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
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

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.

Note from the Executive Director
Erik Halvorsen, PhD
**Fiscal Year 2012 Summary**

<table>
<thead>
<tr>
<th>Invention Management Activity</th>
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<tbody>
<tr>
<td>Inventions under Active Management</td>
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<tr>
<td>Technology Development Funded Inventions</td>
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<table>
<thead>
<tr>
<th>Sources of Licensing Revenue</th>
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<tbody>
<tr>
<td>Namenda® 5%</td>
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<tr>
<td>Pomalyst® 5%</td>
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<tr>
<td>Dystrophin Diagnostic 4%</td>
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<tr>
<td>Neumega® 2%</td>
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<tr>
<td>Quick Change® 1%</td>
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<tr>
<td>Other 13%</td>
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<tr>
<td>Thalidomide® 70%</td>
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<table>
<thead>
<tr>
<th>Issued US Patents</th>
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<tr>
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<tr>
<td>Rao, Anjana</td>
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<td>12/6/11</td>
</tr>
<tr>
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<td>12/13/11</td>
</tr>
<tr>
<td>Frank, Markus</td>
<td>12/13/11</td>
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<td>Levy, Hara</td>
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<td>1/3/12</td>
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<tr>
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<td>1/10/12</td>
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<tr>
<td>Zon, Leonard</td>
<td>1/24/12</td>
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<td>Klagesbrun, Michael</td>
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<td>Lieberman, Judy</td>
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<td>Rogers, Gary</td>
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<td>8/14/12</td>
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<td>Springer, Timothy</td>
<td>8/21/12</td>
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<tr>
<td>Folkman, Judah</td>
<td>9/25/12</td>
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<tr>
<th>Fiscal Year 2012 Agreements</th>
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<tr>
<td><strong>Exclusive Licenses</strong></td>
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<tr>
<td><strong>Non-Exclusive Licenses</strong></td>
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<td><strong>Options</strong></td>
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<td><strong>Total</strong></td>
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<td><strong>Corporate Sponsored Research/Collaborations</strong></td>
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<td><strong>Clinical Trials</strong></td>
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<td><strong>Confidentiality Amendments</strong></td>
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<td><strong>Agreements Involving the Receipt of Equity</strong></td>
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<td><strong>Inter-Institutional Invention Administration</strong></td>
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<td><strong>CRO</strong></td>
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<tr>
<td><strong>Other</strong></td>
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| Current Licenses | 301 |
| **Issued US Patents** | 450 |
| **Issued Foreign Patents** | 640 |

<table>
<thead>
<tr>
<th>Gross Licensing Revenue Distribution: $10.3 Million</th>
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<tbody>
<tr>
<td><strong>Departments</strong></td>
<td>18%</td>
</tr>
<tr>
<td><strong>TIDO</strong></td>
<td>7%</td>
</tr>
<tr>
<td><strong>Legal Expenses &lt;1%</strong></td>
<td></td>
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<tr>
<td><strong>Other Institutions</strong></td>
<td>28%</td>
</tr>
<tr>
<td><strong>Inventors</strong></td>
<td>25%</td>
</tr>
<tr>
<td><strong>General Research Endowment</strong></td>
<td>22%</td>
</tr>
</tbody>
</table>

<p>| Gross Revenue | 10.3 Million |</p>
<table>
<thead>
<tr>
<th><strong>New Patents Filed</strong> Breakdown of <strong>License &amp; Options Executed</strong></th>
<th></th>
</tr>
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<tbody>
<tr>
<td><strong>US</strong></td>
<td>60</td>
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<tr>
<td><strong>PCT</strong></td>
<td>20</td>
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<tr>
<td><strong>Provisional</strong></td>
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<tr>
<td><strong>Foreign</strong></td>
<td>30</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>150</td>
</tr>
</tbody>
</table>

| **Clinical Trial Agreements** | 40 |
| **Collaboration Agreements** | 15 |
| **Invention Disclosures** | 60 |
| **Corporate Sponsored Research & Development** | 20 |
| **New Patents Filed** | 90 |
| **Non-Exclusive Licenses** | 25 |
| **Exclusive Licenses** | 10 |
| **Options** | 10 |

| **Inventors** | 25% |
| **Other Institutions** | 28% |
| **General Research Endowment** | 22% |
| **Inventors** | 25% |
Invention Management Activity
Fiscal Year 2012 Summary

- **Issued US Patents**
  - Folkman, Judah 9/25/12 8,273,383 Methods and compositions for treatment of preeclampsia
  - Springer, Timothy 8/21/12 8,247,185 Conformation specific antibodies
  - Springer, Timothy 8/14/12 8,241,627 Modified polypeptides stabilized in a desired conformation and methods for producing same
  - Clapham, David 7/3/12 8,211,666 Sperm-specific cation channel, CATSPER1, and uses therefor
  - Rogers, Gary 5/29/12 8,186,354 Orthotic device for preventing and/or correcting deformational posterior plagiocephaly
  - Lieberman, Judy 5/1/12 8,168,601 Method of delivering RNA interference and uses thereof
  - Zon, Leonard 5/1/12 8,168,428 Method to modulate hematopoietic stem cell growth
  - Klagsbrun, Michael 4/10/12 8,153,585 Peptide antagonists of vascular endothelial growth factor and methods of use thereof
  - D’Amato, Robert 4/10/12 8,153,806 Synthesis of 4-amino-thalidomide enantiomers
  - Zetter, Bruce 4/3/12 8,148,086 Methods to predict and prevent resistance to taxoid compounds
  - He, Zhigang 3/27/12 8,142,782 EGFR inhibitors promote axon regeneration
  - D’Amato, Robert 3/27/12 8,143,283 Methods for treating blood-borne tumors with thalidomide
  - Clapham, David 3/20/12 8,137,918 Sperm-specific cation channel, CATSPER1, and uses therefor
  - Zon, Leonard 3/13/12 8,133,974 Ferroportin1 nucleic acids, proteins, antibodies and methods
  - Atala, Anthony 3/6/12 8,128,707 Bladder reconstruction
  - Zon, Leonard 1/24/12 8,101,412 Method of enhancing proliferation and/or hematopoietic differentiation of stem cells
  - Levy, Hara 12/20/11 8,080,394 Method for determining predisposition to pulmonary infection
  - Frank, Markus 12/13/11 8,076,091 Gene encoding a multidrug-resistance human P-glycoprotein
  - Lock, James 12/6/11 8,070,800 Transcatheter heart valve prostheses
  - Rao, Anjana 11/1/11 8,048,864 Regulators of NFAT and/or store-operated calcium entry
  - D’Amato, Robert 8/17/12 5066505 Japan Synthesis of 3-amino-thalidomide and its enantiomers
  - 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, Dennis 11/17/11 2006257073 Australia ADAMTS15-comprising compositions having thrombolytic activity
  - Lock, James 11/23/11 1,765,453 EPO* Cannula for in utero 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 20058002909.8 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 505438 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

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*France, Germany, Ireland, Israel, Luxembourg, Monaco, Switzerland, Great Britain*
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 Epidemiico (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.
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), 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.”
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.

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 ABCBS, 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.
**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.

**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 (IFEs) 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.
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 pravastin 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.

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-inflammatory agents, 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 Clinical Trial Agreements

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

THERAPEUTICS
- Inhibition of viral infection-triggered asthma with c-Kit inhibitor – Dale Umetzu, 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

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

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Find our searchable list of promising healthcare and research technologies at
www.childrensinnovations.org