Office of Technology Licensing
Intellectual property newsletter
St. Jude Children's Research Hospital
ALSAC • Danny Thomas, Founder
2011 Issue

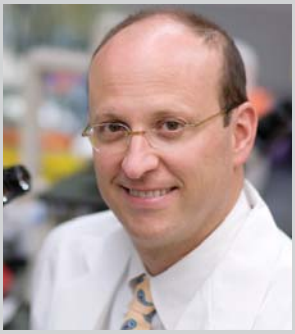
Hemophilia B treated with gene therapy vector from St. Jude

Hemophilia B, a disease in which the patient's blood fails to clot properly, affects about one in 30,000 individuals, mainly males. It is caused by a mutation in the gene coding for Factor IX (FIX), a factor involved in blood clotting. People with hemophilia B suffer from lower than normal levels of Factor IX.

Hemophilia B is well suited for gene therapy replacement because the lack of a single protein is responsible for the disease and achieving even a modest rise in FIX levels is enough to alleviate a subject's clotting deficiency. Several groups of researchers have conducted research with gene therapy vectors designed to express FIX, but have not been able to achieve stable production of therapeutic levels in humans.

Drs. John Gray, Andrew Davidoff and Amit Nathwani jointly designed a FIX expression vector that may finally reach this goal. It includes two significant improvements for which St. Jude sought patent protection. The first is a specific coding sequence designed for optimal expression of FIX. The second is a transcriptional regulatory control region that regulates the expression of FIX in liver cells. This transcriptional regulatory control region consists essentially of a smaller version of a known liver specific enhancer and promoter, both of which are reduced in size but still retain their function. By reducing the size of this control region, the chimeric FIX gene was able to fit into a self-complementary virus vector which is more efficiently transduced into cells than standard virus vectors.


Arthur Nienhuis, MD


Andrew Davidoff, MD


John Gray, PhD

Standard treatment is directed toward stopping the bleeding associated with the disease by infusion of factor IX concentrates to replace the defective clotting factor. Current recombinant protein treatment causes peaks and troughs; whereas, gene therapy replaces the defective gene and yields stable FIX levels. It is hoped hemophilia B gene therapy will be successful enough to replace all recombinant FIX products.

The University College London, in collaboration with Drs. Arthur Nienhuis and Andy Davidoff, initiated a Phase I/II study in adults using the St. Jude vector. Six patients with severe hemophilia B have been treated with vector produced at St. Jude in the Children's GMP. To date, all six patients have demonstrated increased circulating factor IX levels for the duration of the trial, which has been over a year in some of these cases. Four of the six have been able to discontinue their previously necessary prophylactic factor IX protein injections.

St. Jude filed a patent application claiming the aforementioned improvements to this expression vector, which was recently granted on October 4, 2011 as U.S. Patent No. 8,030,965. These patent rights have been licensed to Amsterdam Molecular Therapeutics.

View a video about St. Jude's contribution to Xalkori, an ALK inhibitor used to treat non-small cell lung cancer that recently received FDA approval, on the St. Jude internet site: *http://www.stjude.org/technology-licensing*

OTL FY 2011 Activities

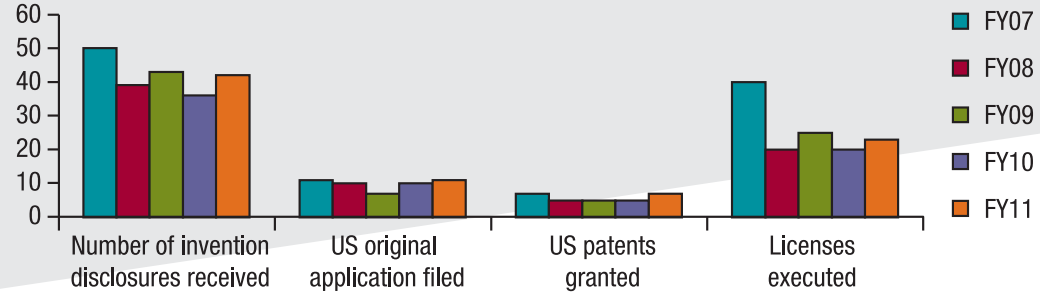


Figure 1. OTL activities related to patenting and licensing over the last 5 years.

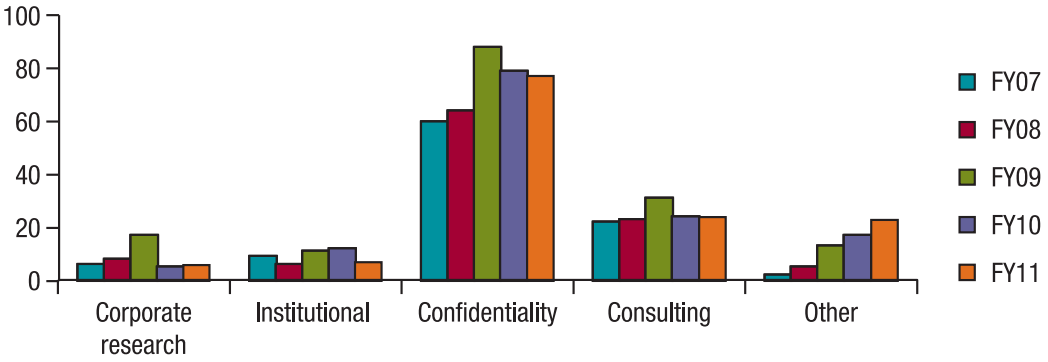


Figure 2. Types and number of various agreements executed by the OTL over the last 5 years. Other agreements include evaluation before licensing, option to license, service, in-license for software, transfer of clinical data to companies, and access to databases.

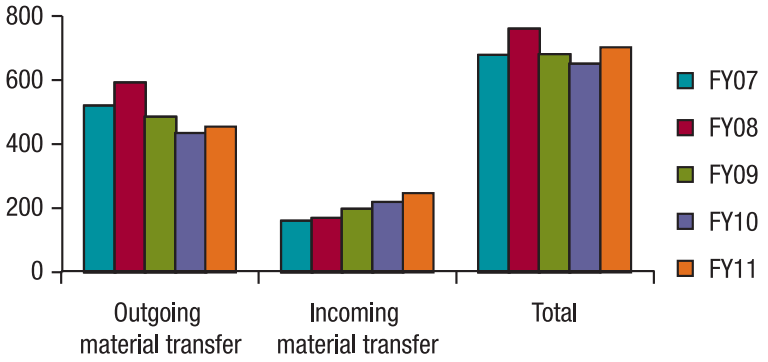


Figure 3. MTAs, both outgoing and incoming, increased in FY 2010.

Licensing income from St. Jude's portfolio grew to over $3M in 2010, with $1M allocated to 70 different inventors.

Addendum replaces editing of consulting agreements and streamlines review process

This fall the OTL changed its procedure for reviewing consulting agreements. The OTL now provides faculty and staff who wish to consult with a company or other for-profit entity with a standardized addendum that protects St. Jude's interests and supports compliance with internal consulting and conflict of interest policies. A copy of the addendum is available on the OTL website and can be provided by OTL personnel upon request. A copy of the fully executed consulting agreement and addendum must be provided to the OTL so that it can continue to track consulting activities. Investigators who consult with for-profit entities are encouraged to familiarize themselves with internal consulting policies as they remain ultimately responsible for their own compliance with these rules.

Table 1. New U.S. Patent Applications Filed in FY 2011

Filing Date	Inventor(s)	Department	Title
06/01/11	Erich Hoffmann		DNA transfection system for the generation of infectious influenza virus
02/18/11	Elisabeth Adderson (John Bohnsack)	Infectious Diseases	Group B streptococcus polypeptides nucleic acids and therapeutics compositions and vaccines thereof
02/04/11	Philip Potter, Monika Wierdl, Matthew Redinbo	Chemical Biology and Therapeutics	mutant hCE
11/12/10	Charles Mullighan, James Downing	Pathology	ALL Subtype with ERG Deletion
11/02/10	Mark Bix, Melanie Van Stry, Masato Kubo	Immunology	Genetic mapping of an IL4 regulatory locus called Dicel.2
12/15/10	Thomas Webb, Chandraiah Lagisetti	Chemical Biology and Therapeutics	Anticancer compounds and methods of making and using same
06/08/11	Lijun Chen, Jie Zheng, Youming Shao	Structural Biology	DKK2 in E. coli
04/14/11	Gerard Grosveld	Genetics	Alternate mTOR pathway
05/05/11	Thomas Webb	Chemical Biology and Therapeutics	Non-nucleoside,broad spectrum anti-influenza inhibitors that target RNA dependent RNA polymerase.
03/25/11	Jerry Aldridge, Robert Webster, (Megan MacDonald, Katharine Magor)	Infectious Diseases	RIG-I transgenic chicken
10/01/10	David Ellison	Pathology	Diagnostic Assay for SHH positive Medulloblastoma
10/06/10	Wing-Hang Leung, Rafijul Bari	Oncology	Molecular determinant based functional KIR allele typing(KIR2DL1 as prototype)
03/28/11	Elaine Tuomanen	Infectious Diseases	CbpA-pneumolysin Fusion Vaccine
09/30/10	Kip Guy, Yiqun Zhang	Chemical Biology and Therapeutics	Nutlin Analogs
09/29/10	Richard Lee, Julian Hurdle	Chemical Biology and Therapeutics	"Use of Reutercyclin analogues to treat Clostridium difficile infections"
05/17/11	Brenda Schulman, Daniel Scott, Julie Monda	Structural Biology	SCCRO Inhibitor
04/28/11	Julia Hurwitz	Infectious Diseases	"Modified Sendai Virus Vaccine Vector"
03/31/11	Dario Campana	Oncology	"MRD Detection Assay"
05/02/11	Jonathan McCullers, Julie McAuley	Infectious Diseases	"Diagnostic Assay for Influenza Virulence"

Table 2. U.S. Patents Issued in FY 2011

Patent #	Issue Date	Subject Matter	Inventor(s)
7,892,552	02/22/11	Group B streptococcus polypeptides nucleic acids and therapeutics compositions and vaccines thereof	Elisabeth Adderson (John Bohnsack)
7,820,115	10/26/10	Automated laboratory rack system	D. Zatechka (Francis Gomes, David Landsberger)
7,871,626	01/18/11	Modified Influenza Virus for Monitoring Vaccine Efficiency	Elena Govorkova, Erich Hoffmann, Aleksandr Lipatov, Richard Webby, Robert Webster
7,906,637	03/15/11	mutant hCE	Philip Potter, Monika Weirdl (Matthew Redinbo)
7,879,326	02/01/11	Neutralizing human monoclonal antibodies to H5N1 influenza viruses	Richard Webby (Steven Foung, Zhen-Yong Keck)
7,850,956	12/14/10	Immunization by inoculation of DNA transcription unit	Robert Webster (Harriet L. Robinson, Ellen F. Fynan, Shan Lu)
7,906,331	03/15/11	Relationship of ABC transport proteins with hematopoietic stem cells and methods of use thereof	Brian Sorrentino, John Schuetz