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“Innovation.” The word has been relegated to the realm of business jargon and gets tossed around all too casually. It conveys a “new,” “fresh” or “cutting-edge” idea. To innovate generally means to introduce something new, but notably absent from such a definition is any reference to a “product,” “adoption” or “impact.” If an innovation is simply an idea or concept that gets introduced, it begs the question: Is it enough to simply innovate? The answer is no.

Since arriving at Children’s Hospital Boston more than three years ago, I’ve seen that clinicians, researchers and administration are not content with the status quo or simply come up with new ideas. They are committed to resourcing and developing innovations in ways that lead to new products, novel ways to diagnose illness, better treatments and patient-centric models of care delivery.

The Technology & Innovation Development Office (TIDO) pursues this essential mission. Each group within TIDO is a partner to Children’s investigators, our industry counterparts and other departments within the hospital throughout the long process of translating an innovation into a product. TIDO has played a role in advancing a number of Children’s research and clinical innovations, several of which reached milestones this past year:

• Led by Charles Berde, MD, PhD, chief, Division of Pain Medicine, a major international collaboration was formed with pharmaceutical manufacturer, Proteus S.A. of Chile, to develop a novel, long-acting local anesthetic that could revolutionize surgery and pain management.

• Under the direction of Mark Puder, MD, PhD, associate professor in Surgery, with the support of Fresenius Kabi, Children’s received orphan drug status for a parenteral nutrition product, Omegaven, and advanced the product through a Phase II/III clinical trial in the United States.

• Clinical trials initiated by David Hunter, MD, PhD, ophthalmologist-in-chief, are set to begin with an easy-to-use prototype to detect amblyopia and strabismus. The Pediatric Vision Scanner was built with an investment from the Technology Development Fund in 2009.

• Led by researchers David Williams, MD, chief of Hematology/Oncology, Sung-Yun Pai, MD, attending in Medicine, and Luigi Notarangelo, MD, director of the Research and Molecular Diagnosis Program on Primary Immunodeficiencies, a new FDA approved gene therapy trial for SCID-X1 (otherwise known as the “bubble boy disease”) is now accepting patients.

With the business environment in health care and life sciences evolving rapidly and deal structures becoming increasingly complex, TIDO will continue to display creativity and flexibility to forge highly coordinated, multi-party partnerships such as the ones described on this page. TIDO is adapting to meet the changing needs of Children’s and the external marketplace, and I’m proud to announce a selection of accomplishments and changes we made in 2010:

• TIDO’s agreements increased by 40 percent compared to FY09.

• Kathleen Bass, PhD, was promoted to the position of associate director, and she will oversee the operations within TIDO.

• The Clinical Trials Office, which handles clinical and preclinical collaborations with industry, went through a significant reorganization to improve efficiency, decrease transaction time and better support clinical research at Children’s.

• The Business Development and Marketing team, led by Nurjana Bachman, PhD, launched new marketing initiatives, including TIDO’s own Twitter account and, in conjunction with the Public Affairs and Marketing Department, the science and innovation blog, Vector (www.vectorblog.org).

• Now in its second year, the Technology Development Fund, led by Monique Yoakim-Turk, PhD, invested $1.3 million in 11 projects in 2010, and we’re encouraged to see that many of the 2009 projects have not only received significant commercial interest, but also $4.3 million of additional funding.

Looking forward to next year, innovation around health care informatics, clinical decision support, genomic medicine and a renewed focus on unmet medical needs in orphan diseases, make it a great time to be at the center of it all here at Children’s.

Our goal and our charge is to find ways to harness the innovative ideas and discoveries made here at Children’s and turn them into products that can benefit our patients. We will continue to strive to do so at a world-class level because that is what our patients deserve.
With more than $225 million in annual funding and 800,000 square feet of space, Children’s Hospital Boston’s research enterprise is the world’s largest and most active at a pediatric center. Our investigators—basic scientists, clinical researchers and epidemiologists—are Harvard Medical School faculty who are accelerating the pace of medical discovery from brainstorm to bench to bedside. The National Institutes of Health (NIH) is our largest sponsor. The hospital is home to seven members of the National Academy of Sciences, 11 members of the Institute of Medicine and 11 investigators supported by the Howard Hughes Medical Institute (HHMI), the nation’s largest private nonprofit source of funding for biomedical research and science education. Children’s 1,100 scientists are experts in many fields, including stem cells, oncology, cardiology, neuroscience, rare diseases, genomics, vascular biology and medical informatics.

Invention Management Activity

In FY10, the Technology and Innovation Development Office (TIDO) had 700 inventions under active management. One-hundred-and-eighty-two of these were marketed within the fiscal year. Licensing managers supervised 233 ongoing license agreements, and facilitated the activities of outside patent attorneys to manage 1,003 pending patent applications on 399 inventions and maintain 1,101 issued U.S. and foreign patents.

Patent Filings

TIDO filed a total of 123 patent applications in FY10. Forty-two were provisional patent applications and 27 were filed for U.S. and foreign rights under the Patent Cooperation Treaty mechanism. Forty-five applications were filed in the United States, and nine were filed in individual foreign countries.

Patent Issuances

Children’s was granted 18 patents by the U.S. Patent and Trademark Office and 34 by foreign patent offices. (Children’s patents are filed with the Assignee designation of Children’s Medical Center Corporation.) These new patents are listed in Appendix 3.

Invention Disclosures

TIDO received 117 new invention disclosures from Children’s clinicians and researchers, which is a slight decrease from FY09.

Invention Management Activity

<table>
<thead>
<tr>
<th>Invention Management Activity</th>
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<tr>
<td>Inventions under active management</td>
<td>700</td>
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<tr>
<td>Under initial evaluation</td>
<td>76</td>
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<tr>
<td>In marketing campaigns</td>
<td>182</td>
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<tr>
<td>In development</td>
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<td>With license pending</td>
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<td>With other institute leading</td>
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<tr>
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<td>432</td>
</tr>
<tr>
<td>Issued foreign patents</td>
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</tbody>
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Patent Filings

| Patents filed | 123 |
| Provisional | 42 |
| PCT | 27 |
| U.S. | 45 |
| Foreign | 9 |
| Patents issued | 52 |
| U.S. | 18 |
| Foreign | 34 |
| Licenses & options granted | 30 |

| Gross revenue ($M) | 12,550,700 |
| Net revenue (less external institutions; $M) | 9,335,571 |
| Revenue from new licenses and options ($M) | 279,223 |

Licensing Activity

TIDO negotiated and executed 30 license and option agreements for Children’s technologies: nine exclusive licenses, 16 non-exclusive licenses and five options. This is an increase of 7 percent in FY10. The revenue recognized from these new license and option agreements was $279,223. TIDO’s overall performance and licensing and patenting activities over the past six years are illustrated in Appendices 1 and 2.

Clinical Trials Office

In collaboration with TIDO’s licensing managers, the Clinical Trials Office (CTO) negotiated and executed 902 agreements in FY10: 31 clinical trial agreements, 860 academic and industry material transfer agreements and nine corporate sponsored and collaborative research agreements. The funding realized from these agreements was approximately $2 million.

Distribution of Licensing Revenue

Gross revenue received in FY10 from all licenses was $12.55 million, a decrease from the previous year. Of the 233 active license agreements, 76 generated revenue. Forty-one of these 76 licenses brought in less than $10,000 each, but three produced more than $500,000 each. The net revenue received by Children’s was $9.34 million, which is $12.55 million in gross revenue less $3.22 million distributed to other institutional co-owners. Of the $9.34 million in net revenue, $2.84 million was distributed to the inventors and $2.14 million was distributed to the inventors’ departments and laboratories. The remaining $4.36 million distribution to the hospital was apportioned to the general research endowment, unrecovered legal expenses and TIDO’s operations.
Managing Licenses & Patents

Significant Revenue-Generating Inventions

Seventy-one percent of the total revenue was generated by sales of Thalomid® brand drug and Revlimid® brand drug for the treatment of cancer. Other significant sources of revenue were royalties from the sales of CardioSEAL® and StarFlex® for minimally invasive repair of heart defects; Namenda® for the treatment of Alzheimer’s disease; BioStar® to treat cardiac sources of migraine headaches, strokes and other potential brain attacks; and Neumega®, which stimulates platelet production and is used in combination with chemotherapy in patients with cancer.
Children’s Hospital Boston’s Technology Development Fund (TDF) announced its second annual awards for 2010 and significantly advanced the stage of development of its 2009 first-time award winners. With guidance from its advisory board and in partnership with multiple contract research organizations (CRO), TDF brought its projects to relevant inflection points, which resulted in new commercial partnerships, $4.3 million in additional funding from the NIH, the Department of Defense (DOD), foundations and donors, and generated data submitted for publication.

In the spring of 2010, the TDF issued its second request for proposals and received more than 40 letters of intent. After a preliminary internal review by TIDO, 20 applicants were invited to submit full grant proposals and present their projects to the TDF’s external advisory board of industry experts with extensive product development experience.

In August of 2010, TDF announced the award of $1.3 million to 11 technologies that range from pharmaceuticals, diagnostics and medical devices to drug delivery and software. The investigators for the 11 projects will be paired with members of the TDF advisory board, who will work with Monique Yoakim-Turk, PhD, technology development manager of TIDO, to guide each project.

“As funding to advance early-stage discoveries and innovations continues to lag, the Technology Development Fund seeks to fill that gap for our most promising technologies,” says Erik Halvorsen, PhD, director of TIDO. “This mechanism, which brings capital and industry experts to bear on Children’s innovations, is critical for translating our research into new diagnostics, devices and therapeutics that can benefit our young patients.”

“The Technology Development Fund has allowed us the freedom to innovate and form collaborations that are essential to further the development of early-stage technology,” says John Kheir, MD, department of cardiology and award recipient. “Without the unique resources and expertise from this fund, we might never see our concepts come to fruition.”

Below is the list of 2010 funded projects and investigators:

**Site 1 sodium channel blocker as a prolonged duration local anesthetic**  
— Charles Berde, MD, PhD, Anesthesiology

Dr. Berde and his colleagues have shown that a class of site 1 sodium channel blockers has prolonged action as local anesthetics and has some very desirable safety features, including no toxicity to the heart and no entry into the brain. The goal of the project is to perform animal toxicology studies as part of the final package of data for an investigator-initiated investigational new drug (IND) submission to the FDA and for clinical trials for use as a prolonged-duration local anesthetic.

**Optical device to monitor capillary refill**  
— Vassilios Bezzerides, MD, PhD, Cardiology

Currently, the diagnosis of dehydration is based on a combination of clinical signs and symptoms that have limited sensitivity and specificity. Dr. Bezzerides developed a hand-held prototype that accurately measures capillary refill time and conducted a pilot study in Children’s Emergency Department to determine the device’s effectiveness. The purposes of this project are to improve the device and perform clinical studies to diagnose patients with various degrees of dehydration.

**Early autism diagnosis and risk assessment using complex systems analysis of EEG signals**  
— William Bosl, PhD, Medicine/Informatics Program

The primary goal for this technology is to enable early detection of autism and routine monitoring of infants’ cognitive development through EEG measurements. Dr. Bosl envisions a diagnostic service based on novel analysis of EEG data recorded during a pediatric well-visit. A risk profile and cognitive assessment based on Dr. Bosl’s analysis will be sent to the health care provider for use and follow up.

**A GDNF receptor agonist for topical treatment of peripheral neuropathies**  
— Gabriel Corfas, PhD, Neurology and Otolaryngology

The goal of this project is to develop a new therapy to treat peripheral neuropathies (PN) by targeting the underlying physical and/or functional defects in peripheral nerves to stop (and potentially reverse) nerve damage. Using two mouse models of small fiber PN,
Dr. Imam’s team showed that topical application of a non-peptidyl GDNF receptor agonist to the skin of affected mice has dramatic therapeutic effects. They used last year’s TDF grant to perform chemical manufacturing control studies on their compound, and pharmacokinetic and pharmacodynamic studies are underway. The 2010 award will be used to perform studies to move the compound towards IND submission to the FDA.

**Novel transillumination PICC line catheter — Farhad Imam, MD, PhD, Newborn Medicine/Surgery**

Dr. Imam has developed a novel transillumination method and device to improve the safety and efficiency of peripherally inserted central catheter (PICC) line insertion. The device allows the external observer to see light emission from the internal catheter through the skin. A functional prototype has been constructed and tested successfully in cadaver tissue and live animals. The goal of this project is to construct and optimize a functional transilluminating PICC catheter that can be used in cadaver, animal and ultimately human testing.

**I.V. oxygen using injectable microbubbles — John Kheir, MD, Cardiology**

When systemic oxygen levels are low, irreversible and severe injury occurs to the brain, heart and other organs. The goal of this project is to develop a platform technology allowing therapeutic gas to be injected intravenously. Dr. Kheir has demonstrated that oxygenated microbubbles can be manufactured and stored in bulk for weeks. Oxygenated microbubbles have been successfully tested in a rabbit model of hypoxic ventilation. The purpose of this project is to expedite further optimization of the lipid formulation and examine the possibility of using well-established processes for drug manufacturers to make size-limited, gas-filled microparticles.

**Platform to deliver vaccines and drugs across the intestinal wall — Wayne Lencer, MD, Gastroenterology/Nutrition**

Dr. Lencer will test his recent discovery that “short” or “unsaturated” ceramide-based lipids may act as molecular carriers to deliver therapeutic peptides across mucosal epithelial barriers and extend drug half-life. The goal of this project is to provide proof-of-principle for this novel nanotechnology designed to transport peptides and proteins across the epithelial membrane. If successful, this technology could become a platform for oral or nasal administration of therapeutic proteins and/or vaccine adjuvants.

**Novel myocardial imaging agent — Alan Packard, PhD, and S. Ted Treves, MD, Nuclear Medicine and Molecular Imaging**

This project proposes the development of an 18F-labeled rhodamine B for myocardial perfusion imaging in patients with known or suspected coronary artery disease using positron emission tomography. In preliminary studies, the investigators have demonstrated that 18F-labeled rhodamine B accumulates in the heart. The goal for this project is to optimize the synthesis of the compound and obtain sufficient toxicity data to support a physician-sponsored IND.

**Development of saposin A derivatives as a cancer therapeutic — Randolph Watnick, PhD, Surgery/Vascular Biology Program**

Dr. Watnick has identified a peptide that retains the in vivo activity of the full-length prosaposin protein. He has shown that prosaposin is secreted by weakly aggressive human breast and prostate cancer cells, and that it inhibits metastasis in a prostate cancer model in vivo. Dr. Watnick is currently working with TD2 (a CRO) to perform pharmacokinetic stability studies on the peptide as part of the initial funding he received from TDF last year. For this next phase of the project, he will continue to work with TD2 to perform preclinical efficacy studies using multiple xenograft models including breast, colon and pancreatic cancer.

**Ion channel blockers to manage neurogenic inflammation — Clifford Woolf, MD, PhD, Neurobiology Program**

The goal of the project is to use certain large-pore cation channels, located on sensory neurons that are activated in allergic conditions, as drug entry ports to introduce charged calcium channel blockers into bronchial sensory fibers. This will disrupt the neurogenic inflammation produced by the calcium-dependent release of pro-inflammatory mediators from the targeted nerves, for treatment of conditions such as asthma, rhinitis, conjunctivitis and Crohn’s disease. This project will study respiratory diseases because the evidence for a neurogenic component is very compelling, there is an unmet need and preclinical models are available.

**Novel therapeutic approach for metastatic prostate cancer — Bruce Zetter, PhD, Surgery/Vascular Biology Program**

Dr. Zetter and colleagues developed a screen that relies on differential cytotoxicity of drugs for highly metastatic cells to select novel therapeutic agents for late-stage cancer. From a library of 1,120 non-toxic FDA-approved drugs, they identified benzimidazoles as a class of compounds that are preferentially active against highly metastatic prostate tumor cells and exhibit minimal cell killing in normal cells. They aim to bring forward a member of this class of compounds as a potential treatment for androgen-resistant metastatic prostate cancer and develop a novel formulation suitable for cancer patients. They will also conduct efficacy and pharmacokinetic studies.
with a renewed collaboration agreement, Children’s, Genocea and PATH will move toward the next vaccine development milestones together, with the goal of bringing a vaccine candidate into the clinic in the near future.

Start Cart – an unusual success story

Eight years ago, Mark Rockoff, MD, associate anesthesiologist-in-chief, searched for a mobile workstation among hundreds of exhibitors at the
American Society of Anesthesiologists annual meeting. He wanted an operating room cart that could safely transport and discard the needles and tubes he inserts before surgery, thereby eliminating the current inefficient system in most operating rooms. At the time, the needles and supplies he used were individually carried to a patient’s bedside, and the patient’s bed served as an unsafe, temporary work surface for the equipment used to set up the lines for I.V. fluids, medications and arterial monitoring. He did not find what he envisioned.

Frustrated, he spent the flight home sketching out the cart he wanted. Starting from these early sketches, Dr. Rockoff collaborated with the Harloff Company, a medical supply manufacturer based in Colorado. This fall saw the debut of his vision. The Start Cart, which Dr. Rockoff perfected for use in Children’s operating rooms, consolidates the supplies and disposal containers, features an adjustable worktop and attached needle disposal bin, and can be wheeled to each patient’s bed or operating table, offering a safer and more efficient system for handling needles and catheters. The cart is now part of the Harloff catalog and has generated considerable interest and resulting sales.

Shire options sickle cell technology
Shire Pharmaceuticals, a global specialty biopharmaceutical company with a strong business model around developing therapeutics for orphan diseases, optioned the rights to a hemoglobin disorder technology invented by Stuart Orkin, MD, chairman, Department of Pediatric Oncology at Children’s/Dana Farber and an HHMI Investigator. Dr. Orkin developed a nucleotide-based therapeutic for sickle cell anemia and other major hemoglobin disorders that up regulates fetal hemoglobin (HbF, α2γ2) in adult red cells. There is no cure for sickle cell disease, an orphan disease affecting 72,000 individuals in the United States alone.

Dr. Orkin has a long history of studying transcriptional regulation of blood stem cell progenitors. As humans develop from embryos to adults, tight regulation of globin genes results in the expression of successive forms of globin molecules. Mutations in the coding or regulatory sequences of globin genes result in the major clinical disorders, sickle cell anemia and the β-thalassemias. With Vijay Sankaran, MD, PhD, he discovered...
that RNAi knock-down of BCL11A, a zinc-finger repressor of the γ-globin genes, led to reactivation of expression of HbF. Therapeutic RNAi technology has been shown to be promising but notoriously difficult to deliver to the target site.

To solve the delivery issue, Shire, as part of an active collaboration with the Orkin lab, has agreed to make a proprietary antisense oligonucleotide formulation and delivery technology available to Dr. Orkin’s lab in the effort to create a therapeutically relevant molecule. Shire will also complement the Orkin group’s deep disease-specific knowledge with its complementary drug development expertise and an opportunity to bring the technology to the clinic.

**Children’s enters multi-party collaboration to use protein structure to inform vaccine design**

Pioneer in structural biology Stephen Harrison, PhD, chief of Children’s Division of Molecular Medicine and an HHMI investigator, is working with investigators from Brandeis University and Novartis Vaccines and Diagnostics to develop new ways to design vaccines based on the understanding of protein structure. The collaboration, which arose from recent improvements in protein structure determination using electron cryomicroscopy, tests a new platform approach for rational vaccine design. If validated by these studies, this structure-based approach could become a powerful strategy for development of novel and potent vaccines.

**Axonis enters option agreement for spinal cord injury treatment**

Axonis, a startup company founded by Robert Yant, Jr., a member of the national board of directors of the Christopher and Dana Reeve Foundation, entered into an option agreement with Children’s for technologies that promote the regeneration of nerves to treat spinal cord injuries. Zhigang He, PhD, research associate in the Department of Neurology at Children’s, has developed a technology to promote the regeneration of injured nerves by inhibiting an enzyme called PTEN (a phosphatase and tensin homolog) and activating mTOR, a regulator of cell growth.

PTEN is in the mTOR pathway and inhibits mTOR thereby stopping cell growth. As reported in Nature Neuroscience in September, Dr. He and colleagues at Children’s, UC Irvine and UC San Diego used this technology in rodents after spinal cord injury, and PTEN deletion in the rodents resulted in nerve cell proliferation and regeneration of the neural connections. This agreement also includes another unpublished neuron regeneration technology developed by Dr. He and Axonis plans to fund his laboratory at Children’s to develop these regeneration technologies for functional repair of CNS injury in adults.

**Lundbeck options and sponsors research to improve epilepsy treatment**

Children’s entered into an exclusive option and sponsored research agreement with Lundbeck, Inc. for a technology to reduce the retinal and CNS adverse effects of vigabatrin with NKCC1 inhibitors, invented by Frances Jensen, MD, senior associate in Medicine and director of Epilepsy Research. Lundbeck’s drug Sabril® (vigabatrin) is an inhibitor of GABA transaminase and an anticonvulsive drug that has FDA approval for treatment of certain forms of epilepsy. However, vigabatrin can cause serious side effects, including irreversible retinal toxicity, bilateral visual field narrowing and white matter abnormalities, resulting in one of the most restrictive Risk Evaluation and Mitigation Strategies required by the FDA. Dr. Jensen hypothesized that bumetanide and other NKCC1 inhibitors can reduce the adverse effects of vigabatrin on the retina and brain tissue. This sponsorship will fund the development of bumetanide in combination with vigabatrin for treatment of
seizures. If successful, the FDA may approve the combination treatment for additional types of epilepsy.

Lundbeck sponsors research to study vigabatrin’s effects on retinas

Lundbeck Inc. and Children’s entered into a sponsored research agreement to support Anne Fulton, MD, senior associate in Ophthalmology, to study the effects of vigabatrin on the retina. Vigabatrin is a highly effective treatment for infantile spasms and seizures that can cause irreversible loss of peripheral vision in approximately 30 percent of patients. Dr. Fulton has observed that patients being treated with vigabatrin exhibit retinal function similar to that in children with mitochondrial disorders. Building on these observations, this study aims to look at the effects of vigabatrin on the retinas of rats, testing the hypothesis that the basis for the retinal and visual dysfunction effects of vigabatrin are due to injury to the mitochondria. Dr. Fulton and her team hope to get a better understanding of how vigabatrin acts on the retina and the retinal neurons.

Collaboration with Proteus S.A. to develop novel, long-acting local anesthetic

Children’s Hospital Boston signed a deal with Chilean company Proteus S.A. to develop NeoSaxitoxin (NeoSTX) as a local anesthetic, with the goal of moving it further down the path of regulatory approval and clinical adoption. NeoSTX is a Site 1 sodium channel blocker derived from freshwater micro-algae. As part of the deal, Children’s investigators will carry out preclinical and early-stage clinical trials, while Proteus will provide the compound and additional expertise and data.

Tens of millions of patients undergo surgical procedures requiring local anesthesia each year. Current local anesthetics and analgesics based on opioids have a short duration of action, leaving patients to cope with postoperative pain, and cause substantial side effects, such as cardiac adverse effects, nausea, sedation, shallow breathing, confusion and itchiness.

Charles Berde, MD, PhD, chief of the Division of Pain Medicine, and Daniel Kohane, MD, PhD, a clinician-researcher in Critical Care Medicine, have been working to change the standard of care for local anesthesia. In an extensive body of work in animals, they have shown that by combining Site 1 sodium channel blockers with local anesthetics, a nerve blockade can be prolonged to periods of two to four days with minimal local or systemic side effects.

NeoSTX’s chief analgesic ingredient is a saxitoxin produced by the algae. It is part of a larger class of anesthetics based on toxins from marine organisms, which also includes tetrodotoxin, derived from the puffer fish venom.

These channel blockers have advantages over existing analgesics and anesthetics because they do not cause effects mentioned above, are not addictive, and do not cross the blood-brain barrier, thereby avoiding the risk of seizures occasionally seen with existing local anesthetics. They also cause minimal local tissue reaction, thereby avoiding the local toxicity to nerves and muscles seen with high concentrations of existing local anesthetics.

The collaboration with Proteus will help overcome a major obstacle to bringing this technology to market: the synthesis and purification of the chemical compound. Chile’s shore line frequently faces problems with Red Tide, where the harmful toxin released by the algae is a type of saxitoxin. The company learned from this problem and used their expertise in saxitoxin chemistry to develop novel culture methods for freshwater micro-algae and perfected techniques for extraction and purification of the active compound, which led to a new STX formulation known as NeoSTX.

Proteus conducted preliminary clinical tests of NeoSTX solutions in healthy volunteers in Chile and saw exciting results: use of NeoSTX led to more prolonged skin numbness compared to bupivacaine (another commonly used local anesthetic), was well tolerated and no local or systemic toxicities were observed. Compared with patients receiving bupivacaine-based local anesthesia, patients receiving NeoSTX were less likely to experience severe pain, were more likely to experience complete pain relief and recovered approximately two days sooner.

The hope is that this collaboration will bring a new class of anesthesia compounds to market and fundamentally improve the standard of care worldwide.
ParinGenix sponsors a drug clinical trial for protein losing enteropathy

Research by Doff McElhinney, MD, associate in Cardiology, focuses on improving the health of children undergoing catheterization procedures. These interests have afforded him a number of opportunities to work with and study a variety of cardiac devices and implants.

Dr. McElhinney is the principal investigator on a clinical trial sponsored by ParinGenix Inc., to study a new drug treatment for pediatric patients with protein losing enteropathy (PLE) associated with single ventricle Fontan palliative surgery. Heparin has been shown to improve symptoms in patients with PLE, but these children face a high risk of bleeding due to the blood thinning effects of heparin. However, the drug being studied in the clinical trial, ODSH (2-0, 3-0 desulfated heparin) has only 5 percent of the anticoagulation effects of heparin and at the doses planned for the study, the risk of bleeding is none or minimal. In previous studies, ODSH has been shown to stop the gastrointestinal protein loss in an animal model of PLE.

This study aims to look at the safety and effectiveness of ODSH in children with PLE. Dr. McElhinney is one of four principal investigators participating in this study in collaboration with ParinGenix nationally. He plans to enroll three patients for the study at Children’s.

Milk allergy clinical study with Xolair®

Milk allergy is one of the most common food allergies in children today. Although cows’ milk is the usual cause of the allergic reaction, milk from other animals can also cause a reaction. Approximately 2.5 percent of children younger than 3 are allergic to milk in the United States, and nearly all infants who develop this allergy do so in their first year of life. Dale Umetsu, MD, PhD, senior associate in Medicine in the Division of Immunology and professor of Pediatrics at Harvard, is studying the medication Xolair® (omalizumab), provided by Genentech, in conjunction with a gradually escalating dosage of milk to see if patients with severe milk allergy can be desensitized to milk. Xolair® is an antibody therapeutic that helps to block IgE, which is responsible for allergies and allergic symptoms. Although the study is still ongoing, the outcome of some patients enrolled has been very promising. The success of this study could translate into a treatment for children suffering from milk allergies and could lead to similar food allergy studies in the future.

Clinical trial for treatment of Rett syndrome

While Rett syndrome, a neurological disorder affecting one in 10,000 children and almost exclusively girls, is thought to be an irreversible neurodevelopmental disease, recent studies have shown that the disease may be treatable and that the gene that regulates the hormone/growth factor IGF-1 is disabled in patients with the disease. This suggests that by correcting that gene disability, the disease can, in fact, be treated and hopefully reversed. One treatment strategy is to introduce more of the IGF-1 hormone into the Rett syndrome patients.

As Director of Children’s Rett Syndrome Program and Assistant in Neurology, Omar Khwaja, MD, PhD, is one of the world’s expert clinical researchers studying the condition. Dr. Khwaja is launching a clinical study in which he will introduce a clinically approved form of IGF-1 to Rett syndrome patients, thereby aiming to reverse the symptoms of the disease. For this study, he is using funds from several foundation grants (Autism Speaks, International Rett Syndrome Foundation and Harvard Catalyst), and is working with Ipsen U.S., who is providing IGF-1 for the study.

Cystic Fibrosis Center conducts clinical trials to improve cystic fibrosis treatments

In FY10, Children’s Cystic Fibrosis Center conducted 11 observational and interventional clinical research studies including quality-of-life surveys, nutritional supplementation and anti-infective and anti-inflammatory treatments. An increasing area of interest within the cystic fibrosis community is CFTR modulation—the modulation of the defective CFTR gene and its protein product—where therapies are designed to treat the basic defect in cystic fibrosis. Children’s center is currently participating in all three CFTR modulation studies supported by the Cystic Fibrosis Foundation Therapeutics Development Network, which is sponsored by Vertex Pharmaceuticals and PTC Therapeutics.
## Appendix 1 Summary of Technology Transfer Activity FY2005 - FY2010

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APPENDIX 2  SIX YEAR TREND OF TECHNOLOGY TRANSFER ACTIVITY

GROSS REVENUES ($M)

PROVISIONALS FILED

INVENTION DISCLOSURES

PCTS FILED

FOREIGN APPLICATIONS FILED

U.S. PATENTS FILED

APPENDIX 2  SIX YEAR TREND OF TECHNOLOGY TRANSFER ACTIVITY

GROSS REVENUES ($M)

PROVISIONALS FILED

INVENTION DISCLOSURES

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FOREIGN APPLICATIONS FILED

U.S. PATENTS FILED

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Christopher Walsh, MD, PhD, is the chief of the Division of Genetics and an HHMI Investigator at Children’s Hospital Boston. Dr. Walsh earned his BS degree at Bucknell University in chemistry and his PhD (1983) in neurobiology and his MD (1985) at the University of Chicago. He completed his residencies at Massachusetts General Hospital and then became a postdoctoral fellow at Harvard Medical School. During his fellowship, he performed some of the first direct studies of cell lineage and cell migration in the developing brains of mammals, specifically in the cerebral cortex, which is essential for memory, thinking, consciousness and other complex functions. Dr. Walsh established his own lab in 1993 to identify and analyze the genes that regulate the development and normal function of the human cerebral cortex.

We sat down with Dr. Walsh to discuss how the Division of Genetics works to improve treatments for children with genetic conditions.

**What role will genetics have in the future of health care?**

It has been said for a long time—since the human genome project—that genetics will permeate all aspects of health care. And some people might say we’ve been slower to deliver on those promises than we should have been. But I think in the field of pediatric medicine, genetics has had, and will have, an extremely big impact because almost all aspects of pediatric medicine are about genetics. Kids are usually healthy, and when they aren’t healthy, they usually have a rare disease or a genetic disorder that predisposes them in a very strong way to a specific illness. So genetics will be critical for diagnosis. It’s already critical for classification and risk assessment. It’s increasingly guiding our therapy, too. Genetics is all about discovering mechanisms, and mechanisms are guides to therapy. That wave of translation of genetics into therapies is really starting to hit.

**How is Children’s Division of Genetics helping make this future vision a reality?**

I see three ways in which our division is contributing. First, we’re pioneering the use of full exome and whole genome sequencing to understand the root causes of childhood disease. Second, we’re translating those genetic advances into a partnership with patients through the Gene Partnership, in which geneticists Ingrid Holm, MD, MPH, and Louis Kunkel, PhD, have leadership roles. Third, we’re translating genetic advances into the improved clinical care of patients by developing specialty clinics devoted to individual rare diseases where we can house clinical trials in gene-specific ways.

**Children’s cares for many children with rare diseases for whom treatment options are limited. How is your research and that of your colleagues in the division helping these children?**

Our division cares for some children with rare diseases that are treatable. We have had a Phenylketonuria (PKU) clinic at Children’s for 30 years. Here, we can take a child with an incurable lethal illness, put them on the right diet and give them a long productive life. We follow people in the clinic who are now lawyers and policemen. And now we have a maternal PKU clinic to help patients have healthy children. So we have already pioneered ways to treat and follow these patients, monitor their cognitive function, know when to change approaches and know when they need to be hospitalized.

We’ve developed expertise in treating rare diseases, including those that affect the brain. We’re now trying to leverage that expertise to treat an increasing number of rare diseases that we thought were not treatable—but now we think might be—by using small molecules and other drugs. We have joint clinics with many departments at Children’s and we’re starting new clinics as the opportunity arises, such as our Fragile X clinic. We’ll continue to start new clinics as we see opportunities to develop treatments for rare diseases and provide a platform on which pharmaceutical companies can work with us to test new treatments.

We also want to improve the diagnosis rate for kids with rare disease. Forty percent of kids currently leave our clinic without a specific genetic diagnosis and we want to decrease this percentage and provide a specific genetic diagnosis. We think that many of these kids probably have a disease that we already have understood on a scientific level but have not yet been able to translate into an accurate clinical diagnosis because the diagnosis is not always widely available, paid for by insurance or practical. The newest DNA sequencing technologies allow us to make diagnosis practical and useful in the clinic, and will allow us to recognize that a few of the kids who were considered untreatable may actually be treatable with present day technology. So it really is a combination of building opportunity for treatment and trying to find ways of directing as many kids as possible to the proper treatment.
CHILDREN’S NEW SCIENCE AND INNOVATION BLOG LAUNCHED IN SEPTEMBER OF 2010

Called Vector, it reports on and discusses science and innovation in pediatric and adult medicine, from the bench to the bedside. Vector, co-run by the Technology and Innovation Development Office and Public Affairs and Marketing department, covers topics such as scientific advances, clinical innovations, drugs and diagnostics, emerging trends in biomedicine, collaboration with industry, personal stories of discovery and ethics and policy. Geared toward an audience of biomedical researchers and opinion leaders, health care professionals, industry, investors, donors, government, media and interested laypeople, Vector aims to be a leading voice in clinical care and research.

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