be reassured that every research study at Nationwide Children's is federally mandated to undergo rigorous review and oversight to ensure the safety and well-being of participating children and families. Any study that includes children must obtain approval from the Nationwide Children's Institutional Review Board. All clinical research with children also has additional protections to ensure minimal risk to participation or that the benefits outweigh any known risks.

Parents and children should know their rights as participants. Families have the right to understand the risks and benefits of participating, alternative options and any associated costs and/or compensation. Parents and children also have the right to know how their privacy and confidentiality will be protected and whom to contact with questions about the research or any research-related injury. Parents are encouraged to discuss the study with the research team and their child, so they feel fully informed and comfortable participating. Lastly, they should know that participating in research is incredibly valuable and critical to improving how we care for children!

"Cultivating an organization where clinical care drives research and research drives clinical care ensures that children receive the most advanced therapies possible. It also brings together bright minds from every corner of the organization dedicated to solving the most challenging problems affecting pediatric health."

Cynthia Gerhardt, PhD, is chief clinical research officer at Nationwide Children's Hospital, a professor of Pediatrics and Psychology at The Ohio State University and program director for the Center for Clinical and Translational Science, a collaboration between The Ohio State University, Wexner Medical Center and Nationwide Children's Hospital. She also is the Janet Orttung-Morrow and Grant Morrow, III, MD, Endowed Chair in Pediatric Behavioral Health at Nationwide Children's.

The integration of the highest quality clinical care with the most innovative research is at the heart of the Nationwide Children's Hospital Strategic Plan.

Q&A with Health Equity Expert Deena Chisolm, PhD

Your research extends beyond a clinical setting to factors that can impact children on a daily basis in their schools, homes and neighborhoods. What are some areas you are currently studying?

One of my active research projects is exploring the impact of structural racism on maternal and child health and how investments by a health system in an affected community can be guided by a better understanding of the neighborhood's history. Another is focused on implementing and evaluating a novel approach for meeting the whole-child needs of Medicaid enrolled children, including school-based health interventions, home visiting and care navigation. My research covers a broad spectrum of health (for example, infant mortality, chronic disease, mental health and preventive health care). The common thread is addressing health needs by meeting families where they are, and identifying and addressing the real issues that underly their health challenges.

How do you develop the research to determine what disparities are impacting access to health care?

Knowing that disparities exist is only the beginning. We start by identifying health outcomes that differ across population groups (such as race, primary language, income) and then conduct research to understand the underlying causes of the differences. Using our knowledge of those underlying causes, we test interventions that can close the gaps. We focus on both individual and system-level causes. Individual level approaches include patient and family mentoring and education to promote healthy behaviors, and programs to support health-related social needs like food insecurity, housing instability and transportation. There also are novel approaches to medication adherence. System-level approaches include providing access to care in health care deserts, developing payment models that reward reducing disparities and addressing the neighborhood effects of structural racism.

How is Nationwide Children's working within the community to create opportunities to improve the health and well-being for children and families in underserved populations?

For more than two decades, Nationwide Children's has prioritized community investment of time and money to improve community well-being through the Healthy Neighborhoods Healthy Families Initiative. This work has focused on housing, health, education, economic well-being and community enrichment on the south side of Columbus and more recently in the Linden area. This work is done with the understanding that health is not just the absence of disease. A truly healthy community, supported by an engaged health care system, also strives toward high kindergarten readiness, high graduation rates, safe and affordable housing, low rates of unintended pregnancy and more.

The study of health equity can have ripple effects in how future generations experience health care systems. How do you see your work now contributing to the future?

I'm encouraging the field to focus more on creating solutions than identifying problems. Importantly, my research seeks to demonstrate that health care systems are not the whole problem or the whole solution. They must be part of the broader environment that influences health. Most importantly, I hope that my work inspires young people to take the baton and move it forward: To believe that they can achieve in academia and research even if that is not a path that others they know have taken. I see training, mentoring and celebrating the next generation of diverse researchers as the greatest contribution that I can have to the future.

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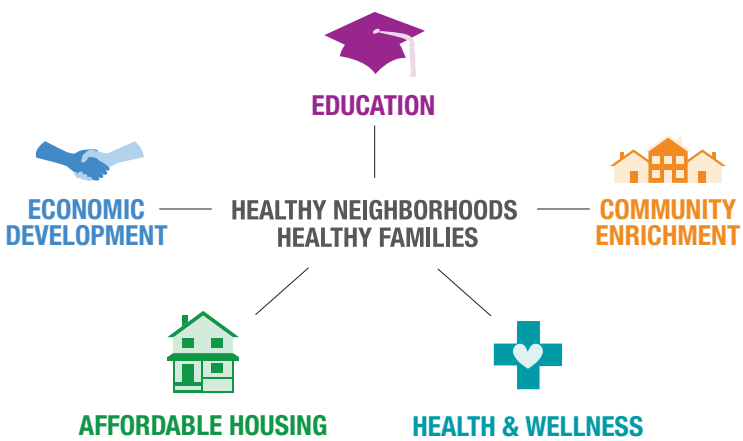
Deena Chisolm, PhD, is the director of Center for Child Health Equity and Outcomes Research, vice president of Health Services Research, the Nationwide Foundation Endowed Chair of Health Equity Research at Nationwide Children's Hospital and a professor of Pediatrics at The Ohio State University College of Medicine and Public Health.



The Healthy Neighborhoods Healthy Families Initiative began in 2008 and targets five impact areas that affect communities' overall health.

Q&A with Genomic Medicine Expert Elaine Mardis, PhD

Would you provide a basic Genomics description?
We should first define what a genome is: essentially, it is the DNA-based "blueprint" from which an organism can be built. DNA encodes genes and other sequences that regulate the genes and their expression into RNA and then into proteins. Proteins are the working components of cells that determine their biology. Genomics is the science of studying genomes, which requires an interplay of technology to produce sequencing data and bioinformatics to analyze and interpret the sequencing data.

Your expertise is internationally recognized—including significant contributions to the Human Genome Project, which is considered one the most ambitious and important biomedical research endeavors in history. What was your role in the Human Genome Project?
Our center at Washington University in St. Louis was one of three large National Institutes of Health-funded centers that executed the Human Genome Project in the U.S. It was, of course, a multi-national project. Our center produced about 20 percent of the draft human genome coverage (announced in 2001), coordinated all U.S. and many international centers on the strategic approach to the sequencing and finished to high quality the 2, 4, 7 and Y chromosomes. My role was leading a group of technicians and engineers to oversee how technologies were utilized in the sequencing aspects of the Human Genome Project, including robotics, molecular biology and the sequencing instrumentation.

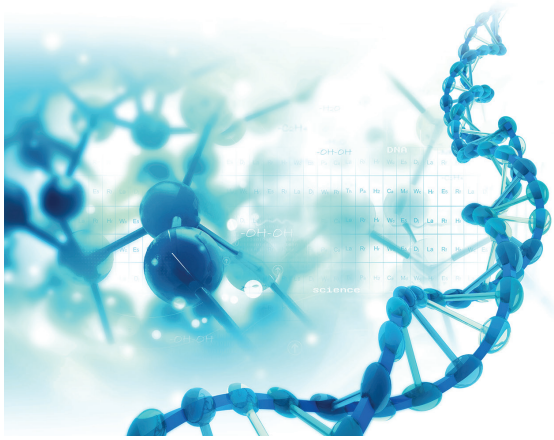
Can you explain what real-world impacts come out of the Steve and Cindy Rasmussen Institute for Genomic Medicine at Nationwide Children's?
We utilize genomics to study patients in real time, providing information relevant to their disease diagnosis and to identify best care for these children. Our studies span a range of diseases from cancer to epilepsy to cardiac defects to immunology and beyond. We partner with the physicians providing care for these patients, to help them answer specific questions and to familiarize them with the impact that genomics can have on their understanding of the underlying causes for specific health challenges.

What is genomics' biggest impact on the treatment of children with cancer?
In early discovery efforts, genomic studies of pediatric cancers demonstrated how truly unique their genomes and underlying causes for cancer development are, when compared to adult cancers. In daily practice, genomics can identify therapeutic targets in pediatric cancer genomes—effectively identifying specific treatments that may eradicate their cancer. These have largely been applicable in the genomic drivers that overlap with adult cancers. So much more is needed in drug development for genetic drivers unique to pediatric cancers.

With rapid advancements and applications in the field, what excites you most about the future of genomic medicine?
Two things, in particular: First, gaining increasing understanding of genomics in diverse populations is on the increase and may clue us in to the unique disease underpinnings in these patients, which is the first step to effective medical care. Second, the sophistication with which we are beginning to use data science in placing each child's genome into context relative to the universe of genomic knowledge achieved by studying other children's genomes. In effect, our efforts are to impact each child in terms of their diagnosis and care while enhancing our ability to understand the next child relative to those studied before. This is really the spirit with which most patients and parents consent to genomic studies, and we want to honor that intent.

"We utilize genomics to study patients in real time, providing information relevant to their disease diagnosis and to identify best care for these children. In effect, our efforts are to impact each child in terms of their diagnosis and care while enhancing our ability to understand the next child relative to those studied before. This is really the spirit with which most patients and parents consent to genomic studies, and we want to honor that intent."

Elaine Mardis, PhD, an internationally recognized expert in cancer genomics, is co-executive director of the Steve and Cindy Rasmussen Institute for Genomic Medicine at Nationwide Children's Hospital and holds the Rasmussen Nationwide Foundation Endowed Chair in Genomic Medicine. She also is a professor of Pediatrics at The Ohio State University College of Medicine.



The Molecular Characterization Initiative

Nationwide Children's Hospital's Institute for Genomic Medicine and Biopathology Center were both chosen to collaborate with the National Cancer Institute (NCI) and the Children's Oncology Group (COG) to create the Molecular Characterization Initiative: a project that aims to collect, analyze, and report clinical molecular data to support more than 200 COG member hospitals around the world that treat children with cancer.

This collaboration helps pediatric cancer patients receive a precise diagnosis based on the molecular characteristics of their specific tumor, which means their doctor can provide the best possible treatment option. Children facing cancer from across the world now benefit from the expertise of the Nationwide Children's Institute for Genomic Medicine and Biopathology Center.

Q&A with Data Sciences Expert Peter White, PhD

You were recently named the first Chief Data Sciences Officer (CDSO) at Nationwide Children's. Why was this role so important for the hospital to create?

From discovery science to population health, our researchers are generating masses of data that hold immense potential to transform pediatric research, diagnostics, treatments and even disease prevention. To make sense of this data deluge, we've been harnessing the power of cloud computing and cutting-edge data science techniques, like AI, machine learning and big data analytics.

And that's why we took the bold step of creating the Office of Data Sciences. Our mission is to unleash the true potential of biomedical data sciences across our research enterprise to support cutting-edge research and translation into the world-class care that defines Nationwide Children's.

Do you see genetic/genomic testing becoming a standard of care in the near future?

We have been performing rapid genome sequencing in newborn infants in our neonatal intensive care unit. The goal of this study was to perform the genome sequencing and analysis as rapidly as possible — what used to take months can now routinely be done in three to five days. About 35 percent of the patients we have enrolled in this study had a genetic finding that informed their care.

We believe that genomics will impact multiple areas of care in pediatrics. As a father of a daughter born with a congenital heart defect, I am very excited to be leading a new translational protocol, which will use genomics to analyze all Nationwide Children's patients born with a critical congenital heart defect and patients admitted to our Cardiothoracic Intensive Care Unit.

What do you think is most important for patients and families to keep in mind with the availability of new tools such as artificial intelligence (AI)?

AI is undoubtedly set to revolutionize the healthcare landscape! In my group, we've been thoroughly evaluating Large Language Models (LLMs), the powerful technology that drives applications like ChatGPT. Our belief is that LLMs hold tremendous potential to glean valuable research insights.

Our primary focus is to rigorously assess this technology to ensure its application is free from any potential harm. We're working diligently to understand its biases and making careful recommendations to ensure ethical AI use and avoid creating health inequities.

You also lead Nationwide Children's rare disease genomics program. What is the significance of this program?

I have had the privilege to be part of a team that has used genomics to end the diagnostic odyssey for hundreds of patients and their families. We started the program back in 2011, which allowed us to perform research genomic analysis for patients with a suspected rare genetic disorder, but the family had no diagnoses. The success of that program showed us just how powerful genomic testing could be, and in 2015 we launched clinical exome sequencing diagnostic testing. Since then, clinical exome sequencing has become the standard of care for patients seen by our genetics clinic, and our Institute of Genomic Medicine (IGM) has performed the test for thousands of patients now.

As a parent, not knowing why your child is sick is an awful thing to go through. The quicker we can diagnose a patient's rare genetic disorder, the better; it helps our clinicians determine how best to care for the patients.

"Our mission is to unleash the true potential of biomedical data sciences across our research enterprise to support cutting-edge research and translation into the world-class care that defines Nationwide Children's. We believe that genomics will impact multiple areas of care in pediatrics. As a father of a daughter born with a congenital heart defect, I am very excited to be leading a new translational protocol, which will use genomics to analyze all Nationwide Children's patients born with a critical congenital heart defect."

Peter White, PhD, is chief data sciences officer and the Battelle Chair in Quantitative and Computational Biology at Nationwide Children's Hospital. He is also a Professor of Pediatrics in the College of Medicine at The Ohio State University.

Nearly a decade ago, a team from Nationwide Children's, led by Dr. Peter White, won the CLARITY Undiagnosed Challenge presented by Boston Children's Hospital.

These challenges brought together the best teams in the world to address genomic research and clinical challenges. Nationwide Children's prevailed over 24 other teams including those from Emory, Stanford, USC and Geisinger.

In 2021, Nationwide Children's Hospital was selected as a Rare Disease Center of Excellence by the National Organization for Rare Disorders (NORD).

Q&A

with Cell Therapy Expert Dean Lee, MD, PhD

Briefly explain what is meant by "cell therapy."
"Cell therapy" refers to the preparation and delivery of living cells as therapeutic drugs. This is in contrast to typical drugs that are defined by their chemical composition (which includes everything from aspirin to chemotherapy to insulin), or entire organs that are defined by their anatomy. When we think of cells as drugs, we are most often talking about cells from our immune system that are selected on the basis of their appearance and function. These cells may be prepared from patients or from healthy donors, and are infused into patients much the same way as we give blood transfusions to patients. In many cases — such as the recently approved CAR T cells — the cells are modified with new genes that give them added function.

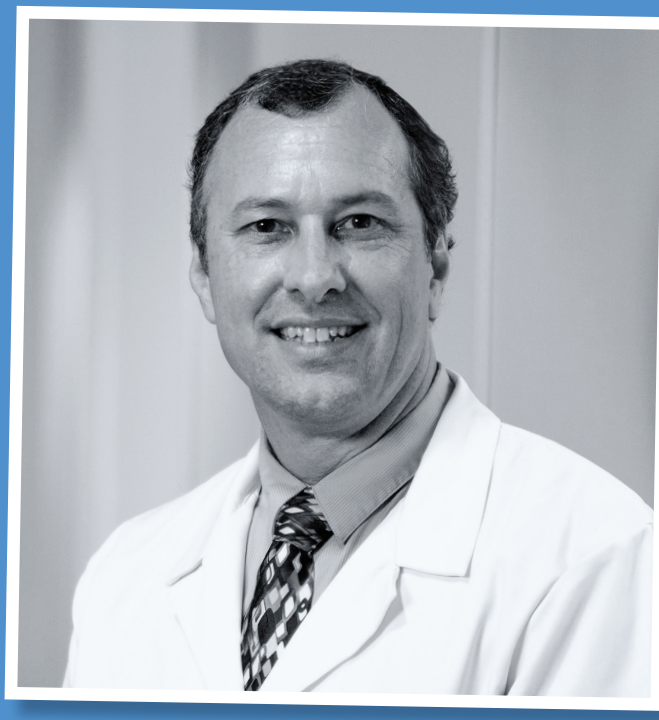
What are NK cells and their role in cell therapy?
NK cells get their name from their original description in the 1970s as "natural killers" of cancer cells. They are white blood cells that are part of the immune system that play an important role in our defense against infection and cancer. They have broad activity against cells in our body that they recognize as dangerous, without being restricted to specific viruses or cancers the way other parts of the immune system are (such as the B cells and T cells that are activated by vaccines). Because they have broad activity, these cells may have broad potential across many kinds of cancer and viral infections.

Why did you choose NK cells as a focus of your research?
It was a little bit of an accident. People had studied NK cells for more than 30 years, but NK cells were very hard to grow in the lab. If you can't grow them, they are hard to study, and if you can't study them, it is hard to know how they work and figure out how to use them. My early research was focused on T cells, and while trying to grow T cells we stumbled on a way to grow and activate large numbers of NK cells. This fueled an entire new area of research in the lab, and we have shared the knowhow and materials with dozens — maybe hundreds — of other labs around the world. But it also enabled us to think about how to give large numbers of these highly active NK cells to cancer patients as a way to restore their immune function and improve cancer cures.

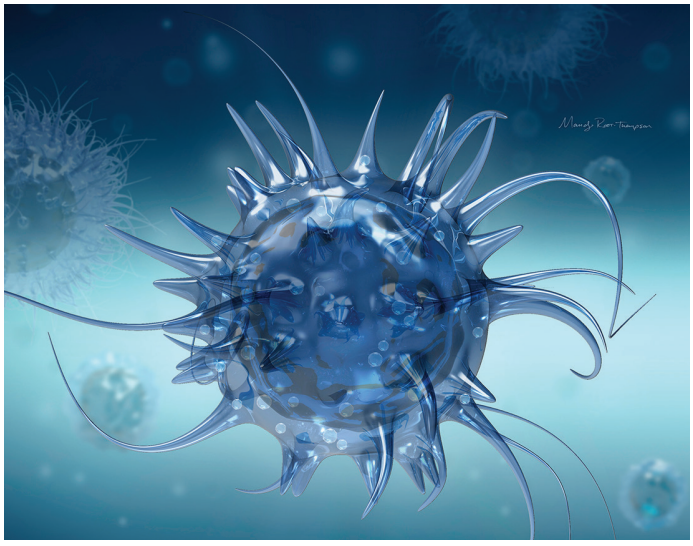
What are the successes achieved so far with NK cell therapy?
Lots of mice have been cured with NK cells over the last 50 years since they were discovered, but NK cells are still very early in their clinical development and proof of success in human patients. As of yet there are no FDA-approved NK cell products. However, we've made major progress in solidifying our manufacturing methods and showing that NK cells are very safe to give to patients. Several initial studies by us and other groups have been recently completed showing that the addition of NK cells can improve remission of leukemias and lymphomas in adults, and we are currently running the first studies focused on pediatric leukemia patients. New studies at Nationwide Children's and OSU are testing NK cells for sarcomas, neuroblastoma, brain tumors, breast cancer and skin cancer.

What excites you the most about the future for cell therapy?
The most exciting thing to me is how broad the possibilities are. We've only started to scratch the surface in cancer, and there are many other possible uses for NK cells in autoimmune diseases, infections, and aging.

"We've made major progress in solidifying our manufacturing methods and showing that NK cells are very safe to give to patients. Several initial studies by us and other groups have been recently completed showing that the addition of NK cells can improve remission of leukemias and lymphomas in adults, and we are currently running the first studies focused on pediatric leukemia patients."



Dean A. Lee, MD, PhD, is director of the Cellular Therapy and Cancer Immunology Program at Nationwide Children's Hospital and The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute. He is a professor of pediatrics at The Ohio State University College of Medicine and the DiMarco Family Endowed Chair in Cell Based Therapy at Nationwide Children's.



Natural killer (NK) cells are the innate immune system's first line of defense for viral infections and help keep tumor cells at bay. But while these critical components of the immune system have held promise for treating cancer, progress has been challenging. NK cells have been difficult to obtain, reproduce and manipulate for maximum benefit — until now.

Advances in technology and methodology have led to new strategies that use NK cells to improve outcomes for children (and adults) with cancer.

Q&A with Microbial Disease Expert Lauren Bakaletz, PhD

How would you define microbial pathogenesis to a non-scientist?

Microbial pathogenesis is the study of how viruses, bacteria and other microscopic organisms cause disease. We then use this information to devise a better cure and/or figure out how to stop them from causing disease by developing new therapeutic drugs or, ideally, new vaccines. We also often use the advanced understanding gained from our studies to devise better ways to detect the microbe or diagnose the disease, similar to what was done during the COVID-19 pandemic.

Your team's groundbreaking research and continued contributions to the field provide insight into a variety of bacterial infections. What is the real-world application of your research?

Ideally, the real-world application of my team's research will lead to a broadly applicable way to cure a variety of infections caused by bacteria, and even a vaccine that will prevent these infections. We focus on diseases that are chronic, recurrent and/or very difficult to treat with antibiotics like chronic sinus infections, urinary tract infections, middle ear infections, wound infections, infections of implanted joints and necrotizing enterocolitis, as well as cystic fibrosis and COPD, among many others. It's a very exciting time for us as we have moved our work forward from the laboratory to testing these new applications in human clinical trials, which is a major milestone! And we need to mention that our work is in collaboration with the laboratory of Nationwide Children's researcher Steven Goodman, PhD.

Biofilms are referenced in much of your work. Can you explain what that means and their significance?

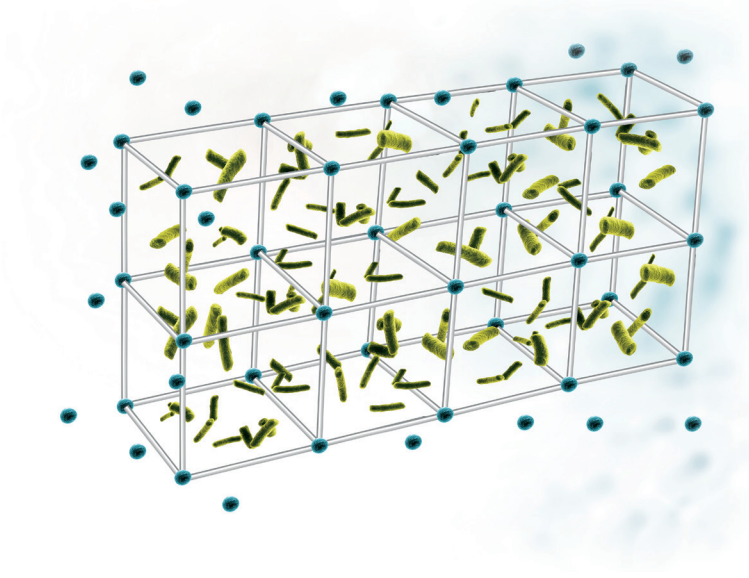
A biofilm is a 3D community of many bacteria living together in a "fortress" of their own construction that protects them very well from antibiotics and even our own immune systems. These communities of bacteria are very sophisticated, they have a system of communication with each other, a division of labor and even ways to avoid being detected by our immune systems. As such, they are extremely difficult to get rid of when they are responsible for causing a disease. There are, however, healthy biofilms that are good for us, such as those in our gut, our mouth and on our skin. A biofilm in itself is not necessarily a 'bad' thing, but rather it is simply the way that all bacteria in nature prefer to live anywhere they exist. However, when these biofilms are built and reside where they don't belong in or on our bodies, or are occupied by disease-causing bacteria, we very much are in need of better ways to get rid of them as, unfortunately, this happens more often than ideal.

What have been the most exciting developments in your research?

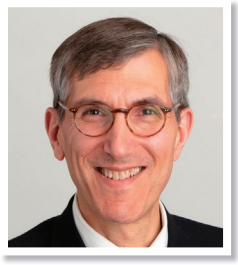
There have been many, including being able to watch my trainees and staff make so many new discoveries and get excited when they have a chance to present their work at meetings all over the world that we've traveled together to. But, certainly, being able to make discoveries that have progressed all the way through the many years of diligence required to get them FDA-approved and into human clinical trials has been absolutely priceless and incredibly exciting for me, my collaborators and our hard-working lab teams!

"The real-world application of my team's research will lead to a broadly applicable way to cure a variety of infections caused by bacteria, and even a vaccine that will prevent these infections. It's a very exciting time for us as we have moved our work forward from the laboratory to testing these new applications in human clinical trials, which is a major milestone!"

Lauren Bakaletz, PhD, is the director of the Center for Microbial Pathogenesis and vice president for Basic Research at the Abigail Wexner Research Institute at Nationwide Children's Hospital and the Tillie E. Coleman Endowed Chair in Pediatric Research at Nationwide Children's Hospital. She is a Professor in the Departments of Pediatrics and of Otolaryngology at The Ohio State University College of Medicine.



Biofilms are highly organized communities of bacterial cells shielded by an extracellular matrix — a fortress of their own construction. Dr. Bakaletz, Dr. Goodman and their teams focus on ways to disrupt biofilms and their protection of harmful bacteria — and ways to use the protective power of biofilms for good.



"Onasemnogene (gene therapy for spinal muscular atrophy) is probably the poster child for what goes right and how well this can work when a gene therapy is truly effective. This, to me, is about as amazing as it gets in medicine."

– Peter Marks, MD, PhD, Director, Center for Biologics Evaluation and Research U.S. Food and Drug Administration

(Quoted from the 2023 Nationwide Children's Hospital Technology Showcase Keynote Presentation)

"I am extraordinarily proud of the significant impact that Nationwide Children's has, not only on the well-being of central Ohio's children but also on the advances in research that support the health of children around the world. One simply cannot help but be inspired and want to do as much as possible to fuel further advances."

– Abigail Wexner

"Ten years ago, Nationwide Children's undertook a strategic initiative aimed at commercializing our research. Amazingly, just 10 years later, we are a national leader in commercialization returns. But this was never the reason. The aspiration was baked in a belief that the best and brightest scientists and researchers would be attracted to a place that prioritized the culture of spinning out as well as spinning in technology and knowledge —and that knowledge would improve the health of our kids. It was also baked in a belief that this is one of the most important ways we can impact the economic future of Columbus and Ohio."

– Alex Fischer, former CEO of the Columbus Partnership, former chair of the board of Nationwide Children's Hospital and current board member for Nationwide Children's Hospital and the Abigail Wexner Research Institute.

"Nationwide Children's leadership has had the willingness to take risks and make investments. That has truly made a difference. I consider the hospital and research institute critical engines of continued industry growth, creating a flywheel effect that will sustain a robust life sciences industry here in central Ohio."

– Eddie Pauline, MBA, OhioCED, President and CEO of Ohio Life Sciences (formerly BioOhio)

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