TRANSFER to TRANSFORM

THE OFFICE OF TECHNOLOGY COMMERCIALIZATION
AT NATIONWIDE CHILDREN’S HOSPITAL

2021
Rev1 Ventures partners with the Abigail Wexner 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 Abigail Wexner Research Institute at Nationwide Children’s has been a Pillar Member of BioOhio for the past 10 years.

OhioX is Ohio’s statewide technology and innovation partnership dedicated to helping make Ohio a leading tech hub. OhioX powers connections, tells impactful stories, and advocates for growth on behalf of Ohio technology and innovation. As a founding member of OhioX, Nationwide Children’s joins industry-leading organizations across Ohio in building the future.
The dedication to high-quality clinical care and high-impact research has made Nationwide Children’s Hospital a destination for families seeking hope and innovation.

However, it’s also a destination for some of the most talented clinicians, pioneering researchers and bold thinkers from around the world. Why? The answer lies in our willingness to think creatively, invest in the best people and programs, and take a few risks to do the right thing.

For more than a decade, the Office of Technology Commercialization has played an essential role at Nationwide Children’s to ensure that answers to complex medical conditions can be found more efficiently. We are the convergence point for their inventive thinking, their entrepreneurial spirit and their genuine compassion for children.

A hospital environment is a fertile ecosystem for new ideas. Innovators from every corner of the organization have a unique perspective on what can help a patient or a fellow clinician or researcher. Quite often their foresight is focused on a newly identified market need. Our Office of Technology Commercialization (OTC) is a key component of this ecosystem, and their track record of assisting faculty to move their discoveries along the development pathway is well known and serves as a magnet to draw the most innovative scientists.

The excitement and momentum continues to grow as the OTC builds on our successes and takes full advantage of the rich pipeline of novel discoveries being made at Nationwide Children’s Hospital. We are especially excited about the recent approval of a new gene therapy for spinal muscular atrophy, Zolgensma, to treat a devastating condition.

As a result, Nationwide Children’s Hospital has earned its reputation as an institution with a remarkable track record of moving discoveries into the marketplace. And the hospital’s physicians and researchers haven’t slowed down in their quest to bring more life-saving therapies to children everywhere.

How has generating startups benefited AWRI, Nationwide Children’s Hospital and children overall? Several of the start-ups have been critical to advancing early stage new therapies to the point where they become more commercially viable. AveXis stands as perhaps the best example of this, as AveXis was able to advance our early stage gene therapy for spinal muscular atrophy to the point where Novartis, a major global pharmaceutical company, acquired AveXis, and was able to get the therapy to the point of FDA approval.

A company with the resources that Novartis has is often needed to develop a therapy to the point of FDA approval and able to enjoy global distribution. Our track record with start-ups has positioned Nationwide Children’s Hospital as a leading pediatric research center with a very forward-thinking approach to advancing our discoveries in partnership with industry. This reputation attracts continued interest on the part of industry in our discoveries, and again, helps us to recruit and retain the most innovative scientists.
Centers and Institutes at the Abigail Wexner Research Institute

- Battelle Center for Mathematical Medicine
- Biobehavioral Health
- Cardiovascular Research
- Childhood Cancer and Blood Diseases
- Clinical and Translational Research
- Gene Therapy
- Child Health Equity and Outcomes Research
- Injury Research and Policy
- Microbial Pathogenesis
- Perinatal Research
- Regenerative Medicine
- Vaccines and Immunity
- The Steve and Cindy Rasmussen Institute for Genomic Medicine

Funding at the Abigail Wexner Research Institute

2020 ANNUAL PERFORMANCE INDICATORS

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2020 EXTERNAL AWARDS BY SOURCE

- Program $1.6
- Industry $22.3
- Other $22.9
- Federal Other $25.9
- NIH Prime $47.7

2020 $120.4 MILLIONS

RESEARCH BY THE NUMBERS

*Includes faculty from the Abigail Wexner Research Institute and faculty from Nationwide Children’s Hospital with $50,000 or more in research funding support.
Milo Biotechnology
Milo Biotechnology 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. Phase I/II clinical trials evaluating the safety and efficacy of Milo’s follistatin therapy in patients with Becker muscular dystrophy, Duchenne muscular dystrophy and Inclusion Body Myositis took place at Nationwide Children’s Hospital.

AveXis
AveXis, recently renamed Novartis Gene Therapies, is a commercial gene therapy organization developing treatments for patients with neuromuscular diseases, including Nationwide Children’s Hospital’s licensed programs for Rett syndrome, a genetic form of amyotrophic lateral sclerosis (ALS), and spinal muscular atrophy (SMA), a motor neuron disease that is the leading genetic cause of death of children under the age of 2. The SMA gene therapy technology allows for the delivery of a replacement gene to target motor neurons throughout the brain and spinal cord. The gene therapy product for SMA, Zolgensma®, was approved in mid-2019 by the Food and Drug Administration.

Abeona Therapeutics
Abeona Therapeutics, formed in early 2013 based on gene therapy technologies developed at Nationwide Children’s Hospital, is a clinical stage company initially 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. These diseases lead to progressive muscular and cognitive decline in children after the age of 2 years. With no cure or approved treatments, children with Sanfilippo syndrome usually die before the age of 20. Two separate multi-site phase I/II clinical trials for MPS IIIA and MPS IIIB are underway to evaluate the safety and efficacy of the treatment.

ENTvantage Dx
ENTvantage Dx 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.

Myonexus Therapeutics
Myonexus Therapeutics, a startup formed in 2017, is a clinical stage gene therapy company developing first ever treatments for limb-girdle muscular dystrophy (LGMD) types 2D, 2B, 2E, 2L and 2C based on research at Nationwide Children’s Hospital, a leader in muscular dystrophy gene therapy discovery and translational research. In early 2019, Myonexus was acquired by Sarepta Therapeutics.

Scioto Biosciences
Scioto Biosciences was founded in 2017 to develop treatments for diseases associated with microbial dysbiosis. The technology platform, developed by researchers at Nationwide Children’s Hospital, is a novel formulation that primes the colony-forming mechanisms of probiotic bacteria by combining beneficial bacteria with polysaccharide microspheres. These natural mechanisms induce biofilm formation, enhance probiotic function and allow for nonspore-forming bacteria to survive passage through the gastrointestinal system. Among the first therapeutic indications being pursued is necrotizing enterocolitis, a high-morbidity disease that affects 7% of premature births.

Zotarix, LLC
Zotarix, LLC, is a Columbus-based startup focused on patient safety during surgical procedures. Their first-in-kind product is a disposable medical device which provides protection against thermal and physical injury to the patient’s lips during oral surgery.
LYST Therapeutics
LYST Therapeutics, based in Columbus, Ohio, was founded in 2017 to develop a platform technology for treatment of fibrotic diseases. The technology, invented by researchers in the Center for Tissue Engineering at Nationwide Children’s Hospital, is a novel immunomodulatory therapeutic antibody and has potential applications in treating stenosis, myocardial infarction and other conditions involving fibrosis.

LittleSeed
LittleSeed, Inc. was formed in 2018 in Powell, Ohio, with the goal of delivering clinically driven, evidence-based fun to pediatric patients. The foundational technology, Voxel Bay, was developed by a team of clinicians and game designers at Nationwide Children's Hospital. Voxel Bay provides an interactive virtual reality platform designed to distract and calm children undergoing uncomfortable medical procedures. The Voxel Bay VR platform is being expanded to include other virtual environments and games tailored to specific needs within the pediatric environment.

Celenex
Celenex is a clinical stage gene therapy company targeting Batten diseases and other genetic diseases. In late 2018, Celenex was acquired by Amicus Therapeutics, a biotechnology company focusing on rare and orphan diseases. Phase I/II clinical trials for Batten diseases CLN3 and CLN6 are underway at Nationwide Children's Hospital.

Deep Lens
Deep Lens is augmenting VIPER, one of the world's first digital pathology cloud platforms, to include new features. For over 10 years, VIPER has allowed pathology groups to collaborate on groundbreaking cancer research across dozens of cancer types. Based on feedback from hundreds of expert global users, Deep Lens is enhancing the system to include clinical trial enrollment, AI-powered image detection and workflow support, telepathology, cloud storage and built in APIs for integration by hardware and software vendors and biopharma companies.

Thrive NeuroMedical
Thrive NeuroMedical, an Ohio-based startup based on technology developed at Nationwide Children's Hospital is developing the SmallTalk™ platform to enrich the neurological development of babies who don’t have regular, consistent access to their parent’s voice. The SmallTalk™ device is a unibody Bluetooth-enabled speaker that transmits the parent’s recorded voice with the appropriate sound characteristics to provide a clinical, therapeutic effect.

Clarametyx Biosciences
Clarametyx Biosciences is developing a platform therapeutic for the eradication of bacterial biofilms which are responsible for approximately 80% of human bacterial infections. Their lead composition CMTX-101 is a monoclonal antibody that causes rapid biofilm collapse, enabling host immune clearance and potentiating antibiotic activity.

Andelyn Biosciences, Inc.
Andelyn Biosciences is a viral vector contract and development manufacturing organization. It was established in 2020 as a spin-out of Nationwide Children’s Hospital’s manufacturing division, which has expertise in manufacturing several adeno-associated virus (AAV) serotypes of gene therapy products.

Invirsa
Invirsa is developing a unique, broad platform based on a naturally occurring small molecule (INV-102) that has demonstrated enhanced immune response to infection. INV-102 not only reduces viral infection, and potentially bacterial replication, it also reduces inflammation, while enhancing the body’s wound healing response. Invirsa’s technology is first being developed in the ophthalmology and pulmonary space in partnership with the Biomedical Advanced Research and Development Authority (BARDA) of the Office of the Assistant Secretary for Preparedness and Response in the U.S. Department of Health and Human Services.

Tasseogen
The Tasseogen platform relies on the genome dashboard technology developed at Nationwide Children's Hospital to allow researchers or clinicians to upload genome sequencing data and interactively explore the data to identify gene variants, if any, that may be causal for a patient’s disease. Tasseogen and Nationwide Children’s Hospital RISI team are the recipients of a 2020 Ohio Development Services Agency Technology Validation and Startup Fund (TVSF) Phase I award.
Growth in Technology Commercialization at Nationwide Children’s

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DISCLOSURES

LICENSES/OPTIONS

ISSUED PATENTS

U.S. PATENT APPLICATIONS FILED

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, startup companies and innovations. All along the way the OTC helps assess, support and make decisions about the innovations and technologies.

GOALS FOR TECHNOLOGY COMMERCIALIZATION

Engagement With Industry  Faculty Retention  Revenue  Economic Development  Public Utilization
Natural killer (NK) cells are critical for immune surveillance and host defense. These white blood cells respond to a variety of pathological challenges within the body, including cancer cells, as part of the innate immune system. Their cancer-killing ability led Dean Lee, MD, PhD, and his laboratory at Nationwide Children’s Hospital to study NK cells and develop them as a cancer immunotherapy.

“I think of NK cells as a military unit,” says Brian Tullius, MA, MD, a former Navy officer who is now a fourth-year Hematology, Oncology and Blood and Bone Marrow Transplant fellow working under the supervision of Dr. Lee. “They have two things: a gun, which is their cytotoxic ability to secrete granzyme and perforin, and a radio, which is their ability to call the adaptive immune system for back-up by secreting effector cytokines such as interferon gamma.”

Boosting Natural Killer Cells for the Treatment of COVID-19

While a postdoctoral fellow in Dr. Lee’s lab, Meisam Kararoudi, DVM, PhD, who is now a principal investigator in the Center for Childhood Cancer and Blood Diseases at Nationwide Children’s, developed a method to genetically modify human NK cells (which are notoriously resistant to foreign DNA) to enhance their ability to target cancers. Then, the COVID-19-causing virus, SARS-CoV-2, began to spread worldwide, leaving researchers scrambling to find treatments to reduce the disease’s severity and save lives.

While driving to the laboratory one day in April 2020, Dr. Tullius had an epiphany. “I thought, ‘Wait a minute. We work with a cell that kills cancer — but it also kills viruses,’” says Dr. Tullius.

Over the course of the next eight hours, Drs. Tullius and Kararoudi reviewed all the available literature on the immune response to SARS-CoV-2, which at this time (April) was still limited, and to SARS-CoV-1, which caused the SARS outbreak in 2003.

“NK cells recognize viruses and virus-infected cells, and they prevent the virus from spreading all over the body,” says Dr. Kararoudi. “When we were reviewing the data from SARS-CoV-2 and SARS-CoV-1, we saw that the SARS outbreak in 2003.

“NK cells recognize viruses and virus-infected cells, and they prevent the virus from spreading all over the body,” says Dr. Kararoudi. “When we were reviewing the data from SARS-CoV-2 and SARS-CoV-1, we saw that the numbers of lymphocytes, in particular NK cells, were very low in patients with severe disease.”

This aligns well with our experience in the clinic, where we focus on getting NK cells to cancer patients in settings where they don’t have enough of them, to help restore their NK cell numbers for a better anti-cancer effect,” explains Dr. Lee, who is also a physician in the Division of Hematology and Oncology at Nationwide Children’s and director of the Cellular Therapy and Cancer Immunology Program at Nationwide Children’s and The Ohio State University Comprehensive Cancer Center.

In collaboration with colleagues at OSU, Dr. Lee’s team has developed universal donor NK cells, meaning they can be used “off-the-shelf” to reduce the time and cost of making patient-specific NK cells and without the concern for graft-versus-host disease.

“That is critical because of how rapidly COVID-19 progresses,” says Dr. Kararoudi, who is also director of the CRISPR/Gene Editing Core at Nationwide Children’s. “With this off-the-shelf possibility, we do not need to wait for a donor and are not limited in the number of doses we can deliver.”

Two weeks after their initial literature search, the team worked with the Office of Technology Commercialization to submit a patent. Within the next four weeks, they had FDA approval for a clinical trial of their novel COVID-19 therapeutic.

The technology has been licensed to Kiadis, the company Dr. Lee is working with to develop the off-the-shelf NK cells. The investigational new drug (IND) application and protocol management have been transferred to New York Medical College, where they will initiate an adult-focused clinical trial.

“As we move forward, members of our team will continue to be involved in the protocol, even though the treatment won’t initially be tested in children,” says Dr. Lee. “We’re very proud that our children’s hospital led design and IND approval for a novel cell therapy for adults in the midst of this historic pandemic.”

Chronic and recurrent bacterial diseases, such as infections of the middle ears, sinuses and urinary tract, are resistant to treatment because the bacteria live in biofilms, highly-organized communities of cells that act as fortresses to protect groups of bacteria from the immune system — and from antibiotics.

Some antibiotics only work on dividing cells, and because bacteria in biofilms have slowed metabolism and are no longer dividing, these treatments are rendered ineffective. The Centers for Disease Control estimates 2.8 million antibiotic-resistant infections occur in the United States each year.

Additionally, a single biofilm might contain several species of bacteria, making it difficult to tackle them all with a single treatment.

But what if physicians could find a way to knock down the entire complex structure of biofilms, leaving bacteria vulnerable and exposed?

That’s exactly what Lauren Bakalezt, PhD, director of the Center for Microbial Pathogenesis in the Abigail Wexner Research Institute at Nationwide Children’s Hospital and Steve Goodman, PhD, principal investigator, also in the Center for Microbial Pathogenesis, and their teams have done: for the past 11 years, the researchers have been working to understand biofilms, dismantle them and bring that technology to clinicians everywhere.

Drs. Bakalezt and Goodman discovered the protein most essential to all biofilms’ structures, DNABII protein, then developed a monoclonal antibody that can be delivered therapeutically to target that protein and collapse the biofilm. As a result, the bacteria become susceptible to lower and fewer doses of antibiotics that would not have previously impacted the infection. And the researchers say that it has worked on every type of biofilm tested.

“Once you disrupt the biofilm, a quarter of the usual dose of antibiotics is effective,” says Dr. Goodman. “Here’s a way to address the massive problem of antibiotic resistance and the need for new antibiotics without actually needing to find any new antibiotics.”

In developing a strategy to defeat biofilms in the setting of chronic infections, Drs. Bakalezt and Goodman realized they had developed a platform technology — one that had many diverse applications.

“What started with a focus on biofilms within the context of otitis media quickly expanded,” says Dr. Bakalezt, who is also a professor in the Departments of Pediatrics and of Otolaryngology at The Ohio State University College of Medicine and the Tillie E. Coleman Endowed Chair in Pediatric Research. “We can use what we’ve learned to attack biofilms in many contexts, from treating chronic infections to disinfecting medical equipment — and there are even non-medical applications.”

Biofilms form on human and animal tissue, but they can form on almost any other type of surface. They can be on catheters, implanted artificial joints, medical equipment and kitchen cutting boards, says Dr. Bakalezt. They foul water and oil pipes. They create drag on ship hulls and airplane wings.

Recognizing the importance of bringing technologies based on their portfolio of patents to the marketplace, Drs. Bakalezt and Goodman began working with the Office of Technology Commercialization (OTC) at Nationwide Children’s to search for an industry partner — a pharmaceutical company.

The OTC helped guide the researchers towards continually creating new Intellectual Property (IP) that was driven by composition of matter, the claims a pharmaceutical company would use, and helped them, and the hospital, protect it. They connected the researchers with resources and helped them get in front of the right CEOs. And when the doctors’ initial attempt to partner with a pharmaceutical company didn’t quite develop into the licensing agreement they had hoped for, the OTC helped them pivot.

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Steve Goodman, PhD, principal investigator in the Center for Microbial Pathogenesis at Abigail Wexner Research Institute
“There are some business aspects you can’t control,” says Dr. Bakaletz. “It became clear to us that starting a new company was probably the best way to go, and we have an amazing management team now.”

Together, Drs. Bakaletz and Goodman founded preclinical stage biotechnology startup Clarametyx Biosciences to develop biofilm-combatting therapies. Now, they serve as co-chairs of the company’s scientific advisory board.

“The hardest part of the process is knowing what you don’t know,” says Dr. Bakaletz. “When it comes to the idea, we’re on pretty good footing — when it comes to commercialization and understanding the market, you need a whole team of people that can help you. That’s where the OTC comes in.”

Additionally, because the doctors’ journey with this new technology has spanned over a decade, there have been changes in patent and IP law. By working with the OTC, they’ve been better equipped to navigate these changes and protect their IP. As IP matures, the OTC oversees and mitigates patent challenges and advises researchers on their portfolios, offering funding opportunities and resources along the way.

“Not having their support would delay the progress we’d be able to make and the growth in our portfolio,” says Dr. Bakaletz. “We’re good at the basic science, and we’re still learning about the rest of it.”

The technology that Drs. Bakaletz and Goodman developed offers an opportunity to shift the paradigm for clinical management of a multitude of diseases that evade effective intervention today. The next step is to secure more funding and see if these same results are observed in clinical trials.

“Filing a patent and licensing the technology is just the start of the rest of the journey,” says Dr. Bakaletz. “We’re still innovating, still creating new IP and still working with Clarametyx to bring things to practice. This is the start of the marathon, not the end.”

“This relationship between inventors and innovators and the OTC is very important now and going into the future,” says Dr. Goodman. “Science today is very entrepreneurial — the prioritization of translating innovative discoveries has been transformative for the institution, the health of the community and global health.”

Bacteria in biofilms are responsible for approximately 80% of human bacterial infections. Organized communities of bacteria living in biofilms are shielded from immune system attacks.

These bacteria can be up to 1,000 times more resistant to antibiotics than those unprotected by biofilms.

The technology developed by Drs. Bakaletz and Goodman and licensed to Clarametyx captures and removes the proteins that keep biofilms intact, resulting in their rapid collapse.

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University, believed a new device could help prevent in 2008. Dr. Jatana and Charles Elmaraghy, MD, chief of the Department of Otolaryngology (ENT) at Nationwide Children’s and professor in the Department of Otolaryngology (ENT) at Nationwide Children’s. “There was no existing medical device to achieve lip protection needed.”

“Rather than wait for the solution, we decided to create one ourselves,” says Dr. Elmaraghy.

“We saw this as an opportunity for our institution to continue to be a national leader in the patient safety space,” adds Dr. Jatana, who is also a professor in the Department of Otolaryngology – Head and Neck Surgery at The Ohio State University.

The pair reached out to the Office of Technology Commercialization (OTC) in 2015 to launch a new partnership and begin developing their solution. The office encouraged the doctors to apply for its Technology Development Fund (TDF), which provides up to $50,000 in pre-commercial funding support to either one or multiple awardees twice a year. It paid off: that year, Drs. Elmaraghy and Jatana were awarded $25,000.

With the support of the OTC, the surgeons innovated a novel disposable device made from medical grade silicone, working with design firm Priority Designs on concepts and prototypes. The device, now known as the LabraGuard, is designed to aid in the retraction of the lips and protect the areas that are at the highest risk for preventable burns, mechanical trauma and lacerations during oral surgeries.

In 2019, OTC recognized Drs. Elmaraghy and Jatana for their successful track record creating patient safety medical devices with its Excellence in Innovation Award. The doctors had also worked with the OTC to create the Comfort Collar, the first medical device developed by a surgeon at Nationwide Children’s to be commercially available, and they were awarded a $25,000 TDF grant in 2011 to support its development as well. The Comfort Collar (Marpac Inc., Albuquerque, New Mexico) helps protect tracheostomy patients’ neck skin from pressure wounds, which were a common complication of the procedure, and is now used in hospitals across the country.

“The technology development support here has been outstanding,” says Dr. Elmaraghy. “It provides the initial resources to get ideas off the ground.”

In addition to providing the clinicians with funding and patent support, the OTC helps inventors at every step necessary to bring a technology to market.

Throughout the development of both the LabraGuard and the Comfort Collar, Drs. Elmaraghy and Jatana worked closely with Kyle Murrah, PhD, senior licensing associate in the OTC.

Dr. Murrah assisted Drs. Elmaraghy and Jatana with determining strategies to protect their intellectual property, developing the content and format of FDA regulatory documentation (with support from The Ohio State University Center for Clinical and Translational Science) and marketing the technologies, and marketing the technologies.

The surgeons established and licensed the LabraGuard device to a new venture: surgical safety device company, Zotarix LLC (Columbus, Ohio). Zotarix LLC has continued to collaborate locally with Priority Designs and has involved the CMD MedTech for its FDA regulatory expertise.

“The OTC created a seamless process,” says Dr. Jatana. “They’re available to guide you through next steps and connect you with industry members when relevant or to help you license your technology to startup companies.”

Soon, Zotarix LLC plans to support a medical device trial for the LabraGuard at Nationwide Children’s.

“Nationwide Children’s clearly supports innovation to achieve the best outcomes for pediatric patients,” says Dr. Jatana.
Therapeutics

This model shows the protein that allow the human respiratory syncytial virus (RSV) to enter healthy cells. Unraveling the mechanisms of these viral proteins has paved the way for the development of vaccines and other novel therapeutics to fight RSV.

Method for Inhibiting the Growth of Intrabacterial Pathogens Salmonella and Francisella in the Infected Cells (Reference # 2019-050/070)
Antimicrobials are agents used to treat infections by killing or inhibiting the growth of microorganisms. However, the increasing problem of antimicrobial resistance has resulted in more than 2 million infections and 23,000 deaths every year. Researchers at Nationwide Children’s Hospital have developed a novel method to control infections by intracellular pathogens. This method deploys specific anti-infective agents that target the host immune pathway to effectively help the infected cell control bacterial growth. Hence, this strategy will be efficient in treating infection caused by multidrug resistant strains and intracellular pathogens such as salmonella and francisella.

Generation of Universal and Off-the-Shelf Airway Epithelial Stem Cells for Treatment of Acute and Chronic Airway Diseases (Reference # 2019-015)
Airway epithelial cells (AECs) in the lungs play a crucial role in maintaining a conduit for air and defend against pathogens. Various acute and chronic pulmonary diseases damage AECs resulting in their altered structure and function. However, the AEC renewal is a slow process. Researchers at Nationwide Children’s Hospital have generated Airway Epithelial Stem cells using gene editing technology that will provide unlimited cell source for AECs. Notably, these cells evade immune rejection in recipients. This preclinical invention may provide “off-the-shelf” product paving the way to regenerative respiratory therapeutics.

Didesmethyrocaglamide (and Rocaglamide) as Potential Treatments for Malignant Peripheral Nerve Sheath Tumors (MPNSTs) and Other Nervous System and Soft-Tissue Tumors (Reference # 2018-052)
Malignant peripheral nerve sheath tumors (MPNSTs) are aggressive soft tissue sarcomas of neural origin. The only known curative therapy is complete resection. Researchers at Nationwide Children’s Hospital have shown that methyl-deficient viruses trigger high innate immune response while ensuring sufficient attenuation and enhanced genetic stability. As result, this method could make the rational design of live attenuated vaccine candidates for human respiratory syncytial virus (RSV) and other similar viruses.

Oncolytic HSVs That Stimulate an Immune Mediated Anti-Tumor Response Against Tumor Antigens (Reference # 2018-032)
Oncolytic viruses infect and replicate in tumor cells without harming normal tissue. Researchers at Nationwide Children’s Hospital have genetically engineered sophisticated ‘Herpes Simplex Viruses’ (HSV) that express tumor associated antigens. These HSVs have elicited superior antitumor immune response against tumors in preclinical mouse models. These next generation HSVs are a valuable therapeutic option for controlling cancers.

The Utilization of Nuclear Export Inhibitor Drugs in the Treatment of Calcific Aortic Valve Disease (Reference # 2018-031)
Heart valve disease results in over 23,000 annual deaths in the United States with calcific aortic valve disease (CAVD) being the most prevalent. CAVD is a slow progressive disorder that ranges from mild valve thickening to severe calcification reducing the cardiac output. At present, the only effective treatment for CAVD is surgical repair or replacement. Researchers at Nationwide Children’s Hospital have developed a pharmacological approach to treat the valve calcification by repressing causative signaling pathways. This preclinical finding could lead to a new effective medical therapy for this common disorder.

Vaccines for Prevention of Respiratory Syncytial Virus (RSV) Infections (Reference # 2017-079)
Respiratory syncytial virus (RSV) is the most frequent cause of lower respiratory disease and hospitalization in infants, but there is currently no vaccine available to prevent or treat RSV disease. Researchers at Nationwide Children’s Hospital and The Ohio State University have developed a novel method for designing RSV vaccines using a Vesicular Stomatitis Virus (VSV) vector. VSV is attenuated in humans, so it can infect people and express inserted genes without causing disease. Additionally, VSV grows to high titers in culture, allowing for efficient vaccine production.

Novel VSV-Based Vaccine Platform for Zika Virus (Reference # 2017-028)
There is currently no vaccine available for protecting against Zika virus (ZIKV) infection and disease. Researchers at Nationwide Children’s Hospital and The Ohio State University have developed novel candidate ZIKV vaccines that use vesicular stomatitis virus to express ZIKV proteins. The protection conferred by our vaccines does not rely on antibodies against the ZIKV envelope protein, eliminating the potential problem of antibody dependent enhancement of other species of flavivirus. Our candidate vaccines are highly attenuated while still inducing a protective immune response against ZIKV infection.

Methods for Increasing Autophagy and CFTR Expression in Patients With Cystic Fibrosis (Reference # 2016-037)
Cystic fibrosis (CF) is a systemic disorder caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR). Multi-drug resistant pathogens remain a major cause of chronic morbidity and mortality in CF patients, due in part to deficient autophagy in CF macrophages. Researchers at Nationwide Children’s Hospital and The Ohio State University have identified a novel therapeutic agent that increases CFTR expression and restores autophagy function in CF affected cells.

Therapeutics

Novel Method for Attenuating Live Vaccine Candidates for Nonsegmented Negative-Sense RNA Viruses (Reference # 2018-049)
Stability is a major challenge for live attenuated vaccine candidates because of the ability of viruses to revert to the wild-type phenotype. Virologists at Nationwide Children’s have shown that m6A-deficient viruses trigger high innate immune response while ensuring sufficient attenuation and enhanced genetic stability. As result, this method could make the rational design of live attenuated vaccine candidates for human respiratory syncytial virus (RSV) and other similar viruses.

Oncolytic HSVs That Stimulate an Immune Mediated Anti-Tumor Response Against Tumor Antigens (Reference # 2018-032)
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Heart valve disease results in over 23,000 annual deaths in the United States with calcific aortic valve disease (CAVD) being the most prevalent. CAVD is a slow progressive disorder that ranges from mild valve thickening to severe calcification reducing the cardiac output. At present, the only effective treatment for CAVD is surgical repair or replacement. Researchers at Nationwide Children’s Hospital have developed a pharmacological approach to treat the valve calcification by repressing causative signaling pathways. This preclinical finding could lead to a new effective medical therapy for this common disorder.

Vaccines for Prevention of Respiratory Syncytial Virus (RSV) Infections (Reference # 2017-079)
Respiratory syncytial virus (RSV) is the most frequent cause of lower respiratory disease and hospitalization in infants, but there is currently no vaccine available to prevent or treat RSV disease. Researchers at Nationwide Children’s Hospital and The Ohio State University have developed a novel method for designing RSV vaccines using a Vesicular Stomatitis Virus (VSV) vector. VSV is attenuated in humans, so it can infect people and express inserted genes without causing disease. Additionally, VSV grows to high titers in culture, allowing for efficient vaccine production.

Novel VSV-Based Vaccine Platform for Zika Virus (Reference # 2017-028)
There is currently no vaccine available for protecting against Zika virus (ZIKV) infection and disease. Researchers at Nationwide Children’s Hospital and The Ohio State University have developed novel candidate ZIKV vaccines that use vesicular stomatitis virus to express ZIKV proteins. The protection conferred by our vaccines does not rely on antibodies against the ZIKV envelope protein, eliminating the potential problem of antibody dependent enhancement of other species of flavivirus. Our candidate vaccines are highly attenuated while still inducing a protective immune response against ZIKV infection.

Methods for Increasing Autophagy and CFTR Expression in Patients With Cystic Fibrosis (Reference # 2016-037)
Cystic fibrosis (CF) is a systemic disorder caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR). Multi-drug resistant pathogens remain a major cause of chronic morbidity and mortality in CF patients, due in part to deficient autophagy in CF macrophages. Researchers at Nationwide Children’s Hospital and The Ohio State University have identified a novel therapeutic agent that increases CFTR expression and restores autophagy function in CF affected cells.
Increasing the Yield of Respiratory Syncytial Virus Live Attenuated Vaccines (Reference # 2014-045)

A widespread economic problem of RSV vaccine candidates is their inefficient production. RSV vaccine candidates are produced in Vero, a cell line isolated from African green monkey kidney. Infectious disease experts at Nationwide Children’s Hospital have discovered RSV grown in Vero cells has a cleaved, non-functional attachment glycoprotein (G protein). Our experts identified mutations in the G protein that prevent its cleavage during production in the Vero cell line. Importantly, these mutations increase RSV vaccine production efficiency up to 10 times, making vaccine production now economically feasible.

Sustained Expression of MHC Class I Protects Motor Neurons from ALS Astrocyte-Induced Toxicity (Reference # 2014-033)

Ninety percent of cases of amyotrophic lateral sclerosis (ALS) are sporadic and lack a familial association, but the etiology of sporadic ALS remains largely unknown. Researchers at Nationwide Children’s Hospital have 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.

Novel Treatment for Otitis Media by Preventing NTHI Invasion of Host Epithelial Cells (Reference # 2014-029)

Otitis media (OM) is a leading cause of hearing loss in children in the United States. Nontypeable Haemophilus influenzae (NTHI) is a major causative agent of OM and other diseases of the respiratory tract. NTHI-mediated OM 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.

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.

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

Marine Double Minute 2 (MDM2) is an E3 ubiquitin ligase and negative regulator of the tumor suppressor protein MDM2. 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.

Calcific aortic valve disease (CVD) is a condition in which calcium deposits form on the aortic valve in the heart, reducing the flow of blood through the heart. Researchers at Nationwide Children’s have developed a novel pharmacological approach to treat CAVD.

A Novel Therapeutic Agent for the Treatment of Neisseria gonorrhoeae (Reference # 2015-033)

Resistance of Neisseria gonorrhoeae to antibiotics has developed rapidly in recent years, leading to increased efforts to identify novel antimicrobials. Researchers at Nationwide Children’s Hospital and The Ohio State University have found that AR-12, a drug used in oncology, has antimicrobial properties in the context of N. gonorrhoeae infection of normal human mucosa. Further, AR-12’s antimicrobial activity targets the human pathways required for infection, not the pathogen itself, suggesting that it is unlikely to encourage the development of bacterial resistance mechanisms.

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.

Inhibitors of Covalent Protein Cross-Linking as Antiviral Agents against Respiratory Syncytial Virus (Reference # 2014-051)

Respiratory syncytial virus (RSV) infection is one of the main causes of infant hospitalization and mortality. However, there is no vaccine to prevent RSV infection yet. Virologists at Nationwide Children’s Hospital have characterized a large protein from viral origin in vivo that is responsible for 90% of the infectivity of RSV. These inventors further show that a drug inhibiting protein crosslinking reduces the infectivity of RSV. Such a drug will be used prophylactically to prevent RSV infection.
### Therapeutics

**HIGHLIGHTED TECHNOLOGIES**

**Therapeutics**

- **Enhanced Immunogenicity of a Modified RSV Vaccine with Mutations in One or Both Non-Structural Protein (Reference # 2011-001)**
  
  Respiratory syncytial virus (RSV) is the leading cause of upper and lower respiratory tract infections in infants and young children, and the most common cause of bronchiolitis and pneumonia in children younger than 1-year of age. A vaccine does not exist in part because RSV non-structural protein genes (NS1 and NS2) suppress the immune system rendering the host unable to elicit an appropriate adaptive immune response. Researchers at Nationwide Children's Hospital have identified a previously undescribed disease mechanism in which microglial cells use killing pathways typically ascribed to the innate immune system and can use these mechanisms as targets for therapeutic intervention in ALS.

- **Microglia Induce Motor Neuron Death via the Classical NF-kB Pathway in Amyotrophic Lateral Sclerosis (ALS) (Reference # 2013-028)**
  
  Nuclear factor-kappa B (NF-kB) 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-kB 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. The USPTO has issued a patent for this application in May 2016.

- **ALS Astrocytes With Natural Killer Properties (Reference # 2012-023)**
  
  ALS, commonly referred to as Lou Gehrig’s disease, is characterized by 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 developed a novel method for modulating SMN2 splicing in a therapeutic context by inducing the heat shock response. This novel splicing-corrective treatment is capable of increasing protein levels of SMN in vitro and is being further developed for use in murine models of SMA.

- **Methods of Treating and Preventing Intestinal Injury Related to Hemorrhagic Shock and Resuscitation (Reference # 2007-006)**
  
  Hemorrhagic shock and resuscitation (HS/R)-induced injuries often result from trauma or severe blood loss and can quickly progress to organ failure. Researchers at Nationwide Children's Hospital have developed a novel method for treating subjects at risk for HS/R by administering Heparin Binding-Epidermal Growth Factor (HB-EGF). Administration of HB-EGF protects intestinal epithelial and endothelial cells from HS/R-induced injury in a rat model. This novel method may have broad clinical availability for treating or preventing a range of intestinal injuries in pediatric and adult patients.
Gene Therapies and AAV Production

AAV-Mediated HIT1 Gene Editing for Correction of Diverse DMD Mutations in Patients With Muscular Dystrophy (Reference # 2020-001)

Dystrophinopathies are a group of disorders caused by mutations in the DMD gene which codes for dystrophin, the vital, muscle-specific structural protein. Currently, there is no cure for muscular dystrophy, and patients only rely on palliative care options. Our gene therapy researchers at Nationwide Children’s Hospital have developed an AAV-mediated gene editing method for correcting deleterious DMD mutations in affected patients. This therapy uses a homology-independent targeted integration (HIT1) to replace any missing or aberrant exons in affected patients; therefore, correcting the underlying cause of muscular dystrophy.

Cerebrospinal Fluid Delivery as a New Route for AAV Gene Therapy Targeting Cells of the Cochlea (Reference # 2019-071)

AAV mediated gene therapy is a leading candidate for the treatment of hearing disorders. However, finding a safe and effective delivery route for a gene therapy has been proven difficult to achieve as traditional routes of administration can cause additional damage to cells of the inner ear. To circumvent this challenge, researchers at Nationwide Children’s Hospital have developed a cerebrospinal fluid delivery route to prevent procedural damages and better target cells of interest. Our researchers have also designed vectors to include cochlea-cell type promoters to achieve cell type specific expression. Therefore, they have designed a subset of highly effective AAV gene therapy candidates to treat hearing disorders.

Reduction of Toxic Small Huntingtin Protein by Targeting Both Exon 1 mRNA and Mutant Huntingtin Protein Cleavage Pathways (Reference # 2019-007)

Huntington’s disease (HD) is a late onset progressive neurodegenerative disorder that results in death in 10-15 years after the first sign of symptoms. Existing oligonucleotides (AONs) based therapies are imperfect as they knockdown wildtype protein, require consistent re-injections, and use potentially harmful molecules. Gene therapy experts at Nationwide Children’s Hospital have devised a gene therapy approach that uses a specific siRNA to stably and safely reduce the highly pathogenic protein HTT. By enabling a continuous expression of the therapeutic RNA in the nervous system (and other targets), this technology may delay the age of onset, slow symptom progression, and reduce symptom severity of HD. Hence, it has the potential to become the optimal therapeutic strategy for the treatment of HD.

New Indication for Small Molecule CuATSM (Reference # 2019-040)

Neurodegenerative diseases often stem from the loss of critical molecular pathways. Small molecule therapies, such as CuATSM, have been of great interest in treating these diseases. Researchers at Nationwide Children’s Hospital have identified a new target of the existing CuATSM therapy. This discovery expands the current therapeutic use of CuATSM to now encompass nervous system disorders involving mitochondrial abnormalities and seizure disorders.

Optimizing Gene Therapy for Targeting of Specific Cell Types in the Retina Using Different Viral Vectors, Different Promoters and Different Delivery Routes (Reference # 2019-010)

Gene therapy experts at Nationwide Children's Hospital are utilizing adeno-associated virus (AAV) mediated gene therapy to target specific cell types within the retina to treat vision impairment, retinal degeneration and vision-related disorders. Although, use of ocular administration of gene therapy vectors has shown some promising results, there is a need for improved gene therapy methods. Our experts have designed various viral vectors, promoters and multiple delivery routes to target particular cell types in the retina. This preclinical study offers hope for treating vision loss.

AAV-Mediated CRISPR/Cas9 Gene Editing for Correction of DMD Exon Duplications in Patients With Muscular Dystrophy (Reference # 2019-008)

Gene therapy experts at Nationwide Children’s Hospital have developed an AAV-mediated CRISPR/Cas9 gene editing method for the correction of exon duplications in patients with DMD (Duchenne muscular dystrophy). This therapy has the potential to permanently correct DMD by stopping and potentially reversing the progression of muscle wasting and fibrosis in affected individuals. Currently about 11% of DMD cases are caused by exon duplications and our experts plan to use this invention to correct for this underlying cause within muscle tissues.

DUX4 RNA Silencing Using RNA Targeting CRISPR-Cas13b as a New RNA Interference Tool (Reference # 2018-040)

Facioscapulohumeral muscular dystrophy (FSHD) is one of the most prevalent hereditary muscle disorders affecting an estimated half million individuals worldwide. FSHD is caused by the double homeobox 4 (DUX4) gene mis-expression leading to muscle differentiation defects and atrophy. Gene therapy experts at Nationwide Children's Hospital have developed a novel strategy silencing DUX4 expression using Clustered Regulatory Interspersed Short Palindromic Repeats (CRISPR) - Associated 13b (Cas13b). This therapeutic gene correction has yielded efficient and specific DUX4 reduction in vitro and holds a significant promise for FSHD treatment.

AAV1RF2BP1 Mediated Gene Transfer for 1RF2BP1 Related Disorder (Reference # 2018-037)

1RF2BP1-related disorders are a group of neurodegenerative disorders, characterized by abnormal movements, loss of speech, and seizures, caused by mutations within the 1RF2BP1 gene. Researchers at Nationwide Children's Hospital have devised a gene therapy approach using adeno-associated viruses together with specific promoters to mediate the transfer of a functional gene in affected individuals. This approach is designed to restore 1RF2BP1 protein levels which could lead to drastic health improvement for these patients.
Gene Therapies and AAV Production

Increasing Tissue Specific Gene Delivery by Capsid Modification (Reference # 2018-002)
Researchers at Nationwide Children’s Hospital have identified modified capsid sequences of the adeno-associated virus rh74 (AAVrh74) native capsid that improve delivery of genes to specific target cells or overall global gene delivery. These include modifications that increase specific gene delivery to either the heart or muscle stem cells.

Protein and Gene Therapy for Congenital Muscular Dystrophy Type 1A (Reference # 2017-070)
Congenital muscular dystrophy type 1A (CMD1A) usually presents in the neonatal period with marked muscle weakness and severe hypotonia. CMD1A patients show deficiency in laminin-alpha2 (LAMA2) protein caused by the genetic mutations leading to weaker and unstable muscle tissue. Gene therapy experts at Nationwide Children's Hospital have developed a gene and protein therapy approach enabling delivery of key domains of LAMA2 using adeno-associated virus (AAV). In addition, our experts have engineered fusion proteins that assist in anchoring LAMA2 to the muscle membrane thereby improving the muscle-matrix interaction and muscle integrity.

Functional Cas9 Expressed Internally in AAV Particle (Reference # 2016-012, 2017-009)
CRISPR/Cas9 gene editing technology is a promising tool for treating disease but requires the delivery of the large Cas9 enzyme. Gene therapy experts at Nationwide Children’s Hospital have taken two different approaches to couple the CRISPR gene editing machinery with AAV, including constructing Cas9 as a stable component of the AAV particle, as well as expressing Cas9 on the surface of the viral particle.

Induction of Dystrophin DelCH2 Insom (Reference # 2016-069)
Absence of the dystrophin protein leads to the severe muscle disorder Duchenne muscular dystrophy. Nearly asymptomatic patients have been identified to produce a functional N-terminal truncated dystrophin protein. Gene therapy experts at Nationwide Children's Hospital are developing a U7-snRNA exon skipping strategy to facilitate expression of a functional truncated dystrophin protein for patients carrying mutations within exon 6 to 9 of the DMD gene, rendering their dystrophin nonfunctional. Our experts have effectively skipped exon 8 in patient-derived cell lines and, in turn, produced a functional truncated dystrophin protein product.

Site-Specific Integration of Recombinant Adeno-Associated Virus (AAV) Vector Genomes by Rep68 Protein Expressed on the Surface of AAV Particles (Reference # 2016-055)
Adeno-associated virus (AAV) vectors are replication defective viruses that are engineered to deliver therapeutic genetic cargo to cells. The structural and enzymatic AAV proteins are traditionally supplied in trans to generate engineered particles for gene delivery. One constraint of AAV vectors is the size limitation of the genetic insert. Gene therapy experts at Nationwide Children’s Hospital have engineered an AAV vector that expresses the Rep78 protein on the surface of the viral particle thus eliminating the need to package the rep coding region within the particle. This strategy allows for delivery of a functional Rep78 protein while increasing the overall therapeutic gene insert size.

Improved Adenovirus Helper Plasmid for the Production of Clinical Grade AAV Vectors (pHELP-kanV4) (Reference # 2016-045)
Adeno-associated virus (AAV) remains a leading viral vector candidate for gene delivery. However, the standard production of AAV makes use of ampicillin containing materials which can increase the risk of unwanted beta-lactam reactions in some sensitive patients. Researchers at Nationwide Children’s Hospital have developed a novel plasmid, namely pHELP-kanV4, to replace the standard plasmid and allows for the production of recombinant AAV vectors without the chance of ampicillin gene or protein being retained as a contaminant in the final product. As a result, this will help increase the production of AAV for sensitive patients and especially in Europe where there is a strict guidance in the making of AAV.

Optimized GMP-Grade Adeno-Associated Viral Vector (AAV) Products (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.

Stem Loop RNA Mediated Transport of Mitochondria Genome Editing Molecules (Endonucleases) Into the Mitochondria (Reference # 2016-032)
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Gene therapy experts at Nationwide Children’s Hospital have made significant advancements in designing optimal viral vectors for producing Good Manufacturing Practice (GMP)-grade viral vector products. Our experts have optimized properties of vectors for a wide variety of adeno-associated virus (AAV) serotypes, including AAV1, 2, 2.5, 5, 5.6, 6, 8, 9 and r74. In particular, our experts have optimized virus packaging efficiency, reduced potential to form replication competent AAV and replaced the beta-lactam resistant gene with kanamycin in order to be compliant with European Union (EU) regulations. Our experts have made additional optimized vectors for AAVrh74 and AAV9 that allow for more efficient purification and improved CNS transduction, respectively.

Recombinant Adeno-Associated Virus Gene Therapy for MPS II (Reference # 2016-001)
Mucopolysaccharidosis (MPS II) is a disorder caused by a genetic defect in iduronate-2-sulfatase (IDS), an essential enzyme for the degradation of glycosaminoglycans. Researchers at Nationwide Children’s Hospital and the University of North Carolina at Chapel Hill have developed a gene therapy-based approach that uses a recombinant AAV to deliver a therapeutic IDS gene to the CNS, somatic organs and tissues via a single intravenous injection in patients. Unlike currently available treatments, this novel route ensures a homogenous distribution of the transgene delivery to its targets and therefore represents an effective treatment for MPSII at early and even advanced stages of the disease.
Gene Therapies and AAV Production

Researchers at Nationwide Children’s Hospital have made significant advancements in designing optimal viral vectors for producing Good Manufacturing Practice (GMP)-grade viral vector products. Our gene therapy experts have optimized properties of vectors for a wide variety of adenovirus-associated virus (AAV) serotypes.

**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 DUOX4 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 nontoxic. Researchers at Nationwide Children’s Hospital have developed U7-based snRNAs that bias protein production toward the short nontoxic version of DUOX4 or to block incorporation of exon 3. This new strategy represents a novel therapy for FSHD.

**GARS Knock Down and Replacement Gene Therapy for CMT2D (Reference # 2014-039)**
Charcot-Marie-Tooth (CMT) diseases are the most common, progressive and hereditary peripheral neuropathies leading to loss of normal function and/or sensation in the legs and arms. A subtype of this disease, CMT type 2D (CMT2D), is caused by dominant mutations in a gene encoding the ubiquitously expressed enzyme glycyl-transfer RNA synthetase (GARS). There are currently no treatments for CMT2D or any other inherited peripheral neuropathy despite a cumulative incidence of 1:2500 people affected by these diseases. Gene therapy experts at Nationwide Children’s Hospital have developed an effective adenovirus-based virus-based treatment strategy to knockdown the mutant (defective) form of GARS while preserving essential function of wild type (normal) form using RNA interference. This preclinical invention provides proof-of-concept for CMT2D gene therapy.

**RNAi Therapy for Dominant Limb Girdle Muscular Dystrophy Type 1A (Reference # 2011-002)**
Researchers at Nationwide Children’s Hospital have developed the first RNA interference (RNAi)-based preclinical treatment for limb girdle muscular dystrophy type 1A (LGMD1A), which is caused by dominant mutations in one allele of the myotilin (MYOT) gene. Our researchers have designed novel microRNAs (miRNAs) that reduce mutant MYOT by exploiting the natural RNAi pathway and have demonstrated therapeutic efficacy of their MYOT-targeted miRNAs in a LGMD1A mouse model. This RNAi strategy can also be adapted to broadly impact a large class of dominant muscle disorders.

**MicroRNA Delivery as a Novel Therapeutic Strategy for Liver Cancer (Reference # 2009-002)**
Therapeutic strategies based on small RNA-guided gene regulatory pathways hold great promise for many diseases. Gene therapy experts at Nationwide Children’s Hospital and John Hopkins University have identified a microRNA (miRNA) that when expressed can induce cell-cycle arrest in a hepatocellular carcinoma (HCC) cell line. Our experts further demonstrated systemic adeno-associated viral (AAV) delivery of this particular miRNA protected mice from liver cancer progression without toxicity. This invention identifies a miRNA with potent tumor suppressor activity that exhibits great promise as a liver cancer therapeutic agent and further demonstrates safety of delivering a miRNA-based therapy with AAV in an animal model.

**Production of rAAV in Vero Cells Using Simian Adenoavivirus 13 as Helper (Reference # 2008-004)**
Infectious recombinant adeno-associated virus (rAAV) are exclusively used as gene transfer vehicles for an ever-widening array of human applications such as for use as vaccines and gene therapy vectors. A requirement for the clinical use of rAAV for DNA delivery is a highly efficient, reproducible and commercially scalable production. The most common methods of scalable rAAV production use HeLa cells. HeLa cells are derived from malignant cervical tumor and therefore, raises potential safety concerns. Gene therapy experts at Nationwide Children’s Hospital have developed new methods and materials achieving higher titers of rAAV in mammalian cells other than transformed cell lines. A team of researchers at Nationwide Children’s Hospital have developed a simple and cost-effective technique to ease the production of rAAV. Compared to existing methods, this approach allows more rAAV genomes to be encapsulated into infectious rAAV particles while allowing the production of rAAV in several cell types. The materials and methods of this invention are covered in the U.S.-issued patent 8,409,842.

**Targeted Expression of Apoptosis-Inducing Genes for Treating Cancer (Reference # 2004-005)**
One of the most promising forms of cancer gene therapy is delivery of genes directly to the tumor to facilitate cancer cell death. Gene therapy experts at Nationwide Children’s Hospital have developed a tumor-targeted novel molecular treatment by fusing two genes, Survivin and Granzyme B. Survivin is expressed at high levels in all tumors and Granzyme B induces apoptosis in tumor cells. The recombinant DNA is delivered to the target cells by another agent, such as liposome. This approach represents a universal method for targeting tumor cells that express Survivin and induce death of those cells, leaving minimal effect on healthy cells, unlike conventional chemotherapeutic approaches.

**Methods and Materials for Recombinant Adeno-Associated Virus Production (Reference # 2003-001)**
Recombinant adenovirus-associated virus (rAAV) is one of the most used viral vectors for gene therapy. However, large-scale rAAV production is labor intensive and costly due to the requirement for an efficient rAAV synthesis in stable cell lines. A team of researchers at Nationwide Children’s Hospital have developed a simple and cost-effective technique to ease the production of rAAV. Compared to existing methods, this approach allows more rAAV genomes to be encapsulated into infectious rAAV particles while allowing the production of rAAV in several cell types. The materials and methods of this invention are covered in the U.S.-issued patent 8,409,842.
Gene Therapies and AAV Production

Adeno-associated viruses (AAV) are small viruses with a genome of single stranded DNA that infect humans but do not cause disease in most people. This makes AAV an effective and versatile viral vector for gene therapy applications; the virus can be engineered to safely deliver DNA to target cells without facing a strong immune response. Nationwide Children's Hospital researchers have developed simple and cost-effective techniques to scale the production of these vectors.

Regions Within the Adeno-Associated Virus Type 2 (AAV2) Capsid Amenable to Foreign Epitope Insertion, Scaffolding Sequences Required for Efficient Epitope Display, and Construction of AAV2 Vectors With Altered Tropism (Reference # 2000-004)

Gene therapy experts at Nationwide Children's Hospital have recognized there is a need for constructing adeno-associated virus (AAV) vectors that display immunogenic peptides/polypeptides or display targeting peptides that promote delivery of DNA to a specific target cell. Our inventors have elucidated regions of the AAV2 capsid protein that are amenable to insertion of peptides that cause altered characteristics in comparison to wildtype AAV, including, but not limited to, altered cellular tropism and/or antigenic properties. Our experts' technology could vastly increase the utility of AAV vectors for clinical gene transfer. This technology is covered in U.S.-issued patents 6,962,815 and 7,749,492.

Biomarkers

Relying on only patient perception and reporting of their own medical symptoms can present challenges for early and accurate detection of conditions and complications. Researchers at Nationwide Children's continually develop new biomarkers that allow for more accurate screening and diagnosis of a variety of conditions. Biomarkers are any substance, structure or process that can be used to directly, objectively and reproducibly measure and evaluate normal biological processes, pathogenic processes or pharmacologic responses to therapeutic interventions in a patient.

Uroepithelial Proteins as Biomarkers of Urinary Tract Obstruction (Reference # 2019-034)

Urinary tract obstruction (UTO) is one of the most common etiologies of prenatal hydronephrosis, a condition that can lead to permanent kidney damage if left untreated. A group of researchers at Nationwide Children's Hospital have developed a new way to use specific uroepithelial proteins such as antimicrobial peptides (AMPs) as biomarkers of obstructive uropathy. This noninvasive procedure tremendously improves early detection of UTO, informs surgical management and enables postoperative monitoring of patients.

Factor XIII EC-ELISA Activity (Reference # 2018-063)

Factor XIII deficiency is a genetic bleeding disorder characterized by deficiency of clotting factor XIII resulting in prolonged, uncontrolled bleeding episodes. Unfortunately, the currently available, clinically approved Factor XIII activity assays are technically challenging. Researchers at Nationwide Children's Hospital have developed a new method for the determination of blood coagulation factor XIII enzymatic activity in a conventional enzyme-linked immunosorbent assay (ELISA). This method enables direct quantification of factor XIII as opposed to currently available indirect methods of measurement. This proof-of-principle technology provides improved, sensitive and simplified procedure for factor XIII estimation.

Novel Diagnostic Tools for Acute Peritonitis (Reference # 2017-044)

Infectious peritonitis is a serious complication in patients undergoing chronic peritoneal dialysis (PD) leading to patient morbidity and mortality. Currently available, nonspecific diagnostic criteria of peritonitis can lead to missed or overdiagnosis. Researchers at Nationwide Children's Hospital have discovered more sensitive and specific biomarker for peritonitis in the PD population that entails measurement of antimicrobial peptide levels. This new process will aid practitioners in early, accurate diagnosis of acute peritonitis in patients undergoing PD.

Use of LPS Serotypes as Predictors of Disease Severity (Reference # 2013-022)

Determining the severity of urinary tract infections (UTIs) relies on patient reporting of symptoms, a difficult task when working with pediatric populations. Failure to identify severe cases of UTI can result in dangerous complications including renal scarring and urosepsis. Researchers at Nationwide Children's Hospital have found that lipopolysaccharide (LPS) serotype correlates with magnitude of pro-inflammatory responses and is predictive of clinical UTI severity. Screening for the predominant LPS serotype in a sample will determine which patients are likely to develop severe disease and require therapeutic interventions.
End User Innovation

Physicians, researchers and technology experts at Nationwide Children's have developed virtual reality experiences that address a variety of clinical challenges, from reducing patient psychological stress during appointments to assessing cognitive function and facilitating rehabilitation among patients with traumatic brain injuries.

All in One IV Pole: Tape dispenser, sharps bins and medical trash containers (Reference # 2019-002 and 2019-007)

Inventors at Nationwide Children's Hospital have developed a device consisting of an intravenous pole (IV) that harbors a clamp for adhesive tape dispenser, sharp bins and medical trash container. This prototype "all in one" equipment is a convenient and practical site for adhesive tape dispensation and surgical trash disposal while ensuring patient safety in the operating suite.

"Facing Takeoff" - A Day-Long Workshop for Those Interested in Easing their Fear of Flying (Reference # 2018-089)

Flying phobia is a highly prevalent anxiety disorder, which causes sufferers significant distress and life interference. There are multiple interventions addressing flying anxiety provided through airports, commercial airlines as well as online materials. However, these services either charge fees or do not provide any aircraft/airport simulation experience.

There are multiple interventions addressing flying anxiety provided through airports, commercial airlines as well as online materials. However, these services either charge fees or do not provide any aircraft/airport simulation experience. These educational interventions facilitate increasing tolerance of and comfort with air travel.

Congenital Anomalies Surgical Simulation Models (Reference # 2017-051)

Congenital defects have low birth prevalence and therefore, pediatric surgeons have limited opportunity to repair these anomalies. Physicians at Nationwide Children’s Hospital have developed a suite of high-fidelity surgical simulation models to recreate congenital defects. These models are modular and offer an immersive and realistic way of learning surgical skills enabling minimally invasive surgery.

End User Innovation

Integrated Process and Apparatus to Prepare and Predict Pediatric Patients Who Will Successfully Undergo MRI Procedures Without Sedation (Reference # 2017-047)

To ensure image quality and reduce repeat MRI exams, sedation is typically required for younger pediatric patients who will undergo MRI exams. Researchers at Nationwide Children’s Hospital have developed a new process combining devices, immersive virtual reality simulation and predictive analytics to better educate and prepare pediatric patients or research participants for routine MRI exams. Additionally, this technology will aid in predicting which patients are best suited to undergo an MRI without sedation and in predicting which research participants are likely to successfully complete a functional MRI study. This technology will improve pediatric MRI clinical throughput and reduce patient and family apprehension towards MRI exams.

Transcranial Doppler Ultrasound Determination of Pathologic Mechanisms and Treatment Strategies for Cerebral Malaria (Reference # 2017-045)

Worldwide, malaria affects 2 million individuals annually. Cerebral malaria is the most severe neurological manifestation of malaria with case fatality rates ranging from 15-40%. Researchers at Nationwide Children’s Hospital have developed a method for using transcranial doppler to detect distinct waveform morphologies and identify pathogenic mechanisms leading to neuronal injury in children with cerebral malaria.

Computerized Screening Tool for Behavioral Health (Version 2) (Reference # 2016-061)

Despite the high prevalence of mental health, many cases go without treatment, in part because their disorders go undiagnosed. Scientists at Nationwide Children’s Hospital have developed a computerized screening tool for behavioral health that is able to administer and score a set of mental health symptom questionnaires. This web application enables earlier identification of mental health disorders leading to earlier care.

Virtual Reality-Based Pediatric Traumatic Brain Injury Assessment and Rehabilitation Platforms (Reference # 2016-011; 2017-033)

Researchers at Nationwide Children’s Hospital have developed virtual reality (VR)-based programs for assessing cognitive function and providing subsequent rehabilitation. This pediatric TBI assessment software provides VR-based cognitive-assessment tasks and an additional training platform that pairs with the Oculus Rift virtual reality viewer. The training program is designed with a series of environmentally enriched three-dimensional cognitive exercises that aid in rehabilitation of executive core functions among pediatric patients with TBI in a highly controlled, safe and automated manner.

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. Scientists at Nationwide Children’s Hospital have developed a 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.

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. Physicians 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

Mobile Safety App (Reference # 2013-013)
Injuries are a major source of childhood emergency department and hospital admissions. Nearly 9,000 children and young adults, aged 0-19 years, die from unintentional injuries each year. Known effective safety devices are readily available, however, there is no centralized and authoritative information available to parents on how to achieve a safe home and which products are most suited to their homes and families. Researchers at Nationwide Children's Hospital have developed a mobile safety app and a corresponding website to provide correct, reliable and trusted child and home safety information to help parents identify injury hazards “room-by-room” to make their homes safe for their families. This mobile safety app will allow parents to select and purchase safety products that are best suited to the features of their homes and will provide tips for proper installation as well as reminders for correct and consistent use.

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 multidhead testing devices with fixed horizontal surfaces do not provide consistent intradevice 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. Clinical studies of PS Rocker are currently underway at Nationwide Children’s Hospital testing effectiveness of PS Rocker.

Gearbox (Reference # 2012-016)
Data scientists at Nationwide Children's Hospital in collaboration with The Ohio State University have developed a medical data visualization software package, Gearbox. This is a general-purpose library that combines widgets, utility, image handling, volume rendering, and any networking capabilities all under one library. Gearbox enables improved and interactive visual representation of medical data.

Braincase (Reference # 2012-015)
Skull base surgeries are ranked among the most difficult of the surgical subspecialties since minor errors can have disastrous consequences. Successfully navigating through tiny spaces between nerves, arteries and bone requires a masterful grasp of neuroanatomy. Hence, there is a growing interest in the use of simulation to complement conventional surgical training. Inventors at Nationwide Children's Hospital have developed a skull base surgical simulator that combines visual, haptic and auditory output into a cohesive learning experience for users. This simulation model is a useful tool that may improve surgical proficiency while minimizing risk to patients.

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.

End User Innovation

Using surgical simulation to complement conventional training can improve surgical proficiency while minimizing risk to patients. New simulation models developed by inventors at Nationwide Children's can recreate complex neuroanatomy and rare congenital defects, offering an immersive and realistic way of learning and improving surgical skills.

Medical Line Safety Enclosure (Reference # 2006-015)
In health care 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.

Literacy in Children With Hearing Loss (“Hear Me Read” app) (Reference # 2016-024)
The Hear Me Read app is the product of an interdisciplinary collaboration between ENT surgeons and speech language pathologists to assist hearing impaired children to read. The program uses curated content and recorded parental voice to narrate a story and guide children through exercises.
**Tissue Engineering**

Congenital heart defects are the most common birth defects, and those involving underdeveloped or blocked blood vessels may require surgery utilizing vascular grafts. Tissue-engineered vascular grafts (TEVG) are superior to other options for pediatric congenital heart patients because they are made up of the patient’s own cells, eliminating the need for immunosuppressive or anti-rejection medications, and they grow with the child, decreasing the number of follow-up surgeries needed with conventional grafts.

**Closed Seeding System for the Tissue Engineered Vascular Graft (Reference # 2015-076; 2016-010)**

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 patient. 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.

**Cell-Free Tissue Engineered Vascular Grafts (Reference # 2015-034; 2015-035; 2015-036)**

Researchers at Nationwide Children's Hospital have developed a novel method for increasing the potency of biodegradable, synthetic vascular grafts. Administration or controlled release of one or more cytokines or chemokines was found to promote outward tissue remodeling of the vascular grafts and vascular neotissue formation. As a result, this method does not require cell seeding of the vascular graft, eliminating many problems associated with cell seeding such as contamination, loss of clinical utility due to added time for cell expansion, and difficulty in obtaining healthy autologous cells from diseased donors.

**Production of Tissue Engineered Intestine 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. 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.

**Bioinformatics**

**The Superbaby Project (Reference # 2019-059)**

Preterm birth is the leading cause of mortality and morbidity in young children with over a million deaths per year worldwide arising from neonatal complications (NC). Research scientists at Nationwide Children's have developed a scoring grid that can be used for the early detection of NC in premature infants. Infant-specific risk knowledge which can be derived from this invention could help design individualized treatment for each preterm infant, thus reducing hospitalization cost.

**Vitals Risk Index (Reference # 2017-021)**

Each year, a significant number of code blue and emergent transfer events occur in pediatric hospitals. Current prediction methods do not have a high level of success with alerting medical staff to an imminent code blue event. Researchers at Nationwide Children's Hospital have developed an algorithm for calculating a pediatric early warning index score designed to correlate with the risk of cardiopulmonary failure and/or emergency transfer to the ICU based on only objective vital sign measurements. The Vitals Risk Index (VRI) alerts medical staff when early warning index scores exceed a specified threshold. VRI prototype technology has the potential to help prevent code blue events and increase emergency medical staff preparedness.

**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 Hospital 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.

**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.


Next Generation Sequencing (NGS) is a sequencing technology characterized by the large volume of generated DNA/RNA sequencing data. However, the cost to analyze NGS data is outstripping the cost to actually produce the data. To circumvent this challenge, the Institute for Genomics Medicine have developed a fully automated and comprehensive analysis tool called Churchill. Churchill's patented novel parallelization strategy analyzes raw NGS data in a record time.
Research Tools/Clinical Tools/Other

General Movements Assessment maT (GMAT) (Reference # 2020-029)

General movements (GM) are distinct spontaneous movements that are used for the early diagnosis of cerebral palsy in infants. However, the training cost associated with a limited field expert and the unreliability of current GM assessment tools remain the main challenges. To circumvent these challenges, a group of researchers at Nationwide Children’s Hospital have developed General Movements Assessment maT (GMAT). GMAT is an assessment tool that uses a combination of pressure sensor technology and machine learning to detect GM rapidly and with high accuracy. Effectively, this new technology ensures an improved surveillance and delivery of targeted early interventions in our hospitals.

WHAAP: Wound Healing Automated Analysis Pipeline (Reference # 2020-023)

Wound healing assay is a common laboratory method used to study cell migration and interaction. However, current assay methods involve tedious manual processing between steps of analysis. Researchers at Nationwide Children’s Hospital have developed a wound healing automated analysis pipeline (WHAAP), an automated software that tracks cell movements and proliferation in live culture. WHAAP analyzes images with a very high accuracy and provides enhanced data visualizations, all in record time.

Neuromuscular GRO Worksheet (Reference # 2020-005)

Spinal muscular atrophy (SMA) is a severe neuromuscular disease and the leading genetic cause of infant mortality. Moreover, existing treatments suffer from notable floor and ceiling effects and also poorly discriminate improved motor performance in patients. To circumvent these challenges, researchers at Nationwide Children’s Hospital have developed the Neuromuscular Gross Motor Outcome (GRO) worksheet. The GRO worksheet is a gross motor outcome measure designed to assess whole body strength, motor development and function for all levels of ability across the lifespan in those diagnosed with SMA. Hence, the GRO worksheet is the ideal outcome measure tool for SMA or similar conditions to answer the need to quantify gross motor ability across a wide age span.

Gene Therapy Immersion Training Program (Reference # 2019-075)

With the recent success of gene therapy, a consistent approach is needed to perform clinical trials as well as administration of approved gene therapy products in multi-sites. The Center for Gene Therapy at Nationwide Children’s Hospital has extensive experience in designing and performing gene therapy clinical trials. They have developed a comprehensive gene therapy training program for medical professionals initiating new gene therapy programs at their facilities or research sites. This training program covers detailed aspects on the use of gene therapy for neuromuscular diseases and ensures that the recipients are fully immersed in the challenges and latest innovations in the gene therapy field.

AAV Viral-Mediated Gene Therapy Pharmacy Training Manual (Invention # 2019-017)

Adeno-associated virus (AAV)-mediated gene therapy has emerged as a highly promising and efficacious therapeutic over the last decade. Despite the versatility, relative safety and popularity of AAV, several challenges remain that still impede its mainstream use in the clinic, one of it being unavailability of detailed pharmacy recommendations. Pharmacists at Nationwide Children’s Hospital have developed a pharmacy training manual that describes in-depth pharmacy procedures and expert opinions related to the handling and manipulation of viral mediated gene therapy. This document would allow the harmonization of pharmacy procedures between multiple sites in a clinical trial.

Gene Therapy Immersion Program for Neuromuscular Disorders Module 6: Physical Therapy Outcome Measures (Reference # 2020-059)

Neuromuscular disorders (NMD) are a group of diseases characterized by a progressive weakness and loss of functional mobility of muscles. Currently, there is no cure for NMD and gene therapy has since emerged as a leading candidate for its treatment. NMD and gene therapy experts at Nationwide Children’s Hospital have developed a physical functional assessment to evaluate the efficacy of gene therapies. This data-driven guide uses specific psychometric properties to match different outcome measures to their targeted interventions. Hence, ensuring the effectiveness of new therapeutic interventions and clinical management strategies aimed at the treatment of NMDs.

Lowes Lab Ambulatory Status Algorithm (LASA) (Reference # 2019-072)

Research in the field of neuromuscular disease is increasing at an astonishing pace. However, there is no current standardization in the evaluation of the ambulatory status of patients. Researchers at Nationwide Children’s Hospital have devised a guide that stratifies patients into ambulatory statuses for data analysis and group assignment. Unlike the traditional binary stratification, this method adds a third stratification which is very important for clinical trial planning and an accurate assessment of the ambulatory status of patients.

From bench to bedside, experts at Nationwide Children’s Hospital have developed a variety of tools to improve training, documentation, testing and more. In one case, recognizing that consumer software solutions are inadequate tools for effectively documenting every regulatory aspect of multiple clinical trials, specialists developed a new and unique, web-based software platform to streamline clinical research processes.
Research Tools/Clinical Tools/Other

The Roadmap to Navigating Clinical Research: Your Survival Guide to Compliant Study Management (Reference # 2019-065)

Clinical research is the vehicle through which new diagnostics, therapeutics and prevention strategies are developed in the medical field. Researchers at Nationwide Children's Hospital have designed an unmatched clinical research training program that provides an in-depth foundation in multisite study management. This new training program incorporates different evaluation and exercise tools to maximize understanding and applicability for all learning styles.

Clinical Trial and Investigator Initiated Research Tracking Platform (Reference # 2019-012)

Proper documentation is critical to the success of the daily management of a clinical trial. Every aspect of the clinical study must be documented in order to obtain useful data and demonstrate compliance with applicable regulations. Typically, the documentation relies on using programs like Microsoft Excel and Word often resulting into lack of reliable, accurate and adequate information. Clinical trial specialists at Nationwide Children's Hospital have designed a software platform to support, track and manage regulatory aspects of multiple clinical trials. This prototype web-based system provides a reproducible tool to streamline clinical research processes.

SpeakHealth: A Shared, Voice-Enabled, Real-Time and AI Powered Home Medical Diary App (Reference # 2018-086)

Children with special health care needs (CSHCN) require complex care provided by parents and health professionals. The Research Information Solutions and Innovation (RISI) team has developed a patient-centered and AI-driven mobile app called SpeakHealth to facilitate the communication between everyone involved. SpeakHealth utilizes speech recognition and real-time information capturing technologies to reduce delays and miscommunication which in turn help CSHCN achieve the best health outcomes.

Glass (Tissue) Slide Holder for Scraping (Reference # 2018-076)

Glass slides are exclusively used for histopathological studies in biomedical research for tissue mounting purpose. Many downstream applications of these slides often lead to tissue/label loss and slide damage. Inventors at Nationwide Children's Hospital have designed a glass slide holder with a unique design that reduces difficulty of scraping labels, keeps them still for experimental purposes and prevents breakage. This prototype glass slide holder provides safety and functionality for those working with glass tissue slides.

Titin (TTN) Based Cardiomyopathy Mouse Model TTN219 (Reference # 2018-023)

Experts at Nationwide Children's Hospital have developed a novel titin-deficient mouse, TTN 219, in order to study limb girdle muscular dystrophy type 2J (LGMD2J) based on a documented patient mutation. The TTN 219 mouse model was developed using CRISPR/Cas9 technology therefore the time required to modify the titin gene is reduced as well as off-target insertions into the mouse genome. Our experts have demonstrated functional deficits in skeletal muscles of the TTN 219 mouse model and plan to use this model to test therapeutic strategies intramuscularly and systemically to restore titin protein function.

Titin (TTN) Based Cardiomyopathy Mouse Model TTN326 (Reference # 2018-022)

Titin (TTN) plays essential roles in both skeletal and cardiac muscle and when functioning improperly has devastating effects on muscle like dilated cardiomyopathy. Gene therapy experts at Nationwide Children's Hospital have utilized CRISPR/Cas9 technology to develop a new mouse model of dilated cardiomyopathy referred to as TTN326. Utilizing the CRISPR/Cas9 technology to produce a mouse model instead of traditional methods has reduced the time required to modify the Titin gene as well as off-target insertions into the mouse genome. Our experts have demonstrated functional deficits in skeletal muscles of the TTN-326 mouse model and plan to test therapeutic strategies intramuscularly and systemically in this model to restore Titin protein function.

Research Tools/Clinical Tools/Other

An Inducible Facioscapulohumeral Muscular Dystrophy (FSHD) Mouse Model Expressing DUX4 (Reference # 2014-019)

Facioscapulohumeral muscular dystrophy (FSHD) is the third most common muscular dystrophy, affecting 1 in 20,000 individuals. There is no current treatment for FSHD; therefore, animal models of the disease are essential for testing potential therapies. Researchers at Nationwide Children’s Hospital have developed a mouse model that recapitulates the FSHD phenotype and develops myopathy. This is an inducible FSHD mouse model that stably expresses the disease-causing gene, DUX4, from the mouse genome using the human DUX4 promoter. Importantly, in comparison to other FSHD mouse models, this particular inducible model circumvents lethality and leanness problems seen in past models of the disease.

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.

A Novel Mouse Model of Duchenne Muscular Dystrophy With a Duplication of DMD Exon 2 (Reference # 2013-037)

A novel mouse model for testing exon skipping therapies for Duchenne muscular dystrophy 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)

Putative cytidine monophosphate-N-acetylneuraminic acid hydroxylase-like protein is an enzyme that in humans is encoded by the CMAH gene. A new CMAH-deficient mouse model for Duchenne muscular dystrophy (DMD)-related research has been created at Nationwide Children's Hospital in association with research done at University of California, San Diego. The CMAH-deficient mouse model mimics the human disease better than the current standard model thus providing a model for DMD that facilitates translational research to be more relevant to issues affecting the human disease.

Transfected Cell Line for Drug Discovery Aimed at Splicing Correction (Reference # 2009-014)

Researchers at Nationwide Children's Hospital have developed a stably transfected cell line that expresses wild type survival motor neuron gene-2 (SMN2) that can be used as a drug discovery tool aimed at gene splicing correction. SMN2 is a potential therapeutic target for proximal spinal muscular atrophy (SMA), an autosomal recessive neuromuscular disease. SMA is caused by a homozygous loss of the SMN1 gene. Humans have two nearly identical SMN genes, SMN1 and SMN2. SMN2 generates a truncated protein due to a nucleotide alteration in exon 7, which leads to inefficient RNA splicing of exon 7. Stable cell lines expressing SMN2 minigene have been generated that allow for detection of correct splicing of the SMN2 gene.
Matthew McFarland, RPh, PhD, Vice President, Commercialization and Industry Relations
Matthew joined Nationwide Children's Hospital as director of the Office of Technology Commercialization in the spring of 2012 and currently serves as vice president of Commercialization and Industry Relations. In this role, 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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Susan S. Allen, BS, Senior Intellectual Property Coordinator
Susan joined Nationwide Children's Hospital in the summer of 2013. She manages the intellectual property and patent portfolio 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 nongovernment 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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Margaret Barkett, PhD, Associate Director
Margaret joined Nationwide Children's Hospital as a licensing associate in February 2010, and currently serves as associate director 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 Nationwide Children's. 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 cellular 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 Nationwide Children's, she completed a full time, one-year technology licensing internship at Massachusetts Institute of Technology focusing on medical devices and biotechnology.

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Andrew M. Corris, PharmD, JD, Senior Licensing Associate
Andrew joined Nationwide Children's Hospital in March 2015. In his role as a senior 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 degree 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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Cristina Crimaldi, BA, Marketing and Business Coordinator
Cristina joined Nationwide Children’s Hospital in May 2019 and as of December 2020, was promoted to Marketing & Business Coordinator within the Office of Technology Commercialization. Her primary responsibilities include the management of OTC engagement efforts with multiple stakeholders, both internal and external. She is the lead for managing outreach and publication efforts and helps to develop and execute on marketing campaigns for select high priority Nationwide Children’s technologies.

She has a Bachelor of Arts degree in political science from Ohio University. She has 15 years of experience in administration, business development and customer service.

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Jocelyn Eidahl, PhD, Licensing Associate
Jocelyn joined Nationwide Children’s Hospital as a licensing associate in the Office of Technology Commercialization in December 2018. In her role as a licensing associate, she promotes technology transfer through the evaluation, protection and out-licensing of technologies developed at Nationwide Children’s Hospital.

Jocelyn has a Bachelor of Science degree in biology from the University of Akron and a PhD in pharmaceutics and pharmaceutical chemistry from The Ohio State University. Jocelyn then completed her postdoctoral training in the Center for Gene Therapy at Nationwide Children’s Hospital. Her postdoctoral research focused on developing therapies to treat musculoskeletal disorders. While carrying out her postdoctoral studies, she completed a technology transfer internship at Nationwide Children’s.

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Ellen Hanna, BS, Lead Administrative Assistant
Ellen joined Nationwide Children’s Hospital in July 2020 and joined the Office of Technology team in December 2020. Her primary responsibilities include supporting Amy Roscoe, vice president of Strategic Planning and Finance, and Matt McFarland, vice president of Commercialization and Industry Relations, as well as the Office for Technology Commercialization. Ellen is responsible for calendar management and meeting coordination as well as assisting each member of the Office of Technology Commercialization with various duties as needed. Ellen also supports the team with department projects, event coordination, supply orders and provides assistance with record keeping.

She has a Bachelor of Science Degree in family studies from Ohio State University. She has 12 years of experience in customer service, Human Resources, and administration.

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Isabella Gomez Rueda, LLB, LLM, Esq., Agreements Coordinator
Isabella joined Nationwide Children’s Hospital in March 2018. As agreements coordinator she is responsible for the negotiation and administration of Material Transfer Agreements, Data Use Agreements and Confidential Disclosure Agreements. Isabella also manages the agreements docket and provides assistance to the office’s licensing team.

Isabella has a Bachelor of Laws LLB from the Universidad Industrial de Santander, a Graduate Degree in Trade Law from the Universidad Autonoma de Bucaramanga and a Master of Laws LLM in Intellectual Property and Technology Law from The Ohio State University. She is a licensed attorney in Colombia and the State of New York. She has experience in the areas of university transactions, contracts, commercial and intellectual property law.

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Patrick Kennedy, MBA, Alliance Manager
Patrick joined Nationwide Children’s Hospital in 2008. He worked in Human Resources Talent Acquisition for 11 years before joining the Office of Technology Commercialization in 2019 as the Alliance Manager. He is responsible for relationship and program management with commercial partners. This position functions as a liaison between Nationwide Children’s stakeholders and licensing partners to ensure effective program development to the commercial market.

Patrick has a Bachelor’s Degree in health sciences from Ohio State University and a Master’s in Business Administration from Ohio Dominican University.

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Kyle Murrah, PhD, Senior Licensing Associate
Kyle joined Nationwide Children’s Hospital as a licensing associate in the Office of Technology Commercialization in July 2014 and currently serves as a senior licensing associate. In his role, 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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### Our Team

**Susannah Wolman, BA, Operations and Business Manager**

Susannah joined Nationwide Children's Hospital as the business compliance and finance coordinator in July 2016, and currently serves as the operations and business manager. In her role, Susannah manages the activity of the office's financial transactions as well as the operational projects and reporting.

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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**Amy Yoder, BA, Intellectual Property Coordinator**

Amy joined Nationwide Children's in June of 2018. She manages the intellectual property and patent portfolio for the Office of Technology Commercialization. She works with external law firms, inventors, and licensing staff to coordinate the execution of all legal documentation associated with the patent application process.

Amy has her bachelor's degree in political science from the University of Kentucky and her paralegal certificate from Columbus State Community College. She has experience in the areas of intellectual property and corporate law.

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