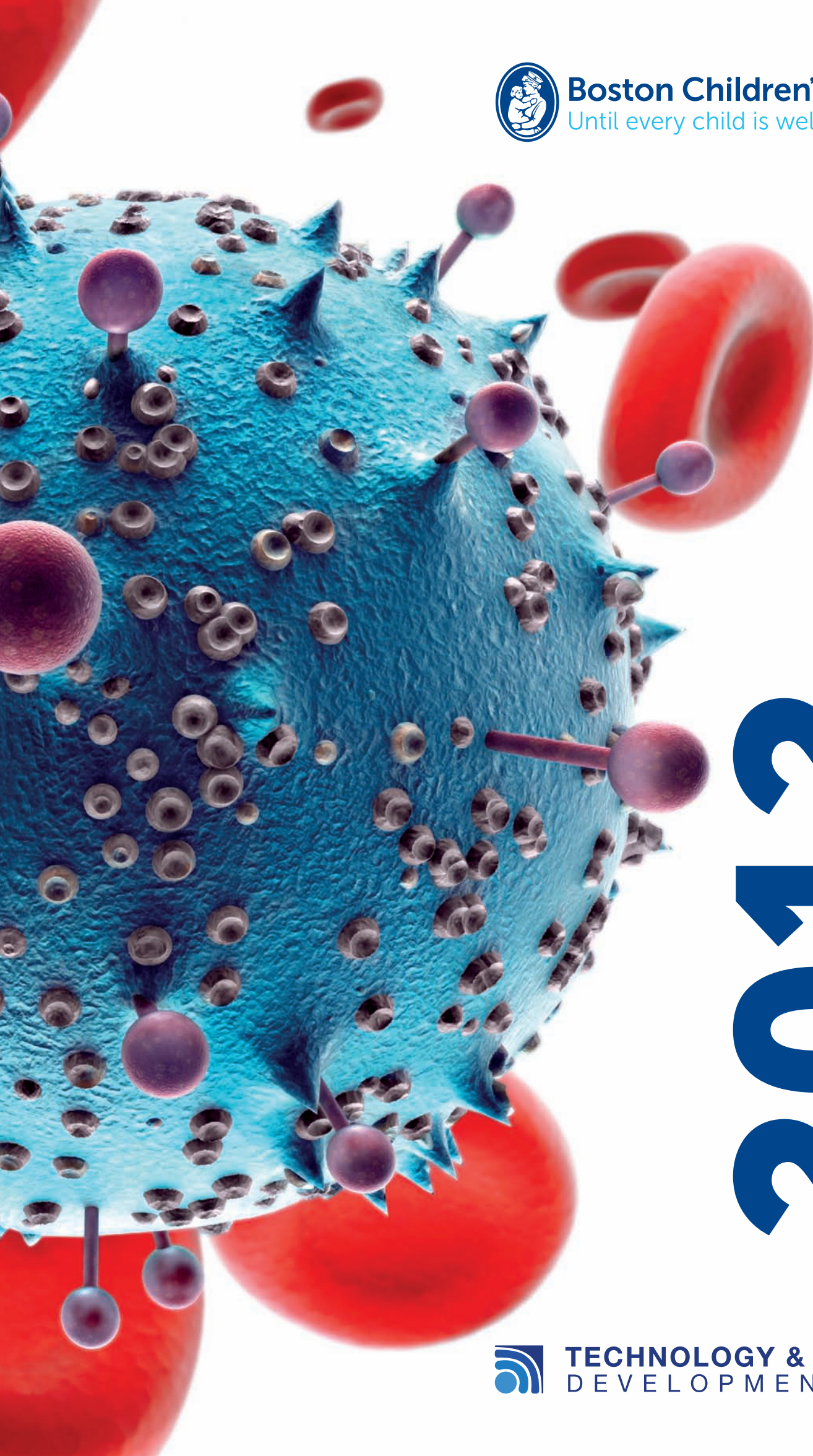




**Boston Children's Hospital**  
Until every child is well<sup>SM</sup>



# 2012

## Annual Report



**TECHNOLOGY & INNOVATION**  
DEVELOPMENT OFFICE



# Technology & Innovation Development Office Team



## Leadership

Erik Halvorsen, PhD  
*Executive Director of TIDO;  
Managing Partner, Technology  
Development Fund*

Jane Amara, PhD  
*Associate Director,  
Licensing & Operations*

## Patents & Licensing

### Licensing Managers

Alexander Augst, PhD  
*Licensing Manager*

Connie Caron, MBA,  
Patent Agent  
*Licensing Manager*

Ryan Dietz, JD  
*Licensing Manager*

Rajinder Khunkhun, JD  
*Licensing Manager;  
Patent Specialist*

Abbie Meyer, PhD  
*Licensing Manager*

Alan Yen, PhD  
*Licensing Manager*

### Contracts & Intellectual Property

Christopher Geehan, JD  
*Contracts & Intellectual  
Property Specialist*

Stanley Tabi, JD  
*Patent Coordinator*

Karen Lai  
*Contracts Specialist*

## Business Development & Marketing

Maude Tessier, PhD  
*Assistant Director, Business  
Development & Strategic Initiatives*

David Altman  
*Senior Marketing &  
Communications Specialist*

## Technology Development Fund

Monique Yoakim-Turk, PhD  
*Partner, Technology Development  
Fund; Associate Director of TIDO*

Meridith Unger, MBA  
*Principal, Technology  
Development Fund; Associate,  
Business Planning & Analysis*

## Clinical Trials Office

Fernando Vallés, JD  
*Senior Contracts Associate*

Elizabeth (Lianne) Cleary, JD  
*Senior Contracts Associate*

## Business & Administration

Sharon Jordan-Prioleau, MBA  
*Business Manager*

Lisa Pight  
*Financial Assistant*

Katherine Fox  
*Administrative Associate*

## About Boston Children's Hospital

Boston Children's Hospital is home to the world's largest research enterprise based at a pediatric hospital, with \$272 million in research expenditures annually. More than 1,100 scientists, including nine members of the National Academy of Sciences, 11 members of the Institute of Medicine and 12 members of the Howard Hughes Medical Institute, comprise our research community. The Technology & Innovation Development Office (TIDO) manages and develops Boston Children's Hospital's intellectual property, innovations and technologies for further investment and development by industry partners to bring new therapies, diagnostics and devices to market to benefit patients worldwide.

- **\$272M NIH and Industry Research Funding**
- **\$10.3M Gross Licensing Revenue**
- **\$7.7M Net Licensing Revenue – up 3%\***
- **30 Licenses and Options – Up 76%\***
- **55 Clinical Trial Agreements – Up 28%\***
- **144 Invention Disclosures – Up 8%\***

\* over FY11



### Note from the Executive Director

Erik Halvorsen, PhD

Five years ago when I joined Boston Children's Hospital, I was asked to take a fresh look at how a successful technology development and licensing office should be organized to serve the mission and meet the challenges. This was during a time when the healthcare business climate was increasingly dynamic and volatile, and the status quo academic "tech transfer" structure was quickly becoming a relic.

At its core, Boston Children's has first-class researchers, cutting-edge technologies, and world-renowned clinical expertise—a very good base to work with. The market, however, was demanding novel, flexible, creative, and at times complex partnering strategies that required forward-thinking institutions and their leadership to adapt or become irrelevant. When your mission is to translate your research discoveries and clinical innovations into new products that can improve the lives of children—you quickly learn to adapt.

By creating specialized functions including business development, market analysis and our Technology Development Fund, as well as the move of the Clinical Trials Office to TIDO, we have been able to fully support our core licensing and technology commercialization activity.

By making these changes, Boston Children's has become the partner of choice for companies looking to collaborate on projects from early-stage laboratory research through clinical trials.

In FY12, TIDO hit an all-time high in the number of executed licensing and research agreements, and our net licensing income has increased for the first time in five years. Since FY09, we have seen a 150% increase in industry collaborations and some novel partnerships with innovative structures that have us excited about the future of TIDO. These unique relationships include two collaborations with Pfizer CTI (page 8). We are also proud to have licensed two Technology Development Fund projects to newly founded companies in FY12: the Pediatric Vision Scanner to REBIScan (page 7) and the MedWatcher and HealthMap platforms to Epidemico (page 7), with two more transactions in active negotiations.

Looking forward, TIDO will continue to bolster the momentum created in FY12 to further build novel alliances with industry to fulfill our mission of translating the excellence of laboratory research and clinical care at Boston Children's into lifesaving biomedical products, devices and procedures for the public benefit.

## Fiscal Year 2012 Summary

Invention Disclosures	144
Patent Applications Filed	173
Provisional	65
PCT	35
US	59
Foreign	14
Patents Issued	52
US	32
Foreign	20
Licenses & Options Executed	30
Gross Revenue	\$10,320,164
Net Revenue (less external institutes)	\$7,720,689
Revenue from New Licenses and Options	\$128,525

## Fiscal Year 2012 Agreements

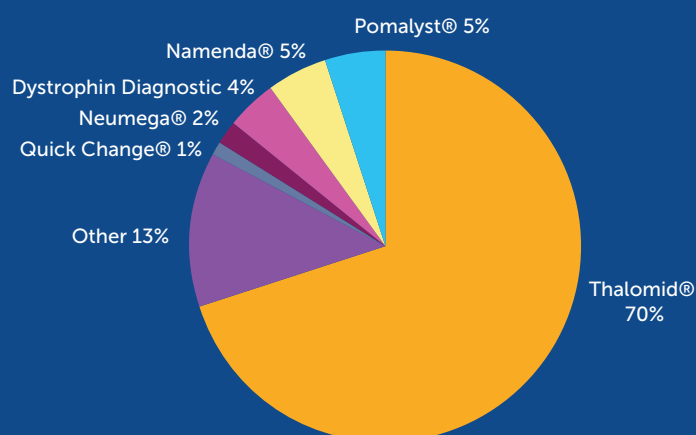
Exclusive Licenses	8
Non-Exclusive Licenses	19
Options	3
Total	30
Corporate Sponsored Research/Collaborations	20
Clinical Trials	55
Material Transfer	1108
Confidentiality	182
Amendments	8
Agreements Involving the Receipt of Equity	2
Inter-Institutional Invention Administration	11
CRO	21
Other	13

## Invention Management Activity

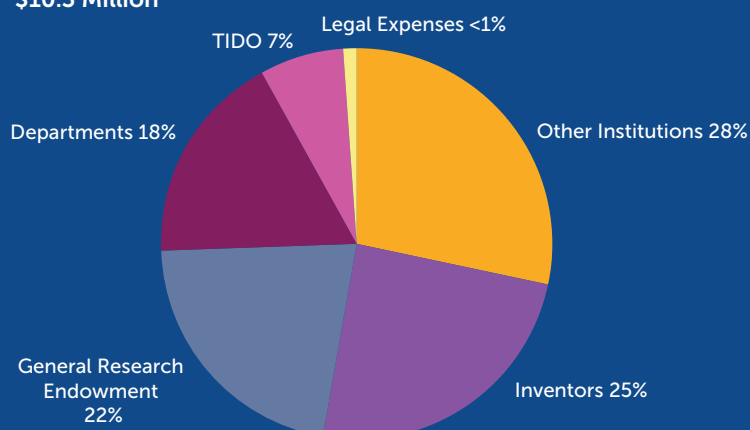
Inventions under Active Management	794
Technology Development Funded Inventions	19

Current Licenses	301
Issued US Patents	450
Issued Foreign Patents	640

## Sources of Licensing Revenue



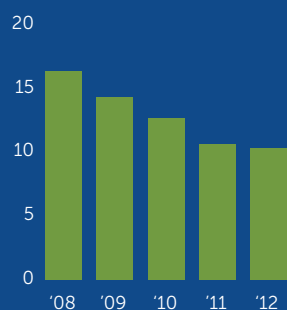
## Gross Licensing Revenue Distribution: \$10.3 Million



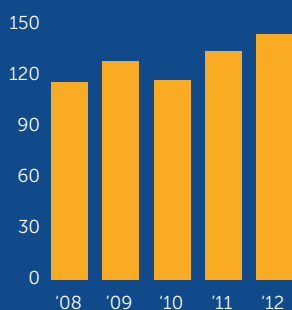
## Issued US Patents

Lead Inventor	Issue Date	Patent Number	Application Title
Rao, Anjana	11/1/11	8,048,864	Regulators of NFAT and/or store-operated calcium entry
Lock, James	12/6/11	8,070,800	Transcatheter heart valve prostheses
Imam, Farhad	12/13/11	8,078,261	Light-guided transluminal catheter
Frank, Markus	12/13/11	8,076,091	Gene encoding a multidrug-resistance human P-glycoprotein homologue on chromosome 7P15-21 and uses thereof
Levy, Hara	12/20/11	8,080,394	Method for determining predisposition to pulmonary infection
Mulligan, Richard	1/3/12	8,088,585	Methods for purifying hematopoietic stem cells
Lock, James	1/10/12	8,092,524	Transcatheter delivery of a replacement heart valve
Zon, Leonard	1/24/12	8,101,412	Method of enhancing proliferation and/or hematopoietic differentiation of stem cells
Clapham, David	2/7/12	8,110,668	Sperm-specific cation channel, CATSPER1, and uses therefor
Atala, Anthony	3/6/12	8,128,707	Bladder reconstruction
Zon, Leonard	3/13/12	8,133,974	Ferroportin1 nucleic acids, proteins, antibodies and methods
Clapham, David	3/20/12	8,137,918	Sperm-specific cation channel, CATSPER1, and uses therefor
D'Amato, Robert	3/27/12	8,143,283	Methods for treating blood-borne tumors with thalidomide
He, Zhigang	3/27/12	8,142,782	EGFR inhibitors promote axon regeneration
Zetter, Bruce	4/3/12	8,148,086	Methods to predict and prevent resistance to taxoid compounds
D'Amato, Robert	4/10/12	8,153,806	Synthesis of 4-amino-thalidomide enantiomers
Klagsbrun, Michael	4/10/12	8,153,585	Peptide antagonists of vascular endothelial growth factor and methods of use thereof
Zon, Leonard	5/1/12	8,168,428	Method to modulate hematopoietic stem cell growth
Lieberman, Judy	5/1/12	8,168,601	Method of delivering RNA interference and uses thereof
Rogers, Gary	5/29/12	8,186,354	Orthotic device for preventing and/or correcting deformational posterior plagiocephaly
Clapham, David	7/3/12	8,211,666	Sperm-specific cation channel, CATSPER1, and uses therefor
Springer, Timothy	8/14/12	8,241,627	Modified polypeptides stabilized in a desired conformation and methods for producing same
Springer, Timothy	8/21/12	8,247,185	Conformation specific antibodies
Folkman, Judah	9/25/12	8,273,383	Methods and compositions for treatment of preeclampsia

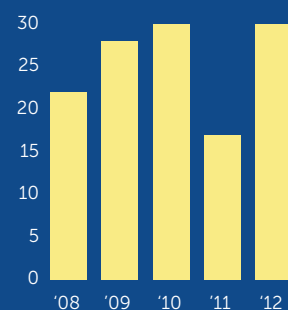
Gross Revenue (\$M)



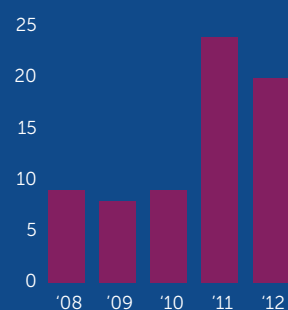
Invention Disclosures



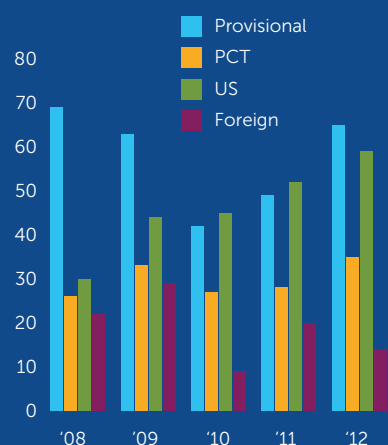
Licenses &amp; Options Executed



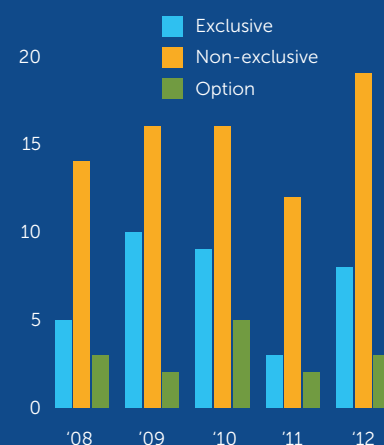
Corporate Sponsored Research &amp; Collaboration Agreements



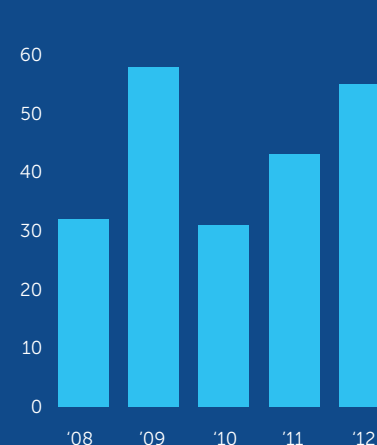
New Patents Filed



Breakdown of License &amp; Option Agreements



Clinical Trial Agreements



### Issued Foreign Patents

Lead Inventor	Issue Date	Patent Number	Country	Application Title
Moses, Marsha	10/21/11	4847873	Japan	Methods for diagnosis and prognosis of cancers of epithelial origins
Hirschhorn, Joel	11/3/11	2005286944	Australia	Compositions and methods for obesity screening using polymorphisms in NPY2R
Springer, Timothy	11/3/11	2005215024	Australia	Conformation specific antibodies
Wagner, Denisa	11/17/11	2006257073	Australia	ADAMTS13-comprising compositions having thrombolytic activity
Lock, James	11/23/11	1,765,453	EPO*	Cannula for <i>in utero</i> surgery
Lieberman, Judy	12/8/11	2005277547	Australia	Methods of delivering RNA interference and uses thereof
Atala, Anthony	12/16/11	HK1099528	Hong Kong	Augmentation of organ function
Atala, Anthony	1/6/12	4897176	Japan	Methods and compositions for organ decellularization
Lieberman, Judy	1/13/12	4903146	Japan	Methods of delivering RNA interference and uses thereof
Atala, Anthony	2/2/12	2008258204	Australia	Methods of isolation, expansion and differentiation of fetal stem cells from chorionic villus, amniotic fluid and placenta and therapeutic uses thereof
Carroll, Michael	2/17/12	200580012909.8	China	Natural IgM antibodies and inhibitors thereof
D'Amato, Robert	3/1/12	2010200186	Australia	Methods and compositions for inhibition of angiogenesis
Satchi-Fainaro, Ronit	3/6/12	2,480,666	Canada	TNP-470 polymer conjugates and use thereof
Carroll, Michael	3/8/12	2005219839	Australia	Natural IgM antibodies and inhibitors thereof
Lieberman, Judy	4/25/12	1789447	EPO	Methods for delivering RNA interference and uses thereof
Moses, Marsha	5/17/12	2005207318	Australia	Methods for diagnosis and prognosis of cancers of epithelial origin
Orkin, Stuart	5/30/12	2011/01964	South Africa	Modulation of BCL11A for treatment of hemoglobinopathies
Moses, Marsha	6/1/12	5006802	Japan	CYR61 as a urinary biomarker for breast and ovarian human cancers
Snyder, Evan	7/24/12	2,339,411	Canada	Engraftable human neural stem cell lines
Springer, Timothy	8/3/12	5054385	Japan	Conformation specific antibodies (LFA1)
D'Amato, Robert	8/17/12	5066505	Japan	Synthesis of 3-amino-thalidomide and its enantiomers
Folkman, Judah	8/29/12	200410085778.3	China	Angiostatin and method of use

\*France, Germany, Ireland, Israel, Luxembourg, Monaco, Switzerland, Great Britain



# Technology Development Fund FY12 Portfolio

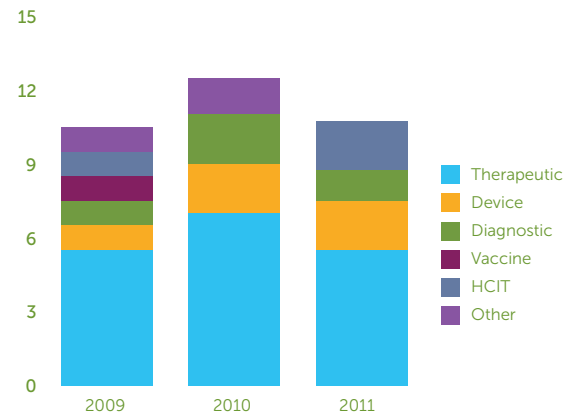
Boston Children's Hospital is proud to announce the selection of six projects for funding in its fourth Technology Development Fund (TDF) cycle in 2012:

1. **Bioenhanced repair of ACL injuries for the skeletally immature patient** – *Martha Murray, MD, Orthopedic Center*
2. **Development of a multiple antigen presentation system (MAPS) vaccine platform** – *Richard Malley, MD, Division of Infectious Diseases*
3. **Contact lens drug delivery platform** – *Daniel Kohane, MD, PhD, Department of Anesthesiology*
4. **Inhibiting sepiapterin reductase for treating pain and inflammation** – *Clifford Woolf, MD, PhD, F.M. Kirby Neurobiology Center and Program in Neurobiology*
5. **Drug screening of an acetyl transferase as a novel drug target in neuroblastoma** – *John Powers, PhD, Department of Hematology/Oncology*
6. **Communicating audiological results: A new and improved software tool** – *Brian Fligor, ScD, Department of Otolaryngology and Communication Enhancement*

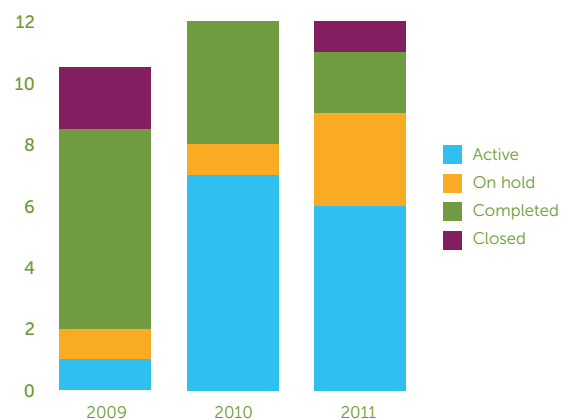
In addition to funding the new FY12 projects, TDF continued to manage its existing portfolio of technologies spanning multiple sectors. As of September 2012, 13 of the 35 TDF-funded projects since TDF's start in 2009 had been completed. Two completed projects were licensed to NewCos in 2012: the Pediatric Vision Scanner to REBIScan (page 7) and MedWatcher to Epidemico (page 7), while two other projects are in active discussions with industry partners. Fourteen of our active projects have progressed on their development plans and received mentoring from our advisory board and support from our network of CROs and engineering/design firms.

TDF's investment to date of \$3.7M over three years has led to approximately \$6.8M of follow-on funding from government, foundation and philanthropic grants. To further strengthen the program, TDF is excited to welcome Patrice Milos, PhD, Boston site head and precision medicine lead, Pfizer CTI, to its advisory board.

## Funded Projects



## Portfolio Status as of 9/30/12



## Selected Agreements

### Myriad Genetics licenses cancer treatment prediction technology

Myriad Genetics has exclusively licensed a treatment response-prediction technology to help clinicians better tailor treatment to cancer patients. This innovation, co-developed by researchers at Boston Children's Hospital, Brigham and Women's Hospital, Dana-Farber Cancer Institute and Technical University of Denmark, is based on understanding the relationship between DNA repair in cancer cells and sensitivity of cancer cells to chemotherapy treatment. The technology uses genomic signatures indicative of defective DNA repair to predict whether a patient will respond to chemotherapy treatments such as Cisplatin. Myriad aims to develop the prediction technology into a widely available laboratory test.

### Epidemico licenses HealthMap and MedWatcher technologies to expand population health monitoring

Boston Children's and Epidemico ([www.epidemico.com](http://www.epidemico.com)), a Boston-based healthcare analytics startup company, entered into an exclusive license to commercialize the MedWatcher and HealthMap technologies created by a research group led by John Brownstein, PhD, in the Boston Children's Hospital Informatics Program (CHIP). HealthMap and MedWatcher harness the power of the Internet and crowdsourcing to monitor disease, report adverse events, and disseminate health information. Epidemico will develop HealthMap and MedWatcher into commercial products and services for the healthcare industry, government agencies and consumers.

### Collaboration with Seaside Therapeutics to examine fragile X syndrome and autism

Researchers at Boston Children's and Seaside Therapeutics have entered into a research agreement to expand the understanding of fragile X syndrome and autism. Isaac Kohane, MD, PhD, chair of CHIP, and Louis Kunkel, PhD, director of the Program in Genomics, are examining the effect of a new class of fragile X syndrome medication, developed by Seaside Therapeutics, on gene expression patterns in patients. The study will lead to a better understanding of the medication's impact and to the identification of biomarkers that may improve the efficacy of the medication.

### REBIScan exclusively licenses Pediatric Vision Scanner for early detection of amblyopia

REBIScan has exclusively licensed the Pediatric Vision Scanner (PVS), developed in Boston Children's Department of Ophthalmology, for early detection of amblyopia ("lazy eye").

If amblyopia is caught early – ideally, before age 3 – it can easily be treated by patching the fellow eye, requiring the child to use and strengthen the weaker eye. If amblyopia goes unnoticed, the weak eye can slowly go blind because the brain starts ignoring its visual input. Once children reach 8 to 10 years of age, their loss of vision due to amblyopia often cannot be restored with any form of treatment.

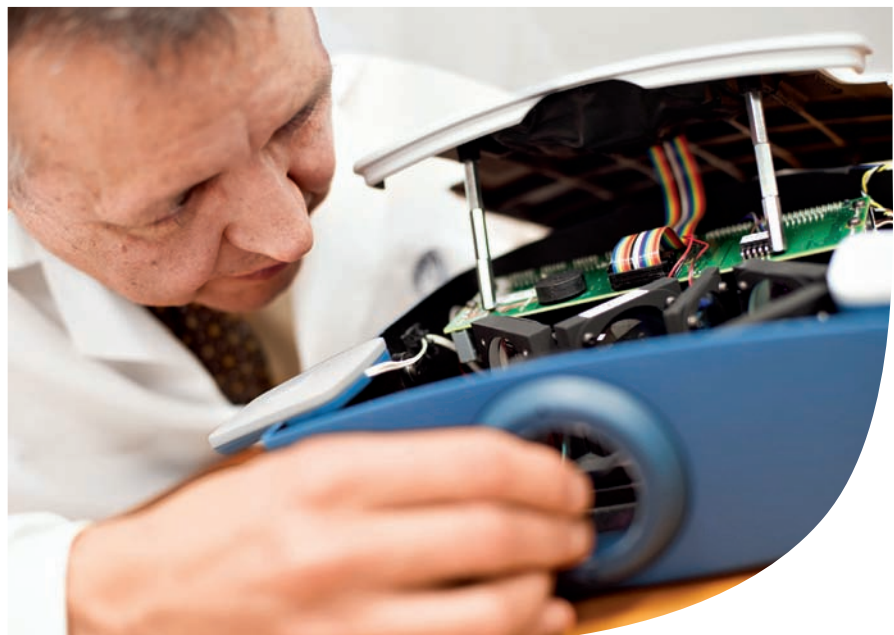
David Hunter, MD, PhD, ophthalmologist-in-chief, has developed a new, easy-to-use device for the early detection of amblyopia. This invention will enable pediatricians and community programs to test for amblyopia in preschool-age children as part of a routine checkup. Dr. Hunter developed the PVS with help from Boston Children's Technology Development Fund as well as outside funding through the National Eye Institute and private donors.

REBIScan was founded in 2009 to further develop the PVS and to obtain FDA clearance using funding from a Small Business Innovation Research grant and private investors. REBIScan expects the first devices to enter the market in mid-2013.

### Collaboration with Roche to screen and identify treatments for autism

Roche has brought together three Harvard-affiliated organizations in a collaboration to identify new drugs for the treatment of autism spectrum disorders (ASDs). Led by Mira Irons, MD, associate chief of the Division of Genetics, investigators at Boston Children's will obtain skin biopsies from patients with specific genetic conditions causing ASDs. These samples and associated clinical data will be provided to the Harvard Stem Cell Institute, where scientists will isolate fibroblasts and reprogram them into induced pluripotent stem cells (iPSCs). Researchers at Harvard Medical School will differentiate the iPSCs into lines of functional neurons that will be used to identify potential therapeutic targets and, eventually, as a platform for testing candidate drugs.

"Despite a high unmet need, ASD is characterized by a lack of suitable cellular models for drug development," notes Anirvan Ghosh, PhD, head of Central Nervous System Discovery at Roche. "Our intention is to build cell lines from ASD patients to identify signaling and synaptic defects associated with ASD, and to develop drug screening platforms. This should greatly facilitate the discovery of the next generation of drugs to fight the condition."



David Hunter, MD, PhD, with the Pediatric Vision Scanner

## Selected Agreements

### **CoStim Pharmaceuticals sponsors research to identify therapeutic monoclonal antibodies to treat cancer**

Dale Umetsu, MD, PhD, director, Boston Children's Hospital Asthma Center, and Rosemarie DeKruyff, PhD, staff scientist, Division of Immunology, have begun a research project sponsored by CoStim Pharmaceuticals, an MPM Capital startup company, to identify key therapeutic monoclonal antibodies in the treatment of cancer. The project is an effort to advance the technology, invented jointly by Drs. Umetsu and DeKruyff, along with colleagues at Dana-Farber Cancer Institute and Harvard Medical School. The background technology, designed to help the body's immune system attack and kill cancer cells by activating costimulatory pathways, was previously licensed to CoStim Pharmaceuticals.



*Dale Umetsu, MD, PhD*

### **Genocea Biosciences licenses pneumococcal vaccine candidates**

Infectious diseases remain an urgent and persistent global health threat in both the developed and the developing world. Scientists at Genocea Biosciences, along with Richard Malley, MD, senior associate physician, Division of Infectious Diseases, have identified promising new T cell antigen-stimulating pneumococcal vaccine candidates using Genocea's unique transformational technology. Boston Children's has licensed the rights to these candidates to Genocea Biosciences to develop next-generation pneumococcal vaccines. These discoveries are the result of collaborative research with Genocea Biosciences that was funded by the philanthropic organization PATH Vaccine Solutions.

### **Collaboration with Pfizer CTI to develop a therapeutic against bone loss**

Xi He, PhD, neuroscience research chair, is a leading expert on molecular signaling mechanisms of the Wnt family of proteins. Over the past decade, Dr. He's laboratory has identified a number of key molecules in Wnt signaling, including kinases and transmembrane receptor components, and elucidated their mechanisms of action in signal transduction. His

laboratory studies how the Wnt pathway regulates embryonic and neural development in vertebrates and how defective regulation leads to human diseases. Dr. He's project, selected by Pfizer's CTI program, aims to validate and create drug candidates for a target that Dr. He has identified as being involved in bone mass regulation.

### **Collaboration with Pfizer CTI to develop large molecule therapeutics for malignant melanoma**

The laboratory of Markus Frank, MD, staff scientist in the Division of Nephrology, focuses on the physiological and pathological roles of the human P-glycoprotein family of ATP-binding cassette (ABC) transporters. Dr. Frank's lab has identified and characterized ABCB5, expressed by cancer stem cells in human malignant melanoma, which serves as a multidrug resistance transporter in this aggressive melanoma subpopulation, conferring resistance to chemotherapy. Dr. Frank's project was selected to participate in Pfizer's CTI program to develop large molecule therapeutics for cancer in collaboration with a Pfizer scientific team.



*(Left to right) Alberto Visintin, PhD, Pfizer, Inc.; Snehal Naik, PhD, Pfizer CTI; Markus Frank, MD, Boston Children's; and Brian Wilson, PhD, Boston Children's.*



## Selected Agreements

### **Pfizer ARTS program funding to study the regulation of endothelial cell activation in the development of allograft rejection**

Boston Children's Hospital and Pfizer have entered into a research agreement to fund a two-year study conducted by David Briscoe, MD, director of the Transplant Research Program and senior associate in medicine, Division of Nephrology. Dr. Briscoe was awarded one of five Pfizer ARTS competitive grants following an independent board review. This study aims to characterize the role of DEP domain containing mTOR-interacting protein (DEPTOR) in endothelial cell activation responses and allograft rejection. DEPTOR is reported to be a negative regulator of mTOR activity in cancer cells and is hypothesized by Dr. Briscoe to inhibit allograft rejection. In this study, Dr. Briscoe will determine whether DEPTOR promotes inflammation resolution by inhibiting signaling networks in vascular endothelial cells. His laboratory plans to study the biology of DEPTOR in human endothelial cells and to create mouse models to study DEPTOR in the development of allograft rejection.



David Briscoe, MD



Clifford Woolf, MD, PhD

### **Collaboration with GlaxoSmithKline to study potential therapy for cough**

As part of the GlaxoSmithKline (GSK)/Harvard Stem Cell Institute alliance, GSK has entered into a collaborative sponsored research agreement with Boston Children's to fund a study by Clifford Woolf, MD, PhD, director of the F.M. Kirby Neurobiology Center, to develop and validate new cell-based models of sensory neurons with respiratory disease applications. This research project involves transdifferentiating sensory neurons from mouse and human fibroblasts to use in drug testing, and could lead to new therapies for cough.

### **Collaboration with EMD Millipore to improve glycomics and proteomics simultaneously (GAPS) technology**

Richard S. Lee, MD, assistant in the Department of Urology, and Hui Zhou, PhD, postdoctoral fellow in the Department of Urology, have devised an innovative sample preparation called GAPS to capture both glycans and deglycosylated proteins, allowing the characterization of glycans, glycosylation sites and proteins in a single workflow. As one of the most abundant post-translational modification of proteins, glycosylation is involved in numerous biologic functions and affects the activity and toxicity of therapeutic proteins such as monoclonal antibodies. This collaboration with EMD Millipore will assess specific EMD Millipore reagents for suitability with the GAPS method.

### **Collaboration with Pronova Biopharma to study intravenous nutrition in pre-term infants**

Mark Puder, MD, PhD, associate in Surgery, and Kathy Gura, PharmD, pharmacist, are collaborating with Pronova Biopharma to investigate new intravenous clinical nutrition compositions in pre-term infants. Pronova Biopharma's commercialized product, Omacor/Lovaza™, is the first FDA-approved prescription drug containing omega-3 fatty acids from fish oil. This preclinical study will investigate Lovaza™ and new compositions of fish oil-based intravenous fat emulsions (IFE) as novel components of the nutrition given to patients unable to absorb adequate nutrition orally or enterally due to medical conditions such as short bowel syndrome. When conventional IFEs based on soybean oils are used long term, they cause severe complications such as parenteral nutrition-associated liver disease (PNALD), which can lead to death. To date, no IFE with a high content of omega-3 fatty acids has been approved by the FDA. This collaborative project with Pronova Biopharma builds on the original work from Drs. Puder and Gura, who identified that fish oil-based IFEs can prevent and even reverse PNALD in patients receiving parenteral nutrition.



Mark Puder, MD, PhD

## Selected Clinical Trial Agreements

### Phase II clinical trial for treatment of progeria

In 2007, Mark Kieran, MD, PhD, director of Pediatric Neuro-Oncology, began the first-ever clinical trial using lonafarnib for the treatment of progeria, a rare genetic condition that produces rapid aging in children and death due to heart attack and stroke. The results of the triple-drug clinical trial, published in October 2012, are promising. After two years of treatment, a significant number of patients had stopped losing weight or experienced weight gain. More importantly, the majority of patients had less blood vessel stiffness, a risk factor for strokes and heart attacks. Many patients also had improved bone density, flexibility and hearing. Based on these exciting results, a phase II trial evaluating the addition of zoledronic acid and pravastatin in combination with lonafarnib is now under way. The single-agent lonafarnib trial and the triple-drug trial have been funded through the Progeria Research Foundation, the National Institutes of Health and Boston Children's Hospital. Based on new preclinical data, a four-drug trial is being planned for the near future.



*Progeria Research Foundation photo*

*Progeria patient Claudia, Portugal, 14 years old.*

### Half-pint pediatric blood sugar management clinical study

Stress hyperglycemia, a state of abnormal metabolism with supranormal blood glucose levels, is often seen in critically ill patients. Michael Agus, MD, director, Medicine Critical Care Program, has designed his second multicenter clinical trial to study whether close management of blood sugar in critically ill children improves overall recovery. The first study, conducted in 980 babies after open-heart surgery, was recently published in the *New England Journal of Medicine*. The ongoing study, which is being conducted at more than 20 intensive care unit (ICU) sites over a period of four years, examines survival, organ failure, the length of ICU stay, and brain function in children with high blood sugar and critical illness. These studies use cutting-edge technology to continuously monitor glucose and computer-driven algorithms to titrate insulin delivery to control glucose levels. Study partners Nova Biomedical Corporation and Edwards Lifesciences are providing the devices required to carry out the trial.

### Multicenter pediatric status epilepticus clinical study

Tobias Loddenkemper, MD, assistant in the Department of Neurology, is exploring prolonged seizures, a condition medically known as status epilepticus (SE). During SE, a life-threatening condition, the brain is in a state of persistent seizure. This condition can be divided into subtypes with multiple underlying etiologies. Dr. Loddenkemper is currently running a registry to enable researchers to compare data from multiple participating clinical sites to establish a cohort of well-identified patients by identifying biomarkers of short-term and long-term outcomes of SE. If successful, this registry could utilize emerging genetic studies to determine markers for genetic susceptibility or predictors of SE, ultimately leading to improved management of SE.

### Industry-sponsored clinical trial with Isis Pharmaceuticals for the treatment of spinal muscular atrophy

Basil Darras, MD, associate neurologist-in-chief, is the lead investigator in an industry-sponsored clinical trial with Isis Pharmaceuticals, Inc. Isis has discovered and developed a potential drug to treat spinal muscular atrophy (SMA), a devastating disease caused by a mutation in the survival of motor neuron (SMN) gene. Decreased SMN protein in the spinal cord of children with an SMA mutation results in death of motor neurons in the anterior horn of the spinal cord and subsequent system-wide muscle wasting and weakness. This trial will assess the safety of a single dose of the drug in children with SMA and calculate how long it stays in the body. Effectiveness of the treatment will also be assessed.

### Boston Children's Cystic Fibrosis Center studies

The Cystic Fibrosis (CF) Center at Boston Children's conducted 15 interventional and observational clinical research projects supported by the Cystic Fibrosis Foundation and therapeutic and industry partners Gilead Sciences, MPEX Pharmaceuticals, Grifols Therapeutics, Vertex Pharmaceuticals and PTC Therapeutics. These projects focused on multiple approaches to treatment, including anti-infectives, anti-inflammatories, and cystic fibrosis transmembrane regulator (CFTR) modulation to address the underlying cause of CF. The CF community achieved an exciting milestone this year with the FDA approval of KALYDECO™ (ivacaftor), the first medicine to treat the underlying cause of cystic fibrosis for people ages 6 and older who have at least one copy of the G551D mutation in the CFTR gene. KALYDECO™ had been tested in clinical trials at Boston Children's.

## Selected Research and Technology Highlights

### MEDICAL DEVICES

- **Medical imaging biomarkers for the early diagnosis of abnormal brain development** – Simon Warfield, PhD, Department of Radiology
- **Devices for transapical beating heart surgery** – Pedro del Nido, MD, Department of Cardiovascular Surgery
- **Intravenous oxygen microbubbles for the treatment of hypoxic tissues** – John Kheir, MD, Department of Cardiology
- **PET radiopharmaceutical for the evaluation of myocardial perfusion** – Alan Packard, PhD, Department of Radiology
- **Mylar head wrap to reduce hypothermia in surgical patients** – Karen Sakakeeny, Nursing

### HEALTHCARE IT

- **SMART healthcare IT platform to support “app store for health”** – Kenneth Mandl, MD, MPH, Boston Children’s Hospital Informatics Program
- **ICISS: ADHD disease management web portal** – Eugenia Chan, MD, MPH, Division of Developmental Medicine; and Eric Fleegler, MD, MPH, Division of Emergency Medicine
- **BEAPPER: Emergency room clinician communications software** – Debra Weiner, MD, PhD, Division of Emergency Medicine
- **My Passport inpatient care mobile application** – Hiep (Bob) Nguyen, MD, Department of Urology
- **T3 software for critical care patient monitoring and clinical decision support** – Peter Laussen, MBBS, Division of Cardiovascular Intensive Care



Zebrafish from Boston Children’s Aquatic Resources Program

### THERAPEUTICS

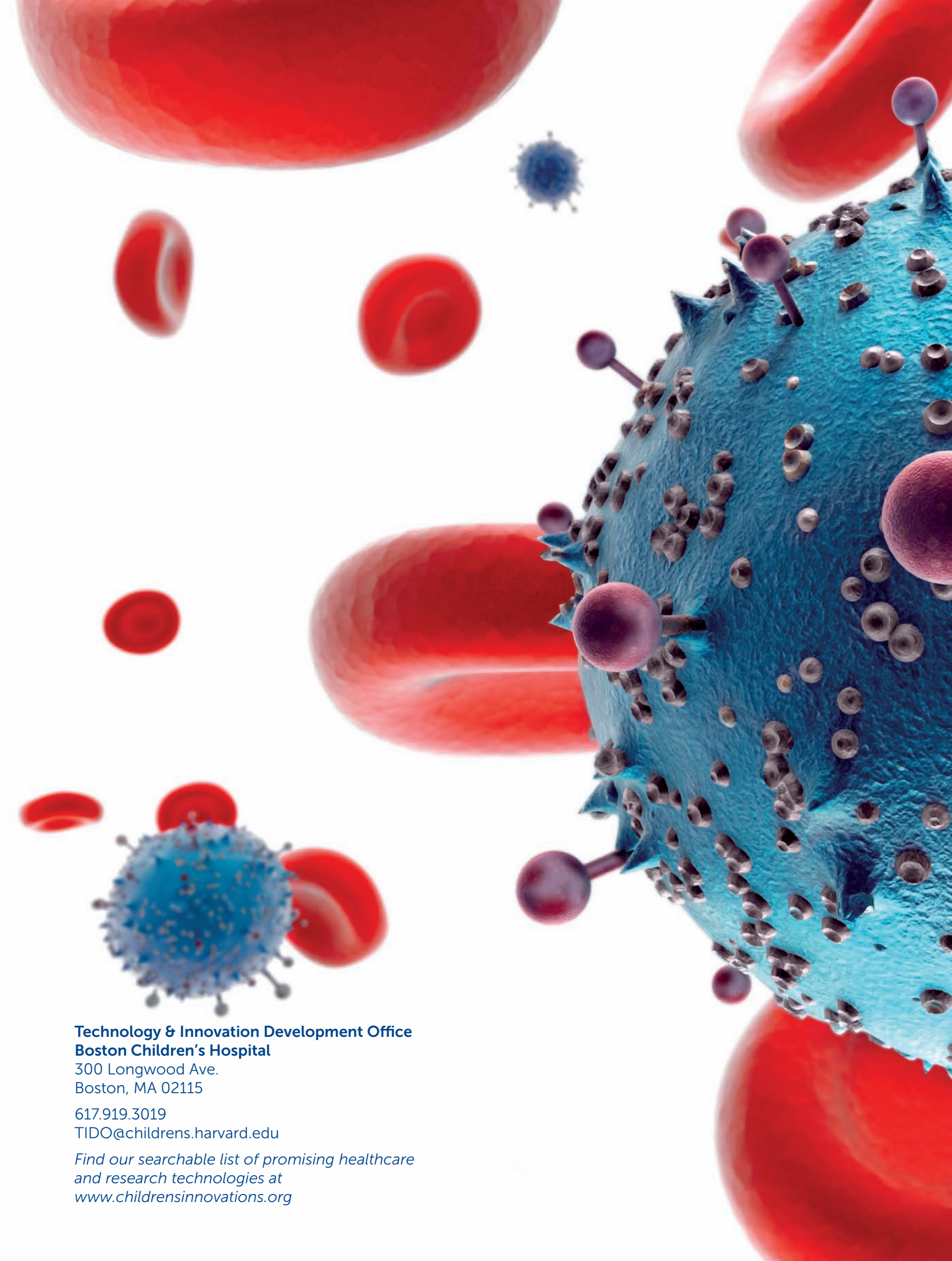
- **Inhibition of viral infection-triggered asthma with c-Kit inhibitor** – Dale Umetsu, MD, PhD, Division of Immunology
- **Lin28A, Lin28B and let-7 for the treatment of cancer** – George Daley, MD, PhD, Stem Cell Transplantation Program and Stem Cell Program; and Richard Gregory, PhD, Stem Cell Program
- **Use of matrix-associated proteins from gram-negative bacterial biofilm to spatially localize, concentrate and present enzymes or antigens** – Paula Watnick, MD, PhD, Division of Infectious Diseases
- **Small molecule modulators of neural crest development discovered in zebrafish models as potential therapeutics in melanoma** – Leonard Zon, MD, Stem Cell Program and Department of Hematology/Oncology
- **Therapeutic to increase proliferation of skeletal precursor cells** – Leonard Zon, MD, Stem Cell Program and Department of Hematology/Oncology
- **A topical treatment for peripheral neuropathies** – Gabriel Corfas, PhD, Department of Neurology and Department of Otolaryngology
- **Targeting respiratory diseases by delivery of ion channel blockers via large pore channels to block neurogenic inflammation** – Clifford Woolf, MD, PhD, F.M. Kirby Neurobiology Center and Program in Neurobiology
- **Inhibiting the voltage-gated proton channel Hv1 to curb stroke’s inflammatory damage** – David Clapham, MD, PhD, Department of Cardiology
- **Tiki 1 and Tiki 2 inhibitors as treatment for osteoporosis** – Xi He, PhD, Department of Neurology
- **Targeting ABCB5 to treat cancer** – Markus Frank, MD, Division of Nephrology
- **Prominin-1 derived proangiogenic peptide** – Robert D’Amato, MD, PhD, Vascular Biology Program
- **Lodamin: A topical, slow-release anti-angiogenic drug for treating eye diseases** – Robert D’Amato, MD, PhD, and Ofra Benny-Ratsaby, PhD, Vascular Biology Program
- **Saposisin A derivatives as a cancer therapeutic** – Randolph Watnick, PhD, Vascular Biology Program
- **Stem cell exosomes for pulmonary diseases** – Alex Mitsialis, PhD, Division of Newborn Medicine

### DIAGNOSTICS

- **Diagnostic test for developmental delay and autism** – Bai-Lin Wu, PhD, M Med, FACMG, Department of Laboratory Medicine
- **Genetic markers for diagnosis of autism spectrum disorders and intellectual disabilities** – Christopher Walsh, MD, PhD, Division of Genetics







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