Transfer to Transform

THE OFFICE OF TECHNOLOGY COMMERCIALIZATION
AT NATIONWIDE CHILDREN'S HOSPITAL

SPRING 2014

NATIONWIDE CHILDREN'S

When your child needs a hospital, everything matters.℠

Our Mission

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

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

Affiliations

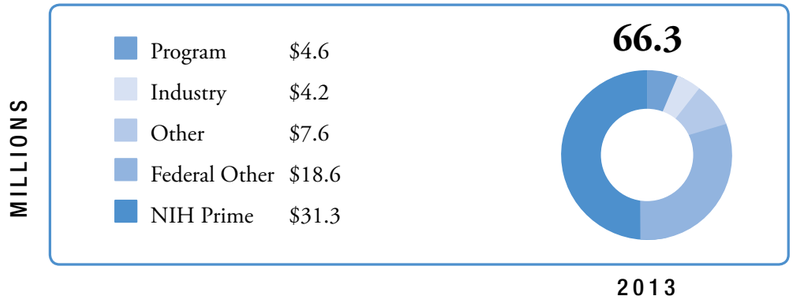
TechColumbus partners with The Research Institute at Nationwide Children's Hospital to accelerate the formation and growth of life science companies in central Ohio. Through our partnership, we seek out high growth opportunities and advise entrepreneurs who are developing innovative therapies and technologies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

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

13 Research Centers

Battelle Center for Mathematical Medicine
Biobehavioral Health
Biopathology Center
Cardiovascular and Pulmonary Research
Childhood Cancer and Blood Diseases
Clinical and Translational Research
Gene Therapy
Injury Research and Policy
Innovation in Pediatric Practice
Microbial Pathogenesis
Molecular and Human Genetics
Perinatal Research
Vaccines and Immunity

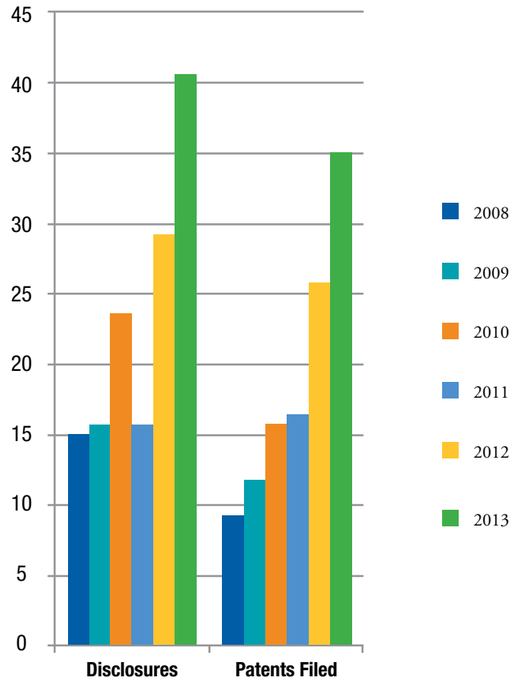
2013 External Awards by Source

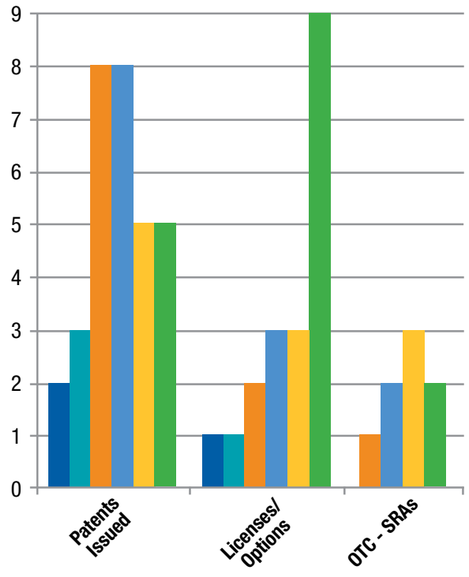


	2011	2012	2013
Principal Investigators*	156	160	161
Research Fellows	70	51	55
Graduate Students	48	43	45
Employees	944	934	1007
Publications	577	522	609
Patents Filed	17	27	35
Patents Issued	7	5	5
Inventions	16	29	41

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

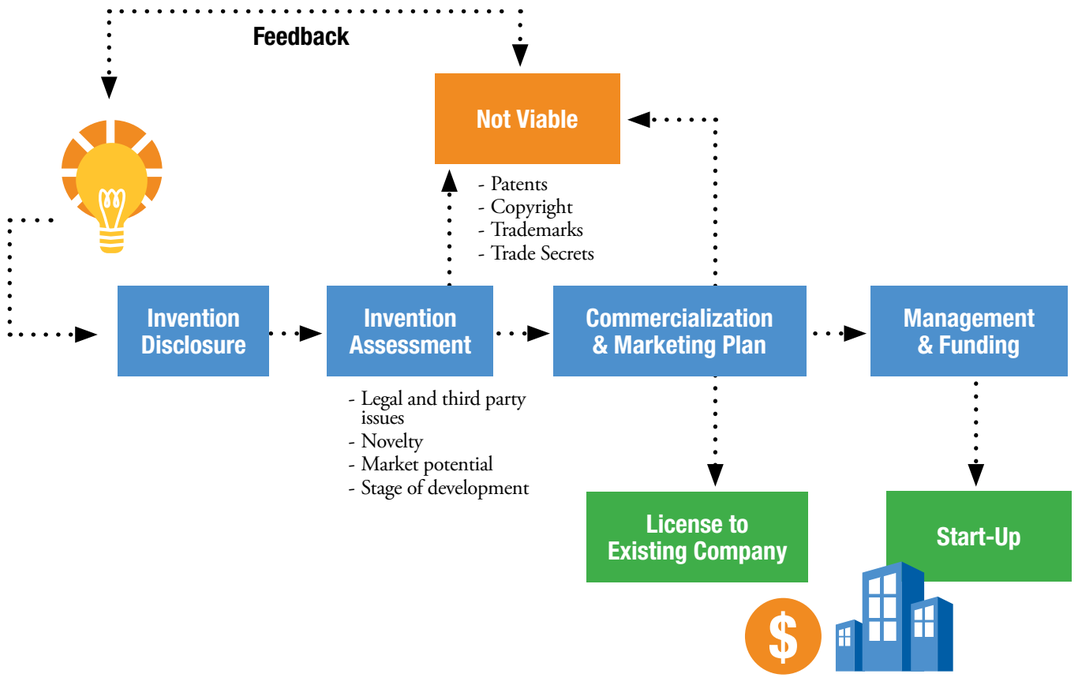
Metrics





Our Process

1. Cutting edge research leads to the generation of novel ideas.
2. An invention disclosure is submitted to OTC.
3. OTC meets with the inventor to gather additional information and also reviews any third-party encumbrances associated with the disclosed technology.
4. OTC performs a technology assessment and determines the patentability, market potential, and readiness of the technology for commercialization.
5. A decision is made to: a) actively market the technology via direct and/or indirect marketing approaches, b) delay a final decision regarding the technology until additional information is produced, or c) not move the technology forward due to lack of commercial viability.
6. Part of the commercialization plan for a technology moving forward often includes an IP protection strategy (Patent, Copyright, Trademark).
7. An assessment report is provided to the inventor(s).
8. OTC oversees the marketing of the technology and identifies a viable commercial partner.
9. OTC manages the out-licensing of technologies to either an existing company, or to an entrepreneurial partner to establish a new venture.
10. OTC is responsible for all post-license alliance management, license compliance, and distribution of royalties.



Designing the Optimal Tissue-Engineered Intestine

Researchers collaborate with an Ohio start-up company to build scaffolds with the goal of replacing intestine in critically ill patients

Building body parts is no simple task—especially when those body parts have to replace entire missing segments of human intestine. They must be fully functional and indistinguishable from the body's native tissue so that the immune system doesn't mount an attack, but they must also be practically produced as needed for individual patients.

Although the field of tissue engineering is advancing quickly, the technology is still wide open for innovation. From blood vessels to entire organs, human tissue scaffolds designed in a lab and implanted into patients could be the basis of future regenerative medicine. In the case of Gail E. Besner, MD, chief of pediatric surgery and principal investigator in the Center for Perinatal Research in The Research Institute at Nationwide Children's Hospital, tissue-engineered intestine may offer the cure for a deadly condition that plagues her most fragile patient population: premature babies.

Many babies born too early develop necrotizing enterocolitis (NEC), a dangerous infection in the gut that, despite six decades of research, still has a mortality rate of up to 50 percent. The primary treatment for NEC involves surgical removal of a large portion of the baby's small intestine. If the remaining intestinal tissue can't perform the body's required digestive functions, it can result in short bowel syndrome—a deadly complication requiring bowel transplant or nutritional support.

"Our experience with these babies shows that surgery is not the answer to this disease," Dr. Besner says.

Transplants require long-term immunosuppression so that the body doesn't reject the new tissue, she notes, and other therapies offer only partial fixes. If the new intestine or remaining intestine is unable to absorb ample nutrients, the result can be severe malnutrition, driving many patients to lifelong nutritional support.

"These therapies carry with them another host of potentially dangerous complications," says Dr. Besner. "We have to search elsewhere for a cure."

That's where tissue-engineered intestine comes into the picture.

"If we could develop a biocompatible, biodegradable scaffold and infuse it with the patient's own intestinal stem cells, we could implant new intestine into these patients," Dr. Besner explains. "The patient's body would essentially rebuild a totally functional length of intestine and would recognize it as native tissue. That means immunosuppression and nutritional support could be avoided."

Enter Nanofiber Solutions, LLC, an Ohio-based start-up company best known for its expertise in tissue-engineered tracheas used in numerous life-saving implants worldwide.

"We were so fortunate that the best people to help us develop this technology were right here in Columbus," Dr. Besner says.

Once she had identified them as the ideal company to work with, the Office of Technology Commercialization at Nationwide Children's guided the contract agreements and licensing process.

"Being a clinician requires dedicating a lot of time to one's patients, and combining that with bench research leaves limited time for venture capitalism searches or meeting with clients," says Dr. Besner. "Knowing that the people in the technology commercialization group took a personal interest in my work was very gratifying and beneficial to the advancement of the project. They really look out for you."

Dr. Besner's lab collaborates with bioengineering colleagues at The Ohio State University and the specialists at Nanofiber Solutions to design the scaffolds used in her research, which the company then builds to spec.

"Building any sort of tissue-engineered organ or vessel is complex," Dr. Besner says. "But building one that has so many functional requirements is very challenging. You need a tissue-engineered intestine to be able to absorb nutrients and you need a muscular layer to push food through the intestine. You then have the challenge of the non-sterile environment in the intestines, which requires a barrier function of the new tissue as well."

The group meets monthly to improve the scaffold design and explore new materials, nanofiber sizing and cell infusion options.

It will be several years before tissue-engineered intestinal implants are ready for clinical trials, Dr. Besner says, but the purposeful process is important for the protection of human patients. "You're dealing with people's lives, so it's critical to have the very best product."

The next step is to attach the engineered scaffolds to existing intestine in animal models with short bowel syndrome. This will allow researchers to see how the implants are gradually replaced by native tissue and whether they perform the necessary functions of the intestines.

"As much as I love working in the operating room, I think it is incredibly important to discover something in the lab to help generations of patients in the future," Dr. Besner says. "Tissue-engineered intestine has the potential to do that."

RELATED CITATIONS:

Boomer L, Liu Y, Mahler N, Johnson J, Zak K, Nelson T, Lannutti J, Besner GE. Scaffolding for challenging environments: materials selection for tissue engineered intestine. *Journal of Biomedical Materials Research*. 2013 Nov 28. [Epub ahead of print.] PMID: 24288210.

Yang J, Su Y, Zhou Y, Besner GE. Heparin-binding EGF-like growth factor (HB-EGF) therapy for intestinal injury: Application and future prospects. *Pathophysiology*. 2013 Dec 14. [Epub ahead of print.] PMID: 24345808.

Yang J, Watkins D, Chen CL, Zhang HY, Zhou Y, Velten M, Besner GE. A technique for systemic mesenchymal stem cell transplantation in newborn rat pups. *Journal of Investigative Surgery*. 2012 Dec, 25(6):405-14. PMID: 23215798.

Creative Clinicians

When physicians set their minds to solving the problems they face in everyday practice, inventions abound

Most clinicians don't begin their careers expecting to be inventors. But for a number of doctors at Nationwide Children's Hospital, exciting ideas for devices that could help children was enough to set those initial expectations aside, leading them to make prototypes out of play-dough or search sporting goods stores for soft, waterproof materials. To them, these departures from the traditional role of physicians amount to an extension of best practices in patient care.

Amber M. Patterson, MD, director of the Center for Immunotherapy at Nationwide Children's, had always wanted to bring efficiency and convenience to her allergy and immunology practice—for both physicians and patients. So, when she and her colleagues started noticing that existing allergy tests either took too long to administer or gave false negatives that required repeat tests, they hit the craft stores for modeling clay and wooden dowels.

Current skin allergy tests either require single picks to be dipped one at a time into potential allergen extracts and pricked on the skin or a multi-test tool that allows up to ten allergens to be tested at once. The first method is time-consuming but precise, and the second is theoretically convenient but often results in unreliable application of the skin pricks on wiggly children or uneven surfaces, such as patients' arms and backs.

"We wanted a tool that would have the precision of a single pick and the efficiency of a multi-test, so we came up with a model that rolls along the arm or back," Dr. Patterson says of her ergonomically designed multi-test tool. "You can grip it with your hand and quickly get consistent pressure for every single test placed."

They made prototypes from play-dough and modeling clay, then engaged the Office of Technology Commercialization to explore possible avenues for patenting their invention and identifying a commercial partner. The team worked with **William C. Ray, PhD**, principal investigator in the Battelle Center for Mathematical Medicine in The

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– Matthew McFarland, RPh, PhD, director of the Office of Technology Commercialization

Research Institute, to produce a more sophisticated prototype with 3-D printing technology. From there, a series of Skype meetings with a list of potential companies led to an option agreement for market testing with a commercial partner that produces allergy extracts.

"It's been almost a two-year process so far," says Dr. Patterson. "But it's been a blessing to have the people in the Office of Technology Commercialization bring their expertise to help make this dream a reality."

BUILDING A BETTER TRACHEOSTOMY COLLAR

Kris R. Jatana, MD, a surgeon in the Department of Pediatric Otolaryngology at Nationwide Children's, and **Charles A. Elmaraghy, MD**, interim chief of that department, started meeting on the weekends three years ago to discuss ways to improve the traditional tracheostomy collar.

"Existing collars have no protective barrier where the tracheostomy tube meets the skin, which can lead to patient discomfort and pressure ulcers, so collars are often padded with bulky, obtrusive dressings to improve comfort," says Dr. Jatana. "There are also security concerns in children—the collars can fall off because of the limitations of the Velcro strap design."

Drs. Jatana and Elmaraghy scoured the aisles of sporting goods stores to find a soft, durable and water-resistant material to incorporate into a new tracheostomy collar design. They wanted the material to try to reduce skin irritation and pressure ulcers, make care of the wound easier and improve the appearance of the collar.

Their new design allows for improved adherence of the Velcro to make sure the collar can securely fit tiny necks. The collar is compatible with commonly used, commercially available tracheostomy tubes.

"From our clinical testing so far, a majority of patients and their caregivers prefer the new tracheostomy collar design," says Dr. Jatana.

The team worked with a series of companies to develop the prototype and licensed their most recent design to a medical tube securement device company. Their goal is to get the product to market in 2014,.

"There is no data to support use of any of the current commercially available collars. We plan to collect data on long-term use of the new collar and to continue to find ways to optimize it," Dr. Jatana says. "We want to keep improving the design based on the feedback of patients, parents and physicians."

FROM PRACTICE TO PROTOTYPE

When it comes to innovation, doctors shouldn't feel limited by the fact that they don't have business experience, explains **Matthew McFarland, RPh, PhD**, director of the Office of Technology Commercialization at Nationwide Children's. "Our office is here to help creative clinicians bring their ideas to fruition by walking them through the process, from patent searches and prototypes to licensing or start-ups."

The assistance in bringing practical patient care solutions to market is what both Dr. Patterson's and Dr. Jatana's teams hailed as the primary benefit of the Office of Technology Commercialization.

"It allowed us to keep focusing on why we do what we do," says Dr. Patterson. "It all comes back to the patients—we want to give them a better experience."

IN GOOD COMPANY

New start-up companies help to take inventions by Nationwide Children's Hospital's scientists and clinicians from bench to bedside

A number of discoveries by scientists in The Research Institute at Nationwide Children's Hospital have great potential for new therapeutics to treat diseases that affect children and have resulted in new start-up companies, including Cleveland-based Milo Biotechnology.

The company was founded in 2013 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. The therapy uses an adeno-associated virus (AAV) delivered follistatin protein, which inhibits the activity of myostatin, a protein that impedes muscle differentiation and growth. A clinical trial evaluating the safety and efficacy of Milo's follistatin therapy in patients with Becker muscular dystrophy is underway at Nationwide Children's.

Abeona Therapeutics, a company formed in early 2013 based on technology developed at Nationwide Children's Hospital, is focused on developing a cure for Sanfilippo Syndrome, a rare genetic disorder caused by the body's inability to properly break down certain sugars. The disease leads to progressive muscular and cognitive decline in children after the age of 2. With no cure or approved treatments, children with Sanfilippo Syndrome usually die before the age of 20. The company is using technology invented by Nationwide Children's researchers to deliver a corrective gene to the central nervous system in children with the disorder. The company plans to begin clinical trial for a drug to treat Sanfilippo Syndrome in 2014.

Another company, founded as BioLife and now renamed AveXis, is developing a new gene therapy treatment for patients with spinal muscular atrophy, a motor neuron disease that affects one in 6,000 live births in the U.S. and is the leading genetic killer of children under the age of 2. The technology, invented by researchers at Nationwide Children's, allows for the delivery of a replacement gene to target motor neurons throughout the brain and spinal cord. The Dallas-based company recently received "Fast Track" designation from the Food and Drug Administration and plans to begin clinical trials in 2014.

Research on Biofilms Prompts New Platform Technology to Treat Bacterial Infections

"Platform technologies are quite exciting because they usually represent an opportunity to impact healthcare — and potentially other industries — in multiple ways"

– Matthew McFarland, RPh, PhD, director of the Office of Technology Commercialization

While science appears to be winning the battle against acute bacterial infections with the aid of available vaccines and antibiotics, chronic and recurrent bacterial infections are a different story. Cases of chronic otitis media, sinusitis and bronchiolitis are on the rise around the world, due in large part to an apparent resistance to even the strongest antibiotics. The reason, scientists now know, is that in chronic and recurrent infections, bacteria form a complex structure called a biofilm, a closely knit community that offers protection against the body's immune system and most widely available drugs.

Researchers at Nationwide Children's Hospital have figured out a way to infiltrate these bacterial communities using an antibody against a family of bacterial proteins that stabilize biofilms. The work, led by Lauren Bakaletz, PhD, and Steven Goodman, PhD, has far-reaching potential for the development of new vaccines and therapeutics targeted at everything from patients with cystic fibrosis to periodontal disease to chronic ear infections.

"Biofilms are a consortium of multiple bacterial species that are living together in the same city, in buildings that all have a similar structure," says Dr. Goodman, a principal investigator in the Center for Microbial Pathogenesis in The Research Institute. These bacterial structures are strengthened by extracellular DNA, which act as steel girders that hold those buildings upright. Drs. Goodman and Bakaletz figured out that a protein family called DNABII binds to the extracellular DNA in biofilms. Remove those proteins and the girders buckle and give way, leaving individual bacteria exposed and vulnerable to antibiotics or antibodies directed against them.

"In terms of the biofilm disruption technology, in very general terms, we have been most active in developing a therapeutic approach where we administer a therapy — in this case antibodies directed against the protein, or a particular portion of it — to breakdown a bacterial biofilm, then also administer antibiotics to kill the released bacteria thus attempting to effect a 'cure'," says Dr. Bakaletz, director of the center and vice president of basic sciences at The Research Institute.

The DNABII protein family is expansive. While the amino acid makeup of family members varies, their structure and function is highly similar. Scientists knew that these proteins bind to bent architectures of intracellular DNA, but it was preliminary work by Dr. Goodman, then at the University of Southern California, that revealed the proteins were also found extracellularly.

Meanwhile, Dr. Bakaletz' lab at Nationwide Children's had made strides in the biofilm structures of nontypeable *Haemophilus influenzae* (NTHI) bacteria biofilms, the culprit behind chronic and recurrent otitis media. Her work had provided strong evidence that extracellular DNA of biofilms possessed a complex basket-weave architecture.

In 2008, following a seminar on Dr. Bakaletz's findings, the researchers began to compare notes about the presence of both the DNABII family of proteins and the novel structure of the extracellular DNA in the bacterial biofilms. That discussion led to a collaboration to investigate whether these proteins bind at key junctures in the extracellular DNA structures within biofilms and if they did, what it all meant.

In work published in 2011 *Mucosal Immunology*, the researchers demonstrated that members of the DNABII family were present not only on extracellular DNA but were also highly localized to regions of complex DNA architecture. They devised an experiment to see if removal of the DNABII protein from the biofilm matrix with a highly specific antibody would affect the biofilm architecture. In studies of NTHI biofilms, treatment with the antibody against the DNABII family proved dramatic. The biofilm collapsed and the resident bacteria were released. They've now successfully used the antibody to break down biofilms comprised of about a dozen different types of bacteria.

Preliminary studies by the pair suggest that their biofilm-busting technology could be used in the development of new therapeutics to treat existing infections, as well as vaccines to prevent new infections. In the world of technology transfer, that's called a "platform technology," says Matthew McFarland, RPh, PhD, director of the Office of Technology Commercialization at Nationwide Children's.

"Platform technologies are quite exciting because they usually represent an opportunity to impact healthcare — and potentially other industries — in multiple ways," Dr. McFarland says "They can be applied across many disease states and may enable different therapeutic modalities. I am most excited about the fact that the technology seems to be, based on data to date, broadly effective against diverse strains and species of bacteria. In other words, our intellectual property enables a therapeutic or vaccination strategy that will be effective for most biofilms."

In collaboration with the University of Southern California, Nationwide Children's filed the first patents on the biofilm technology in 2010 and applications for patents outside the United States are in process. Working with Dr. McFarland's team has enabled Drs. Bakaletz and Goodman to focus on furthering their understanding of biofilms, endeavors that could unveil even more potential applications for their discovery.

"The Office of Technology Commercialization staff had indeed truly enabled us to focus our time on moving the research forward and considering new applications and uses for our technology rather than dealing with the labor-intensive patent and licensing process," Dr. Bakaletz says.

Therapeutics

Therapeutic Strategy for the Removal of Biofilms (Reference #: 2010-002)
Bacterial biofilm formation is a major problem not only for patients with inner ear infections, cystic fibrosis, pneumonia and COPD, but also for patients requiring implanted medical devices. Once a biofilm is formed, treatment of the infection with antimicrobial agents is difficult if not impossible. Reducing the protective, impenetrable biofilm barrier is necessary to make the bacteria accessible to antibacterial treatments. Researchers at the Research Institute at Nationwide Children's Hospital and at the University of Southern California have identified a protein, IHF, which is a central component of the bacterial biofilm formed by several pathogenic bacteria. It constitutes an important structural component of the biofilm, and has been targeted to resolve biofilm-related infection in several in vitro and in vivo models.

Novel Therapy for the Treatment and Prevention of Necrotizing Enterocolitis (Reference #: 2010-018)
Necrotizing enterocolitis (NEC) is the most common gastrointestinal emergency in infants and is a leading cause of death in premature infants. Researchers at Nationwide Children's Hospital have demonstrated that heparin-binding EGF-like growth factor (HB-EGF) effectively decreases the severity of intestinal injury in NEC and will prove to be a clinically viable means of reducing the incidence of NEC. No growth factor-based therapies are presently available for NEC. Exogenous administration of HB-EGF represents both a safe and logical way to reduce intestinal injury. HB-EGF is naturally present in both human amniotic fluid and breast milk. Also, decreases in HB-EGF have been well documented in NEC intestine. This patented treatment method has been evaluated and found to be effective in vitro and in vivo. Accordingly, optimal doses, treatment intervals and drug efficacy have been established in severe laboratory models of NEC.

New Methods of Treating Intestinal Injury using Heparin-Binding Epidermal Growth Factor and Stem Cells (Reference #: 2012-004)
Researchers at Nationwide Children's Hospital have developed new methods for treating, abating and reducing the risk for intestinal injury by administering a combination of HB-EGF and stem cells. This innovative treatment approach also provides methods of promoting engraftment of stem cells within the intestine of a patient. The combination of HB-EGF and somatic stem cells represents a promising therapeutic strategy for intestinal diseases, including, but not limited to, necrotizing enterocolitis, hemorrhagic shock, ischemia-related intestinal injuries and inflammatory conditions.

A Novel Class of STAT3 Small Molecules Inhibitors as a Potential Cancer Therapeutic Agent (Reference #: 2012-024)
The Signal Transducers and Activators of Transcription (STAT) proteins are transcription factors that participate in oncogenesis. STAT3 activity plays a role in disease progression in a wide variety of human malignancies, including breast cancer and sarcoma. In normal cells, blocking STAT3 is neither harmful nor toxic to cells, thus promoting the direct targeting of STAT3 signaling as an attractive therapeutic approach to treating cancer. Currently, there is no FDA-approved drug targeting STAT3. Researchers at Nationwide Children's Hospital and The Ohio State University have successfully designed and synthesized LY5, a novel non-peptide, cell-permeable, small molecule that targets STAT3 and inhibits its activity. This molecule has shown efficacy against several cancer types in in vitro assays and further assessment is currently underway.

Therapeutics

A Novel Technique for Generating Tissue Engineered Intestine for the Treatment of Short Bowel Syndrome (Reference #: 2013-009)
Short bowel syndrome (SBS) is a consequence of massive small bowel resection performed in patients presenting various diseases. Many thousands of patients with SBS each year depend on total parenteral nutrition (TPN) for survival. The cost for TPN exceeds $50,000 per year per patient; and the mortality rate remains high. Researchers at Nationwide Children's Hospital have developed a state-of-the-art technology to fabricate tissue engineered scaffolds that mimic the architecture and properties of native intestine and enhance the bio-environment for cell adhesion, proliferation and differentiation. Combining the newly identified and characterized intestinal stem cells (ISC) and enteric neural stem cells (NSC) with this novel nanofiber technology, a full thickness, functional intestine can be generated to treat and manage SBS in neonates, as well as in pediatric and adult patients.

Peptide Targeting Microvascular Alpha 2C-Adrenoceptor Cell-Surface Translocation as a Therapy for Raynaud's Phenomenon (Reference #: 2013-010)
Raynaud's phenomenon (RP) is a condition that mostly affects women, resulting in a series of discolorations of fingers and toes due to abnormal spasm of the blood vessels when exposed to cold temperature. Emerging evidence implicates that alpha 2C-adrenoceptors (AR) play a major role in the abnormal vasoconstriction in RP. Alpha 2C-ARs are stress receptors of vascular smooth muscle cells that generally reside intracellularly in a silent state, and translocate to the cell surface under conditions of environmental stress, including cold temperature, leading to vasoconstriction of cutaneous blood vessels. The amount of cell surface receptors is crucial to the pathogenesis and progression of RP. Currently, no targeted therapies are available for early control of the disease. Researchers at Nationwide Children's Hospital have identified a novel protein-protein interaction between microvascular smooth muscle alpha2C-ARs and the actin binding protein filamin-2, which is necessary for receptor translocation to the surface and for receptor function. Blocking this interaction can inhibit receptor translocation and may lead to a new approach for treating cold-induced vasospastic attacks in Raynaud's phenomenon.

RCn: a New Class of Micellar Antitumor Drugs with Specific Affinity for Tumor Cell Membranes and Ability to Behave as Nanocarriers for Other Bioactive Molecules (Reference #: 2013-024)
Recent generations of anti-cancer therapies provide more effective treatment with reduction of toxicity by two approaches: the use of a new drug with specific tumor-targeting properties, and the use of drug-loaded nanosized carriers. RCn molecules represent a novel class of compounds that demonstrate effective anti-tumor properties and limited toxicity as both a tumor-targeting drug and a micelle carrier.

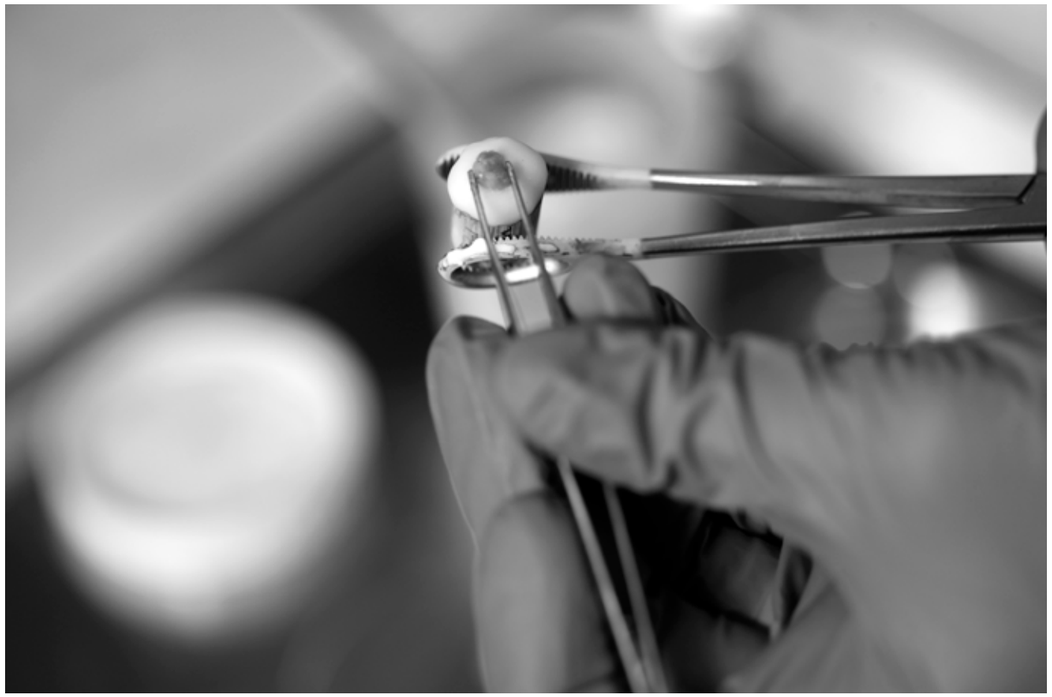
Enhanced Protection against Nephrotic Syndrome with Thiazolidinedone and Combination with Glucocorticoids (Reference #: 2013-035)
A novel combination therapy, pioglitazone (thiazolidinedione) and methylprednisolone (glucocorticoids), demonstrates improvements in clinical efficacy and reduction of proteinuria when used for patients with nephrotic syndrome.

Gene Therapies

Mini-Dystrophin Gene Delivery via Isolated Limb Perfusion as a Therapeutic Potential for Duchenne Muscular Dystrophy (Reference #: 2013-011)

Duchenne muscular dystrophy (DMD), the most common severe childhood form of muscular dystrophy, is caused by mutations in the DMD gene leading to absence of dystrophin protein in skeletal and cardiac muscles. Dystrophin protects the sarcolemma from eccentric contraction and also anchors a number of signaling proteins in close proximity to sarcolemma. Treatment options for DMD are limited despite continuous research efforts. Due to the packaging limits of adeno-associated virus (AAV) vectors, existing gene replacement studies failed to fully correct the functional defect in DMD muscle in animal models with mini- or micro-dystrophin gene. Researchers at Nationwide Children's Hospital have discovered a novel therapeutic potential for DMD involving the delivery of a dual vector of mini-dystrophin transgene that upon homologous recombination includes components essential to the normal function of the dystrophin protein. In addition, the researchers have also successfully increased transduction efficiency of the transgene by optimizing a vascular delivery route called isolated limb perfusion via the femoral artery. This finding can significantly impact future clinical gene therapy trials for DMD.

Gene Therapies



Exon Skipping as a Treatment for Duplication Mutations in Duchenne Muscular Dystrophy (Reference #: 2013-012)

DMD affects 1 in 5,000 newborn males. It is caused by mutations in the DMD gene leading to an absence of the dystrophin protein in skeletal and cardiac muscles. About 65% of DMD patients carry deletions of one or more exons in the gene. Exon skipping is a therapeutic approach that targets specific exons to exclude them from the mature messenger RNA (mRNA), aiming to restore an open reading frame that allows translation of an internal truncated but still partially functional protein. This type of exon skipping is expected to change the severe DMD symptoms into the much milder symptoms of Becker muscular dystrophy (BMD), and exon skipping therapies are currently in clinical trials for the most common deletion mutations. Researchers at Nationwide Children's Hospital are now working on exon skipping therapies for exon duplication mutations, which affect about 5% of patients. This therapeutic strategy is predicted to result in restoration of an entirely normal mRNA and thus completely intact dystrophin protein. Preclinical studies with a vector enabling this approach are underway.

Enhanced Protection against Nephrotic Syndrome with Thiazolidinedone and Combination with Glucocorticoids (Reference # 2013-035)

Researchers at Nationwide Children's Hospital have generated data to support the re-purposing of an existing FDA approved drug, pioglitazone (used for type II diabetes treatment) in combination with low dose glucocorticoids for the treatment of nephrotic syndrome (NS). NS is currently treated with glucocorticoids alone. Early evidence suggests that a combination therapy of pioglitazone and methylprednisolone (a common glucocorticoid) might demonstrate improvements in clinical efficacy and reduction of proteinuria in patients with nephrotic syndrome.

Gene Therapies

AAV9-Mediated Suppression of Mutant Superoxide Dismutase 1 as a Therapeutic Potential for Mutation in SOD1 in Amyotropic Lateral Sclerosis (Reference #: 2013-031)
Amyotropic lateral sclerosis (ALS), also known as Lou Gehrig's disease, is a rapidly progressive and fatal neurodegenerative disease that is responsible for one in every 200 deaths related to motor neuron diseases. Twenty percent of familial cases are caused by mutation in superoxide dismutase 1 (SOD1). Attempts at improving therapy by reducing synthesis of SOD1 have been the focus of multiple therapeutic approaches. Currently, only one drug is FDA-approved as a therapy for ALS. Researchers at Nationwide Children's Hospital and Ludwig Institute for Cancer Research have identified a groundbreaking therapeutic approach that involves the suppression of SOD1 levels via adeno-associated virus 9 (AAV9) mediated delivery of shRNA. This method has been shown in animal studies to be effective in slowing disease progression and extending survival, even when treatment is initiated after onset.

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

Intravascular Treatment of Spinal Muscular Atrophy by Gene Therapy (Reference # 2008-008)
This invention relates to methods of using adeno-associated virus 9 (AAV9) to cross the blood-brain barrier in the treatment of the neurodegenerative disease spinal muscular atrophy (SMA). AAV9 can cross the blood brain barrier after intravenous injections and reach lumbar motor neurons or areas of the brain allowing for effective transmission of the deficient gene, spinal motor neuron (SMN1), for treatment of this genetically based neurodegenerative disease.

Gene Therapy Approach for Limb Girdle Muscular Dystrophy Type 2D (Reference # 2009-016)
The field of gene therapy for the muscular dystrophies is progressing in a stepwise fashion. Researchers at Nationwide Children's Hospital have developed a new gene therapy approach to restore alpha-sarcoglycan deficiency in Limb Girdle Muscular Dystrophy Type 2D. This therapy can be delivered locally, via intramuscular injection, limb perfusion, or systemically by vascular delivery. This methodology is generalizable to any limb, both upper and lower, and is modifiable to control limb perfusion pressure, oxygenation, pH and removal of blood and plasma. These enhancements to current gene targeting protocols will increase gene targeting efficacy and result in broader whole-limb delivery of the transgene.

Gene Therapy Approach for Muscular Dystrophy Using GalgT2, a Glycosyltransferase (Reference # 2005-008)
DMD is an X-linked inherited disease that causes rapid muscle degeneration. A mutation in the dystrophin gene causes loss of dystrophin protein expression, which is responsible for the disease. Researchers at Nationwide Children's Hospital have developed a gene therapy approach which delivers the glycosyltransferase GalgT2 using a gene therapy vector, adeno-associated virus (AAV) for the potential treatment of several muscular dystrophies. This therapy could potentially be delivered locally, via intramuscular injection, to groups of muscles, via limb perfusion, or systemically, via vascular delivery.

Gene Therapy Approach for Duchenne Muscular Dystrophy Using a Micro-Dystrophin
Despite many lines of research following the identification of the DMD gene, treatment options are limited. Researchers at Nationwide Children's Hospital have developed a gene therapy approach using adeno-associated virus (AAV) to deliver micro-dystrophin, a modified version of the defective dystrophin gene, to replace the missing gene in DMD disease.

Gene Therapies

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

Trans-Blood-Brain-Barrier CNS Gene Delivery for Treating Lysosomal Storage Diseases, MPS IIIA and MPS IIIB (Reference # 2010-014)
This invention involves delivering a specific gene therapy product using intravenous injection of AAV9 vector to restore α-N-acetylglucosaminidas activity in the central nervous system (CNS) and periphery to treat both the neurological and somatic aspects of the lysosomal storage disease Sanfilippo syndrome, also known as Mucopolysaccharidosis type IIIB (MPS IIIB). A similar strategy has also been used to restore Sulfogluvcoasamine Sulfohydrolase (SGSH) activity as a potential therapy for Mucopolysaccharidosis type IIIA, a more prevalent form of MPS III.

Biomarkers

Diagnostic Biomarker Assay for Predicting the Susceptibility of Recurring Urinary Tract Infections (Reference #: 2009-012)
The subject technology has identified specific protein expression levels in patients that have greater susceptibility to urinary tract infections. A number of genes have been described or implicated by looking at the DNA copy number variations. These genetic variations have led to the development of an antibody-based diagnostic assay to detect protein levels that highly correlate with clinical recurrence of UTIs.

A Minimally Invasive System for the Rapid Detection of Bacterial Sinusitis (Reference #: 2011-009)
Investigators at Nationwide Children's Hospital and The Ohio State University have identified biomarkers for the presymptomatic screening and diagnosis of bacterial sinusitis. This technology can be used with traditional balloon sinoplasty devices to offer a minimally invasive, patient-specific way to rapidly diagnose sinusitis in the outpatient clinic.

Human Alpha Defensing 5 as a Test of Cure for Urinary Tract Infection (Reference #: 2012-027)
A novel biomarker, human urinary level of alpha defensing 5 (HD5) has been shown to correlate with urinary tract infection. During infection, HD5 level expression increases in the kidney and levels become detectable in the urine. The results suggest that HD5 may have an important role in maintaining urinary tract sterility as well as determining length of antibiotic therapy.

End User Innovation

Pediatric Venous Thromboembolism Clinical Probability Tool (Reference #: 2012-010)
A novel technology indicating that a clinical probability tool may estimate the likelihood of venous thromboembolism in children accurately. Prospective studies are needed to further validate the clinical implementation.

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

Testing Targets, an Innovative Device to Improve Efficiency and Accuracy of Single-Prick Allergy Skin Tests (Reference #: 2012-029)
Food allergies have long been a significant public health issue, particularly in the pediatric population. Six to 8% of children under the age of three have food allergies, and nearly 4% of adults have food allergies. One of the commonly used allergy testing methods is the skin prick test. This method requires accurate marking of testing sites on the patient's skin prior to the application of an allergen, which could be time consuming and difficult to perform on a moving patient. Researchers at Nationwide Children's Hospital have invented a device called Testing Targets (Lil's Testing Targets for kid-friendly version) to be used with the previously existing single-prick allergy test for improving efficiency and accuracy of testing and interpretation. Testing Targets is a disposable plastic device with hollow projections off of one long side of the device that is used with non-toxic ink to mark placement for allergy skin test. Lil' Testing Targets shares the same design with Testing Targets, except the hollow cylinders are replaced with outlines of animal faces without noses (skin test reaction with make the nose).

A Novel Minimally-Invasive Method for Interrogating, Diagnosing and Treating Lesions in the Small Bowel (Reference #: 2013-023)
Researchers at Nationwide Children's Hospital have developed a novel pull enteroscopy device and pull enteroscopy technique that improves on existing endoscopic technology. This novel technology allows operators to pull, rather than push, an enteroscope through the gut and make multiple passes to the small intestine with relative ease. Using a conventional upper endoscope, an operator can only reach the duodenum. However, gastrointestinal pathology often exists beyond the duodenum, in places like the jejunum and ileum. The new device makes the delivery of therapeutic agents to poorly accessible areas of the small intestine possible. This patent-pending device is easy to use and minimally invasive compared to existing enteroscopes. The technology can be used to obtain biopsy samples, cauterize bleeding, and remove malignancies or polyps from parts of the small intestine that are poorly accessible by other means.

End User Innovation

Medical Line Safety Enclosure (Reference #: 2006-015)
The present technology is a medical line organizer that prevents accidental entanglement, suffocation, and strangulation of hospitalized individuals. It is a first in class device that decreases the incidence of both fatal and nonfatal asphyxiation that results from the entanglement of medical tubing/cords around the neck of patients.

A Highly Durable, Water-Resistant Tracheostomy Collar (Reference #: 2011-007)
Clinicians at Nationwide Children's Hospital have designed a novel tracheostomy collar that minimizes collar-related neck abrasions, provides greater neck security and exhibits enhanced durability compared to currently available tracheostomy collars.

Endoscopic Foreign Body Retrieval Device (Reference 2010-009)
The technology is a medical device that provides the clinician improved foreign body retrieval within anatomical structures such as the gastrointestinal and respiratory tracts. The device enables a minimally invasive procedure with decreased tissue trauma and patient discomfort while allowing the clinician to retrieve the foreign body in significantly less time than other devices on the market.

Self-Catheterization Drainage Aid (Reference 2010-005)
The self-catheterization drainage aide is a device that helps in the draining of urine directly from the user's bladder, when using an intermittent catheter. The device attaches to a commode or urinal to secure the catheter tubing, allowing the patient to focus on inserting the catheter into their bladder and draining thereof.

Kinect™-Based Virtual Reality Game as a Sensitive Measure of Movement Abilities across the Lifespan: A Clinical Outcomes Tool for SMA and DMD Patients (Reference #: 2012-9=011)
This technology is a video-based affordable and entertaining physical therapy assessment tool that measures movement abilities. It can be used as a clinical outcome measure for neuromuscular diseases, stroke, head injury, or other conditions in which the functional abilities of the arms and legs are being investigated.

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 active the mechanism.

Research Tools

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

Cmah-Deficient mdx Mice: A Better Mouse Model for Duchenne Muscular Dystrophy (Reference # 2010-019)
A new mouse model for DMD-related research has been created at Nationwide Children's Hospital. A double knock-out mouse strain was generated that better mimics the human disease than the current standard model and thus provides a model for DMD where translational research will be more relevant to issues affecting humans with the disease.

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

Content

Mobile Safety Application (Reference #: 2013-013)
Each year, nearly 9 million children aged 0 to 19 years are seen in emergency departments for injuries, and more than 9,000 children die as a result of their injuries. While effective safety devices are readily available, there is no centralized and authoritative information available to parents on how to achieve a safe home and which products are best suited to their homes and families. Researchers at Nationwide Children's Hospital have developed a mobile safety application and a corresponding web site to provide correct, reliable and trusted child and home safety information to help parents identify injury hazards "room-by-room" and make their homes safe for their families. This mobile safety app will allow parents to select and purchase safety products (such as stair gates, cabinet locks, smoke alarms, carbon monoxide detectors, etc.) 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.

A Smartphone Application to Improve Spina Bifida Self-Management Skills (Reference #: 2013-029)
Few self-management interventions of any type have been developed and empirically supported for youth with spina bifida. While medical management applications exist for other chronic medical conditions, none are sufficient for the complex spina bifida medical regimen. Researchers at Nationwide Children's Hospital have developed a smartphone app that will improve the ability of youth with spina bifida to manage, initiate, and complete the complex self-care tasks associated with spina bifida. In the future, the app could be generalized to other populations of youth with complex medical conditions, such as spinal cord injury, cerebral palsy, etc.

Churchill (a Pipeline for Human Genome Analysis) (Reference #: 2012-005)
Through a novel parallelization strategy and development of a fully automated pipeline, the Churchill software platform substantially shortens the time needed to take raw sequence data through the multiple steps that are required to identify human genetic variation. Churchill is simple to use and allows for fully automated analysis of next generation sequencing (NGS) data. In addition, Churchill is capable of running on the Cloud and all popular Linux environments. More importantly, Churchill provides results that are identical to the much slower gold standard bioinformatics approach.

Pharmacy Safety Tracking System (PhaST) (Reference 2009-001)
This technology is a web-based software application that facilitates the monitoring of medication adherence, side effects, and patient symptoms. Pharmacy Safety Tracking System (PhaST) is an interactive voice response (IVR) call system that screens and evaluates for adverse medication events or exacerbations of symptoms. If PhaST detects a possible event, such as a suicidal thought in a patient taking antidepressants, it will alert a staff person to call the patient for a live telephone interview. In the interview, the staff person will triage the risk to the patient, provide counseling to the patient or family, and, when necessary, contact the prescribing clinician. PhaST generates electronic reports that document these patient interactions.

| Our Team |

Matthew McFarland, RPh, PhD, *Director*

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

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

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

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Margaret Barkett, PhD, *Senior Licensing Associate*

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

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

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

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

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

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

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Supatra S. Davis,
Business Compliance and Projects Coordinator

Supatra joined The Research Institute at Nationwide Children's Hospital in August 2008. She is primarily responsible for information and business systems. She tracks and invoices license terms and follows up as necessary to insure licensee compliance. She oversees the annual budget, purchasing, and the file management database. Supatra also assists technology transfer professionals with department initiatives, events management, and operational issues. She also serves as a Notary Public for the State of Ohio.

Supatra is a dedicated business and financial support professional with 10+ years of experience in providing outstanding service. She has a Bachelor of Science degree from National Paralegal College and is currently pursuing a Master's degree in business administration with a major in financial management at Franklin University.

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