The Wistar Institute of Anatomy and Biology

Research Development Report

Reporting Period:

July 1, 2013 – June 30, 2014

Commercial Development of Research

Wistar has established procedures in place for the commercial development of new technology from Wistar research. These procedures were originally implemented at Wistar in the 1980's and are regularly updated. The procedures and the supporting documents are summarized as follows:

- Wistar scientists are encouraged to disclose new inventions to the Office of Business Development using the Wistar Invention Disclosure Form. Additionally, the Vice President of Business Development confers regularly with faculty, the Cancer Center Director, COO and the President & CEO of Wistar to identify manuscripts in preparation that may contain new inventions with commercial potential.
- The invention and related technology are then reviewed by the Office of Business Development and assessed for patentability and commercial potential. The Office of Business Development manages the preparation and prosecution of patent applications, which is performed by outside patent counsel. In addition, Wistar intellectual property includes proprietary biological materials which may be licensed exclusively or non-exclusively. The Wistar Material Transfer Agreement is used for materials with significant commercial potential and Wistar uses the Uniform Biological Material Transfer Agreement (UBMTA), as approved by NIH, for transfer of other proprietary materials to academic collaborators.
- Once a new technology has been identified as suitable for licensing and, when appropriate, the necessary patent applications have been filed, the technology is marketed to prospective licensees for commercial development. Technology is marketed via Wistar's web site (http://www.wistar.org/technology-transfer) which features Technology Transfer prominently displayed on the home page and via one-on-one meetings with prospective licensees. The Office of Business Development hosts visitors from biotechnology and pharmaceutical companies and investment firms who come to Wistar to meet our faculty and learn of research that may be of interest to the company for sponsored research support, licensing or startup.
- Once prospective partners have been identified, the Office of Business Development, in conjunction with in-house counsel, will negotiate sponsored research agreements, option agreements or license agreements. Depending on the technology and its applications, these license agreements may be exclusive or non-exclusive.

Wistar has a long history of successfully commercializing the results of its research. Today Wistar has 135 active licenses for a portfolio of technologies that includes research tools, vaccines, monoclonal antibodies and patents for therapeutic agents.

The following table summarizes Wistar's technology transfer activities for 2013 versus 2012. In 2012, 9%, and in 2013, 18%, of Wistar's new patent applications were made jointly with other Pennsylvania institutions, as the result of ongoing research collaborations.

	2013	2012
R&D Spending	$57,801,000	$62,133,000
Invention Disclosures	10	11
New Patent Applications	11	11
Joint New Patent Applications with PA Institutions	2	1
Issued U.S. Patents	5	5
New License Agreements	5	6
License Revenues	$19,285,000	$17,769,000
Corporate Sponsored Research Agreements	3	4

The Association of University Technology Managers (AUTM) annual licensing survey is used as the established benchmark for reporting of technology transfer activities.

To compare Wistar's performance to its peer research institutions we looked at the data from the most recent 2012 AUTM licensing survey. In this survey, Wistar is grouped with U.S. research institutions and teaching hospitals, such as the Mayo Clinic, Massachusetts General Hospital and The Scripps Research Institute. Since these institutions vary greatly by size, we decided that the most relevant comparison could be made by normalizing the technology transfer data to $100MM of R&D funding.

	Wistar (2012)	Average of 26 U.S. Research Institutions (2012)
R&D Spending	$62,133,000	$237,565,677
Invention Disclosures - per $100MM of R&D	16	40
New Patent Applications - per $100MM of R&D	16	27
New License Agreements - per $100MM of R&D	10	15
License Revenues - per $100MM of R&D	$28.60 million	$8.32 million

This data implies that albeit there are fewer, on average, invention disclosures filed at Wistar, the amount of license revenues generated far exceed the revenues generated at Wistar peer institutions.

Wistar uses two strategies, training and relationship development, to ensure that we continue to meet best practice standards. Additionally, Wistar makes a concerted effort to build relationships with both peer institutions and prospective licensees to enhance commercialization opportunities. Wistar has representatives of venture capital firms on its Board of Directors and the chairman of the Intellectual Property Committee is a partner of Novitas Capital. This committee advises the Office of Business Development on how to improve communications with our industrial partners.

Forms of Agreement for Licensure

Wistar has developed standard licensing agreements, including a Material Transfer Agreement, an Exclusive License Agreement, a Non-exclusive License Agreement, and a Research Reagent Master Agreement.

Plan for Training Students and Health Professionals

Wistar has affiliations with several postsecondary schools to train students in the biomedical field and is committed to increasing and broadening these relationships in the future. Wistar's charter, dating from 1893, mandates that it provide training to students in the medical sciences; however, because it is not authorized to grant degrees, Wistar has long collaborated with area colleges and universities to fulfill this obligation, helping to develop courses and provide training to their enrollees. A summary of these programs are provided below:

Post-Doctoral Training Program

Wistar conducts a post-doctoral training program for individuals who have received a Ph.D., M.D. or D.V.M degree from another institution. These post-doctoral fellows work in individual laboratories at Wistar for periods of up to four years. In addition to gaining research experience, they attend seminars and courses at Wistar and the University of Pennsylvania, participate in symposia and journal clubs and contribute to laboratory and scientific meetings. Historically, many of the M.D.s serving as fellows at Wistar have been affiliated with and supported by The Children's Hospital of Philadelphia and the University of Pennsylvania.

Pre-Doctoral Training Program

Through formal agreement with the University of Pennsylvania, Wistar provides training to students enrolled in doctoral programs in immunology, cell and molecular biology, pharmacology, neuroscience, chemistry and biology at the University. During the first two years of their graduate education, these students primarily take courses at the University. Wistar researchers participate actively in the University curriculum committees responsible for developing these courses, and frequently serve as course instructors. Wistar also offers a course on cancer biology each fall, which graduate students may take for credit at the University.

At the end of their first two years, approximately six to ten graduate students annually elect to pursue their training in an individual Wistar laboratory. This training culminates in the writing

and defense of a dissertation. Typically, the head of the student's laboratory at Wistar serves as his or her dissertation advisor. Most students require approximately three years to successfully complete their dissertations, at which time they are awarded a Ph.D. by the University of Pennsylvania.

Biomedical Technician Training (BTT) Program

Wistar and the Community College of Philadelphia (CCP) jointly established the BTT Program in 2000 to train community college students for new careers as biomedical research technicians. Students accepted into the program take courses at CCP designed to give them fundamental knowledge of chemistry, biology, mathematics and English composition. The students receive intensive training in laboratory techniques and develop their practical skills at Wistar and other BTT Program-affiliated biomedical institutes. This dual experience of academic and practical training offers students seeking an associate's degree the opportunity to acquire the skills necessary to qualify for positions as research assistants (technicians) at academic institutions and at biotechnology and pharmaceutical companies. Traditionally, these positions have gone to graduates of four-year baccalaureate programs.

To date (as of June 30, 2014), 101 students have completed the BTT Program (60% are from underrepresented minority populations). Upon successful completion, the students receive an associate's degree from CCP and/or a certificate from Wistar. Students who have completed the program have either found employment as technicians (research assistants) with the degree(s) they hold (53 have been employed [51% underrepresented minorities], 28 have been employed at Wistar) or have elected to continue their studies in a baccalaureate degree program.

Training Opportunities Related to the Commercial Development of Research

Detailed information on the patenting and licensing process is available to our scientists on Wistar's web site (http://www.wistar.org/technology-transfer/guidelines-inventors). Technology Transfer has a section on the web site entitled, "Guidelines for Inventors" . This section contains detailed information on the technology commercialization process, including:

- Wistar Policies and Procedures
- How to Disclose an Invention
- Patent and Licensing Process
- Roles in Technology Transfer
- What is a Patentable Invention?

The Vice President of Business Development meets with all new inventors to introduce them to the patenting and licensing process when the Invention Disclosure form is filed. After a licensable technology has been identified, the Office of Business Development works closely with the inventor/scientist in identifying prospective licensees and refining the licensing strategy.

Wistar faculty members have the opportunity to take business courses at the Wharton School of Business of the University of Pennsylvania and other area business schools. The tuition for these courses is reimbursed by Wistar.

Outreach to Businesses Regarding Recent Research Developments

Wistar's ongoing outreach programs include:

- Providing summaries of Wistar technologies available for licensing on Wistar's web site (http://www.wistar.org/technology-transfer).
- Hosting corporate R&D and venture capital groups at Wistar to enable them to meet with interested faculty with the goal of developing research collaborations.
- Encouraging Wistar scientists to publish their findings in peer reviewed scientific journals. These publications often attract attention from scientists from prospective licensees who then contact the Office of Business Development or the scientists themselves about licensing opportunities.
- Working closely with Wistar's Communications department which prepares and distributes press releases of significant developments and publications arising from Wistar research. These press releases often result in articles in business publications (e.g., *BioWorld Today*) that are read by prospective licensees at biotechnology and pharmaceutical companies.
- Working with local groups, including Christiana Care Health System Helen F. Graham Cancer Center, Lehigh Valley Health Network, Temple University and The Science Center, to establish new programs and projects to advance early stage technology to the point where it will be attractive for licensing and commercialization.

Collaboration for the Development of Research

Wistar has a long history of collaborating with researchers at other institutes and universities in the region, and we expect this practice to continue. Where new intellectual property develops from these collaborations, Wistar and the collaborating organization(s) will enter into an inter-institutional agreement that covers the management of patents and licensing of technology.

Ongoing collaborations between Wistar researchers and scientists at other institutions have resulted in the following new joint patent application in 2013:

- Epimorphic Regeneration and Related Hydrogel Delivery Systems (E. Heber-Katz of Wistar with I. Iossif and P. B. Messersmith of Northwestern University). Filed November 13, 2013.

- Methods and Compositions for Screening Modulators of Oncogene-Induced Senescence (R. Zhang and B. G. Bitler of Wistar with J. R. Peterson of the Fox Chase Cancer Cetner). Filed March 15, 2013.

- Methods and Compositions for Diagnosis of Glioblastoma or a Subtype Thereof (R. V. Davuluri, S. Pal, Y. Bi and L. C. Showe of Wistar and D. M. O'Rourke and L. Macyszyn of the University of Pennsylvania).

Recent Accomplishments Related to Research Development Collaborations

- Ongoing joint research program to study immune responses to AAV-mediated FIX gene transfer – collaboration between Dr. Hildegund Ertl of Wistar and researchers at The Children's Hospital of Philadelphia, University of Florida, and Beth Israel Deaconess Medical Center.

- Ongoing BRAF – Collaboration Dr. Meenhard Herlyn at Wistar and researchers at the University of Pennsylvania.

- Ongoing Melanoma Program Project grant – Dr. Meenhard Herlyn at Wistar, in collaboration with researchers at the University of Pennsylvania and The University of California, San Francisco.

- Active member of the PA Cancer Bioinformatics Consortium (PCABC), which includes Wistar, Thomas Jefferson University, Fox Chase Cancer Center, University of Pennsylvania, University of Pittsburgh and Hershey Medical Center.

- Active member of The Greater Philadelphia Bioinformatics Alliance, which includes Wistar, Thomas Jefferson University, Fox Chase Cancer Center, University of Pennsylvania, Drexel University, Temple University, University of the Sciences, Penn State Great Valley, as well as GSK and Merck.

- Ongoing joint research project to study shaping antiviral immunity by the inflammatory, regulatory and tissue environment – collaboration between Drs. Andy Caton and Jan Erikson and researchers at the University of Pennsylvania and Columbia University.

- Ongoing study on biology of human melanoma metastasis – collaboration between Dr. Meenhard Herlyn and researchers at Harvard Medical School.

- Ongoing study on proteomic analysis of ectopic pregnancy biomarkers – collaboration between Dr. David Speicher and University of Pennsylvania.

- Partnership with University of the Sciences in Philadelphia for Center for Chemical Biology and Translational Medicine.

- Ongoing joint research project to study early innate/IgA anti-HIV/SIV response in exposed uninfected – collaboration between Dr. Luis Montaner of Wistar and researchers at the University of Puerto Rico, University of Nebraska and Duke University.

- Ongoing joint research project to study NK cell activation and function in HIV-1 exposed uninfected IV drug users – collaboration between Drs. Luis Montaner and David Speicher of Wistar and researchers at the University of Pennsylvania.

- Ongoing joint research project to study inflammation and regeneration – collaboration between Dr. Ellen Heber-Katz of Wistar and researchers at Northwestern University.

- Ongoing joint research project to study the initiation and evolution of the ovarian cancer microenvironment – collaboration between Dr. Jose Conejo-Garcia of Wistar and researchers at Dartmouth College.

- Ongoing joint research project to study magnetic nanoparticle immunotherapy against ovarian cancer – collaboration between Dr. Jose Conejo-Garcia of Wistar and researchers at Dartmouth College.

- Ongoing joint research project to study the novel molecular therapies of prostate cancer – collaboration between Dr. Dario Altieri of Wistar and researchers at Thomas Jefferson University and the University of Vermont.

- Ongoing joint research project to study small molecular regulation of microRNAs to understand and treat cancer – collaboration between Dr. Qihong Huang of Wistar and researchers at the University of Pittsburgh.

- Ongoing joint project to study methods for high-dimensional data in HIV/CVD research – collaboration between Dr. Luis Montaner of Wistar and researchers at the University of Massachusetts.

- Alliance with The Moulder Center for Drug Discovery Research at Temple University to accelerate drug development.

- DOD translational grant for targeted-HSP 90 – Dr. Dario Altieri of Wistar and researchers at Harvard University, Thomas Jefferson University, University of Milan and Fondazione IRCCS Cá Granda.

- Ongoing joint research project to study regenerative wound healing via inflammation-modulating biomaterials – collaboration between Dr. Ellen Heber-Katz and researchers at Northwestern University.

- Ongoing joint research project to study the early events in KSHV infection of primary B-cells – collaboration between Dr. Paul Lieberman and researchers at the University of Pennsylvania.

- Ongoing joint research project to study the changes in the RBC proteome during health and disease – collaboration between Dr. David Speicher and researchers at the Children's Hospital of Philadelphia.

- Ongoing joint research project to study the drivers in melanoma susceptibility, development and progression – collaboration between Dr. Meenhard Herlyn and researchers at the University of Pennsylvania, University of Oslo and the University of Leeds.

- Ongoing joint research project to study breast cancer treatment with antibody targeted T cells – collaboration between Dr. Qin Liu and researchers at Wayne State University.

- Ongoing joint research project to study health disparities in prostate cancer – collaboration between Dr. Harold Riethman and researchers at the University of Pennsylvania.

- Ongoing joint research project to study nanomapping-assisted analysis of human telomere regions – collaboration between Dr. Harold Riethman and researchers at Drexel University.

- Ongoing joint research project to study the effects of common polymorphisms in immune sensors in tumor immunosurveillance – collaboration between Dr. Jose Conejo-Garcia and researchers at the University of Pennsylvania.

- Ongoing joint research project to identify diagnostic markers for early-stage lung cancer in PAX gene blood samples – collaboration between Dr. Louise Showe and researchers at the University of Pennsylvania, Temple University, Fox Chase Cancer Center and the Helen Graham Cancer Center of the Christiana Care Health Services.

- Ongoing joint research project to study the rational design of effective multi-modal ovarian cancer immunotherapy – collaboration between Dr. Jose Conejo-Garcia and researchers at the University of Texas at San Antonio.

- Ongoing joint research project to study the chromatin regulatory mechanisms in ovarian cancer – collaboration between Wistar researchers (Drs. Rugang Zhang, David Speicher, Jose Conejo-Garcia, Frank Rauscher) and researchers at the University of Pennsylvania and the University of Miami.

- Ongoing joint research project to study HIV-1 vaccine based on chimp serotypes of adenovirus – collaboration between Dr. Hildegund Ertl and researchers at the University of Pennsylvania and Emory University.

- Ongoing joint research project to study lipids and myeloid cell function in cancer – collaboration between Dr. Dmitry Gabrilovich and researchers at the University of Pittsburgh.

- Ongoing joint research project on Skin Cancer – collaboration between Dr. Dmitry Gabrilovich and researchers at the Moffitt Cancer Center.

- Ongoing joint research project to study the regulation of tumor microenvironment in cancer – collaboration between Drs. Dmitry Gabrilovich, David Speicher and researchers at the Moffitt Cancer Center.

- Ongoing joint research project to study a common link between mammalian regeneration, high fat diets and breast cancer - collaboration between Dr. Ellen Heber-Katz and researchers at the University of Pennsylvania.

- Ongoing joint research project for the development of a novel adjuvant for vaccine sparring – collaboration between Dr. Scott Hensley and the New York Blood Center.

- Ongoing joint research project for alternative pathways for CD4+ T cell epitope

generation from influenza antigens – collaboration between Dr. Scott Hensley and researchers at Thomas Jefferson University.

- Ongoing joint research project to study the effect of human pre-exposure history on antigenic drift of influenza viruses – collaboration between Dr. Scott Hensley and researchers at the Children's Hospital of Philadelphia.

- Ongoing joint research project for the development of a small molecule inhibitor of EBNA1 to treat EBV infection and associated disease – collaboration between Dr. Paul Lieberman and researchers at the Fox Chase Cancer Center.

- Ongoing joint research project towards eradication: reducing proviral HIV DNA with interferon-α immunotherapy – collaboration between Dr. Luis Montaner and researchers at the University of Pennsylvania.

- Ongoing joint research project to study pathogenesis of malignant Mesothelioma by the human polycomb BAP1-ASXL – collaboration between Dr. Frank Rauscher and researchers at the Fox Chase Cancer Center.

- Ongoing joint research project to study a novel single-molecule telomere characterization technology for analyzing cancer – collaboration between Dr. Harold Riethman and researchers at Drexel University.