

HELPING KIDS EVERYWHERE

A LOOK INSIDE THE ABIGAIL WEXNER RESEARCH INSTITUTE
AT NATIONWIDE CHILDREN'S HOSPITAL

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When your child needs a hospital, everything matters.

A NOTE FROM THE PRESIDENT OF THE ABIGAIL WEXNER RESEARCH INSTITUTE AT NATIONWIDE CHILDREN'S HOSPITAL



John A. Barnard, MD
President

May marked an exceptional time in the history of Nationwide Children's Hospital beginning with the dedication of the Abigail Wexner Research Institute in honor of Mrs. Wexner's compelling leadership and vision in support of research activities on our campus. We also announced the first Steve Allen, MD, Distinguished Scholar in Pediatric Research and celebrated the FDA approval of the world's first gene therapy for spinal muscular atrophy.

In her 25 years on the Nationwide Children's Board of Directors, including seven as its chair, Mrs. Wexner has transformed our hospital from an important community resource to an international destination children's hospital and research institute. I am honored to be the president of an institute named after this visionary leader.

The Allen Distinguished Scholar in Pediatric Research is named after CEO Steve Allen, MD. The Allen Distinguished Scholar is a year-long designation, given to a senior, preeminent researcher whose career has been spent pursuing medical and scientific discovery – just as Dr. Allen's career at Nationwide Children's has been spent expanding what it means to be a world-class children's hospital. In the pages that follow, you'll learn more about the work of the first recipient Dr. Jerry Mendell.

Finally, the FDA approval of the gene therapy Zolgensma, which was developed here at Nationwide Children's in collaboration with experts at The Ohio State University, is a remarkable example of our drive to achieve best outcomes for every patient. Through continued dedication and investment in pediatric research, the possibilities seem limitless.

This special publication is a look inside the day's events and one of the largest fundraisers in the history of Nationwide Children's – raising \$3.5 million for pediatric research in a single evening. As you read the following pages celebrating our researchers and the patients we serve, we hope that you will join us in our mission to advance care and cures for children everywhere.

ABIGAIL WEXNER RESEARCH INSTITUTE AT NATIONWIDE CHILDREN'S HOSPITAL



The Research Institute at Nationwide Children's has been renamed in honor of Abigail Wexner, whose ongoing, passionate advocacy has ushered in a period of unprecedented transformation at the hospital. Mrs. Wexner began serving on Nationwide Children's board in 1993 and acted as board chair for seven years from 2005 to 2012. During her tenure as chair, Mrs. Wexner led the hospital through the largest expansion in its 127-year history, including completion of a 12-story hospital building and a third research building, with more than \$1.2 billion in regional economic impact.

"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. Impact of this magnitude doesn't happen without visionary leadership, dedicated staff and a supportive community. It has been an honor to work alongside Dr. Allen and the team and witness firsthand the transformation of this institution. One simply cannot help but be inspired and want to do as much as possible to fuel further advances."

– Abigail Wexner

STEVE ALLEN, MD, DISTINGUISHED SCHOLAR IN PEDIATRIC RESEARCH



In nearly 13 years as CEO, Steve Allen, MD, helped build Nationwide Children's into a renowned pediatric research institution, including overseeing an increase from \$41.7 million to \$105.9 million in external research awards. In recognition of Dr. Allen's role in the evolution of Nationwide Children's as a leader in pediatric research and health care, Nationwide Children's has established the Allen Distinguished Scholar in Pediatric Research. The award will be given to a preeminent Nationwide Children's senior researcher who exemplifies the innovation at the Abigail Wexner Research Institute. The inaugural recipient is Jerry Mendell, MD, leader of the breakthrough clinical trial of gene therapy for spinal muscular atrophy.

"Nationwide Children's is a premier academic medical center creating world-renowned research because of Abigail Wexner's leadership. I am honored by the creation of the Allen Distinguished Scholar in Pediatric Research as part of the hospital's continuing efforts to support scientific pioneers in the Abigail Wexner Research Institute."

– Steve Allen, MD

FDA Approves Zolgensma – A First-Ever Gene Therapy Treatment for Spinal Muscular Atrophy

The approval of the novel therapy stands as a historical milestone for the Abigail Wexner Research Institute and Nationwide Children's Hospital, as well as for children with SMA.

Spinal muscular atrophy or SMA is the No. 1 genetic killer of babies under 2 years of age. In long-term follow-up studies of Zolgensma, babies who received the gene therapy have improved outcomes and reach developmental milestones never before seen in the natural history of the disease.

The drug, Zolgensma, was developed in the Center for Gene Therapy in the Abigail Wexner Research Institute at Nationwide Children's Hospital in collaboration with researchers at

The Ohio State University. It is the second gene therapy ever approved by the FDA.

Jerry Mendell, MD, neurologist and principal investigator in the Center for Gene Therapy, led the pivotal clinical trial. Dr. Mendell, who is also the recipient of the Allen Distinguished Scholar in Pediatric Research, has been a pioneer in the care of neuromuscular diseases for more than 40 years, including groundbreaking work in SMA, muscular dystrophy and gene therapy.

“For most of my career as a physician and researcher, we’ve had very little to offer families with neuromuscular disorders. Now, we’re starting to see that gene therapy can be a safe and effective treatment for some disorders. We’re on the cusp of a new era in targeted therapeutics, and it’s exciting to be part of it.”

– Jerry Mendell, MD

For more information about this historic announcement, including a video of Evelyn's story and media coverage of the approval, visit [NationwideChildrens.org/SMA-approval](https://www.nationwidechildrens.org/SMA-approval)

Evelyn Villareal came with her family all the way from Virginia to celebrate her doctor, Jerry Mendell, MD. Evelyn received Zolgensma as part of the clinical trial led by Dr. Mendell. She is now walking, running and dancing at age 4, surpassing all expectations associated with SMA.



MAY 21, 2019: A SPECIAL DAY IN OUR COLUMBUS HISTORY

Abigail Wexner, Dr. Steve Allen and the Columbus community share a transformational commitment to pediatric research and medicine. In addition to a breakfast event and a special media tour, more than 350 guests came together at a noon luncheon to celebrate this new era of pediatric research. National, state and city leaders including Mayor Andrew Ginther, joined Nationwide Children's patient champions, doctors and researchers to enjoy lunch and hear guest speakers Governor Mike DeWine and "The Innovators" author Walter Isaacson.



Board Chair Alex Fischer, Abigail Wexner and CEO Dr. Steve Allen share their perspectives on what makes a great leader during the Leadership Breakfast for Nationwide Children's faculty and staff.



Abigail Wexner and Patient Champion Evelyn share a fun moment before the lunch begins.



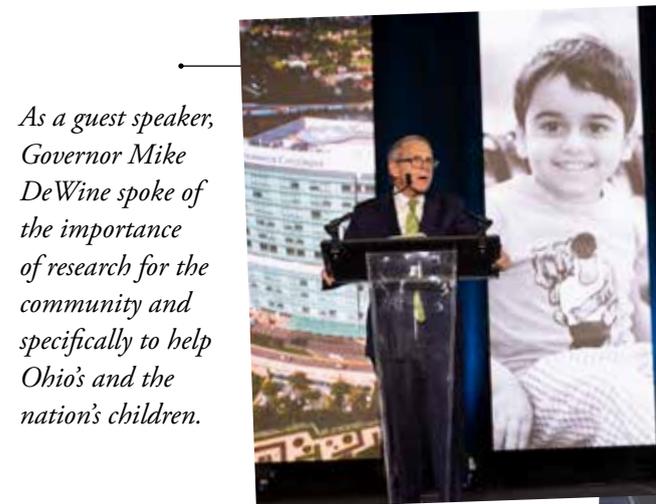
The Institute for Genomic Medicine at Nationwide Children's was a highlight of a special media tour. Abigail Wexner, author and guest speaker Walter Isaacson and IGM Co-Executive Director Elaine Mardis discuss the future of pediatric genomic medicine.



Board Chair Alex Fischer welcomes Dr. Steve Allen to the stage. Dr. Allen retired on June 30 after 13 highly successful years as Nationwide Children's Hospital CEO.



Board Chair Alex Fischer shares the stage with Patient Champion Evelyn Villareal and her mom, Elena. Evelyn boldly told the audience, "Let's eat!"



As a guest speaker, Governor Mike DeWine spoke of the importance of research for the community and specifically to help Ohio's and the nation's children.



Patient Champion Taryn Cook and her mother Sarah are greeted by Gov. Mike DeWine. (See Taryn's story on page 20.)



More than 350 guest and leaders, including the Governor and First Lady, came together to celebrate the dedication of the Abigail Wexner Research Institute.

*Avery, age 6*

TINY PIONEER AMONG THE FIRST CHILDREN TO RECEIVE A TISSUE ENGINEERED VASCULAR GRAFT

*Avery, age 2*

Avery was born with “half a heart.” The medical term for this is hypoplastic left heart syndrome – a type of life-threatening congenital heart disease in which the left ventricle is underdeveloped.

Avery has endured a series of complex surgeries to redirect the blood flow through her heart. The first was at just two days old. At age 3 years, she underwent one of the final major surgeries, called the Fontan procedure.

One of the many challenges of repairing this condition is that children continue to grow, but the materials implanted during the Fontan surgery do not – leading to even more surgeries. As part of a clinical trial at Nationwide Children’s Hospital, Avery received a different type of material – a tissue engineered vascular graft (TEVG), made from her own cells, that could grow with her.

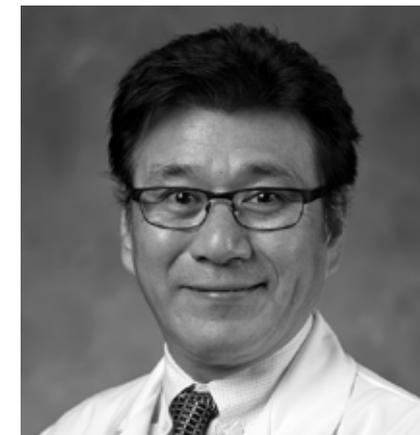
“Tissue engineered vascular grafts are potentially better than other options for pediatric congenital

heart patients for several reasons, the most important of which is the graft’s growth capacity,” says Toshiharu Shinoka, MD, PhD, cardiothoracic surgeon and principal investigator in the Center for Regenerative Medicine.

And while Avery continues to grow and thrive with her TEVG, the researchers are using what they’ve learned from the first clinical trial to continue improving TEVGs to come.

“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 Christopher Breuer, MD, pediatric surgeon, director of the Center for Regenerative Medicine and Nationwide Endowed Chair in Surgical Research.

“Participating in research means hope. Not just for our family, but for those that follow us,” Avery’s mom adds. “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.”

*Christopher Breuer, MD**Toshiharu Shinoka, MD, PhD*

NIGHT OF WONDER

A special evening event was held at the New Albany home of Abigail and Les Wexner to celebrate the launch of the Steve Allen, MD Distinguished Scholar in Pediatric Research fund. Called “A Night of Wonder” the festivities featured remarks by bestselling author Walter Isaacson. Lauren Cunningham, a brave, inspirational cancer survivor also shared her story.

While the evening celebrated the tremendous contributions of Abigail Wexner and Steve Allen, MD, retiring CEO of Nationwide Children’s Hospital, the focus was squarely on the transformation of pediatric health care for future generations. The event was one of the largest fundraisers in the history of Nationwide Children’s, raising \$3.5 million for pediatric research in a single evening.



Left to Right: Steve Allen, the Cunningham family (Lauren is in the floral print dress), Abigail Wexner



John Barnard, MD, president, Abigail Wexner Research Institute at Nationwide Children’s, welcomes guests and recaps the day’s earlier events.



Left to Right: Lisa Bachmann, Tim Johnson, Mike Schlonsky, Rocky Robins, Jeremy Ball, all from Big Lots



Bestselling author Walter Isaacson (center) with Ramon Jones from Nationwide and his wife Erika.



Left to Right: Alex Derkson, Nikki Holsopple, Jamie Reed, all from event lead sponsor JPMorgan Chase & Co.



Left to Right: Ann and Tom DiMarco, Judy and James Beattie

ABIGAIL WEXNER RESEARCH INSTITUTE



The Abigail Wexner Research Institute is spread over three dedicated research buildings, with a fourth planned to open in 2021. Fully integrated within one of America's largest freestanding children's hospitals, AWRI offers unprecedented opportunities for collaboration and innovation.



"A lot of people who come to a pediatric hospital – those kids are still looking for answers. I think what's happening here is pretty inspiring. A large hospital that sees lots and lots of pediatric patients, but has built a research compatibility that's very tightly integrated with that. That's how we make progress in medical research – having the people doing the research right next door."

– Francis Collins, MD, director of the National Institutes of Health

The Big Lots Behavioral Health Pavilion is scheduled to open on the Nationwide Children's campus in 2020. The nine-story pavilion is expected to be the largest facility on a pediatric campus devoted to children and adolescent mental health in the country, supporting expanded access to care and research for families impacted by mental health conditions.

BRINGING INNOVATION FROM THE ABIGAIL WEXNER RESEARCH INSTITUTE TO CHILDREN EVERYWHERE THROUGH TECHNOLOGY COMMERCIALIZATION

The Abigail Wexner Research Institute is dedicated to enhancing the health of children by engaging in high-quality, cutting-edge research. This includes developing promising new technologies to advance the practice of pediatrics and general health care.

STARTUP COMPANIES BASED ON NATIONWIDE CHILDREN'S DISCOVERIES INCLUDE:



To learn more about technology commercialization at Nationwide Children's, visit NationwideChildrens.org/OTC



Tayla, age 6

NEW HOPE FOR PATIENTS WITH BATTEN DISEASE

“When Tayla was diagnosed in Australia, we were told to take her home and love her while we could,” her mother says. “We were devastated and left without hope.”

But her family didn’t give up. They began scouring the research for more information about their daughter’s disease — Batten disease — and found a clinical trial for an enzyme replacement therapy in Columbus, Ohio.

Batten disease is a genetic, progressive and deadly disease of the nervous system. The most common form, CLN2 (neuronal ceroid lipofuscinosis type 2), is caused by the lack of the TPP1 (tripeptidyl peptidase 1) enzyme.

“I always told parents this is a brain disorder that will result in the early death of your child and that you may see your child melt before your eyes,” says Emily De Los Reyes, MD, neurologist and director of the Nationwide Children’s Batten Disease Center of Excellence. “Now, I can tell them that we have a treatment.”

Tayla’s family moved across the world, hoping to find a place in the trial.

“We were fortunate enough to be accepted into the clinical trial at Nationwide Children’s Hospital. I think most parents will do whatever they need to do to save their child,” says Tayla’s mom. “Traveling across the world is what we had to do.”

To date, the drug cerliponase alfa, which was approved for use by children with CLN2 Batten disease by the FDA in April 2017, has an 84% response rate.

For families like Tayla’s, that’s a miracle.

“Researchers are saving lives and giving us precious time with our children to create memories,” Tayla’s mom says. “Our family can now look into the future and have hope.”



Emily De Los Reyes, MD

Nationwide Children’s is a Batten Disease Center of Excellence, as designated by the Batten Disease Support and Research Association.

A Newborn. A Virus. A Novel Treatment. A Life Saved.

Over the course of just six days last year, Nationwide Children's clinician-scientists conceptualized a treatment that had never been tried on a preterm infant before, received an emergency federal approval, and used the treatment to save a life in the Newborn Intensive Care Unit (NICU).

The infant, born about 10 weeks premature, was diagnosed with disseminated adenovirus infection at two weeks after delivery. Given the high death rate associated with this infection in a newborn, Jeffery Auletta, MD, director of the Host Defense and Immunocompromised Infectious Diseases Program in the Division of Infectious Diseases and director of the Blood and Marrow Transplant Program, looked outside the box for answers.

He called Dean Lee, MD, PhD, director of the Cellular Therapy and Cancer Immunology Program at Nationwide Children's and The Ohio State University Comprehensive Cancer Center, and

together they developed a plan: They wanted to give virus specific T cells from the mother, who had successfully cleared the infection, to the infant.

They reached out to Kevin Bosse, PhD, RAC, regulatory operations manager in Drug and Device Development Services at Nationwide Children's, to pave the way for the emergency investigational new drug (EIND) designation. Most IND applications take months to prepare. But with an all-hands-on-deck approach, the team pulled everything together that they needed for the EIND application in less than 36 hours.

After receiving the novel treatment, the infant's infection dramatically cleared. The infant was discharged home and has been doing well ever since.

"We say best outcomes for all children. This is us doing it. Doing things that you can't write a prescription for," says Dr. Bosse.



Kevin Bosse, PhD, RAC



Dean Lee, MD, PhD



Jeffery Auletta, MD

Shaking Up the Scientific Community

A common culprit in ear infections, NTHI bacteria create dense biofilms — complex communities of microorganisms attached to a surface and protected by a fortress-like structure of proteins and DNA. Understanding how biofilms form is an important step in learning how to destroy them and prevent chronic infections. And the more researchers learn about NTHI and their biofilms, the more they understand how complex and surprising these bacteria are.

"Biofilms are sophisticated, three-dimensional, towering communities of bacteria with communication systems, a division of labor and the ability to build and disrupt structures at will. And the bacteria in biofilms are very clever," says Lauren Bakaletz, PhD, director of the Center for Microbial Pathogenesis in the Abigail Wexner Research Institute at Nationwide Children's. "They use a variety of strategies that enable resistance to

antibiotics. It's like a fortress. Nearly every chronic or recurrent infection caused by bacteria involves a biofilm."

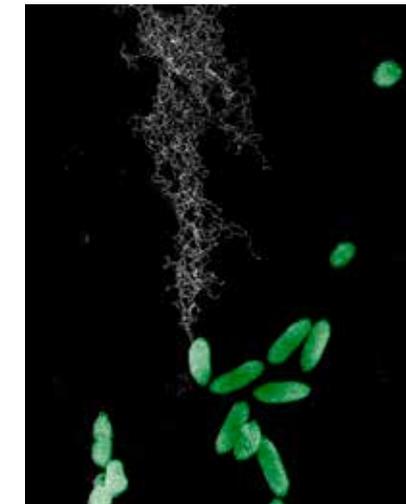
In a previous study, Dr. Bakaletz and her team were the first to observe and describe a method of movement - or motility - for these organisms previously thought to be nonmotile.

Now, they've shaken things up again by being the first to observe and describe how biofilm components get into the biofilms. This discovery generates many more questions, which Dr. Bakaletz and her team are eager to answer.

"In a world where scientists have been studying bacteria for hundreds of years, it's a joy to get at something this fundamental. This is why we do this. We're advancing scientific knowledge for future generations."



Lauren Bakaletz, PhD



Caught on film: Dr. Bakaletz and her team caught NTHI releasing biofilm-building materials into the biofilm environment.

Who? Why? Using Data Analysis to Understand Suicide Risk

Researchers in the Center for Suicide Prevention and Research are on a mission to understand suicide risk. And through understanding who is at risk, they hope to find the keys to early intervention and prevention.

“Our research over the last several years has revealed several emerging trends. By carefully analyzing data, we’re able to uncover those trends that otherwise might be missed,” says Jeff Bridge, PhD, director of the Center for Suicide Prevention and Research.

In a series of publications, Dr. Bridge and his colleagues have outlined racial-, gender- and age-related disparities and trends among youth suicides. For example, they reported that young black children, 5 to 12 years old, have higher

suicide rates compared to young white children, even though the overall rates for suicide in adolescence is higher in white youth. Recently, the team found that while the rates of suicide are increasing overall, they are increasing more rapidly for female youth than males, particularly among youth aged 10 to 14 years.

“We know that certain populations are facing greater increases in suicide risk. By identifying those populations, and quantifying the risk, we provide the building blocks for prevention programs. The data we gather can be used to support funding for prevention programs and targeted outreach,” says Arielle Sheftall, PhD, principal investigator in the Center for Suicide Prevention and Research.



Jeff Bridge, PhD



Arielle Sheftall, PhD

Predicting Severity of Community-Acquired Pneumonia

Community-acquired pneumonia (CAP) is a leading cause of hospitalization and mortality in children.

“When a child comes to the emergency department with CAP, we often don’t know what’s causing it. And we can’t predict if that patient is going to get worse and have to go to the intensive care unit or if we can send them home with antibiotics,” says Rebecca Wallihan, MD, physician in Infectious Diseases and vice-chair for Education in the Department of Pediatrics. “We know a lot about CAP, but the reality is that we still don’t know enough to be practical.”

To address these unknowns, clinicians need a way to quickly and accurately predict disease severity in children with CAP. Dr. Wallihan and her collaborators initiated a clinical study to determine if they could use transcriptional profiling to identify

better markers of disease severity in children hospitalized with CAP.

They used a novel metric called Molecular Distance to Health (MDTH) — a single numerical score that summarizes the overall change in expression of immune-related genes in a patient compared to a healthy, age-matched control.

The approach gives details about how the immune system is responding in each case of CAP, and the MDTH score directly correlated to the severity of the disease, according to the study authors.

By trying to build a database of the knowns, the researchers hope to develop a method to reveal the unknowns. The researchers say that this study is the first of a series that they hope will eventually lead to better outcomes for children with CAP worldwide.



Rebecca Wallihan, MD

Each year in industrialized countries, 4% of children younger than 5 years will develop community-acquired pneumonia.



Taryn, age 3

CHANGING LIVES OF PATIENTS WITH CEREBRAL PALSY



Taryn, age 18 months

Taryn was born at just 27 weeks gestational age. She experienced the most severe type of intraventricular hemorrhage and was diagnosed with

bronchopulmonary dysplasia, retinopathy of prematurity, apnea of prematurity and, ultimately, cerebral palsy.

Taryn received her official CP diagnosis at about 12 months of age during her visit with the Nationwide Children's NICU Follow-up Program. Her parents later enrolled her in the "Early Childhood Constraint Therapy in Cerebral Palsy" clinical trial led by Nathalie Maitre, MD, PhD, director of the NICU Follow-up Program and principal investigator in the Center for Perinatal Research.

"Participating in the trial was personally rewarding because of the benefit we saw for Taryn," says Taryn's mom. "But it was also really important to know that we were contributing to something bigger. We knew that we could help change things for future generations of children with cerebral palsy."

The trial was focused on the use of soft-restraint therapy to encourage the use of the nondominant side of the body. This is beneficial both physically in strengthening the weaker side and neurologically in helping to build new neural pathways in her developing brain.

"The research is important on its own, but it also helps ensure that a clinic is using the most up-to-date, evidence-based care," says Dr. Maitre. "We are not just a research program that documents outcomes. We are a clinical program that fully integrates research into our patients' journeys."

The practicality and application-focus of the trial and clinical education was also much appreciated, says Taryn's parents.

"We understand more now about how we can help her, how we can advocate for her, and what resources are available to her," her dad adds. "We've learned so much from the therapists and other clinic staff. We went from feeling scared and intimidated to knowing that there's something we can do. That's empowering."



Nathalie Maitre, MD, PhD

The Abigail Wexner Research Institute is one of 17 member centers of the Eunice Kennedy Shriver Institute of Child Health and Human Development Neonatal Research Network.



The Sylvester family

FROM PERSONAL TRAGEDY TO RESEARCH PARTICIPANT

When Sarah and Matt Sylvester's infant daughter Addy tragically died of respiratory syncytial virus (RSV) infection, they were devastated.

Years later when their son Michael was born, Sarah noticed a flyer about a clinical trial for RSV at Nationwide Children's Hospital that was enrolling healthy controls.

"RSV is a very common infection in infants and young children — almost everyone will be infected by age 2. In the United States, 2-3% of all infants infected with RSV will be hospitalized," says Octavio Ramilo, MD, division chief of Infectious Diseases and principal investigator in the Center for Vaccines and Immunity.

Dr. Ramilo, Mark Peeples, PhD, and Asuncion Mejias, MD, PhD, and their collaborators are working to understand how the immune system responds to RSV so they can develop a safe and effective vaccine against it.

"I never would have known what RSV was if it hadn't been for Addy. And without being

involved in anything medically, research didn't really cross my mind," says Sarah. "But the flyer caught my eye, and I knew this was something we could do so that someday no family would have to experience the loss that we felt."

They went on to enroll Michael as a healthy infant in the clinical trial when he was 5 months old, and have since become advocates for participating in clinical research — even when your child is healthy. In fact, they plan to enroll their youngest son Noah in the healthy baby study as well.

"Our passion for and personal connection to this research motivate us to participate," says Sarah. "But the caring and understanding we experienced from the research staff have made it a really positive experience. Our children aren't directly benefiting from this research — we're doing it for someone else's children. And that's what the research community is doing, too. We're all connected in that."



Mark Peeples, PhD, M. Asuncion Mejias, MD, PhD, and Octavio Ramilo, MD

The team's RSV vaccine research is funded by a \$6.75 million grant from the National Institute of Allergy and Infectious Diseases.



Deena Chisolm, PhD

Director of the Center for Innovation in Pediatric Practice,
Abigail Wexner Research Institute, Nationwide Children's Hospital

“Research is about moving from where we are to where we need to be. And every day, we are figuring out how we can make the impossible possible.”



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