TRANSFER to TRANSFORM

THE OFFICE OF TECHNOLOGY COMMERCIALIZATION
AT NATIONWIDE CHILDREN’S HOSPITAL

2019 – 2020

NATIONWIDE CHILDREN’S
When your child needs a hospital, everything matters.
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.

Our Mission

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

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

Affiliations
### Centers and Institutes

| Battelle Center for Mathematical Medicine | Injury Research and Policy |
| Biobehavioral Health | Innovation in Pediatric Practice |
| Biopathology Center | Microbial Pathogenesis |
| Cardiovascular and Pulmonary Research | Perinatal Research |
| Childhood Cancer and Blood Diseases | Regenerative Medicine |
| Clinical and Translational Research | Steve and Cindy Rasmussen Institute for Genomic Medicine |
| Gene Therapy | Vaccines and Immunity |

### Funding

#### 2018 Annual Performance Indicators

**Funding**

<table>
<thead>
<tr>
<th>2018 ExternA1 Awards by Source</th>
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#### 2018 External Awards by Source

<table>
<thead>
<tr>
<th>Source</th>
<th>Amount (in millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Program</td>
<td>$0.5</td>
</tr>
<tr>
<td>Industry</td>
<td>$13.5</td>
</tr>
<tr>
<td>Other</td>
<td>$17.9</td>
</tr>
<tr>
<td>Federal Other</td>
<td>$20.4</td>
</tr>
<tr>
<td>NIH Prime</td>
<td>$53.6</td>
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</table>

Total: $105.9 million

#### Research by the Numbers

<table>
<thead>
<tr>
<th>2016</th>
<th>2017</th>
<th>2018</th>
</tr>
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<tbody>
<tr>
<td>Principal Investigators*</td>
<td>182</td>
<td>188</td>
</tr>
<tr>
<td>Research Fellows</td>
<td>75</td>
<td>70</td>
</tr>
<tr>
<td>Graduate Students</td>
<td>34</td>
<td>37</td>
</tr>
<tr>
<td>Employees</td>
<td>1075</td>
<td>1310</td>
</tr>
<tr>
<td>Publications</td>
<td>1067</td>
<td>1171</td>
</tr>
</tbody>
</table>

*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, a Novartis company and a clinical stage gene therapy company, is developing treatments for patients with neuromuscular diseases, including Nationwide Children's Hospital's licensed programs for Rett Syndrome, Amyotrophic Lateral Sclerosis (ALS), and spinal muscular atrophy (SMA), a motor neuron disease that affects one in 6,000 live births in the United States and is the leading genetic killer 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 technology developed at Nationwide Children's Hospital, is focused on developing a cure for Sanfilippo Syndrome, MPS IIIA and MPS IIIB, rare genetic disorders caused by the body's inability to properly break down certain sugars. 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. The company is using technology invented by Nationwide Children's researchers to deliver a corrective gene to the central nervous system in children with these disorders. 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 extending VIPER, one of the world’s first digital pathology cloud platforms that for over 10 years 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 AI-powered image detection and workflow support, telepathology, collaboration, 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 DinoEgg™ platform to enrich the neurological development of babies who don’t have regular, consistent access to their parent’s voice. The DinoEgg™ is a unibody Bluetooth-enabled speaker that transmits the parent’s recorded voice with the appropriate sound characteristics to provide a clinical, therapeutic effect.

Voxel Bay – a virtual reality technology – was originally designed for and tested in children with hemophilia and needle aversion.
Growth in Technology Commercialization at Nationwide Children’s

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.

Our Process

GOALS FOR TECHNOLOGY COMMERCIALIZATION

- Engagement with Industry
- Faculty Retention
- Revenue
- Economic Development
- Public Utilization
Pressure wounds were a common complication following a tracheostomy, often resulting in advanced-stage wounds, national studies showed. Nationwide Children’s Hospital was no different but Kris Jatana, MD, and Charles Elmaraghy, MD, surgeons in the Department of Otolaryngology, knew they could improve these outcomes.

Brendan Boyle, MD, and Alex Green, DO, were fellows in the Division of Gastroenterology, Hepatology and Nutrition, who were frequently called by the emergency department to remove food boluses stuck in a child’s esophagus, most commonly related to swelling of the esophageal lining. The available devices rarely grasped the bolus whole, instead breaking off pieces and making removal a long process. They had ideas for a better tool.

The teams turned to the Office of Technology Commercialization (OTC) and discussed what they had in mind. At the office’s encouragement, they applied for grants and each team received $25,000 from the office’s Technology Development Fund in 2011. With the OTC’s help, their intellectual properties are patented, their technologies licensed and the devices they’d envisioned are now being used in hospitals across the country.

Bringing the Comfort Collar to Market

“We thought pressure wounds could be prevented with consistent barrier protection between the plastic tracheostomy tube and the skin,” says Dr. Jatana, now director of Pediatric Otolaryngology Quality Improvement. “What was historically done — placing gauze under the tube as a barrier — is problematic. The gauze not only obstructs your view of the site, but gets wet, irritating the skin, which is the start of the wound.”

Drs. Jatana and Elmaraghy considered materials used to prevent friction injuries and looked at those used in sports. They believed neoprene would be a soft but sturdy water-resistant barrier and bought a neoprene wetsuit from a sporting goods store. They created a prototype collar from the material in Dr. Elmaraghy’s living room and began testing.

“We spent several years going through prototypes and tweaking the design to get a universal fit for all tracheostomy tubes and designed a more secure Velcro attachment to prevent the tube from accidentally being dislodged,” Dr. Jatana says. “We worked with several potential manufacturers and found Marpac, based in Albuquerque, a good partner.”

The company makes tracheostomy collars and had the machinery and most of the materials required, making the device a good fit for the business, says Dave Mayberry, Marpac’s product development manager. With the assistance of the OTC, Marpac licensed the technology and now manufactures and sells it as the Comfort Collar to hospitals in a dozen states, the U.K., Canada and the United Arab Emirates, Mayberry says. The Comfort Collar is the first clinical device developed by a clinician at Nationwide Children’s to be commercially available.

Dr. Elmaraghy, who is now chief of the Department of Otolaryngology, says “The tracheostomy collar is the result of a great partnership between the OTC and clinical medicine, providing surgeons opportunities to apply practical knowledge and translating it to a product changing outcomes for patients.”

The Abigail Wexner Research Institute at Nationwide Children’s Hospital was no different but was one of the first institutions to be active with the OTC. And while Drs. Jatana, Elmaraghy, Boyle and Green were the first clinicians to bring devices to the market from Nationwide Children’s, many others are following suit.

Dr. Boyle recommends others with ideas for devices pursue them. “I don’t think that we, as the frontline workers, realize how meaningful our insight can be… We can often best recognize the deficiencies in the currently available tools and provide needed insight about the areas for improvement.”

Before this experience, I knew nothing about making a medical device,” Dr. Boyle says. “But the OTC staff guided us through the entire development process – and with our efforts combined and the right partners in place, our idea became a successful product that is now able to help kids in our institution and others.”

Designing the eSuction Solution

With their technology development funding, Dr. Boyle, now an associate professor of Clinical Pediatrics and quality improvement director in the Division of Gastroenterology, Hepatology and Nutrition, and Dr. Green, now a gastroenterologist at Lurie Children’s Hospital of Chicago, reached out to engineering firms to help them develop a prototype.

After the prototype had been tested in a large animal model, Kyle Murrah, PhD, senior licensing associate in the OTC, negotiated the license with Endo-Therapeutics, in Clearwater, Florida.

“Endo-Therapeutics saw this was a technology solving an unmet need,” Murrah says.

The final product, called eSuction, is placed on the tip of an endoscope. Instead of working like forceps, the device has two small wire loops that the operator slides past either side of the bolus. A gentle pull on the loops wraps the bolus and a vacuum seals it to the tip for removal.

Gastroenterology faculty and staff at Nationwide Children’s were recently trained to use eSuction. “We think it will help shorten the duration of the cases which should mean shortened anesthesia times and reduced trauma to the esophagus,” Dr. Boyle says.

A Future Full of New Devices and Technologies

For Drs. Jatana and Elmaraghy, the Comfort Collar experience was just the start. They are now working with the OTC on other devices they believe will improve patient safety during surgical procedures.

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How VIPER Supports a New Era in Pathology

In 2003, Stephen Qualman, MD, former chief of Laboratory Medicine and former director of the Center for Childhood Cancer and Blood Diseases at Nationwide Children’s Hospital, recognized an unmet need in pathology and developed a solution that would become the platform for pathology research at dozens of institutions.

For many years, the only way for a patient to get into a cancer clinical trial was to have cancer samples validated by three separate pathologists. Samples would arrive from the institutions treating the patients to the Biopathology Center at Nationwide Children’s — the repository for samples for Children’s Oncology Group (COG), the National Cancer Institute (NCI) and many other clinical trial consortiums in North America. Those samples would be processed, then packaged into an empty copy paper box with a stack of forms for the other clinical trial consortiums in North America. Those samples would be processed, then packaged into an empty copy paper box with a stack of forms for the pathologists to complete. That box would physically travel around the country from pathologist to pathologist until the assessment was complete. Only then could the patient begin clinical trial treatment.

Dr. Qualman’s idea would go on to solve that problem. And provide an opportunity for research that is continuing to change the way we will understand cancer.

In January 2005, the Virtual Imaging Pilot EndeavoR (VIPER) began to evaluate an automated pathology review process. He led a team to build a system to replace the copy paper box method.

Now, VIPER has evolved to stand for Virtual Imaging Reporting Education and Research. It is a digital system for emailing, reviewing, annotating and storing digital microscopy slides. Using VIPER allows for simultaneous review, no waiting for the mail to arrive, and much faster admission to appropriate clinical trials.

Currently, VIPER can serve as many slides as an institution can physically process and is no longer the rate limiting aspect of pathology research. Using digital microscopy and VIPER is standard practice for clinical trial pathology reviews. Additionally, the digital images serve as a permanent archive, without getting lost or degrading over time. VIPER currently provides access to hundreds of thousands of annotated images and associated data to dozens of the largest research institutions in pathology.

With that much mineable, de-identified data for research, the possibilities for research seem endless. Researchers can request the annotated pathology images for research projects, enabling a range of studies that might be limited by access to physical slides and reports. Also, the large quantity of samples supports researchers studying rare tumors who might otherwise struggle to find a significant number of samples.

Finally, with the promise of artificial intelligence looming, the team suggests that building algorithms to mine the historical data could lead to automated systems that filter pathology samples. Filtered samples could point pathologists to the important parts of the sample, reducing time and accuracy of reviews. Combining VIPER with AI technology could also result in algorithms that help researchers identify trends and changes in cancer pathologies over time.

Those interested in using the VIPER platform can find an augmented version of the software supported by DeepLens, a Nationwide Children’s startup, which is implementing AI enhancements and community engagement features.

Triple Threat

By harnessing the power of viruses, genes and the immune system, a new technology may fight many types of cancer — thanks to Vironexis, a new company formed through Nationwide Children’s.

The mainstays of cancer treatment — radiation therapy, chemotherapy and surgery — have significant risks and side effects. Recent forays into drug combinations in oncology have offered patients the benefit of synergistic treatment effects or reduced side effect profiles. These combinations sometimes hit the cancer from two separate angles, creating a more robust response rate. Emerging therapies offer hope for cancer patients, but the cost, side effects and delivery methods of many current therapies make a truly game-changing innovation appealing for patients and clinicians alike.

Now, a three-pronged approach may tackle cancer in altogether new ways, thanks to the technology behind Vironexis Biotherapeutics, a company formed early in 2019 by physician-scientist Timothy Cripe, MD, PhD, chief of the Division of Hematology, Oncology & Blood and Marrow Transplant at Nationwide Children’s Hospital, through the hospital’s Office of Technology Commercialization.

“The beautiful thing about what we’re trying to do is that we’re building on the shoulders of giants,” says Dr. Cripe, who first conceived the ideas behind the combined approach in mid-2018 and already has multiple patents pending to support the technology. “We’re taking a number of diverse approaches proven to work in humans and putting them together in a way no one has done before.”

The diverse components that make up Vironexis’s hard-hitting portfolio include virotherapy, gene therapy and immunotherapy — three areas that separately have considerable success in the world of medicine, but that have yet to be combined effectively for cancer patients.

A triple threat via triple the treatment strategies. Vironexis aims to leverage the biology of viruses to treat cancer through a novel combination of virotherapy, gene therapy and immunotherapy.

“[You] should not sleep on the shoulders of giants. We’re taking a number of diverse approaches proven to work in humans and putting them together in a way no one has done before.”

— Timothy Cripe, MD, PhD, chief of the Division of Hematology, Oncology & Blood and Marrow Transplant at Nationwide Children’s Hospital

References:

- Cripe, T. M., & Cripe, T. M. (2019). The beautiful thing about what we’re trying to do is that we’re building on the shoulders of giants. [Retrieved from Vironexis Biotherapeutics]


- Vironexis Biotherapeutics (2021). [Retrieved from the company’s website]
First Comes a Virus, Then Comes the Immune System

Dr. Cripe and his research team at the Center for Childhood Cancer and Blood Diseases in the Abigail Wexner Research Institute at Nationwide Children’s have worked for the past two decades on developing virotherapies for cancer. Founded on the idea that you can “give cancer a cold,” these therapies literally infect tumor cells with a virus that prompts the body’s immune system to kill the cancer. To date, they have shown efficacy in several types of cancer, with a modest risk of side effects compared to many other therapies.

Similarly, immunotherapies that have emerged over the past 20 years activate the natural immune system to fight cancer on its own, sometimes by helping to directly connect the body’s immune cells with cancer cells. They also offer a comparatively low risk of the negative treatment consequences seen in other therapies.

Virotherapy and immunotherapy have limitations, of course. As virotherapy infects tumor cells, it essentially kills itself off, resulting in a short-term cycle of therapy. Immunotherapies that have emerged over the past 20 years activate the natural immune system to kill cancer. To date, they have worked for the past two decades on developing virotherapies for cancer.

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INSTITUTIONAL INVESTMENTS IN RESEARCH

The Abigail Wexner Research Institute at Nationwide Children’s Hospital has a wealth of resources available to ensure researchers have the tools they need to advance the hospital’s mission. From core facilities to computational resources and regulatory offices, researchers have the support to enhance the health of children by engaging in high-quality, cutting-edge research according to the highest scientific and ethical standards. Here are just a few of the unique features at Nationwide Children’s that help researchers go from investigators to innovators.

CLINICAL RESEARCH SERVICES
Clinical Research Services is designed to be a portal through which clinical investigators access streamlined coordination of services necessary to initiate clinical research projects, regardless of funding source. Support is provided for all clinical research studies from initiation to completion according to Good Clinical Practice and federal, state and institutional regulations and policies. CRS can also facilitate survey research, large data set analyses and psychometrics.

Nationwide Children’s is accredited by the Association for the Accreditation of Human Research Protection Program (AAHRPP). This accreditation highlights clinical study participant safeguards that surpass state and federal requirements.

CLINICAL AND TRANSLATIONAL SCIENCE
Through the National Institutes of Health Clinical and Translational Science Award, Wexner Medical Center at The Ohio State University, OSU’s seven health science colleges and Nationwide Children’s comprise the OSU Center for Clinical and Translational Science (CCTS). Leaders in the CCTS work to coordinate shared resources, including clinical trial recruitment and retention services, and funding opportunities for clinical researchers at both institutions.

DRUG AND DEVICE DEVELOPMENT SERVICES
Conducting clinical trials is a key step in translating lab discoveries into standard clinical practice. The Food and Drug Administration closely regulates human participation in clinical trials involving new drugs and devices. Drug and Device Development Services at Nationwide Children’s guides investigators through the complex submission, review and approval processes. The team provides streamlined, uniform and consistent approaches to the development and implementation of clinical trials.

Drug and Device Development Services works side-by-side with Clinical Research Services and the Office of Research Compliance and Integrity to ensure compliance with all institutional, state and federal regulations. By working with investigators to discuss pre-clinical plans, the team helps prepare researchers by focusing on the tasks needed to efficiently move the drug or device into the clinic. The team also offers consultation to investigators who are preparing an Investigational New Drug or Device application to the FDA.

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

– Christopher Shilling, MS, director of Drug and Device Development Services

GOOD MANUFACTURING PRACTICES CLINICAL MANUFACTURING FACILITY
AWRI is home to a current Good Manufacturing Practices (cGMP) Clinical Manufacturing Facility that operates according to FDA cGMP guidelines to ensure the safety of manufactured biologic products.

The CMF is 9000 square feet. It consists of a 7,500 square foot clean room suite with ISO Class 5/7/8 spaces and 1500 square foot of quality control lab and research production spaces. The biological drug substances are manufactured according to the FDA Guidance for Industry cGMP for Phase I Investigational Drugs, to ensure product safety, identity, purity and strength.

The Clinical Manufacturing Facility at Nationwide Children’s is a leading cGMP production facility dedicated to advancing the field of Gene and Cellular Therapy.

“Our mission is to apply our knowledge, resources, technology, and experience to move the field of translational and regulatory science forward, in collaboration with our clients, to develop new, safe and effective treatments for diseases once thought untreatable. Our approach and commitment within the cGMP facility is that there are no diseases too rare and no challenges too difficult to make a difference and give hope to every patient and their family.”

– Wade Macedone, executive director and general manager of cGMP

3D PRINTING LAB IN THE DEPARTMENT OF RADIOLOGY
In the 3D Printing Lab, which is part of the Pediatric Advanced Imaging Resource in the Department of Radiology at Nationwide Children’s, a team of physicians, image analysts, digital modelers, coordinators and others translate computed tomography (CT) scans and magnetic resonance imaging (MRI) scans into models. The team develops both computer models and 3D printed models, which are used for presurgical planning, education and research.

“Many institutions utilize 3D printing from a third party vendor, or focus its use for one specific surgical application. We can provide solutions for a variety of pediatric conditions, encompassing several specialties. We do this in-house with a team that has extensive expertise and track record, and in a location that is convenient for all Nationwide Children’s physicians.”

– Jayanthi Parthasarathy, BDS, MS, PhD, manager of 3D Printing

Dr. Parthasarathy, a dental surgeon by background, has a PhD in Industrial and Manufacturing Engineering and has extensive experience in material composition specifically related to 3D printing.

The team uses a CONNEX 3 OBJET 350 3D printer, in addition to a full complement of image processing and 3D modeling and printing software to convert 2D CT and MRI images to 3D physical models. The high-quality printer is capable of 16-micron layers. Multi-color and multi-material capabilities allow for variation of material properties within a single print, depending on the needs of the given application.
**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.

**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.

**Oncolytic Virus for the Treatment of Cholesteatoma (Reference # 2018-092)**

Cholesteatoma (CHST) is an abnormal, recurrent and benign cyst that develops in the middle ear leading to deafness, facial paralysis, meningitis, and death. Currently, no drug is available for CHST treatment except for the surgical intervention resulting in a heavy financial burden. Researchers at Nationwide Children's Hospital have tested peptide lectins and repurposed drugs in vitro that are effective against Gonorrhea and HIV infections. Given the increase in antibiotic-resistant Gonorrhea, these drugs offer an alternative, non-antibiotic approach to STD treatment.

**Didemethylrocaglamide (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 screened two novel compounds (Didemethylrocaglamide and Rocaglamide) that are easy to synthesize owing to their compact structure and low molecular weight. These drugs show anti-tumor activity with no overt toxicity in murine model. This preclinical invention is a promising treatment for MPNST and other tumors.

**New Avenue for Drug Treatment in Sexually Transmitted Diseases (Reference # 2018-058)**

Gonorrhea is the second most common sexually transmitted disease (STD) in the United States and is caused by the Neisseria gonorrhoeae bacterial infection. Moreover, untreated gonorrhea can increase risk of HIV infection. Researchers at Nationwide Children's Hospital have tested peptide lectins and repurposed drugs in vitro that are effective against Gonorrhea and HIV infections. Given the increase in antibiotic-resistant Gonorrhea, these drugs offer an alternative, non-antibiotic approach to STD treatment.

**Novel Syncytial Oncolytic Herpes Simplex Mutants Derived from Directed Evolution and CRISPR/Cas9 Gene Editing Strategies as Potent Cancer Therapeutics (Reference # 2018-046)**

Oncolytic viral therapy (OVT) is a promising strategy to treat malignancies since oncolytic viruses target tumor cells without harming normal tissues. Herpes Simplex Virus (HSV) is one of the most widely used OVs. However, anti-tumor efficacy of OVs is still limited if the viruses are used alone. Cancer researchers at Nationwide Children's Hospital have engineered a couple of HSVs using gene editing CRISPR/Cas9 strategy that show enhanced cytototoxicity leading to elimination of tumor cells. This preclinical OVT offers a multimodal approach to specifically and effectively target and destroy malignant cells.

**Method to Improve Efficiency and Specificity of Human Tumor Targeting and Elimination by Using a Combination of Split & Splice Protein Toxins and Oncolytic Viruses (Reference # 2017-081)**

Oncolytic viruses (OV) 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 tumor in preclinical mouse models. These next generation HSVs are a valuable therapeutic option for controlling cancers.
Therapeutics

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.

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.

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

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

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.

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.

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Therapeutics

HIGHLIGHTED TECHNOLOGIES

Method of Using Neural Stem-Cell Derived Exosomes to Protect Against Necrotizing Enterocolitis (Reference # 2014-003)

Stem cells protect the intestines from necrotizing enterocolitis through a combination of engraftment and release of secreted components such as growth factors. However, local stem cell delivery is linked to increased risks and side effects. Researchers at Nationwide Children’s Hospital have developed a novel cell-free method for delivering secreted components and growth factors to the intestine through the use of exosomes derived from stem cells. This method provides a safer alternative to treat intestinal injury.

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

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

Increasing Expression of HLA-F to Treat Amyotrophic Lateral Sclerosis (ALS) (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. The laboratory of Dr. Brian Kaspar at Nationwide Children’s Hospital has discovered that overexpression of the HLA-F-MHC class I molecule in motor neurons is protective against ALS. Further, they have identified a pharmaceutical composition that increases the expression of HLA-F in motor neurons and would serve as a treatment option for patients with both sporadic and familial ALS.

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.

Novel Live Attenuated Vaccines for Human Pneumoviruses (Reference # 2014-004 & 2015-004)

The syncytial virus (RSV) and metapneumovirus (MPV) is a leading cause of acute respiratory tract infection in infants and children. Despite major efforts, there is no vaccine to combat these diseases due to the difficulty of constructing a virus that is stable, attenuated and can still provoke an adaptive immune response. Infectious disease experts at Nationwide Children’s Hospital and The Ohio State University have developed a panel of recombinant RSV (rhRSV) and MPV (rhMPV) that are defective in zinc binding activity. The inability of these viruses to bind zinc has rendered them genetically stable and highly attenuated in an animal model. Therefore, our rhRSVs and rhMPVs are excellent vaccine candidates for hMPV.

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

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

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

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


Spinal muscular atrophy (SMA) is a neurodegenerative disease that occurs in 1 of every 6,000 births, and is caused by low levels of the SMN protein. SMA patients have inherited deletions or mutations of SMN1, one of two genes encoding SMN. SMN2 contains a translationally silent single nucleotide switch that causes mis-splicing of its transcript, rendering the protein non-functional thus unable to compensate for the loss of SMN1. Current efforts to combat SMA revolve around increasing the stability or altering the splicing of SMN2. 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 vivo and is being further developed for use in murine models of SMA.

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.

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Therapeutics
Therapeutics

**Respiratory Syncytial Virus (RSV) Expressing Two Added Genes, Green Fluorescent Protein (GFP) and Renilla Luciferase, But Not the RSV G (attachment) Glycoprotein (Reference # 2013-043)**

Respiratory syncytial virus (RSV) is the leading cause of upper and lower respiratory tract infections in young children. Preclinical therapeutic studies require simple readouts for viral replication (e.g., readouts for high throughput screening of compound libraries). Researchers at Nationwide Children's Hospital and the National Institutes of Health have constructed a recombinant RSV that expresses both green fluorescent protein (GFP) and Renilla luciferase that in turn allow for rapid quantifiable real-time readout of virus replication or titer. In addition, the RSV virus is constructed with a G glycoprotein mutation that could reduce false positive hits during compound library screens.

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

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

**Enhanced Immunogenicity of a Modified RSV Vaccine with Mutations in One or Both Nonstructural Protein (NS) Genes (Reference # 2011-001)**

Researchers at Nationwide Children's Hospital and University of South Florida have identified mutations in RSV nonstructural protein genes (NS1 and NS2) that allow the virus to induce a measurable interferon response, thus a more robust adaptive immune response. Their findings have built a solid foundation that could be exploited to generate a more immunogenic RSV vaccine.

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

Nuclear Factor-kappa B (NF-κB) is a master regulator of inflammation and is upregulated in the spinal cord of ALS patients and in ALS mice models. Researchers at Nationwide Children’s Hospital have demonstrated that NF-κB inhibition in ALS microglia rescued motor neurons (MNs) from microglia-mediated death in vitro and extended survival in ALS mice by impairing pro-inflammatory microglial activation. This work for the first time provides a cellular and molecular mechanism by which microglia induce motor neuron death in ALS and suggests a new therapeutic target to modulate microglial activation and slow the progression of ALS and other neurodegenerative diseases in which microglial activation plays a role. The USPTO has issued a patent for this application in May 2016.

**Improved Delivery of Antisense Oligonucleotides (Reference # 2012-025)**

A major hurdle for designing effective therapeutics is delivery, especially throughout the neural tissue. Researchers at Nationwide Children's Hospital and The Ohio State University have discovered that when a morpholino is mixed with a particular omnipaque dye, iohexol(omnipaque)-1,N,3-N-bis[(2,3-dihydroxypropyl)-5-(N-[2,3-dihydroxypropyl]-acetamido)-2,6-triodobenzene-1,3-dicarbonamide) the morpholino is delivered efficiently to all regions of the brain. Unlike other methods that have been used to increase delivery, such as charged moieties or peptides, which can elicit toxicity or an immune response, this dye is used routinely in the clinic.

**Microglia Induce Motor Neuron Death via the Classical NF-κB Pathway in Amyotrophic Lateral Sclerosis (ALS) Astrocytes with Natural Killer Properties (Reference # 2012-023)**

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

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

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**Enhanced Immunogenicity of a Modified RSV Vaccine with Mutations in One or Both Nonstructural 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 nonstructural 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 and University of South Florida have identified mutations in NS1 and NS2 that allow the virus to induce a measurable interferon response, thus a more robust adaptive immune response. Their findings have built a solid foundation that could be exploited to generate a more immunogenic RSV vaccine.

**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

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.

Novel Chimeric Antigen Receptor-Primary Natural Killer Cells for Cancer Immunotherapy (Reference # 2019-016)

Chimeric antigen Receptor (CAR)-modified T cells are extensively used against hematological malignancies; however, its application is restrictive for general clinical use. Gene therapy and Cell-based therapy experts at Nationwide Children's Hospital have developed CAR-modified natural killer (NK) cells as an alternative “off-the-shelf” product. Our experts used a combination of sophisticated gene-editing technology and adeno-associated virus for the generation of CAR-NK cells. This preclinical invention eliminates the need for a personalized and patient-specific product that plagues current CAR-T cell therapies.

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 misexpression leading to muscle differentiation defects and atrophy. Gene therapy experts at Nationwide Children's Hospital have developed a novel strategy silencing DUOX expression using Clustered Regulatory Interspersed Short Palindromic Repeats (CRISPR) - Associated 13b (Cas13b). This therapeutic gene correction has yielded efficient and specific DUOX reduction in vitro and holds a significant promise for FSHD treatment.

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 h74 (AAVh74) 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.

Gene Therapy for the Treatment of Galactosemia (Reference # 2017-016)

Galactosemia is a rare metabolic disorder that occurs due to a missing or nonfunctional galactose-1-phosphate uridyltransferase (GALT) gene. Currently, there are no treatment options for Galactosemia other than dietary restriction of galactose-containing food. Even with strict adherence to a galactose-free diet, many patients suffer from long-term mental and physical deficits due to small amounts of galactose found in foods. Researchers at Nationwide Children's Hospital and the University of Utah have developed a concept for a long-term treatment option for Galactosemia patients by efficiently delivering a codon-optimized version of the human GALT gene using adeno-associated virus. Our gene therapy approach is engineered for a sustained expression of functional GALT protein and alleviation of disease symptoms.

Induction of Dystrophin Isoforms Lacking at Least Exon 44 (Reference # 2017-001)

Absence of a functional dystrophin protein leads to the severe muscle disorder Duchenne muscular dystrophy (DMD). Exon skipping strategies are being developed to treat diseases caused by the production of mutated nonfunctional proteins, like DMD. Gene therapy experts at Nationwide Children's Hospital are developing a U7snRNA exon skipping strategy to induce expression of dystrophin (DMD) missing exon 44 as a therapy for patients carrying mutations including exon deletion of exon 43 or 45, and exonic duplication of exon 44 of dystrophin. Our experts have constructed several lead antisense sequences in an adeno-associated virus (AAV) vector to cause skipping of exon 44 and have begun to test their affects in patient-derived cells as well as mouse models of the disease. Injection of antisense sequences has been largely investigated however not explored as an AAV gene therapy.
Induction of Dystrophin DelCH2 Isoform (Reference # 2016-069)

Absence of the dystrophin protein leads to the severe muscle disorder Duchenne muscular dystrophy (DMD). 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 truncated dystrophin protein for patients carrying mutations within exons 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.

Stem Loop RNA Mediated Transport of Mitochondria Genome Editing Molecules (Endonucleases) Into the Mitochondria (Reference # 2016-052)

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.

Recombinant Adeno-Associated Virus Vector Gene Therapy for MPS II (Reference # 2016-001)

Hunter’s syndrome, or macropoly saccharidosis II (MPS II), is a lysosomal storage disease caused by a deficiency of enzyme iduronate-2-sulfatase (IDS). The greatest challenge in developing therapies for MPS II is to achieve efficient central nervous system (CNS) delivery across the blood-brain barrier (BBB). Researchers at Nationwide Children's Hospital are developing a gene therapy vector (systemic delivery) to cross the BBB for treatment of the CNS and also for somatic manifestation of MPS.

DUX4 Exon Skipping Strategies for FSHD Therapy Using U7-snRNA (Reference # 2015-049)

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

Use of Gene Product to Treat Nerve Injury and Sarcopenia (Reference # 2015-008)

High levels of survival motor neuron (SMN) protein is critical for repair of motor unit connectivity after muscle damage. Neuromuscular disease experts at Nationwide Children's Hospital and The Ohio State University predicted high levels of SMN protein will reduce degenerative susceptibility of the motor unit during both injury and aging (sarcopenia). Our experts have designed a method to reduce sarcopenia or nerve damage by administering a SMN protein-increasing substance to be used as a therapy to treat nerve damage from age-related or trauma-induced muscle damage.

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 along with neurobiologists at The Jackson Laboratory have developed an effective Adeno-Associated 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.

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 Adenovirus 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 cancer cells. This invention achieves scalable production of rAAV using clinically safe Vero cells derived from African green monkey kidney cells combined with the simian adenovirus 13 helper virus.
Gene Therapies and AAV Production

Adeno-Associated Virus (AAV) GMP Production (Reference # 2013-033, 2013-044, 2016-017, 2016-047)
Good Manufacturing Practice (GMP) production experts at Nationwide Children's Hospital continually optimize their adeno-associated virus (AAV) production methods. Their diligent work has led to novel methodologies that could be utilized by others in the gene therapy field, including (1) a scalable AAV production and purification scheme utilizing plasmid DNA transfection of human embryonic kidney (HEK) 293 cells, and (2) chromatography and ultracentrifugation purification schemes that reduce contamination and improve yield. Overall, these methods enable development of increased clinical grade vector production to support trials requiring high vector dosing regimens.

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.

Gene Therapies and AAV Production

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, 3, 5, 6, 8, 9 and rh74. 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.

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.

Adeno-Associated Virus (AAV) Vectors Coupled to CRISPR/Cas9 (Reference # 2016-012, 2017-009)
CRIPSR/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 enzyme as a stable component of the AAV particle, as well as expressing Cas9 on the surface of the viral particle.

GMP Quality Control experts at Nationwide Children’s Hospital have been diligently working to develop optimal methodologies for testing adeno-associated virus (AAV) vectors for gene delivery. Their efforts have produced nine novel methods focused on the following: (1) determining replication competent AAV, (2) determining infectious unit titer for AAV, (3) quantifying DNase resistant particles (4) quantifying AAV total protein, (5) assessing AAV purity by SDS-PAGE, (6) determining the ratio of full to empty AAV particles, (7) identifying AAV DNA by NextGen sequencing, (8) identifying AAV capsid by western blot, and lastly (9) measuring the pH of drug product. Overall, these methods enable the successful production and testing of GMP quality AAV vectors.

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. Pharmacist 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.
**Biomarkers**

**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, non-specific diagnostic criteria of peritonitis can lead to missed / overt-diagnosis. 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.

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

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

**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.

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**End User Innovation**

**All in One IV Pole: Tape Dispenser, Sharps Bins and Medical Trash Containers (Reference # 2019-002, 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 air-craft/air-port simulation experience. Inventors at Nationwide Children’s Hospital have designed a unique workshop curriculum which includes PowerPoint slides, a video tape and participant handouts and experimental activities. This educational intervention facilitates increasing tolerance of and comfort with air travel.

**Nasal Cannula for Premature Babies to Reduce Rate of Ulcers (Invention # 2018-079)**

A nasal cannula is a thin, plastic tube that delivers oxygen directly and used extensively in premature babies to support their respiratory needs. However this intervention often results into development of pressure ulcers around nasal area leading to infections. Engineers at Nationwide Children’s Hospital have modified a design and the material of the nasal cannula to reduce pressure and friction inside nose. This prototype device also has an added benefit of deflating in the absence of airflow leading to normal breathing.

**Distraction System for Radiation Therapy (Reference # 2018-060)**

Radiation therapy (RT) requires patients to lie very still for accurate administration of high-energy radiation beams. RT is challenging in pediatrics due to multiple factors: the smaller size of the patients, parent separation anxiety, and treatment resistance. It is therefore common for young children to require sedation during RT. Specialists at Nationwide Children’s Hospital have developed a sophisticated video distraction system that allows the patients to watch movies during RT that shifts child’s attention off stressful procedure promoting comfort and reducing anxiety. This novel, non-pharmacologic intervention could reduce rate of sedation in young patients during RT.

**Handheld Needle Recapping Guard (Reference # 2017-071)**

The Center for Disease Control and Prevention estimates that 380,000 sharps-related injuries occur annually among health care workers in hospitals. Medical professionals at Nationwide Children’s Hospital have developed a handheld needle recapping guard to help prevent needlestick injury. The plastic guard is easily held in the non-dominant hand and is designed to block accidental needle sticks when recapping a needle.

**DeepSuggest (Invention # 2017-062)**

More than 70% of the health information is stored in unstructured clinical notes, and health care providers increasingly rely on the text-search systems for clinical care and research projects. However, clinical notes often contain spelling variations, typos, personal acronyms/synonyms, and informal words that limit efficient searching. Data scientists at Nationwide Children’s Hospital have developed a novel search system, DeepSuggest to expand the input query by suggesting spelling variations and acronyms all identified through an artificial intelligence-driven algorithm.
End User Innovation

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 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.

Virtual Reality Program for Pediatric Pain Management (Reference # 2016-067)
Pain and anxiety are common amongst pediatric patients who undergo medical procedures. However, few non-pharmaceutical interventions have been developed to successfully manage pain and distress associated with these procedures. Researchers at Nationwide Children's Hospital have developed a virtual-reality approach to pain management that provides attentional distraction in an immersive environment. The software consists of active or passive modes and runs on multiple computing platforms that are compatible with smartphones.

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 easier 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)
Impairment of executive functions post-TBI is a leading cause of acquired disability in children and adolescents in the United States. Impairment of executive functions post-TBI has broad and profound implications for everyday life of pediatric patients, and the development of effective rehabilitation strategies is of significant clinical importance. 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. Inventors at Nationwide Children’s Hospital have developed a first-of-its-kind device for securing chest tubes. This flexible device allows for the securing of chest tubes and other main lines while bending and flexing with the patient.

Soothing Asthma Inhaler Spacer for Young Children (Reference # 2015-020)
Using an asthma inhaler can be frightening for young children and a concern for caregivers, leading to reduced compliance. Inventors at Nationwide Children’s Hospital have developed a soothing spacer to be used with an asthma inhaler that makes the experience more enjoyable by incorporating lights and music, when the mask is applied to the face properly. Additionally, the vertical design of the spacer allows for one-handed use which lets a parent hold the child with the other hand, while administering the medication.

Methods and Apparatus to Improve Diagnostic Sensitivity and Scan Efficiency of Brain Diseases (Reference # 2015-013)
Neonatal and infant brain MRI is increasingly utilized to diagnose brain injury and abnormal brain developmental disorders. The T1-weighted sequence provides the most detailed information about injury, lesions and maturation. Perinatal research experts at Nationwide Children’s Hospital and The Ohio State University have designed MP-FAGE, an optimized T1-weighted MRI sequence for neonatal and infant brain imaging. Their optimized methodology has greatly reduced the scan time by two-thirds and improved image quality without the use of additional hardware or increased workload for the MRI technologists or radiologist. This new method will not only reduce cost of the MRI scan but also improve sensitivity for detecting a variety of pediatric diseases/disorders.

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 that recreate congenital defects. These models are modular, and offer an immersive and realistic way of learning surgical skills enabling minimally invasive surgery.

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.

End User Innovation
End User Innovation

Computerized Screening Tool for Behavioral Health (Reference # 2014-017)
Assessing symptoms of and impairment due to mental health problems is important for patient care, but the field of behavioral health rarely makes use of objective screening tools over the course of treatment leading to suboptimal care. Inventors at Nationwide Children’s have developed a screening tool that is able to administer and score a set of existing, well validated mental health questionnaires. This web-based program is entirely self-sufficient and will allow for longitudinal tracking of data leading to improved care.

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.

End User Innovation

PS Rocker: A Multi-Head Skin Allergy Testing Device (Reference # 2012-028)
There are 10 skin testing devices marketed in the United States for diagnosing allergies. These include single-tipped devices for testing allergens one at a time, as well as multi-head devices containing multiple testing tips on one device. One of the recently introduced multi-head devices is designed to decrease pain associated with skin testing. Current multi-head testing devices with fixed horizontal surfaces do not provide consistent intra-device contact with skin, while the single-prick devices can be impractical for children and time consuming. Clinicians at Nationwide Children’s Hospital and The Ohio State University, in collaborations with other independent inventors, have developed a new allergy skin testing device, PS Rocker, which improves upon existing products by combining the precision of a single-prick test with the ease and speed of a multi-head device. Additionally, PS Rocker is less painful than traditional skin prick testing. The PS Rocker’s crescent-shaped, ergonomic design enables more reproducible tip contact with the skin than conventional horizontal multi-head devices, efficiently leading to more reliable results. Clinical studies of PS Rocker are currently underway at Nationwide Children’s Hospital testing effectiveness of PS Rocker.

Gearbox (Reference # 2012-016)
Data scientist at Nationwide Children's Hospital in collaboration with The Ohio State University has 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.

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.
Research Tools

Electronic Whack-A-Mole: An Interactive Device for Measuring Task Performance and Motion Parameters (Reference # 2017-056)

Researchers at Nationwide Children’s Hospital have developed a system for measuring motion (speed or reach) or cognitive (focus or prioritization) variables using an interactive game as an interface. By evaluating these variables using performance on a game-based system, the electronic Whack-a-Mole reduces volitional variation in measured performance and provides a platform for testing the impact of motivational stimuli at the same time as tracking performance variables particularly valuable for benchmarking the severity of muscular dystrophy or other upper extremity mobility disorders.

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 TTN126 (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.

A Novel Genetic Mouse Model of Aging (Reference # 2016-049)

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

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 leakiness problems seen in past models of the disease.

Immunotherapy Potency Assay (Reference #2018-054, 2018-055)

Immunotherapy is a promising therapeutic approach for cancer treatment and harnesses the immune cells such as natural killer (NK) cells to attack cancer cells. Immunotherapy products are evaluated by potency assays to measure quality attributes (for example, high sensitivity and specificity, accuracy and reproducibility) before their clinical use. Available conventional assays have limitations in terms of biological and batch effect variability. Onco-immunologists at Nationwide Children’s Hospital have developed a reproducible and standardized assay to measure potency of therapeutic NK cells. This novel preclinical assay relies on the use of vesicular bodies-fragments derived from tumor cells to stimulate immune response, and will provide sensitive method for measuring potency of NK cells during clinical trials.

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.

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

Glass slides are exclusively used for histopathological studies in biomedical research for tissue mounting purpose. Glass (Tissue) Slide Holder for Scraping 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.

A Novel Genetic Mouse Model of Aging (Reference # 2016-049)

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

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

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

Myotubularin (MTM1) (R69C) Knock-In Mice (Reference # 2012-017)

X-linked myotubular myopathy (MTM) is a severe disease of infancy and is caused by myotubularin (MTM1) mutations. The traditional mouse model of disease, the MTM1 knockout (KO) mouse, exhibits a severe phenotype and short lifespan, which makes testing preclinical therapeutics challenging. Researchers at Nationwide Children’s Hospital have developed a myotubularin-deficient mouse model (MTM1 p.R69C) by modeling the mutation associated with the phenotype seen in MTM-affected individuals. Importantly, the MTM1 p.R69C mouse model exhibits a less severe phenotype than the traditional MTM1 KO model which would be more beneficial for testing preclinical therapies.
Tissue Engineering

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 patients. The Closed Seeding System enables efficient collection and seeding of patient cells onto the TEVG scaffold, which has been further optimized by using patient imaging data and 3D-printing capabilities to create patient-specific vascular grafts for implantation.

Researchers at Nationwide Children’s Hospital have developed a novel method for increasing the patency 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

Variant Identification for Viral Vector Sequence Using a Modified Version of Churchill (Reference # 2016-005)
Currently the cost of next generation sequence data analysis is outstripping the cost to actually produce the data. Through a novel parallelization strategy and development of a fully automated pipeline, previous work at Nationwide Children’s Hospital led to the development of software that substantially shortens the time taken to process the raw (sequence) data through multiple analytical steps required to identify human genetic variations. The Researchers at Nationwide Children’s are using this software to analyze NextGen Sequencing data of viral vectors to verify that the genetic material matches the design and to identify potential contaminants.

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 Intensive Care Unit based on only objective viral 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.

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.
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 genomics 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.

Contact: Matthew.McFarland@NationwideChildrens.org or at (614) 722-2701

Susan 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 non-government research sponsors.

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

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

Contact: Susan.Allen@NationwideChildrens.org or at (614) 355-1603
Cristina Crimaldi, BA, Administrative Support III

Cristina joined Nationwide Children's Hospital in May 2019. Her primary responsibilities include supporting both the Drug & Device Development Services department as well as the Office for Technology Commercialization. Cristina 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. Cristina also supports the team with department projects, event coordination, supply orders and provides assistance with record keeping.

She has a Bachelor of Arts Degree in Political Science from Ohio University. She has 15 years of experience in administration, sales and customer service.

Contact: Cristina.Crimaldi@NationwideChildrens.org or at (614) 722-6962

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 post-doctoral training in the Center for Gene Therapy at the Research Institute at Nationwide Children's Hospital. Her post-doctoral research focused on developing therapies to treat musculoskeletal disorders. While carrying out her post-doctoral studies, she completed a technology transfer internship at Nationwide Children's.

Contact: Jocelyn.Eidahl@NationwideChildrens.org or at (614) 355-2848

Isabella Gomez Rueda, LLB, LLM, 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 and is a licensed attorney in Colombia. She also has 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 has experience in the areas of university transactions, contracts, commercial and intellectual property law.

Contact: Isabella.GomezRueda@NationwideChildrens.org or at (614) 355-4302

Patrick Kennedy, Alliance Manager

Patrick joined Nationwide Children's Hospital in July of 2008 in Human Resources. He recently accepted the alliance manager position in the Office of Technology Commercialization and will be responsible for relationship management with commercial partners. This position will help ensure effective transfer of technology to the commercial market and be a liaison between Nationwide Children's stakeholders and commercial partners.

Patrick has a Bachelor's Degree in Health Sciences from The Ohio State University and 12 years of experience in human resources. He has spent the last several years directly supporting the Research Labs at Nationwide Children's.

Contact: Patrick.Kennedy@NationwideChildrens.org or at (614) 722-2868

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.

Contact: Kyle.Murrah@NationwideChildrens.org or at (614) 355-4551

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.

Contact: Susannah.Wolman@NationwideChildrens.org or at (614) 355-2818

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. She has experience in the areas of intellectual property and corporate law.

Contact: Amy.Yoder@NationwideChildrens.org or at (614) 355-3477