

# Transfer to Transform

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THE OFFICE OF TECHNOLOGY COMMERCIALIZATION  
AT NATIONWIDE CHILDREN'S HOSPITAL

2017





## | Our Mission |

The Research Institute at Nationwide Children's Hospital is dedicated to enhancing the health of children by engaging in high-quality, cutting-edge research according to the highest scientific and ethical standards.

The Office of Technology Commercialization at Nationwide Children's facilitates the transfer of new technologies, research and innovations to outside partners to benefit pediatric care, our community and the general public.

## | Affiliations |



Rev1 Ventures partners with The Research Institute at Nationwide

Children's Hospital to accelerate the formation and growth of life science companies in central Ohio. Through our partnership, we seek out high growth opportunities and advise entrepreneurs who are developing innovative therapies and technologies at Nationwide Children's. The goal is to improve children's health in central Ohio and throughout the world by catalyzing ideas developed by innovators and researchers who may provide solutions that improve patient outcomes.



As Ohio's bioscience membership and development organization, BioOhio is focused on networking the

state's outstanding bioscience assets to accelerate growth of a globally competitive bioscience industry. High on this list of assets is pediatric research, in which Nationwide Children's exhibits leadership every day. The Research Institute at Nationwide Children's has been a Pillar Member of BioOhio for the past seven years.

| Centers and Institutes |

- Battelle Center for Mathematical Medicine

Biobehavioral Health

Biopathology Center

Cardiovascular and Pulmonary Research

Childhood Cancer and Blood Diseases

Clinical and Translational Research

Gene Therapy
- Injury Research and Policy

Innovation in Pediatric Practice

Institute for Genomic Medicine

Microbial Pathogenesis

Molecular and Human Genetics

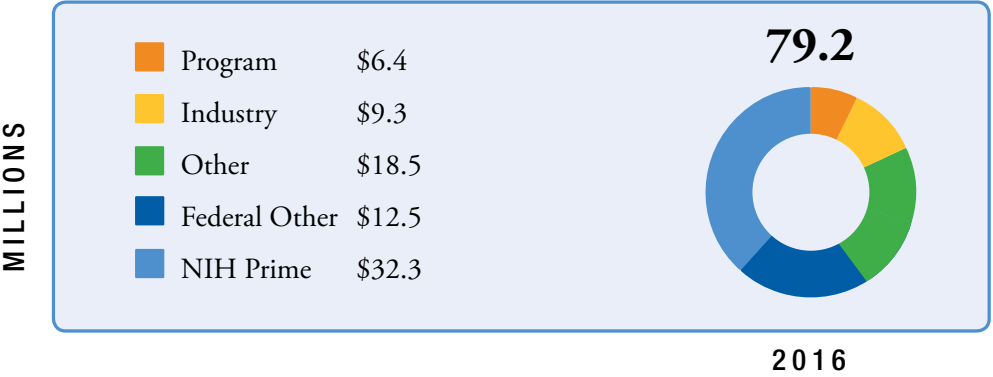
Perinatal Research

Vaccines and Immunity



| Funding |

2016 EXTERNAL AWARDS BY SOURCE



RESEARCH FUNDING BY THE NUMBERS

From research funding support and publications, to patents and inventions, The Research Institute at Nationwide Children’s continues to grow each year.

|                          | 2014 | 2015 | 2016 |
|--------------------------|------|------|------|
| Principal Investigators* | 166  | 184  | 182  |
| Research Fellows         | 61   | 66   | 75   |
| Graduate Students        | 44   | 41   | 34   |
| Employees                | 1103 | 1121 | 1075 |
| Publications             | 713  | 823  | 1067 |
| Patents Filed            | 39   | 62   | 63   |
| Patents Issued           | 12   | 10   | 18   |
| Inventions               | 53   | 76   | 78   |

*\*Includes faculty from The Research Institute and faculty from Nationwide Children’s Hospital with \$50,000 or more in research funding support.*



## | Nationwide Children's Hospital Start-Ups |



### **Milo Biotechnology**

The company was founded in 2012 to develop a therapy that would increase muscle strength and improve the quality of life of muscular dystrophy patients and is based on a discovery by scientists at Nationwide Children's Hospital. The therapy uses an adeno-associated virus (AAV) delivered follistatin protein, which inhibits the activity of myostatin, a protein that impedes muscle differentiation and growth. A clinical trial evaluating the safety and efficacy of Milo's follistatin therapy in patients with Becker muscular dystrophy, Duchenne muscular dystrophy, and Inclusion Body Myositis is underway at Nationwide Children's Hospital.



### **AveXis**

AveXis, a clinical stage gene therapy company, is developing a new gene therapy treatment for patients with spinal muscular atrophy (SMA), a motor neuron disease that affects one in 6,000 live births in the U.S. and is the leading genetic killer of children under the age of 2. The technology, invented by researchers at Nationwide Children's Hospital allows for the delivery of a replacement gene to target motor neurons throughout the brain and spinal cord. The Dallas-based company recently received "Fast Track" designation from the Food and Drug Administration and completed enrollment of Phase I for SMA type I patients.



### **Abeona Therapeutics**

Abeona Therapeutics, formed in early 2013 based on technology developed at Nationwide Children's Hospital, is focused on developing a cure for Sanfilippo Syndrome, MPS IIIA and MPS IIIB, rare genetic disorders caused by the body's inability to properly break down certain sugars. The disease leads to progressive muscular and cognitive decline in children after the age of 2. With no cure or approved treatments, children with Sanfilippo Syndrome usually die before the age of 20. The company is using technology invented by Nationwide Children's Hospital researchers to deliver a corrective gene to the central nervous system in children with the disorder. A Phase I clinical trial for MPS IIIA is underway at Nationwide Children's to evaluate the safety and efficacy of the treatment.



### **ProclaRx**

ProclaRx, based in Athens, OH, is a pre-clinical stage biopharmaceutical company that focuses on developing and commercializing first-in-class anti-bacterial biofilm technology. The technology, invented by researchers at Nationwide Children's Hospital, allows protein-binding antibody to specifically target the protein "bolts" which hold biofilms together. Disruption of the biofilm allows the host immune system and antibiotics to effectively attack and clear the bacterial infection. ProclaRx is developing anti-infectives both as combination devices and as biologics. The company has a growing product pipeline, with multiple candidates in development.



### **ENTvantage Dx**

ENTvantage Dx is an in-vitro diagnostics company that provides primary care physicians and otolaryngologists with rapid, in-office diagnostic tests to determine the cause of ear, nose and throat illnesses. The technology was developed as a result of the research collaboration between The Ohio State University and Nationwide Children's Hospital, for rapid diagnosis of bacterial sinusitis. ENTvantage Dx is currently developing this technology to be used as point-of-care for patients with symptoms of sinusitis.



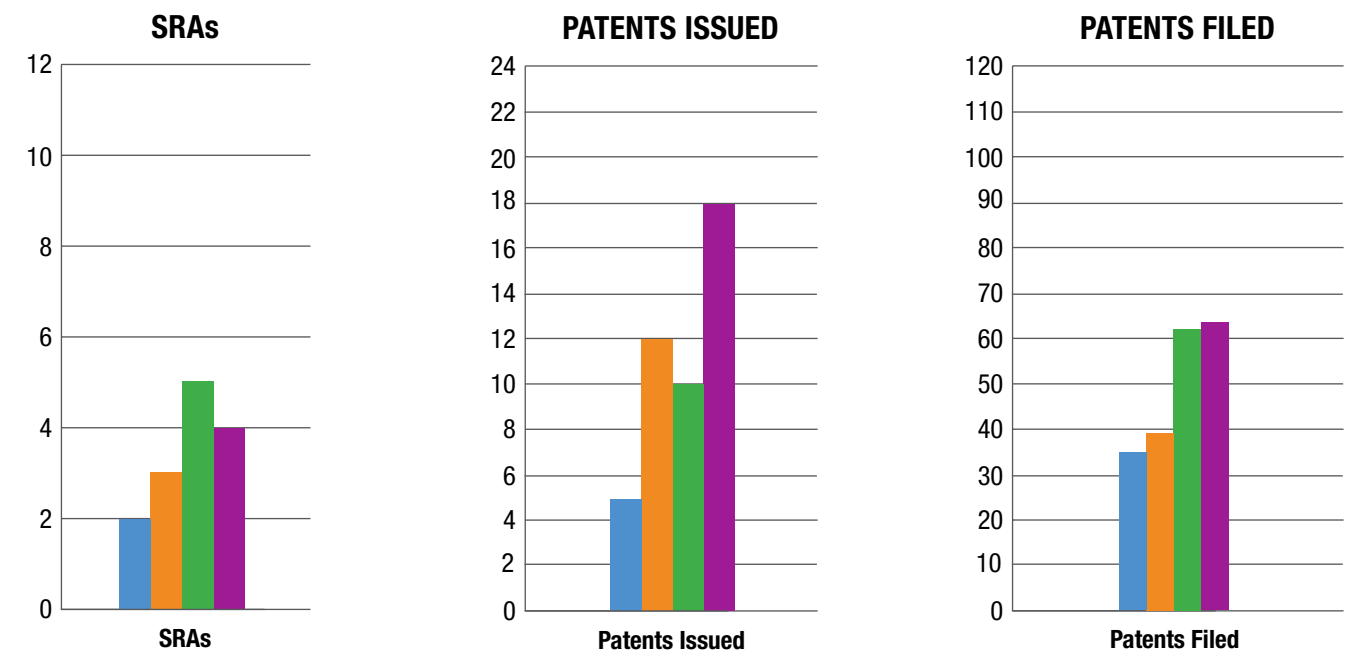
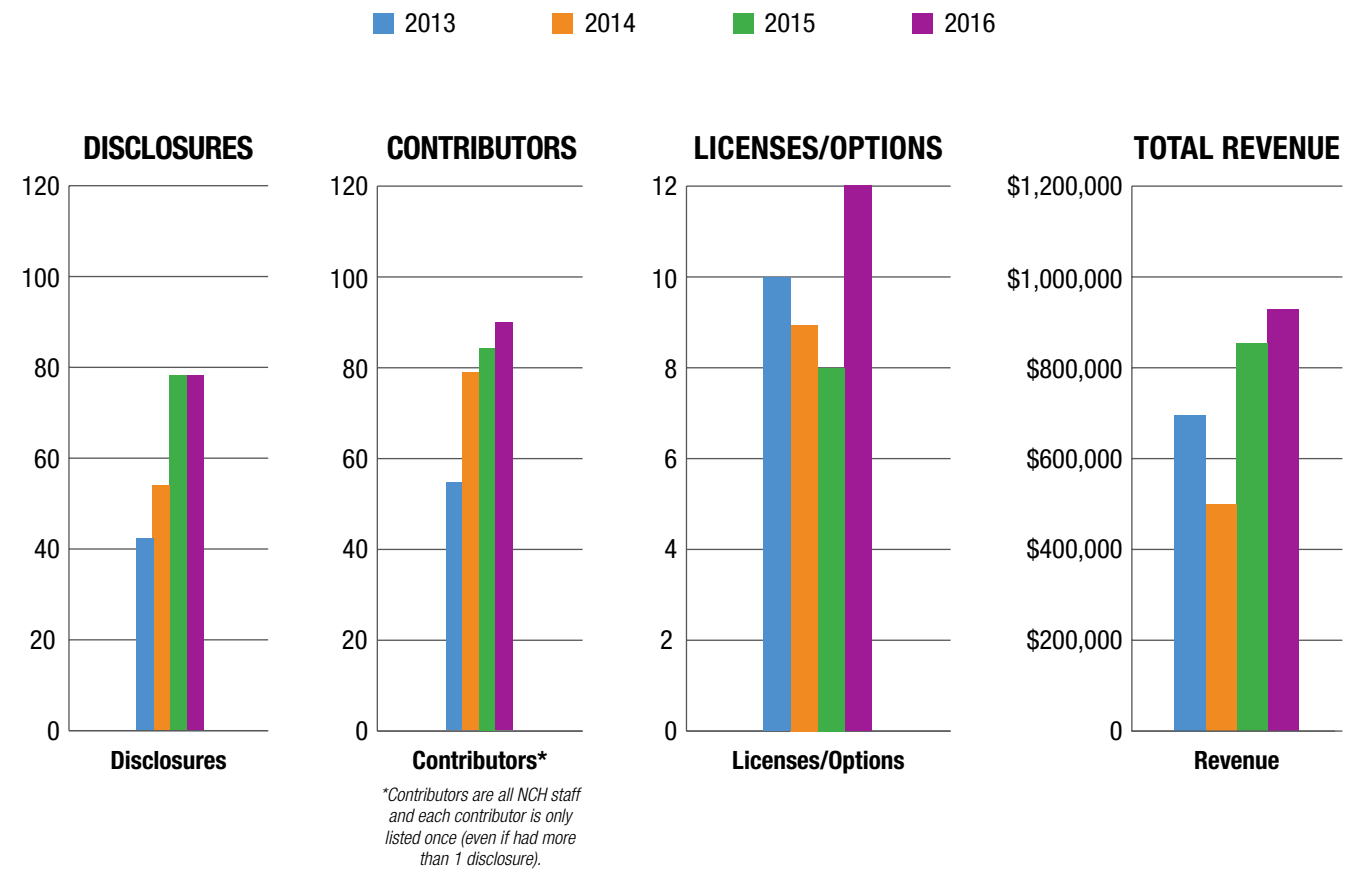
### **GenomeNext**

GenomeNext, LLC, formed in 2014, is a leader in genomic data management and integrated analysis platform. The current strategies for analysis of this data rely upon parallelization approaches that have limited scalability, lack reproducibility and are complex to implement, requiring specialized IT solutions. In order to overcome these challenges, inventors at Nationwide Children's Hospital have developed a unique platform that fully automates the analytical process and provides genomic data and analysis ready for further clinical evaluation.

## | On the Start-Up Horizon |

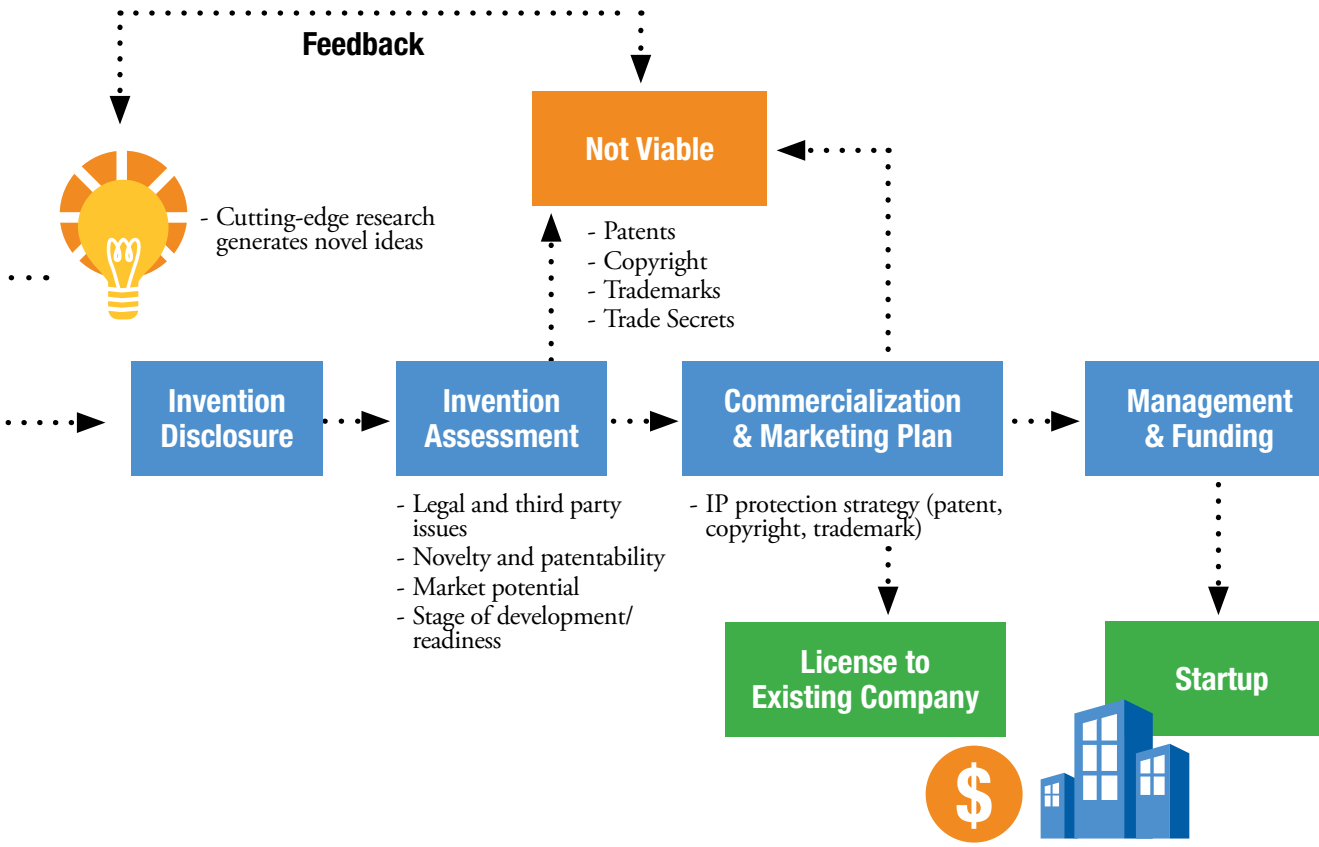
- A clinical stage gene therapy company developing first ever treatments for Limb-girdle muscular dystrophy (LGMD) types 2D, 2B, 2E, 2L, and 2C.
- A clinical stage company developing gene therapy approaches targeting several variants of Batten Disease, a lysosomal storage disorder.
- A preclinical stage RNAi based gene therapy company targeting Facioscapulohumeral muscular dystrophy (FSHD).
- Discovery-stage biopharmaceutical startup focused on developing a novel immunomodulatory therapeutic antibody approach to treating fibrotic diseases.
- A start-up company developing novel formulations for the delivery of probiotic bacteria for treating diseases involving microbial dysbiosis.

# Metrics

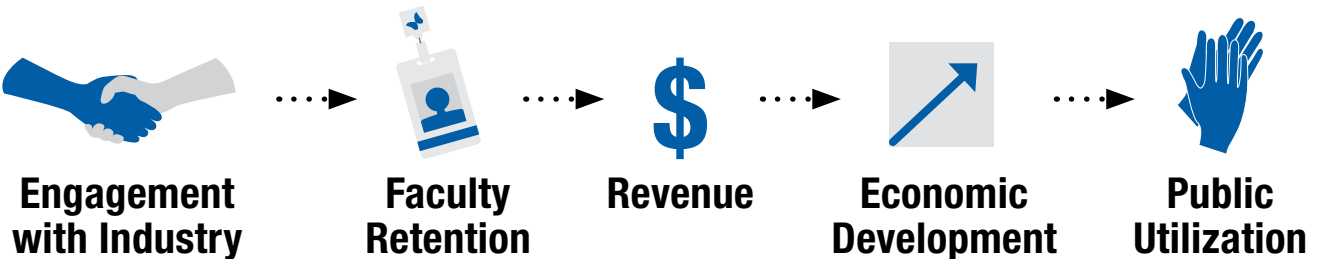


# Our Process

When our doctors, nurses, researchers and other staff members have an idea, they head to our Office of Technology Commercialization. Together, we take these ideas and innovations and translate them into the commercial sector, bringing about new patents, start-up companies and innovations.



# GOALS FOR TECHNOLOGY COMMERCIALIZATION





# Refining Tissue Engineered Vascular Grafts

How two surgeon-researchers are working to improve patient response to tissue engineered vascular grafts through partnership and commercialization

One in every 100 infants is born with a congenital heart defect. For the last 23 years, tissue engineering pioneers Christopher Breuer, MD and Toshiharu Shinoka, MD, have been working together to use tissue engineering techniques in congenital heart surgery to mend these defects. Shortly after they met in 1994 at Yale, they developed the first tissue engineered blood vessels and the first tissue engineered valve.

“We were very fortunate,” says Dr. Breuer. “Usually, when you try things in the laboratory they fail more often than they succeed. We were able to create functional valves and vessels in only about a year’s worth of work.”

Fast forward to 2012, when Dr. Breuer and Dr. Shinoka implanted the first tissue engineered vascular graft (TEVG) in a human patient as part of a landmark clinical trial. Since then, Dr. Shinoka and his surgical colleagues at Nationwide Children’s have implanted numerous TEVGs in children with single ventricle congenital heart anomalies.

“Tissue engineered vascular grafts are superior to other

options for pediatric congenital heart patients for several reasons, the most important of which is the graft’s growth capacity,” Dr. Shinoka says. “Our grafts don’t require immunosuppression or antirejection medications because they are made up of the patient’s own cells. And they grow with the child, decreasing the number of follow up surgeries needed with conventional grafts.”

Briefly, the process of creating and implanting a TEVG is this: a biodegradable scaffold is placed in a vacuum, seeded with cells obtained from the patient’s bone marrow at the beginning of surgery, and then surgically implanted into the patient. Over the next six months, the body acts as a bioreactor to grow a new vessel, and the scaffold disintegrates.

Now, as co-directors of the Tissue Engineering Program at the Research Institute at Nationwide Children’s Hospital, Dr. Breuer and Dr. Shinoka have taken their research a step further and identified novel strategies to combat the leading complication associated with TEVGs. Stenosis, or narrowing of the vessel, is the primary graft-related concern, affecting 30% of patients with TEVGs.

“If narrowing of the graft occurs, less blood will flow to the lungs to be oxygenated, resulting in patients who do more poorly and have worse exercise tolerance. Having a widely open blood vessel is critical to these patients,” says Dr. Shinoka. “It’s the difference between children playing outside at recess or sitting on the sidelines, or worse yet, waiting for another surgery.”

The team has delved into understanding every component of the TEVG process, and how exactly stenosis forms. Research in Dr. Breuer’s laboratory revealed that the process of new vascular tissue formation is orchestrated by the immune system, specifically host-derived macrophages.

“Macrophages orchestrate the whole process,” says Dr. Breuer. “If you can control them, you can control vascular graft formation. It’s all connected. The scaffold causes a host response. The physical and chemical properties of the scaffold affect the macrophages. The cell seeding affects the properties of the scaffold.”

Dr. Breuer and Dr. Shinoka continue to investigate promising interventions which they hope to incorporate into a planned clinical trial. First, the team proposes to seed more cells on the graft before implantation. “This is fairly easy to do,” says Dr. Breuer. “And we can mathematically calculate and analyze risks and benefits of altering the amount of cells seeded to reach optimization.

Secondly, research into the immune response to TEVGs revealed the role of transforming growth factor beta (TGF- $\beta$ ), a cytokine that is involved in many cellular functions, including the regulation of cell growth, proliferation, differentiation and apoptosis. “If you block the receptor for TGF- $\beta$ , you can block stenosis,” Dr. Breuer says. They plan to address the TGF- $\beta$  pathway using medications. Both losartan – a clinically available medication FDA-approved for use in this patient population – and an investigational drug – SB431542 – are promising candidates, according to Dr. Breuer.

“The investigational drug works really well in the models,” says Dr. Breuer. “But losartan is already approved and safe for this population. We’ve included both drugs in our petition to the FDA, but getting losartan to the clinic for their trial is likely to happen more quickly and with less risk.”

Another promising drug is cilastazol, which does not target the TGF- $\beta$  pathway. Instead, it targets another aspect of the immune response – platelets. Cilastazol is

FDA-approved for adults with risk of stenosis, but it is not yet approved for use in children.

Dr. Breuer engaged with the Office of Technology Commercialization at Nationwide Children’s Hospital to manage the patent portfolio protecting these different approaches to improving the TEVG, and the technologies are currently available for partnership opportunities.

More recently, Dr. Breuer’s team made a discovery in a mouse model developed to study stenosis. The team placed TEVGs in mice with varying genetic backgrounds, and found that TEVGs placed in Beige mice almost never developed stenosis. The beige mutation arises from a spontaneous mutation of the LYST gene, or lysosomal trafficking regulator. This mutation causes the LYST gene to be transcribed, but not translated into a functional protein.

Dr. Breuer and his lab recognized the therapeutic potential of inhibiting LYST, and developed a novel method of preventing stenosis through treatment with an anti-LYST antibody. The researchers determined that blocking LYST produces a pro-regenerative immune response, which could have broad implications beyond preventing stenosis in TEVGs. Anti-LYST therapy might have positive effects on tissue regeneration and wound healing in general, could modulate foreign body response, and may improve the longevity of implants and devices such as artificial joints or pacemakers.

The extensive therapeutic potential of this discovery has resulted in the launch of a start-up company, LYST Therapeutics, LLC. The LYST Therapeutics venture will focus on developing various disease treatment modalities within the LYST platform.

Meanwhile, Dr. Breuer and his team continue to make significant strides towards improving patient outcomes through ongoing research projects at Nationwide Children’s Hospital. “It’s great being a doctor when you have the opportunity to make a patient better; however, it is a miserable feeling when someone asks for your help and you have nothing to offer,” says Dr. Breuer. “Performing translational research provides me with an opportunity to offer hope as we continue to push the boundaries of biomedical research and attempt to develop solutions for today’s most vexing clinical problems.”





# An Infrastructure to Support Drug Development

Researchers at academic institutions routinely make discoveries about disease processes and potential therapeutic agents. Translational medicine is bent on moving these discoveries out of the laboratory and into the clinic where they can actually help patients – bench to bedside. But the processes of doing research and discovery and of doing drug development work are more akin to distant cousins than siblings.

The goals and objectives, funding institutional support required for academic research and for drug discovery are different in key ways. And as more researchers embrace the opportunity to do drug development at academic centers as a way to move their discoveries from the bench to the bedside, institutions and the pharmaceutical industry are responding. At NCH we have invested significantly in resources such as

the office of Drug and Device Development Services (DDDS), a GMP facility, and fully integrated Clinical Research Services to support the translation of our pharmaceutical technologies.

## DRUG AND DEVICE DEVELOPMENT SERVICES (DDDS):

“We, at academic centers, have a unique opportunity to develop drugs for patients desperately in need of them,” says Chris Shilling, director of Drug and Device Development Services (DDDS) at The Research Institute at Nationwide Children’s Hospital. “Drug development in academic centers is a viable and challenging option to help patients with diseases in which the pharmaceutical industry is not investing.”

Working with the Office of Technology Commercialization, the DDDS team aims to engage researchers early on in the process.

“We start from the researchers’ vision of what the product would be as a commercial entity,” says Shilling. “Then, we guide the researchers to take the required steps to make their work more acceptable by federal regulators and valued from a commercial standpoint. We go from an initial research concept to engaging the right people, and then guide them towards the appropriate next steps.”

OTC works closely with researchers from the first disclosure of a drug or device to progress the technology through the patenting and eventual licensing processes. Engaging with investigators from the beginning of a research project helps OTC foster a relationship with the inventors and develop intimate knowledge of the technology at hand, allowing more targeted marketing and development of the technology. It also keeps the idea of commercialization fresh in the minds of the scientists doing research at the bench.

Researchers at Nationwide Children’s are encouraged to consider what studies would need to be done to get a drug product to market as they are writing their grants, explains Shilling. In this way, grant funding may support some of the activities needed for drug development.

Another key area of focus for Drug and Device Development Services is building relationships with the U.S. Food & Drug Administration (FDA) and educating all faculty about the opportunities to work with the FDA.

“Our approach is to train researchers to be FDA compliant, to be proactive in doing things in ways that will help ensure a smooth process when the time comes to go to the FDA,” says Shilling. “To be most successful, we want them to look years ahead of their initial research question.”

Academic centers can only take drug development so far and partnering with pharmaceutical companies, either big pharma or smaller startups, is essential to getting the product to market.

“At an academic center, we can’t bring the drugs and devices that we develop all the way to market. We need to create partnerships. This involves engaging with technology commercialization resources at the academic centers to help find and curate industry partnerships,” says Shilling. “By vetting the drugs and getting them into early stage clinical trials, we are able to show safety and efficacy, making them more appealing to companies looking to invest.”

## GMP FACILITY:

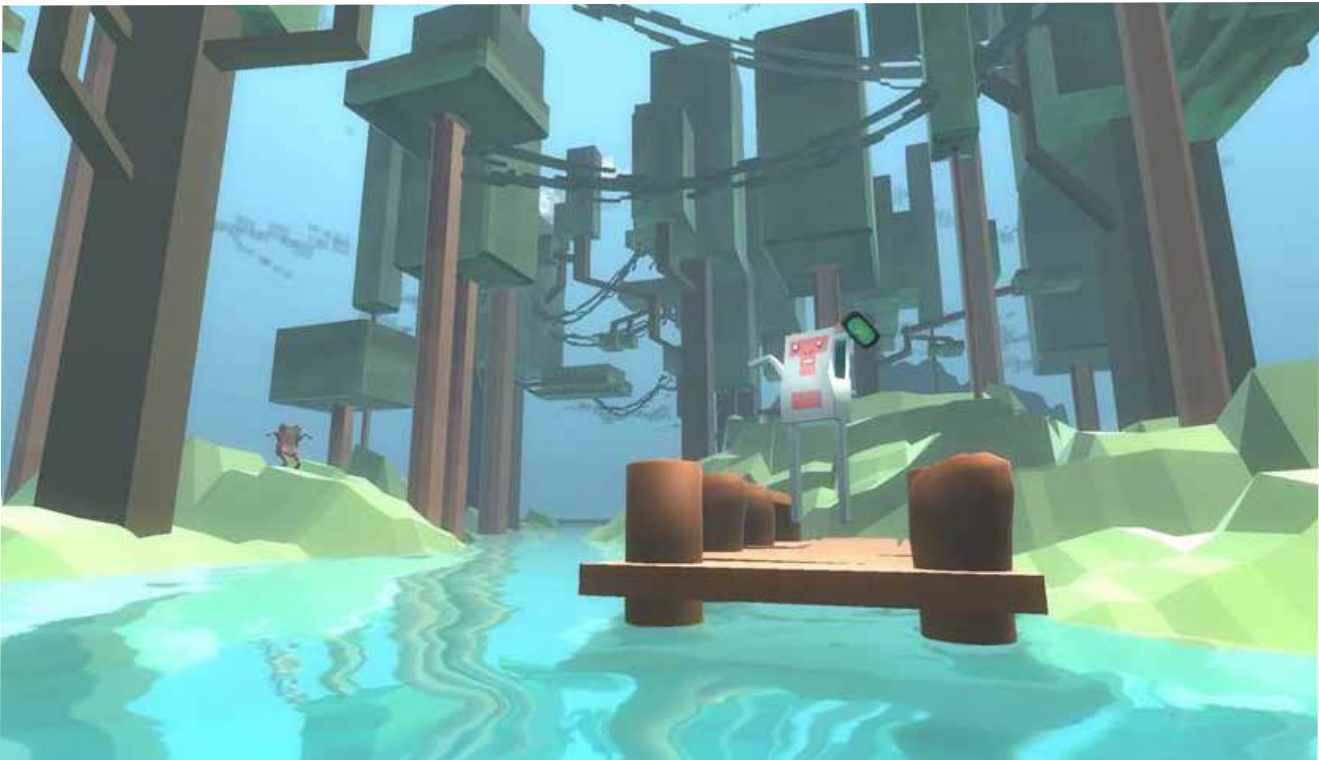
In the Good Manufacturing Practice (GMP) production facility at The Research Institute at Nationwide Children’s, specialized technicians are making materials for first-in-human clinical trials for rare diseases that have no other treatments. The GMP facility space is tightly controlled and staffed by rigorously trained technicians, resulting in an elegantly managed facility with manufacturing capabilities that meets the specific requirements set forth by the Food and Drug Administration.

With a robust, industry-grade facility located in a pediatric academic institution, our GMP facility collaborates with investigators in the Research Institute to develop novel products in areas of viral vectors, cell-based therapy, and genomics on a biologic scale. By working hand-in-hand with the Office of Technology Commercialization, the GMP acts to supply high-quality clinical-grade products that can be tested as investigational new drugs and available for licensing to potential start-ups or industrial partners.

## CLINICAL RESEARCH SERVICES:

As an international leader in pediatric research, the Research Institute at Nationwide Children’s Hospital is actively involved in more than 1,000 clinical research studies. With studies that range from observational to active investigation of promising therapeutics, our Clinical Research Services (CRS) center is innovatively bringing the bench to the bedside through translational research.

CRS actively works to make the process of initiating, designing, and coordinating clinical trials streamlined for investigators. With this goal in mind, CRS fosters the evolution of laboratory discovery to improvements in adverse health outcomes and patient care. CRS works closely with the Office of Technology Commercialization to ensure that technologies and therapies that show promise in pediatric clinical trials have the opportunity to be further developed through collaboration with outside entities. Multiple major pharmaceutical companies have sponsored clinical studies through the Clinical Research Services group. This group has also been a critical part of clinical development by conducting phase I clinical trials for NCH start-up companies such as Milo Biotechnology, AveXis, and Abeona Therapeutics.



# Changing the Game: Virtual Reality Distracts from Pain, Transforming the Patient Experience

As a nurse clinician in the comprehensive hemophilia treatment center at Nationwide Children’s for nearly 30 years, Charmaine Biega, RN, has watched her patients endure hundreds of needle sticks for infusions and other procedures, which can mean tears, frustration, wiggling and – in some cases – lifelong anxiety about the medical system and treatments that patients with hemophilia need to survive. But when she administered six-year-old Brody Bowman’s infusion

in clinic, he was doing something she had never seen him do before a needle stick: having fun. That’s because Brody was engaged in a new virtual reality experience called Voxel Bay, which was developed for his specific patient population as a distraction and pain management technique by design experts at The Research Institute at Nationwide Children’s Hospital. “Brody just started getting his treatments through IV on a regular basis and was having a really rough time,” says

Biega. “But the first time he used Voxel Bay in clinic, he was so completely engaged in the game when the IV was administered, he just barely flinched. The difference in how patients react during a procedure when they are having these interactive experiences is remarkable.”

Biega uses a tablet to control the Voxel Bay experience and see exactly what her patients are seeing in their completely customized headset. Being able to have interaction between the nurse and patient was an important feature clinicians challenged Nationwide Children’s User Experience Technology Research and Development team to create.

“I work with pediatric patients with bleeding disorders and know all too well the fears and anxiety that they and their families experience related to frequent needle sticks,” says Amy Dunn, MD, director of Hematology, at Nationwide Children’s. “I took this problem to our incredible design team and asked them to help our hemophilia team create a solution that would be cost-effective, friendly, safe, engaging for children of any age, and help with adherence to treatments ultimately leading to better outcomes.”

Jeremy Patterson, lead of User Experience Technology Research and Development and creative development lead for the project at Nationwide Children’s, rose to this challenge and his team created a virtual reality environment through Voxel Bay that is customized specifically for patients with hemophilia.

The Voxel Bay experience includes a child-friendly, soft-foam virtual reality headset that is safe, easy-to-use and, importantly for patients who need infusions, hands-free. “The headsets are easy to assemble. Patients can help to put them together, decorate them, and take them home. The headsets become theirs,” says Patterson. This sense of ownership and pride in something they helped to construct can promote positive feelings about going to the clinic or hospital for a procedure or treatment.

A pilot study, funded by the National Hemophilia Foundation, was completed last year to test the feasibility of integrating the virtual reality technology into the clinic setting. The team also collected preliminary data on usability and likability from parents, patients, and nurses. The clinical trial demonstrated that Voxel Bay was able to be successfully utilized in the hemophilia clinic without lengthening the time of patient procedures.

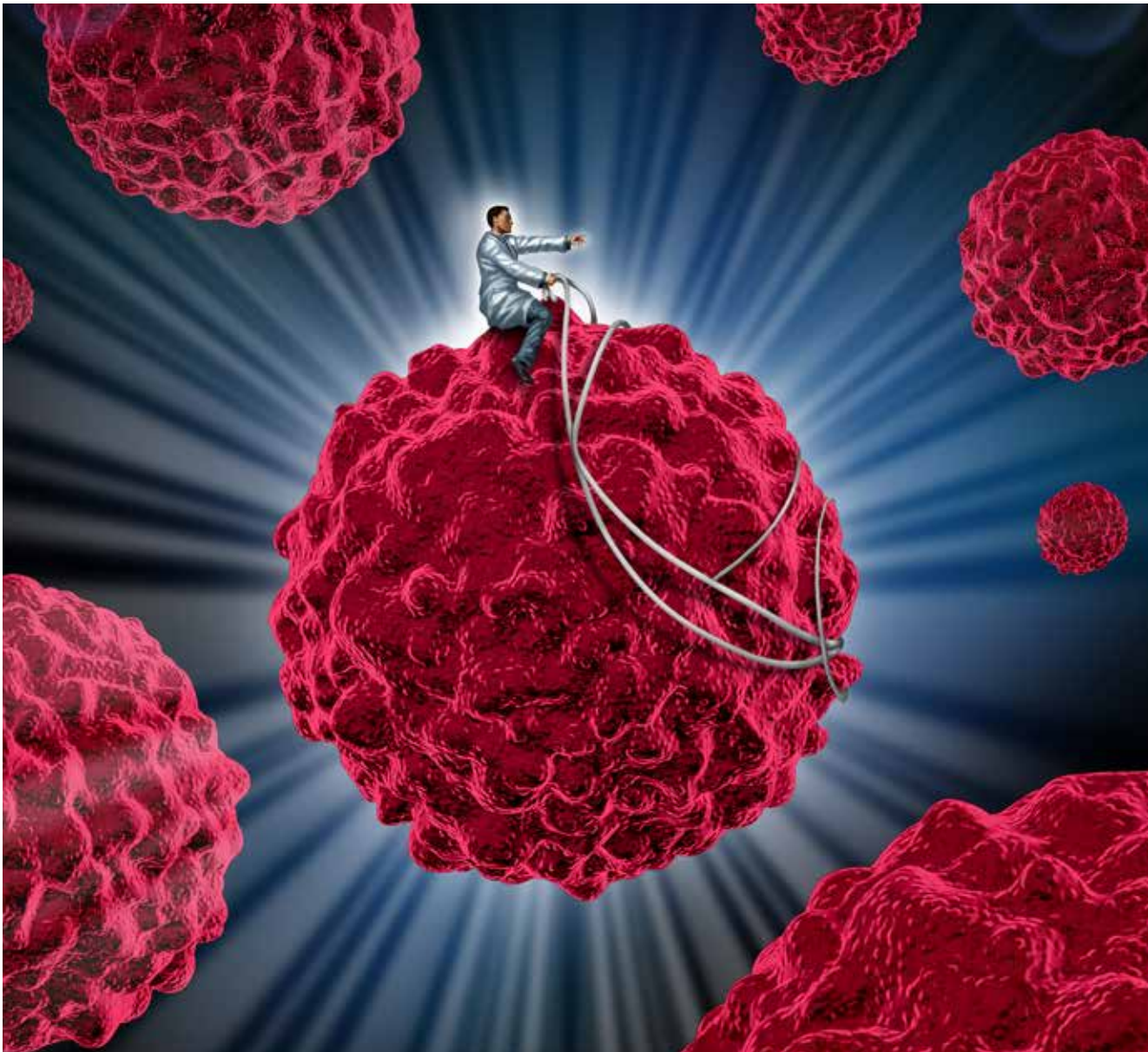
The team at Nationwide Children’s is currently exploring how this technology could be expanded for use in a home setting for the multiple infusions patients with hemophilia receive each week. Pain and anxiety management through virtual reality could be useful for other patient populations as well.

Collaboration with the Office of Technology Commercialization has allowed the active pursuit of options for commercializing Voxel Bay for further development. Interest in the intersection of virtual reality and medicine is rapidly growing, and the team recently had the chance to present their work to an audience of entrepreneurs and thought leaders when Voxel Bay was selected as a finalist in the Health Med and BioTech category of the 2017 Interactive Innovation Awards at the annual South by Southwest Conference and Festival in Austin, TX.

“The feedback we have gotten so far has been really positive,” says Dr. Dunn. “As “One Team” we designed an approach that is truly engaging and immersive for kids and is customized to their needs, and we believe it will really make a difference in their treatment and outcomes.”

“I have made lots of games and know what appeals to kids and what doesn’t, but creating something that has actually helped children have a better patient-experience, there is nothing greater than that,” says Patterson.





CANCER GOES VIRAL:  
HARNESSING ANTIVIRAL IMMUNE  
RESPONSE TO IMPROVE EARLY  
DETECTION AND TREATMENT

Over the last few decades, the use of viruses to eradicate tumor cells based on their heightened susceptibility to infection has increased. Herpes simplex virus (HSV), a human virus with a defined and well-known clinical spectrum, has been an appealing choice for a variety of reasons. It causes side effects that are easily predicted and can infect a wide variety of cell types and tumor types. HSV also has a large nonessential region of its genome that can be removed without substantially affecting its viral potency, so that viral vectors containing large foreign sequences can be developed.

Kevin A. Cassady, MD, principal investigator in the Center for Childhood Cancer and Blood Diseases in The Research Institute at Nationwide Children’s Hospital, has studied HSV virology for nearly 20 years, with a specific focus on how HSV and human cytomegalovirus (HCMV) evade immune recognition in infected cells. His early studies led to the development of an avirulent HSV/HCMV chimeric virus as an anti-tumor therapeutic.

“Preclinical studies have shown that the chimeric HSV, C134, is superior to first-generation HSV oncolytic viruses,” says Dr. Cassady, who is also a physician on the Pediatric Infectious Diseases team at Nationwide Children’s. “In addition to improved viral replication and tumor cell lysis, differences in the adaptive immune response also contribute to C134 efficacy.”

The technology was originally developed while Dr. Cassady was still at the University of Alabama at Birmingham (UAB), prior to his appointment at Nationwide Children’s in 2015.

“UAB provided significant financial and time resources, and their collaboration was crucial in our acquisition of the intellectual property necessary for this technology,” explains Andrew Corris, PharmD, JD, licensing associate in the Office of Technology Commercialization (OTC). “They were very gracious in working on an integrative agreement for mutual institutional benefit.”

The OTC also met with Dr. Cassady before the Investigational New Drug application, to determine National Cancer Institute funding for production of the virus at the Good Manufacturing Production (GMP) facility at Nationwide Children’s.

In addition, Dr. Cassady notes that Drug and Device Development Services (DDDS) at Nationwide Children’s was essential in providing guidance through the complex submission, review and approval process for the FDA.

“Drug and Device Development Services resides within The Research Institute at Nationwide Children’s and exists to assist medical faculty and investigators from pre-clinical to clinical trials,” says Chris Shilling, MS, director of DDDS. “Our services focus on ensuring their success through early engagement and education, ongoing coordination with FDA representatives, and timely and complete submission of necessary applications, as well as careful schedule and budget planning to minimize risk.”

Based on its advantageous anti-tumor and biotoxicology profile, C134 has been manufactured as a GMP product, has undergone biotoxicology testing, and has received approval from the Recombinant DNA Advisory Committee (RAC).

“Our non-human primate studies demonstrate that C134 is safe, like first-generation recombinants,” says Dr. Cassady. “Unlike first-generation recombinants, however, it also evades translational arrest by a more virulent protein kinase – known as PKR – and synthesizes late viral proteins.”

Results from their intracerebral studies are also reassuring, as they have demonstrated a low likelihood of developing virulence mutations, which is a common concern for biologic therapeutics.

The proven safety and efficacy of C134 in preclinical studies offers promise for its utilization in clinical study patient populations in the future, and the OTC continues to work with Dr. Cassady and his team as they move forward with their application for orphan drug designation.

**Related Citations:**  
Cassady KA, Bauer DF, Roth J, Chambers MR, Shoeb T, Coleman J, Prichard M, Gillespie GY, Markert JM. Pre-clinical Assessment of C134, a Chimeric Oncolytic Herpes Simplex Virus, in Mice and Non-human Primates. *Molecular Therapy – Oncolytics*. 2017 Jun 16; 5:1-10.



# Therapeutics



**Live, Attenuated Vaccines Against Pneumoviruses (Reference # 2011-001, 2014-004, 2014-045, 2015-004)**

Respiratory syncytial virus (RSV) is the most frequent cause of lower respiratory disease and hospitalization in infants, but there is currently no vaccine or effective therapy available to prevent or treat RSV disease. Researchers at Nationwide Children’s Hospital and The Ohio State University are working to develop a live, attenuated RSV vaccine to prevent infection in at-risk populations. There are several technologies that have resulted from the RSV research program with more than one performing well in pre-clinical animal trials. Researchers are also working to develop a live, attenuated vaccine to protect against human metapneumovirus (hMPV). For example, a strategic mutation in one of the vaccine candidates has been shown to attenuate virus replication in cotton rats while retaining immunogenicity.

**Inhibition of Notch Signaling Reduces the Incidence of Aortic Abdominal Aneurysm (Reference # 2011-010)**

Abdominal aortic aneurysm (AAA), defined as a localized dilatation of the abdominal aorta, is a life-threatening disease, which has an estimated incidence of 2-4% in the adult population. AAA is characterized by activation of the inflammatory response causing extensive remodeling of the aortic wall. Researchers at Nationwide Children’s Hospital have demonstrated that decreased levels of Notch1 protect against the formation of AAA by preventing macrophage recruitment and down regulating the inflammatory response in the aorta.

**Amyotrophic lateral sclerosis (ALS) Astrocytes with Natural Killer Properties (Reference # 2012-023)**

ALS, commonly referred to as Lou Gehrig’s disease, is characterized by selective, premature degeneration and death of motor neurons (MNs) in the motor cortex, brain stem and spinal cord. Studies have demonstrated that not only MNs but also non-neuronal cell types including microglia and astrocytes play a significant role in disease onset and progression. Researchers at Nationwide Children’s Hospital have identified a previously undescribed disease mechanism in which astrocytes use killing pathways typically ascribed to the innate immune system, and can use these mechanisms as targets for therapeutic intervention in ALS.

# Therapeutics

**Microglia Induce Motor Neuron Death via the Classical NF-κB Pathway in Amyotrophic Lateral Sclerosis (ALS) (Reference # 2013-028)**

Nuclear Factor-kappa B (NF-κB) is a master regulator of inflammation and is upregulated in the spinal cord of ALS patients and in ALS mice models. Researchers at Nationwide Children’s Hospital have demonstrated that NF-κB inhibition in ALS microglia rescued motor neurons (MNs) from microglia-mediated death *in vitro* and extended survival in ALS mice by impairing pro-inflammatory microglial activation. This work for the first time provides a cellular and molecular mechanism by which microglia induce motor neuron death in ALS and suggests a new therapeutic target to modulate microglial activation and slow the progression of ALS and other neurodegenerative diseases in which microglial activation plays a role.

**Long Term Pyruvate Supplementation in Drinking Water add Libitum Ameliorates Neuropathy in the Animal Model for Charcot-Marie-Tooth (CMT) Neuropathy (Reference # 2014-038)**

Charcot-Marie-Tooth neuropathies (CMT) affect approximately 1 in 2,500 people in the United States, but there is currently no treatment for CMT. Researchers at Nationwide Children’s Hospital have found that oral delivery of sodium pyruvate as an energy source for peripheral neurons results in functional improvement in a mouse model of CMT. Sodium pyruvate has been used to safely treat a variety of conditions, suggesting that oral delivery will be a safe, effective treatment for CMT.

**Supplemental Triple Antioxidant Therapy as a Treatment for Anoctamin 5 Deficient Muscular Dystrophies (Reference # 2015-062)**

Limb-girdle muscular dystrophy 2L (LGMD2L) is a progressive disease that results in muscle weakness, pain and exercise intolerance. There is currently no treatment for LGMD2L. Researchers at Nationwide Children’s Hospital have found that impaired mitochondrial function results in disease pathogenesis. The current invention uses triple anti-oxidant therapy to reverse mitochondrial damage and correct exercise intolerance. Because LGMD2L is slowly progressive, this treatment can delay disease progression, either alone or in conjunction with gene therapy.

**Linking PI3K/AKT Signaling to RNase 7 Production and Urinary Tract Sterility (Reference # 2015-039)**

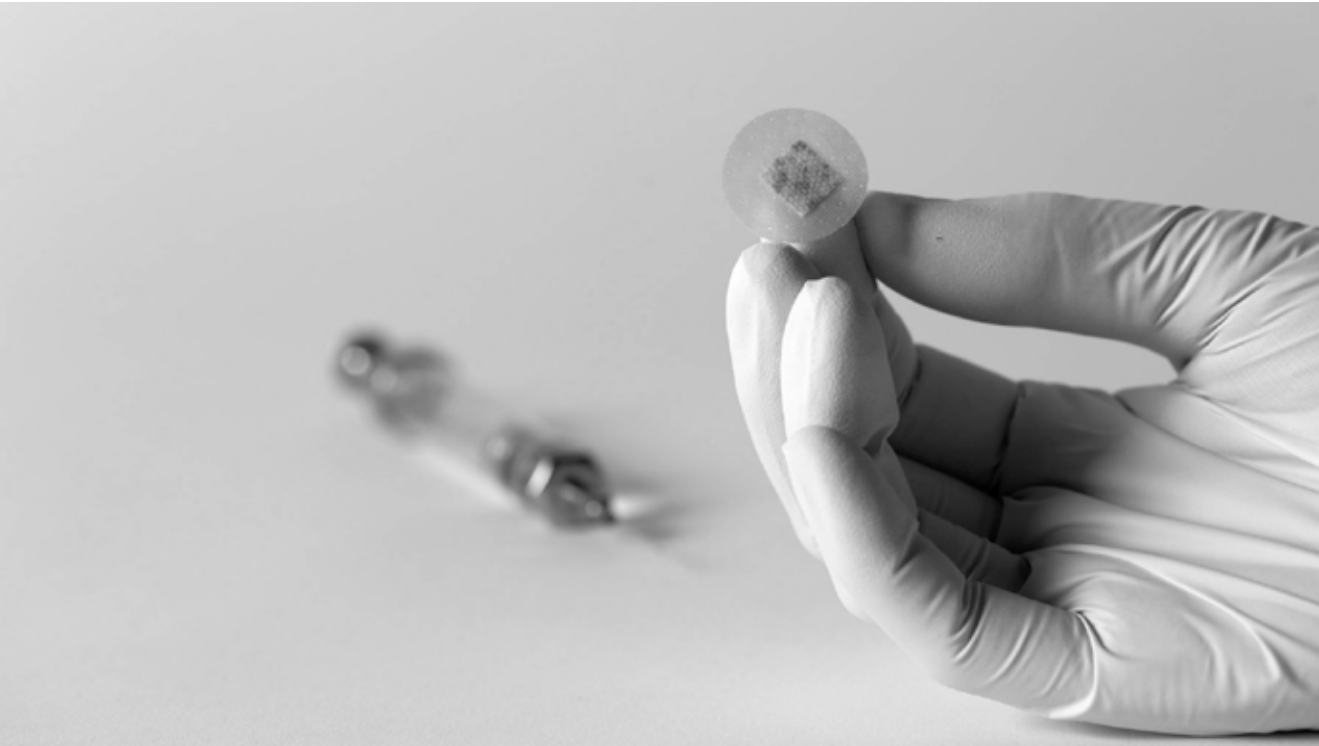
Patients with diabetes mellitus have increased susceptibility to urinary tract infections. Antimicrobial peptides, like Ribonuclease 7 (RNase 7), are important for maintaining urinary tract sterility. Researchers at Nationwide Children’s Hospital have found that insulin induces the expression of RNase 7 through the PI3K/AKT pathway. They have found that patients with diabetes mellitus have low levels of urinary RNase 7 and insulin therapy increases these levels. This demonstrates that insulin may serve as a novel method of inducing antimicrobial peptide production and maintenance of urinary tract sterility.

**An Attenuated Chimeric HSV for Brain Tumor Therapy (Reference # 2015-064)**

Glioblastoma multiforme (GBM) is the most common primary brain tumor and has a 5 year survival rate of less than 5%. Herpes simplex virus-1 (HSV-1) with mutations in a gene that suppresses the host innate immune system, ICP34.5, is effective at killing cancer cells, but replicates poorly. Researchers at Nationwide Children’s Hospital have generated a chimeric herpes virus that lacks ICP34.5, but expresses an innate immune suppressing gene from another virus, allowing it to replicate better than previous viruses and efficiently target and kill cancer cells.



# Therapeutics



**ApoE Treatment for Osteogenesis Imperfecta (Reference # 2015-067)**

Osteogenesis imperfecta (OI) is a genetic disorder characterized by bones that break from little to no apparent cause. Mesenchymal stem/stromal cell (MSC) therapy has been found to effectively treat bone growth impairment in OI, but these treatments are not consistently effective and have safety concerns. Clinicians at Nationwide Children’s Hospital have found that MSC treatment induces release of Apolipoprotein E (ApoE) into the serum, which then stimulates chondrocyte proliferation in the growth plate. This demonstrates that ApoE can be used as a treatment for OI, without the issues related to MSC therapy.

**Simplified Detection and Quantification of Infectious Viruses (Reference # 2016-050)**

Current methods for the detection of infectious viruses rely on Real-time qPCR for the detection of vector genomes that have entered the cells. The methods make it difficult to accurately quantify low number of viruses because of errors introduced during the dilution of the virus and preparation of samples for analysis. In addition, the methods do not discriminate between viruses that enter the cytoplasm versus those infecting the nucleus. Researchers at Nationwide Children’s Hospital have developed a novel method of detection of infectious viruses by engineering proteins to recognize the viral sequence.

**Patch Delivery System for Vaccines Against Ear Infections (Reference # 2013-041)**

Non-invasive immunization tends to be more cost effective and has increased compliance compared to invasive vaccination methods, making it ideal for both the developed and developing world. Researchers at Nationwide Children’s Hospital have developed a method of immunizing against bacterial diseases of the respiratory tract, including ear infections, by applying a vaccine formulation to a patch and placing it on the skin behind the ear. Placement in this unique location is a non-invasive way of promoting an immune response to prevent or resolve infections.

# Therapeutics

**Anti-LYST Therapeutic Immunomodulation (Reference # 2014-002)**

Approximately 1 in 100 infants are born with a congenital heart defect and 10% of these defects result in death. Tissue engineered vascular grafts (TEVG) are an ideal way of mending these defects. Stenosis is the most common graft-related complication for TEVGs, affecting approximately 30% of patients. Inventors at Nationwide Children’s Hospital have discovered that LYST, or lysosomal trafficking regulator, modulates the immune system and thereby contributes to TEVG stenosis formation. The current work focuses on developing an anti-LYST therapy, as a novel method of inhibiting the formation of TEVG stenosis.

**Utilizing Antisense Oligonucleotides to Modulate MDM2 Alternative Splicing (Reference # 2014-014)**

Murine Double Minute 2 (MDM2) is an E3 ubiquitin ligase and negative regulator of the tumor suppressor protein p53. Under normal conditions, *MDM2* is constitutively spliced to generate a full-length protein, and promotes the proteasome-mediated degradation of p53. However, under stress *MDM2* undergoes alternative splicing, generating splice variants that are unable to bind and regulate p53. Subsequently, p53 becomes upregulated and activates downstream targets involved in apoptosis and cell cycle arrest. Investigators at Nationwide Children’s Hospital have developed a novel splicing-corrective treatment to modulate the splicing of p53-modifier MDM2 in cancer.

**Exosomes as a Novel Therapy for Fibrosis (Reference # 2014-024)**

Fibrosis (chronic scarring) accounts for up to 45% of deaths in the developed world, but there are no FDA-approved anti-fibrotic therapies. Researchers at Nationwide Children’s Hospital have found that exosomes from healthy cells contain molecular signals reflective of a healthy state and can be delivered to fibrotic cells that mitigate or reverse fibrosis. This novel therapy will have an impact on numerous diseases, including liver disease, cardiovascular disease, pulmonary fibrosis, kidney disease, and macular degeneration.

**Novel Treatment for Otitis Media (OM) (Reference # 2014-029)**

OM is a leading cause of hearing loss in children in the U.S. Nontypeable Haemophilus influenzae (NTHI) is a major causative agent of OM and other diseases of the respiratory tract. NTHI-mediated otitis media often persists despite repeated antibiotic therapies, due in part to the ability of NTHI to invade host epithelial cells. Researchers at Nationwide Children’s Hospital have developed a novel approach to treating or preventing OM by inhibiting Arp2/3-mediated invasion of host cells.

**Novel Approach for Removal of Caries Causing Bacteria within the Oral Cavity (Reference # 2015-023)**

Dental caries, or tooth decay, affects 84% of adults and is caused by the demineralization of the tooth surface by bacteria (*Streptococcus mutans* and other Streptococcal species) residing in the oral cavity. These bacteria possess surface-associated glucosyltransferases, which convert sucrose to glucan, thus facilitating their attachment to the tooth surface and further colonization. Current treatments for the prevention of tooth decay involve flooding the oral cavity with oral health care products which harm both healthy (commensal) and pathogenic (harmful) bacteria. Investigators at Nationwide Children’s Hospital have developed a Novel Anti-Cariogenic Formulation that provides targeted elimination of cariogenic and harmful bacteria with minimal disturbance of commensals.

**Novel Antibody Fragments for the Treatment of Biofilm-Associated Disease (Reference # 2016-048)**

Biofilms are surface-attached communities of microorganisms that play a critical role in the vast majority of chronic and recurrent infectious diseases. The CDC and the NIH recently estimated that biofilms are responsible for 65% to 80% of all infections. DNABII proteins and extracellular DNA (eDNA) are integral to the structural integrity of biofilms formed by all human bacterial pathogens tested to date. The major challenge with bacterial biofilms is the inability of the host immune system and/or antibiotics and other antimicrobials to gain access to the bacteria protected within the biofilm. Inventors at Nationwide Children’s Hospital have developed novel antibody fragments to disrupt biofilms of diverse bacterial species.

# Therapeutics



**Chimeric Peptide Vaccine for the Treatment of Biofilm-Associated Disease (Reference # 2016-054)**  
65% to 80% of all infections are caused by biofilms. The major challenge with bacterial biofilms is the inability of the host immune system and/or antibiotics and other antimicrobials to gain access to the bacteria protected within the biofilm. Inventors at Nationwide Children’s Hospital have developed a novel chimeric polypeptide vaccine candidate for the disruption of biofilms.

**Airway Progenitor/Stem Cells for Treatment of Pulmonary Disorders and Lung Allografts (Reference # 2017-004)**  
Progressive lung diseases such as cystic fibrosis, primarily ciliary dyskinesia, idiopathic pulmonary fibrosis and few others have no cure, with many of these patients requiring lung transplants. Even after transplant, these patients can develop chronic lung allograft dysfunction, commonly in the form of bronchiolitis obliterans syndrome, which leads to the need for another lung transplant or death. With no cure, cell therapy could make a significant impact across numerous pulmonary diseases and allograft complications. Researchers at Nationwide Children’s Hospital are developing a novel therapy where airway progenitor/stem cells are collected and then administered to patients with pulmonary disorders and lung transplants.

**Composition and Methods for Disruption of Bacterial Biofilms without Accompanying Inflammation (Reference # 2017-008)**  
Biofilms are involved in approximately 80% of all bacterial infections and are strongly implicated in the chronic and recurrent nature of infectious diseases, as well as antibiotic resistance. Researchers at Nationwide Children’s Hospital have developed a novel treatment for biofilm-associated diseases which targets the biofilm extracellular matrix, resulting in disruption of the biofilms and resolution of disease. Importantly, the present treatment does not elicit an excessive inflammatory response.

# Therapeutics

**NICU Safe Developmental Music Player (Reference # 2015-077)**  
Lack of infant directed speech can result in poor brain growth and worsen development throughout early childhood. This has been shown using MRI and long-term language and cognitive outcomes. Between 25-40% of preterm infants have language delays and disorders at school age. New studies show that exposure to a parent’s voice in the NICU can help language development progress in the first two years after discharge from the hospital. Physicians at Nationwide Children’s Hospital have developed a device that is designed to lie inside the isolate of the baby so that the baby can hear the voice of their parents.

**NICU Safe Music Content (Reference # 2016-053)**  
Lack of infant directed speech can result in poorer brain growth and worse development throughout early childhood. Physicians at Nationwide Children’s Hospital have developed a method of producing an audio recording of the parent’s voice to produce developmentally appropriate auditory stimulation content that can be transmitted to infants.

**An Implantable Device Designed to Mimic a Primary Tumor Microenvironment to Remove Tumor Cells from Circulation and Prevent Metastasis (Reference # 2017-006)**  
Osteosarcoma (OS) is the most common bone tumor affecting adolescents. When this cancer spreads, it grows almost exclusively to the lungs. When that happens, children rarely achieve a cure despite the best treatments that are currently available - less than 20% survive beyond three years. Researchers at Nationwide Children’s Hospital are developing a unique approach to treat patients with solid tumors, using a novel device to remove tumor cells from circulation and thereby preventing metastasis.

**Parental Voice Suck-Contingent Pacifier Therapy (Reference # 2017-002)**  
Researchers at Nationwide Children’s Hospital have identified an approach which uses a pacifier-activated device to play parents’ voice in response to infant sucking. This device is commercially available and easy to use by nurses and therapists. The approach improves muscle function, infant neuroregulation, parent-infant bonding, and deep sleep. Preliminary data suggest that the combination of the device and specifically tailored audio of a parent’s voice may improve multisensory cortical processing in preterm infants.

**Method of Using Ankle Weights for Postpartum Weight Loss (Reference # 2016-039)**  
Although the benefits of physical activity (PA) across all populations are well established, less than half of all Americans meet the national guidelines for exercise (CDC). Lack of time is among the strongest perceived barriers to the implementation of regular PA. Overcoming this barrier may be particularly difficult for new mothers. Researchers at Nationwide Children’s Hospital have developed a simple, inexpensive, and practical physical activity intervention, incorporating the use of body weights worn during typical daily activities (e.g. cooking, cleaning, childcare, etc.), that would require no additional time on the mother’s part and could also lay the groundwork for successful prevention or delay of chronic diseases in the future.



# Gene Therapies and AAV Production



**Use of U7snRNA Vector to Skip Duplications in DMD Exon 2 (Reference # 2013-012)**  
Duplicated exons in the DMD gene represent approximately 6% of the Duchenne muscular dystrophy (DMD) patient population, with the duplication of exon 2 being the most common. The laboratory of Dr. Kevin Flanigan at Nationwide Children’s Hospital has found that expression of four U7 small nuclear RNA carrying two new antisense sequences results in efficient skipping of exon 2. This novel treatment will restore protein function and persist over years due to its expression from an AAV vector.

**Rescue of Protein Function by Activating an Internal Ribosome Entry Site in the DMD Gene (Reference # 2014-021)**  
Mutations in exons 1-4 of the DMD gene are present in 6% of patients with Duchenne muscular dystrophy (DMD). Researchers at Nationwide Children’s Hospital have identified a novel internal ribosome entry site (IRES) in exon 5 of DMD and have developed an AAV vector encoding antisense sequences to remove exon 2, resulting in a premature stop codon and activation of this IRES. Activation of this IRES results in production of a functional N-truncated protein and will, thus, correct the pathologic and physiologic features of muscle injury.

**Increasing Expression of HLA-F to Treat Amyotrophic Lateral Sclerosis (ALS) (Reference # 2014-033)**  
90% of cases of Amyotrophic lateral sclerosis (ALS) are sporadic and lack a familial association, but the etiology of sporadic ALS remains largely unknown. The laboratory of Dr. Brian Kaspar at Nationwide Children’s Hospital has discovered that overexpression of the HLA-F MHC class I molecule in motor neurons is protective against ALS. Further, they have identified a pharmaceutical composition that increases the expression of HLA-F in motor neurons and would serve as a treatment option for patients with both sporadic and familial ALS.

# Gene Therapies and AAV Production

**RNAi Therapy for Dominant Limb Girdle Muscular Dystrophy Type 1A (Reference # 2011-002)**  
Researchers at Nationwide Children’s Hospital have designed novel microRNAs that specifically knock down the expression of the protein Myotilin. Animal studies assessing decreased expression of Myotilin suggest that targeting the protein may be a viable therapeutic strategy for treatment of Limb Girdle Muscular Dystrophy Type 1A (LGMD 1A). This RNAi strategy can also be adapted to broadly impact a large class of dominant muscle disorders.

**Gene Therapy Approach for Charcot-Marie-Tooth Neuropathy (Reference # 2008-002)**  
Charcot-Marie-Tooth (CMT) neuropathies are one of the most common inherited neurological conditions affecting 1 in 2,500 people in the United States. Both children and adults are affected, causing sensory and motor dysfunction, pain, and a need for ambulatory aids. Researchers at Nationwide Children’s Hospital have developed a gene therapy approach that delivers neurotrophic factor NT-3 by intramuscular injection to promote nerve regeneration in CMT disease as well as other nerve diseases with impaired nerve regeneration.

**DUX4 Exon Skipping Strategies for FSHD Therapy Using U7-snRNA (Reference # 2015-049)**  
Facioscapulohumeral muscular dystrophy (FSHD) is the third most common genetic disease of skeletal muscle. The dux4 gene is implicated in FSHD and the full-length protein encoded by this gene is toxic to muscles and other tissues. However, a shorter isoform, which lacks the C-terminal transactivation domain, is non-toxic. Researchers at Nationwide Children’s Hospital have developed U7-based snRNAs that bias protein production toward the short nontoxic version of DUX4 or to block incorporation of exon 3. This new strategy represents a novel therapy for FSHD.

**CrispRCas9 Therapeutic Strategies for Titin Based Cardiomyopathies (Reference # 2015-074)**  
Titin is a large protein that is important for muscle elasticity and mutations in titin result in muscle impairment, including cardiomyopathies. Researchers at Nationwide Children’s Hospital have developed a method for correcting mutations in titin. Using the CRISPR/Cas9 system of genome editing, they are able to modify the titin gene and resulting protein. This method can be delivered directly via intracoronary delivery to correct titin mutations and rescue protein function.

**Recombinant Adeno-Associated Virus Vector Gene Therapy for MPS II (Reference #2016-001)**  
Hunter’s syndrome, or mucopolysaccharidosis II (MPS II), is a lysosomal storage disease caused by a deficiency of enzyme iduronate-2-sulfatase (I2S). The greatest challenge in developing therapies for mucopolysaccharidosis (MPS) II is to achieve efficient central nervous system (CNS) delivery across the blood-brain barrier (BBB). Researchers at Nationwide Children’s Hospital are developing a gene therapy vector (systemic delivery) to cross the BBB for treatment of the CNS and also for somatic manifestation of MPS.

**AAV Delivery of Mir29 to Suppress Fibrosis in Muscular Dystrophy (Reference #2016-007)**  
Duchenne muscular dystrophy (DMD) is caused by dystrophin deficiency resulting in muscle loss and progressive muscle weakness and fibrotic scarring. Fibrotic infiltration is profound in DMD and is a significant impediment to any potential therapy. Researchers at Nationwide Children’s Hospital have addressed this problem using an adeno-associated virus (AAV) approach to deliver MicroRNA 29 (miR-29) to suppress fibrosis. Initial results using AAV- delivered miR-29 as an anti-fibrotic therapy suggest that there is significant beneficial effect with reduced collagen and elastin levels, which are key contributors in fibrosis. This work provides a rationale for overexpression of miR-29 to reduce fibrosis along with dystrophin replacement in translational, pre-clinical studies.

# Gene Therapies and AAV Production

## Site Specific Integration of Recombinant AAV Vector Genomes by Rep68 Protein Expressed on the Surface of AAV Particles (Reference # 2016-055)

Recombinant AAV vectors are useful tools for efficient gene delivery and expression of therapeutic genes. To allow for efficient packaging of therapeutic genes into recombinant AAV particles, the normal AAV (rep and cap) genes are removed from the viral genome and the proteins are supplied by plasmids in trans. To allow for efficient delivery of Rep protein in combination with recombinant AAV vector genomes, Researchers at Nationwide Children’s Hospital have developed a novel way of delivering a functional Rep protein into the nucleus for efficient integration of the AAV genome.

## Scalable AAV Production and Purification by Plasmid DNA Transfection of HEK293 Cells (Reference # 2013-033)

Recombinant adeno-associated virus (rAAV) vectors have emerged as one of the most versatile and successful gene therapy delivery vectors. Good Manufacturing Practice (GMP) production Facility at Nationwide Children’s Hospital has developed a process to increase the scale of rAAV production using DNA plasmid based transfection of HEK293 cells. This process allows for the generation of AAV at a 10-fold larger scale than previously produced in the GMP facility thereby supporting trials that require higher doses of clinical grade vector.

## Two-Step Iodixanol Density Gradient by Ultracentrifugation (Reference # 2016-017)

Conventional methods for rAAV purification that are based on cesium chloride ultracentrifugation have often produced vector preparations of variable quality and resulted in significant loss of particle infectivity. GMP production Facility at Nationwide Children’s Hospital have developed novel purification strategies that involve the use of non- ionic iodixanol gradients resulting in higher recovery rate and increase purity of clinical grade rAAV vector.

## Downstream Chromatography Purification for AAV (Reference # 2016-047)

To purify all divergent AAV variants, buoyant density gradients such as CsCl, or iso-osmotic medium iodixanol discontinuous gradients are routinely used. Although quite useful in a laboratory setting, these procedures are neither scalable nor easily adapted for Good Manufacturing Practice (GMP) protocols. GMP production Facility at Nationwide Children’s Hospital have developed an efficient and reproducible protocol that could be applied to particular AAV serotypes and also allows vectors to be purified with high recovery rates.

## Stem Loop RNA Mediated Transport of Mitochondria Genome Editing Molecules (Endonucleases) into the Mitochondria (Reference # 2016-032)

Pathogenic mutations and deletions in the maternally inherited mitochondrial genome (mtDNA) affect as many as 1/500 births and have poor prognosis for treatment. While the CRISPR/Cas9 system for genomic editing has created a new platform for treatment of genetic diseases, researchers have yet to apply the system to mtDNA due to the challenges of transport into the mitochondria. Inventors at Nationwide Children’s Hospital have developed a novel system for importing the CRISPR/Cas9 system into the mitochondria for editing of mtDNA.

# Biomarkers

## Assessment of Cirrhosis and Resolution of Liver Fibrosis Using the MicroRNA Content of Circulating Exosomes (Reference # 2015-047)

Determining the severity or progression of liver fibrosis in patients with Hepatitis B virus (HBV) allows for appropriate treatment management, but current methods to determine this are highly invasive (liver biopsy) or often inaccurate (serum indices or imaging). Inventors at Nationwide Children’s Hospital have developed a minimally invasive method for assessing liver fibrosis by screening for microRNA biomarkers present in circulating exosomes. In addition to defining the current state of fibrosis, this method also predicts which patients will respond to therapy and the effectiveness of therapy.

# End User Innovation

## PS Rocker: A Multi-Head Skin Allergy Testing Device (Reference # 2012-028)

There are 10 skin testing devices marketed in the United States for diagnosing allergies. These include single-tipped devices for testing allergens one at a time, as well as multi-head devices containing multiple testing tips on one device. One of the recently introduced multi-head devices is designed to decrease pain associated with skin testing. Current multi-head testing devices with fixed horizontal surfaces do not provide consistent intra-device contact with skin, while the single-prick devices can be impractical for children and time consuming. Clinicians at Nationwide Children’s Hospital and The Ohio State University, in collaborations with other independent inventors, have developed a new allergy skin testing device, PS Rocker, which improves upon existing products by combining the precision of a single-prick test with the ease and speed of a multi-head device. Additionally, PS Rocker is less painful than traditional skin prick testing. The PS Rocker’s crescent-shaped, ergonomic design enables more reproducible tip contact with the skin than conventional horizontal multi-head devices, efficiently leading to more reliable results.

## Testing Targets: An Innovative Device to Improve Efficiency and Accuracy of Single-Prick Allergy Skin Tests (Reference # 2012-029)

Food allergies have long been a significant public health issue, particularly in the pediatric population. Six to 8% of children under the age of three have food allergies, and nearly 4% of adults have food allergies. One of the commonly used allergy testing methods is the skin prick test. This method requires accurate marking of testing sites on the patient’s skin prior to the application of an allergen, which could be time consuming and difficult to perform on a moving patient. Researchers at Nationwide Children’s Hospital have invented a device called Testing Targets (Lil’s Testing Targets for kid-friendly version) to be used with the previously existing single-prick allergy test for improving efficiency and accuracy of testing and interpretation. Testing Targets is a disposable plastic device with hollow projections along one side of the device that is used with non-toxic ink to mark placement for allergy skin test. Lil’ Testing Targets shares the same design with Testing Targets, except the hollow cylinders are replaced with outlines of animal faces without noses.

## Soothing Asthma Inhaler Spacer for Young Children (Reference # 2015-020)

Using an asthma inhaler can be frightening for young children and a concern for caregivers, leading to reduced compliance. Inventors at Nationwide Children’s Hospital have developed a soothing spacer to be used with an asthma inhaler that makes the experience more enjoyable by incorporating lights and music, when the mask is applied to the face properly. Additionally, the vertical design of the spacer allows for one-handed use which lets a parent hold the child with the other hand, while administering the medication.



# End User Innovation



- Literacy in Children with Hearing Loss (“Hear Me Read” app) (Reference # 2016-024)**

Children with hearing loss are at risk for poor reading and literacy outcomes. Intensive auditory training and individualized therapy can maximize a child’s potential. Researchers at Nationwide Children’s Hospital have developed a mobile iOS application that enables parents and speech language therapists to partner together and help children with hearing impairment achieve evidence based reading and language goals through a fun, interactive multimedia suite.
- ACTIVE Suite: Abilities Captured through Interactive Video Analysis - A Clinical Outcomes Tool for SMA and DMD Patients (Reference # 2012-011, 2014-001)**

This technology is a video-based affordable and entertaining physical therapy assessment tool that measures movement abilities. It can be used as a clinical outcome measure for neuromuscular diseases, stroke, head injury, or other conditions in which the functional abilities of the arms and legs are being investigated.
- Off-Site Critical Medical Incident Management System (OSCMIMS) (Reference # 2016-030)**

Researchers at Nationwide Children’s Hospital have developed a new training tool and process intended to improve and standardize staff responses to simulated and actual critical medical incidents involving anyone within an off-site medical facility, found to be experiencing any medical condition that carries with it the potential to threaten loss of life or permanent disability. The Training Tool can also be used and implemented as a part of the daily routine and is intended to be used during actual medical emergency events.
- Camera Based Rodent Cage Monitoring (Reference # 2016-078)**

Rodents, including mice used for biomedical research, are housed in individually ventilated cages. These cages must be checked daily by an animal technician to ensure animal wellbeing (e.g., animal activity, food and water level). About 20% to 40% of technician time is devoted to this task. Researchers at Nationwide Children’s Hospital are automating this process by using sensors and camera technology to monitor the overall animal wellbeing.

# End User Innovation

- Artificial Intelligence (AI) Tool for Bowel Management (Reference # 2017-003)**

Children can have bowel incontinence for many reasons including anorectal malformations, Hirschsprung disease, and functional constipation. Children with these concerns need medical intervention to assist them in becoming socially continent and obtaining a healthy and effective emptying pattern. This is typically done by attending a Bowel Management Program (BMP), a week long program involving a series of daily evaluations and abdominal x-rays. Researchers at Nationwide Children’s Hospital can automate this process by using artificial intelligence and automatic image recognition program. Such applications can allow processing of more data and as such can produce more replicable and better results with less manpower.
- Multi-Symptom Tracker for Children with Chronic Diseases (Reference # 2017-007)**

Children and youth with chronic diseases experience a myriad of symptoms over the course of their disease, which can interfere with severe developmental milestones, as well as their quality of life. Communications of these symptoms is vital to providing effective management to intervene rapidly and appropriately. Researchers at Nationwide Children’s Hospital are developing a unique web based application to monitor multiple symptoms, quality of life and activities of daily living.
- Medical Line Safety Enclosure (Reference # 2006-015)**

In healthcare settings, accidental suffocation and strangulation can occur due to medical line entanglement. Nurses at Nationwide Children’s Hospital have developed and clinically tested a novel medical line organizer that prevents accidental entanglement, suffocation, and strangulation of hospitalized individuals.
- Child-Proof Spray Bottle (Reference # 2010-020)**

A collaborative team of researchers and engineers from Nationwide Children’s Hospital and The Ohio State University have designed a two-stage trigger system to prevent accidental operation of a spray bottle containing household or other chemical and dangerous solutions. The design restricts the ability of young children to trigger spray bottles in at least two ways. First, young children lack the development capability to perform the correct sequence of pressing down and keeping down the safety level first and then squeezing the trigger. Second, the size and strength of a child’s hand are not sufficient to activate the mechanism.
- Vitrification Insert Device for Cryovials (Reference # 2014-005)**

Vitrification provides many advantages over slow cooling cryopreservation methods, but requires the use of expensive, specialized tools. Investigators at Nationwide Children’s Hospital have invented a vitrification insert device that can be manufactured with inexpensive, sterilization-durable material and fit securely into multiple cryovial models. Further, this cost-effective solution can include various end designs to suit many functions, such as preventing sample contact with cryovial walls.
- Novel Endoscope Cap for Disinfection Quality Control (Reference # 2014-015)**

Sterilization of endoscopes prior to reuse protects patients from the risk of contracting infectious diseases, but accidental use of contaminated endoscopes occurs because current devices to safeguard against this contamination are easy to circumvent. Researchers at Nationwide Children’s Hospital have developed a disposable, single-use, peel away cap that acts as a physical barrier to endoscope use until it is removed. This cap, which is designed to fit a wide variety of devices, will eradicate system shortcuts by inhibiting scope functionality and creating a hard stop checkpoint.
- Disposable Device to Protect Patients’ Lips during Surgery (Reference # 2014-032)**

Lip lacerations and burns can occur during surgical procedures in the mouth and throat. Surgeons at Nationwide Children’s Hospital have developed a disposable device to cover a patient’s upper and lower lips during surgery. This device adjusts to fit the patient’s mouth and will act as a physical and thermal barrier to prevent injury.

# End User Innovation

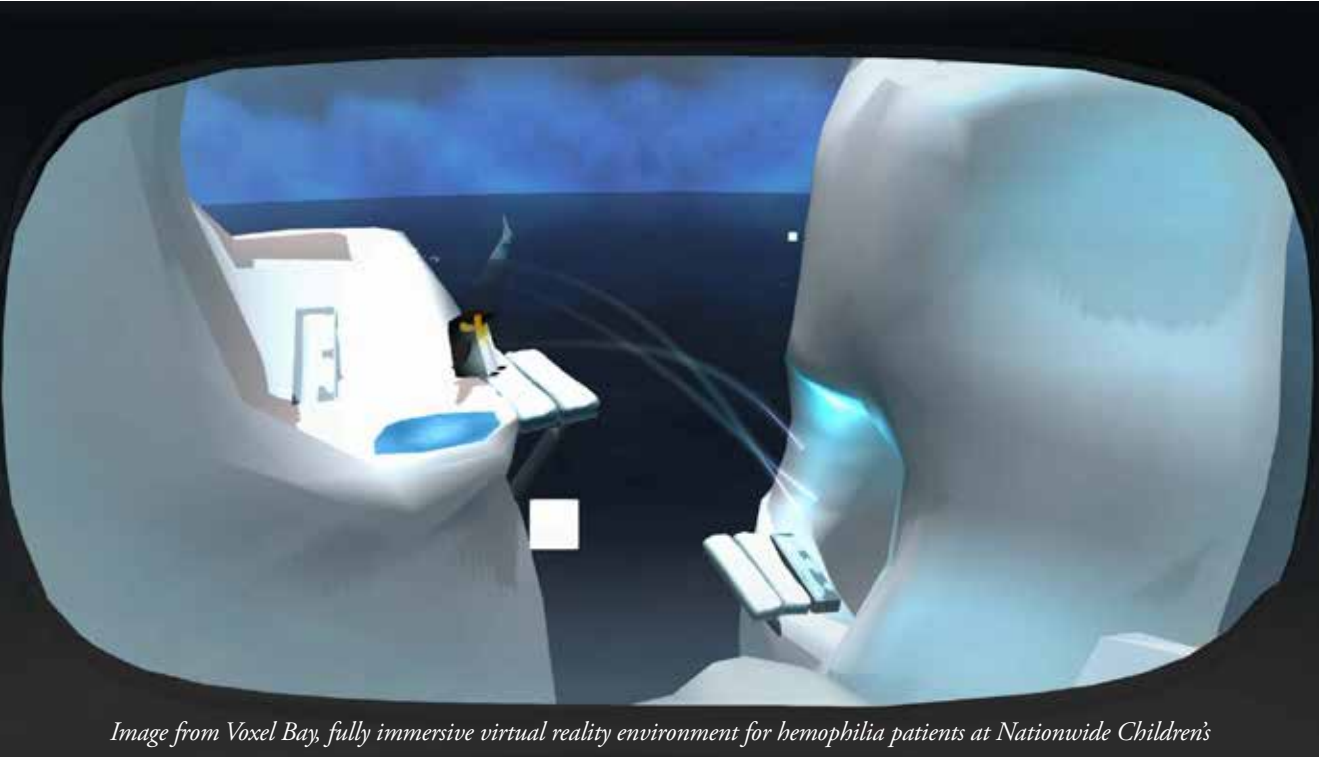


Image from Voxel Bay, fully immersive virtual reality environment for hemophilia patients at Nationwide Children's

## Modified Transgastric-Jejunal Feeding Tubes (Reference # 2014-035)

Transgastric-jejunal feeding tubes are used to provide nutrition to patients who cannot eat enough to grow. However, backing up of food source and mucus from the body can occur, resulting in aspiration, other comorbidities or even death. Physicians at Nationwide Children's Hospital have developed a modified transgastric-jejunal tube that can drain gastric contents into the jejunum, but not affect feeding through another area of the tube. This device will be especially useful in patients requiring long-term feeds and those with special needs of ventilation who are at a high risk of aspiration.

## Chest Tube Securing Device (Reference # 2015-037)

Chest tubes are used to remove air, liquid or pus from the intrathoracic space. Tape or sutures are currently used to prevent unintentional chest tube removal, but these cannot be used on neonatal infants due to the sensitivity of their skin. Inventors at Nationwide Children's Hospital have developed a first of its kind device for securing chest tubes. This flexible device allows for the securing of chest tubes and other main lines while bending and flexing with the patient.

## Novel Coin and Button/Coin Cell Battery Detection, Localization, and Discrimination Method for Objects in the Esophagus (Reference # 2015-045)

Ingestion of button cell batteries by children occurs more than 3,000 times per year in the United States and early identification of a battery in the esophagus is required to prevent severe injury or death. Inventors at Nationwide Children's Hospital have developed a handheld device to detect and localize foreign metallic bodies in a patient. Further, this device will be able to differentiate between a coin and a battery without the use of radiation (x-rays).

## Capacitive Screen Smart Scale (Reference # 2015-046)

Software applications claiming to turn mobile computing devices into digital scales are abundant, but these scales rarely provide accurate measurement of weight. Inventors at Nationwide Children's Hospital have developed a device for accurately weighing objects using a capacitive screen, such as that of a smart phone or tablet. This system is able to use changes in diameter of the detection device to accurately determine the weight of food or other goods in an economical, portable manner.

## Portable Image Diagnostic Device (Reference # 2015-051)

There are many adapters to turn a mobile device, such as an iPod Touch, into an image-capturing, diagnostic device. However, these can yield inconsistent results because there is no standardization of lighting or distance. Inventors at Nationwide Children's Hospital have developed a platform to use with a mobile device that controls for light exposure and sample distance from the camera, thereby allowing for accurate and consistent sample analysis. Additionally, the corresponding software guides the user through the use of the device and encrypts and transfers the image to allow for file sharing.

## Virtual Environment Relaxation and Distraction System for Pediatric Patients undergoing Medical Care (Voxel Bay) (Reference # 2015-060)

Medical treatments can be painful or frightening for children, but virtual reality has been shown to reduce these concerns. Inventors at Nationwide Children's Hospital have developed a virtual environment that can be used to relax and distract patients while they receive treatment. The program is viewed on an iPod touch that is inserted into a disposable cardboard headset that the patient can personalize. The virtual environment is viewed and controlled by a medical caregiver who can customize the program to meet the patient's needs.

## Prepared Infant Formula Instruction Label for Improved Comprehension in Caregivers with Low Health Literacy (Reference # 2016-071)

The majority of infants receive some form of breastmilk substitute within the first year of life. However, few caregivers receive instruction from a healthcare provider on how to properly prepare and store infant formula and, as a result, must rely on step-by-step instructions printed on formula can labels. Current formula labels have been found to be unsuitable for the one-third of American caregivers who have low health literacy skills. Medical professionals at Nationwide Children's Hospital have developed an improved label designed to aid those with low health literacy skills in the preparation, feeding, and storage of prepared infant formula.

# Research Tools

## A Novel Mouse Model of Duchenne Muscular Dystrophy with a Duplication of DMD Exon (Reference # 2013-037)

A novel mouse model for testing exon skipping therapies for DMD disease has been generated at Nationwide Children's Hospital. This mouse model carries a duplicated exon (exon2) in the DMD gene as compared to a point mutation in the most common mdx mouse model. This unique dystrophic mouse can serve as a preclinical testing model to test various therapies that mediate exon skipping.

## Cmah-Deficient mdx Mice: A Better Mouse Model for Duchenne Muscular Dystrophy (Reference # 2010-019)

A new mouse model for DMD-related research has been created at Nationwide Children's Hospital. A double knock-out mouse strain was generated that better mimics the human disease than the current standard model and thus provides a model for DMD where translational research will be more relevant to issues affecting humans with the disease.



# Research Tools



**An Inducible Facioscapulohumeral Muscular Dystrophy (FSHD) Mouse Model Expressing DUX4 (Reference # 2014-019)**  
FSHD is the third most common muscular dystrophy, affecting 1 in 20,000 individuals. There is no current treatment for FSHD. Researchers at Nationwide Children’s Hospital have developed a mouse model that recapitulates FSHD phenotypes and develops myopathy. This is the first FSHD mouse model that stably expresses the DUX4 gene from the mouse genome using the human DUX4 promoter. This model also circumvents lethality, leakiness problems and transient expression inherent in the standard mouse model.

**Anoctamin 5 Deficient Mouse Model for the Study of Limb-Girdle Muscular Dystrophy 2L (LGMD2L) (Reference # 2015-018)**  
LGMD2L is caused by recessive mutations in Anoctamin 5 (ANO5). Researchers at Nationwide Children’s Hospital have developed the only ANO5 deficient animal model. The constitutive knockout of ANO5 in C57BL/6 mice allows for the study of LGMD2L and exceeds current cell culture and in vitro models.

**Monoclonal and Polyclonal Antibodies Against Anoctamin 5 (Reference # 2012-012)**  
Researchers at Nationwide Children’s Hospital have developed a polyclonal antibody directed against human Anoctamin 5 (ANO5). Defects in ANO5 are the causative agent of Limb Girdle Muscular Dystrophy Type 2L (LGMD 2L), an autosomal recessive degenerative myopathy. This antibody can be used as a diagnostic and for research applications.

**Improved Adenovirus Helper Plasmid for the Production of Clinical Grade AAV Vectors (Reference # 2016-068)**  
Researchers at Nationwide Children’s Hospital have developed a novel plasmid by replacing the antibiotic resistant gene in the plasmid backbone. The new version of the plasmid adheres to strict guidelines set up by the European Union in AAV production processes mainly for research and clinical use.

# Research Tools

**A Novel Genetic Mouse Model of Aging (Reference # 2016-049)**  
Demographers predict that the number of people over age 65 will triple over the next 35 years in the U.S. alone. Understanding what contributes to a (healthy) old age begins with understanding the basis of the biological aging process. Currently available rodent models of aging are based on changes in metabolism either by modification of glucose uptake or calorie restriction. Researchers at Nationwide Children’s Hospital have developed a novel model of aging as a result of genetic modification in a murine model. This novel mouse model may be useful for studying the aging process at the most basic level in addition to age-related diseases.

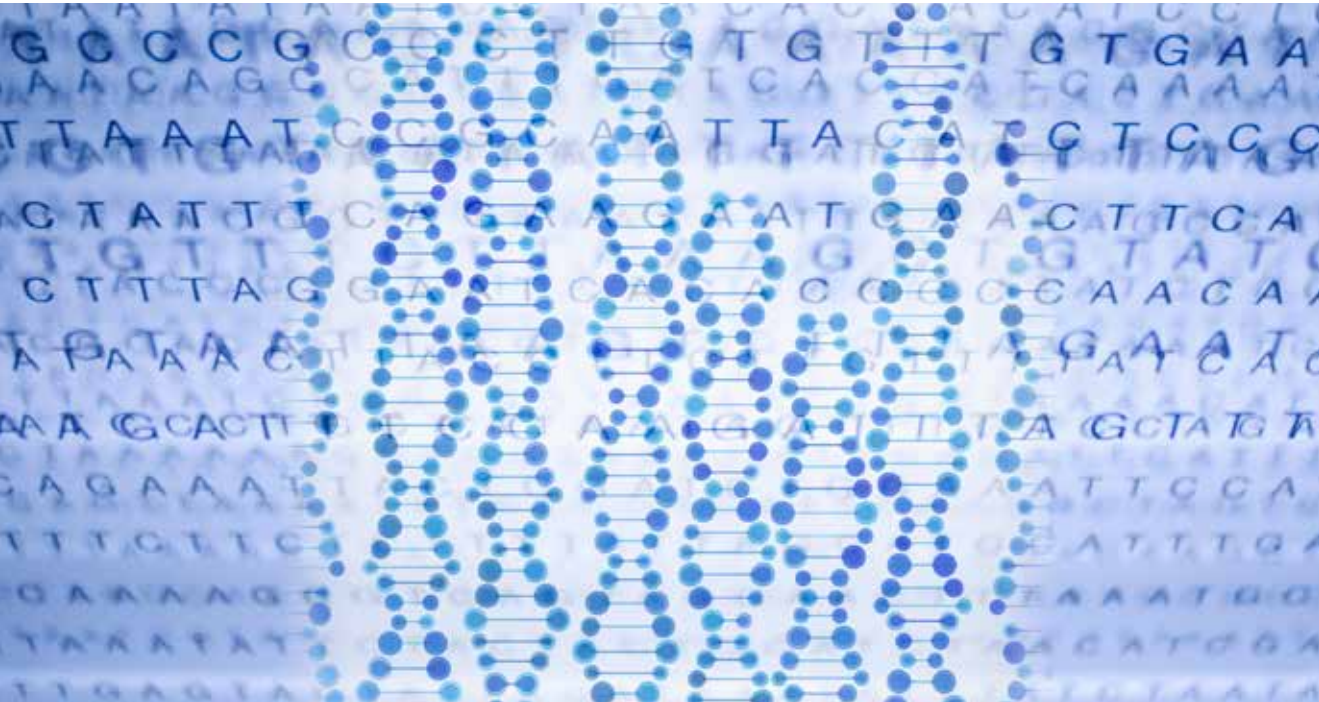
**Novel Screening Assay to Identify and Evaluate Drugs that Target Familial and Sporadic Amyotrophic Lateral Sclerosis (Reference # 2011-016)**  
This is an in vitro cell-based assay that enables investigating molecular disease mechanisms and evaluating potential therapies for Sporadic Amyotrophic lateral sclerosis (ALS) and was developed at Nationwide Children’s Hospital. This assay utilizes human derived cells from individuals with the disease.

# Tissue Engineering

**Production of Tissue Engineered Intestine (TEI) to Treat Short Bowel Syndrome (Reference # 2013-009)**  
Short bowel syndrome is a consequence of massive bowel resection performed in patients with various diseases. Transplantation of the small bowel may be beneficial, but results in risk of graft rejection and complications. Investigators at Nationwide Children’s Hospital and Nanofiber Solutions have developed a method of generating tissue engineered intestine (TEI). This process uses multiple cell types of a patient’s own cells and multi-layered nanofiber scaffolds to generate full thickness, functional intestine that can be used to treat and manage short bowel syndrome.

**Closed Seeding System for the Tissue Engineered Vascular Graft (Reference # 2015-076)**  
Physicians at Nationwide Children’s Hospital have developed a Tissue Engineered Vascular Graft (TEVG) by seeding patient cells onto a biodegradable tubular scaffold. The scaffold degrades by hydrolysis, ultimately leaving only the growing vessel in the patients. The Closed Seeding System enables efficient collection and seeding of patient cells onto the TEVG scaffold, which has been further optimized by using patient imaging data and 3D-printing capabilities to create patient-specific vascular grafts for implantation.

Bioinformatics



Variant Identification for Viral Vector Sequence using a Modified Version of Churchill (Reference # 2016-005)

Currently the cost of next generation sequence data analysis is outstripping the cost to actually produce the data. Through a novel parallelization strategy and development of a fully automated pipeline, previous work at Nationwide Children’s Hospital led to the development of software that substantially shortens the time taken to process the raw (sequence) data through multiple analytical steps required to identify human genetic variations. The Researchers at Nationwide Children’s are using this software to analyze NextGen Sequencing data of viral vectors to verify that the genetic material matches the design and to identify potential contaminants.

Improved Variant Prioritization for Clinical Sequencing (Reference # 2016-046)

Next-generation sequencing (NGS) technologies have fundamentally changed the field of human genetics, and hold numerous potential for improving clinical care. Physicians rely on NGS-based tests- either panel tests that examine a small number of genes, or whole-exome sequencing (WES) assays that analyze in all approx. 20,000 genes- to aid in disease diagnosis and treatment. Researchers at Nationwide Children’s Hospital have optimized an exome-based mapping and variant prioritization solution for rare inherited disorders.

Genome Archiving and Communication System (GACS) (Reference # 2016-056)

To handle the demands of genomic data archiving and access, Researchers at Nationwide Children’s Hospital have created the first validated computer software system that is scalable to archive and query across millions of genomes in a clinical setting, interacting with lab systems and electronic medical records to enable real-time data access.

Dose Wizard: a Method of Calculating Anatomically Correct Radiation Exposure during CT Imaging (Reference # 2015-001)

Calculation of radiation exposure during computed tomography (CT) imaging helps physicians estimate a patient’s risk of future radiation-related cancer. Physicians at Nationwide Children’s Hospital have developed a program that uses anatomically correct models to determine radiation exposure. This program can be used to determine the total radiation dose a patient receives over a period of time and allows for a personalized assessment of the risk of negative effects.

| Our Team |



Matthew McFarland, RPh, PhD, Director

Matthew joined Nationwide Children’s as director of the Office of Technology Commercialization in the spring of 2012. As director, he works closely with Nationwide Children’s faculty and staff to identify intellectual property with commercial potential and to facilitate the transfer of new technologies to outside partners, ultimately for the benefit and enhancement of pediatric care. He has a diverse background in technology transfer, technology valuation and licensing, academic research and pharmacy practice.

Prior to joining Nationwide Children’s, Matthew was the associate director of commercialization, innovation strategy manager and technology manager in the Office of Technology Commercialization at the Purdue Research Foundation. He received a Bachelor of Science degree in pharmacy from Ohio Northern University and his PhD in medicinal chemistry and molecular pharmacology from Purdue University. He also completed a postdoctoral research fellowship in translational genetics and pharmacogenomics of neuropsychiatric disorders at the Institute of Psychiatric Research, Indiana University Medical School.

Matthew has authored several articles for peer-reviewed journals including *Molecular Pharmacology*, *Journal of Biological Chemistry* and *Medical Innovation & Business*. He also received the Jenkins/Knevel Award for Excellence in Research and the Albert and Anna Kienley Award for Excellence in Teaching from the School of Pharmacy at Purdue University.

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Margaret Barkett, PhD, Senior Licensing Associate

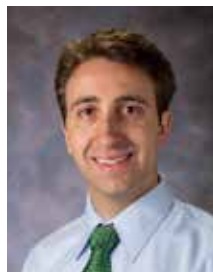
Margaret joined The Research Institute at Nationwide Children’s Hospital as a licensing associate in February 2010, and currently serves as a senior licensing associate for the Office of Technology Commercialization. In her role with the office Margaret manages the assessment, protection, valuation and out-licensing of a portfolio of intellectual property assets owned by The Research Institute. She is also actively involved in managing many of the office’s relationships with both internal and external stakeholders.

Margaret has a Bachelor of Arts degree in biology from Emory University and earned her PhD degree in molecular and cell biology from Boston University, where she continued her training as a postdoctoral fellow. Her doctoral and postdoctoral research in cell death biology spanned different areas including cancer biology and development. Prior to joining The Research Institute, she completed a one-year technology licensing internship at Massachusetts Institute of Technology focusing on medical devices and biotechnology.

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## | Our Team |



**Kyle Murrah, PhD, *Licensing Associate***

Kyle joined The Research Institute at Nationwide Children’s Hospital as a licensing associate in the Office of Technology Commercialization in July 2014. In his role as a licensing associate, he promotes technology transfer through the evaluation, protection, and out-licensing of technologies developed at Nationwide Children’s Hospital.

Kyle has a Bachelor of Science degree in biological sciences from North Carolina State University and a PhD in microbiology and immunology from Wake Forest University. His doctoral research focused on polymicrobial interactions in middle ear infections. While earning his doctorate, he completed a two year technology transfer internship at Wake Forest Innovations.

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**Andrew M. Corris, PharmD, JD, BS, *Licensing Associate***

Andrew joined The Research Institute in March 2015. In his role as a licensing associate, he promotes technology transfer through the evaluation, protection, and out-licensing of technologies developed at Nationwide Children’s Hospital.

Andrew has a Bachelor of Science in chemical engineering and a minor in chemistry from the University of Pittsburgh, a Doctor of Pharmacy degree from The Ohio State University, and a Juris Doctor, cum laude, from Capital University, specializing in intellectual property law.

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**Matthew Moscato, BS, *Agreements Coordinator***

Matthew joined The Research Institute at Nationwide Children’s Hospital in December 2015. As Agreements Coordinator, he is responsible for the negotiation and administration of Material Transfer Agreements, Data Use Agreements, and Confidential Disclosure Agreements. Matthew also manages the agreements docket and provides assistance to the office’s licensing team.

Matthew has a Bachelor of Science degree in paralegal studies with a minor in criminal justice from the University of Cincinnati. He has experience in the areas of compliance, contract, employment, real estate and investment law.

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## | Our Team |



**Susan S. Allen, *Intellectual Property Coordinator***

Susan joined Nationwide Children’s in the summer of 2013. She manages the intellectual property and patent portfolio, as well as agreements records, for the Office of Technology Commercialization. She assists the team with invention evaluation and efforts aimed at marketing and licensing. Susan also manages compliance with regard to reporting requirements for federal and/or non-government research sponsors.

Susan has 23 years of experience including work for federal and state governments, academia, private industry and nonprofits. She has a strong background in intellectual property management and research administration; research education and communications; and budget management and accounting practices including patents, agreements, contracts, and grants management and compliance.

Susan has a Bachelor of Science degree in biology from The Catholic University of America in Washington DC. She is a member of the Association of University Technology Managers. Past professional memberships include: National Council of University Research Administrators, American Medical Writers Association, and American Management Association.

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**Susannah Wolman, BA, *Business Compliance and Finance Coordinator***

Susannah joined The Research Institute at Nationwide Children’s Hospital in July 2016. She is primarily responsible for information and business systems. She tracks invoices, licenses terms and follows up to ensure licensee compliance, in addition to overseeing the annual budget, purchasing and the file management database. Susannah also assists technology transfer professionals with department initiatives, events management and operational issues.

Susannah has over 10 years of experience working in product liability and commercial litigation. She has a Bachelor of Arts degree in Criminology and Psychology from Marquette University.

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**NATIONWIDE  
CHILDREN'S**

*When your child needs a hospital, everything matters.<sup>SM</sup>*