

Fox Chase Cancer Center

Research Development Report

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Commercial Development of Research

The Office of Research and Development Alliances (ORDA) supports the mission of Fox Chase Cancer Center to accelerate the integration of emerging technologies into team-based science to reduce the burden of cancer in all individuals *by facilitating relationships with industry in order to translate clinical and basic research findings into products and services for the public good*. By evaluating and protecting the intellectual assets of Fox Chase, and managing discussions and negotiations with industry, the ORDA enables the effective and efficient transfer of those assets for the benefit of the public and provides a source of revenue to fund further research and to reward, retain and recruit Fox Chase investigators.

The ORDA serves as the liaison between Fox Chase's research community and the pharmaceutical, biotechnological, medical device, diagnostic and venture capital communities. The ORDA continues a long standing policy and tradition at Fox Chase to develop and nurture these collaborations to disseminate intellectual capital for the public benefit. This policy was enhanced when the US Congress sought to incentivize more translation of scientific findings through passage of the 1980 Bayh-Dole Act. That legislation created a uniform patent policy among federal agencies that fund research, enabling small businesses and non-profit organizations, including universities, to retain title to inventions made under federally-funded research programs.

Generally, the ORDA provides three primary services:

(1) The promotion of collaborative research relationships between corporate partners and Fox Chase's academic investigators. Fox Chase has long been recognized as a leader in both clinical research and basic laboratory research. Corporate sponsorship enables early-stage research and technologies to be further developed into pre-clinical and, ultimately, clinical applications, thus promoting academic, clinical and corporate goals. The ORDA is the primary point of contact for establishing industry-sponsored research agreements (SRAs) and clinical trial agreements (CTAs) at Fox Chase. We facilitate the development, negotiation and execution of all SRAs and CTAs within Fox Chase and we work to ensure compliance under all such agreements. Acting as the liaison between Fox Chase, its investigators, and corporate sponsors, the ORDA also consults with other internal departments as necessary while negotiating SRAs and CTAs. Further, the ORDA ensures that all such agreements are consistent with the Fox Chase's Intellectual Property Policies and Procedures Policy and Conflict of Interest Policy, as well as appropriate federal regulations and guidelines. The ORDA also negotiates and manages material transfer agreements and other collaborative agreements with industry on behalf of Fox Chase

investigators. Additionally, the ORDA is charged with development of financial and operational evaluations of proposed technology/ equipment to foster the clinical and research programs of technology-intensive departments. The ORDA is responsible for making recommendations for technology acquisitions, directing a competitive bidding process and closing negotiations for equipment purchases, in conjunction with Finance and Purchasing.

(2) The collection and processing of invention disclosures while working with the inventors to file patent applications when appropriate. The ORDA works with Fox Chase investigators, staff and outside intellectual property law firms to protect intellectual property (IP) that results from activities carried out on Fox Chase time, at Fox Chase expense, using Fox Chase facilities or materials, or under the auspices of Fox Chase. All such IP is protected through patents, copyrights and/or trademarks. In the case of patents, the ORDA works closely with outside IP law firms to evaluate the patentability of invention disclosures, and to draft and file patent applications in the United States and internationally, if appropriate. In addition, the ORDA works with outside counsel to ensure protection of copyrightable materials, secure trademarks, and to protect original artistic or literary work of Fox Chase investigators and staff.

(3) The facilitation of transferring patentable and non-patentable intellectual property, know-how and trade secret technologies to industry through exclusive and non-exclusive licenses, option agreements and the formation of start-up companies. The ORDA identifies discoveries that may be commercially developed, and works with inventors and corporate partners to launch new products into the marketplace. The ORDA strategically markets Fox Chase's intellectual property portfolio, including patented materials, non-patented research materials and software by working with inventors and using the ORDA's extensive network of corporate contacts to partner with companies that are capable of developing our technologies. The ORDA negotiates all option and license agreements with suitable partners in an attempt to introduce technologies into the marketplace as quickly as possible. As an element of this partnership and as part of a license agreement for our technologies, companies oftentimes support additional research within Fox Chase laboratories to further develop the licensed technologies.

Outlined below are the actions and strategies that are implemented by the ORDA to increase commercialization activities and the speed of commercial development.

- The ORDA meets regularly with each current principal investigator and each recently hired investigator to become familiar with the aims of the investigator's research projects. The ORDA staff reminds investigators to disclose results of their research to the ORDA prior to any publications or presentations outside of Fox Chase. ORDA staff also attends internal seminars presented by the investigators in order to benefit from the perspective offered by other researchers in the audience.
- After research results are formally disclosed to the ORDA using an Invention Disclosure Form, the staff performs a thorough scientific and commercial evaluation of the technology. These evaluations include assessment of novelty, utility, unobviousness, stage of development, the problem addressed, and the size and growth rate of the market. Feedback is then solicited from appropriate industry contacts on the level of interest from existing companies. In the event that ORDA staff determines that the disclosure might form the basis

of a new company, efforts are directed towards finding an entrepreneur to lead the company and secure proof-of-concept funding. The assessment also recommends the best means of protecting the discovery in order to maximize its commercial potential and benefit to the citizens of Pennsylvania.

- When it is determined that a patent application should be filed, a patent attorney whose background and experience would allow them to appreciate the technology will be asked to prepare an application with input from the researcher and the ORDA. The ORDA solely contracts with law firms having attorneys with advanced scientific degrees in a field similar to the intellectual property being protected.
- If it is determined that a license to an existing company is the most appropriate route of commercialization, a marketing campaign will be undertaken using the means of contact described in “Outreach to Businesses Regarding Recent Research Developments” below. Particular attention is paid to making small businesses in Pennsylvania aware of the discoveries and the opportunities they present.
- If it is determined that the technology would benefit from further research at Fox Chase to establish proof of principle, an application will be submitted to BioAdvance for review and potential investment. Additionally, Fox Chase has a rich history of making investments in its research programs to help support its investigators conduct applied research, particularly when such support cannot be obtained from conventional funding sources or federal agencies.
- In FY10 Fox Chase recorded 41 invention disclosures, filed 19 patent applications and was awarded 6 US patents. In addition, \$1.1 million in gross revenues was generated during FY10 from payments under its license agreements. In FY10 Fox Chase executed 15 laboratory sponsored research agreements, 187 material transfer agreements, 96 confidentiality agreements and 43 clinical trial agreements with industry. Comparing those data to peer institutions, Fox Chase is on par with its peer institutions (Annual Survey: The Association of University Technology Managers).

Research Licensing Agreements

The ORDA at Fox Chase has developed the following standard licensing agreements for use in the licensing of research results related to medical devices, drugs or other research discoveries:

1. License Agreement
2. Option Agreement
3. Research Materials License Agreement
4. Software Transfer Agreement
5. Material Transfer Agreement
6. Confidential Disclosure Agreement
7. Sponsored Research Agreement
8. Corporate-sponsored Clinical Trial Agreement

Training Students and Health Professionals

- FCCC laboratories provide opportunities for scientific training for undergraduate students. During the summer of 2010, ten students from a variety of colleges were recipients of the Board of Associates undergraduate summer fellowships, funded by a generous donation from the FCCC Board of Associates. An additional twenty-five undergraduate summer assistants were supported from investigators' research funds.
- We recently established an academic relationship with Lincoln University, an Historically Black College/University, for the training of both faculty and undergraduate students in biology; this partnership was recently awarded a P20 grant from the NIH (NIH P20 CA138079, Lincoln University - Fox Chase Partnership in Cancer Research and Training). As part of this training, this summer four Lincoln University students are being housed in Fox Chase housing and will receive 16 weeks of research training in molecular biology and population science.
- Graduate students at FCCC carry out thesis research under the supervision of staff members who hold adjunct faculty appointments at Drexel University College of Medicine, the University of Pennsylvania, Thomas Jefferson University, Temple University, Lehigh University and members who participate in the Fox Chase-Russian State Medical University (RSMU) Sister Institute Program. Generally, these students have completed the major course work requirement for the doctoral degree and are engaged in full-time research. In the year 2010, 6 students from the RSMU program are completing research toward their M.Sc. or Ph.D. at Fox Chase Cancer Center, and 6 students from Drexel University are carrying out their Ph.D. research at Fox Chase Cancer Center. All of these students are supported by investigators' research funds.
- Training in the Ethical Conduct of Research is provided on a yearly basis to members of the postdoctoral and graduate student community at Fox Chase, organized by Dr. Maureen Murphy. This one-day course is required for all postdoctoral and graduate trainees at the Center. Training in the Ethical Conduct in Research will be held in September 2010; faculty mediators will include Drs. Maureen Murphy, Eti Cukierman and Matt Robinson. Topics to be covered include Notebook Keeping, Authorship Issues, Image Manipulation, and Ethical Treatment of Animals. This course is highly interactive and routinely accompanied by extensive discussion.
- Fox Chase Cancer Center maintains several active programs for graduate training of physicians. The activities of these programs range from preceptorship for medical students through research fellowships within the disciplines of medical oncology, surgical oncology, radiation oncology and pathology.

Department of Medical Oncology is responsible for the training of Temple University medical students and residents who rotate at Fox Chase Cancer Center for their training experience. Fourth year medical students are provided a subinternship experience. Second and third year residents do a rotation in the inpatient service during which they receive intensive exposure to medical oncology. These residents are also given the opportunity to

rotate in the ambulatory care department where outpatient oncology can be observed. In addition, the Medical Oncology Department maintains active fellowship training programs in hematology/medical oncology administered jointly with Temple University. The Surgical Oncology Department maintains a fellowship program in surgical oncology as well as providing many training opportunities for Temple University surgical residents. The Pathology Department also provides a fellowship-training program. The Radiation Oncology Program at Fox Chase Cancer Center has an independent residency with its own certification.

The Section of Urologic Oncology in the Department of Surgical Oncology is an active participant in the training of residents and fellows. The Section is a key component of the general urology residency training program of the Temple University Medical College Department of Urology. PGY-4 and PGY-5 level residents gain extensive clinical experience at Fox Chase Cancer Center during 6 months of rotations in each of those resident years. Fourth year medical students from Temple University Medical College are additionally offered one month subinternship elective rotations with the Section. In 2006, the Section initiated a 2-year subspecialty fellowship in urologic oncology, and this training program was recognized and approved by the Society of Urologic Oncology (SUO) in 2008. This SUO accredited fellowship in urologic oncology provides a more in-depth post-graduate training in the surgical and non-surgical management of urologic cancers. Annually two fellows are selected for entry into the training program.

The fellowship in Interventional Endoscopy and Gastroenterology at Fox Chase Cancer Center provides comprehensive training for board-eligible physicians in Gastroenterology. The aim of the one-year fellowship is to prepare the trainee for a career in academic gastroenterology with a concentration in advanced therapeutic endoscopy at a tertiary care referral center. Fellows learn techniques of endoscopic cholangiopancreatography (ERCP) for diagnosis and palliation of cancers of the pancreaticobiliary system, and endoscopic ultrasound (EUS), which is a valuable tool for tissue diagnosis and staging of tumors of the esophagus, stomach, pancreas and rectum. Additionally, the trainee develops proficiency in the placement of palliative stents into the digestive tract for obstruction related to incurable malignancy, endoscopic removal of large precancerous lesions of the esophagus, stomach and colorectum, and current techniques of radiofrequency ablation and cryotherapy for dysplastic Barrett's esophagus and esophageal tumors. Finally, Fox Chase has one of the world's largest experiences with double balloon enteroscopy, a technique to visualize and treat abnormalities along the length of the small intestine. The fellow's responsibilities also include academic productivity: he/she is expected to produce manuscripts for publication as well as research abstracts for presentation at the annual Digestive Disease Week meeting.

- The purpose of the continuing medical education (CME) Program is to plan, develop, implement and evaluate independent, fair-balanced and scientifically rigorous educational activities that improve knowledge, competence and professional performance and effect behavior change with the goal of improving the quality and safety of patient care and healthcare outcomes. CME activities are designed to meet the needs of medical, surgical and radiation oncologists and other oncology subspecialties; primary care physicians; other specialty physicians and other health professionals who interact with cancer patients, cancer survivors, their families and those at risk of developing cancer. Through these activities, the

CME Program supports the mission of Fox Chase Cancer Center (FCCC) to “reduce the burden of cancer by integrating scientific discoveries and technological advances into more effective treatments and prevention strategies.” The CME Program is part of an overall FCCC commitment to quality improvement titled QUEST (Quality-Unity-Excellence-Science-Treatment). The CME activities offered to our learners embrace the standards associated with this commitment-to-excellence initiative.

CME content is based upon educational needs derived from professional practice gaps in knowledge, competence and performance in the context of desirable physician attributes as defined by various state and national organizations. The CME Program plans and executes CME interventions that are evidence-based and focus on new developments in cancer prevention, screening, diagnosis and treatment derived from basic, population and clinical research. Education certified by FCCC encourages safe and compassionate care for all patients that serves to improve the quality of patient outcomes. The CME Program collaborates with numerous stakeholders to address content relevant to patient care and healthcare outcomes, including patient safety, health disparities and health literacy. CME activities are provided to learners in several formats: live courses, regularly scheduled series, internet activities and enduring activities.

The CME Program is expected to improve professional knowledge and competence; performance in the areas of cancer prevention, screening, diagnosis and treatment; and patient outcomes with the goal of improving the quality of care and safety for cancer patients, cancer survivors, their families and those at risk of cancer.

The CME program is nationally accredited by the Accreditation Council for Continuing Medical Education (ACCME).

In 2009, the CME program sponsored nine (9) continuing medical education activities consisting of six (6) live activities and three (3) regularly scheduled series for a total of 61 hours of instruction. This is a 66% increase in the hours of instruction offered. Participants included 1094 physicians and 594 non-physicians, representing 15 states and 6 countries, demonstrating 87% more physician and 63% more non-physician attendees than in 2008.

- In 1998, Fox Chase Cancer Center embarked on a novel partnership with the Russian State Medical University (RSMU) in Moscow to provide training at our Center for RSMU Masters and Ph.D. level students. This partnership, originally conceived by Erica Golemis at Fox Chase and Olga Favorova, Professor of Molecular Biology at RSMU, has provided internship opportunities for 28 RSMU students over these past years. With each passing year, the program has expanded to include not only more students, but also more affiliations with premier Russian research institutions. Despite the growing number of sister institutions, the matching and oversight processes are essentially the same: enthusiastic and talented students are selected by professors at the Russian institute; these students then select potential mentors at our Center based on common research interests. Final matches are made by the Supervisory Committee at Fox Chase. Students typically intern at Fox Chase for approximately 15 months, although a number of them have elected to continue their studies and pursue their Ph.D. research in the host laboratory. Soon after the students’ arrival at Fox Chase, an Advisory Committee is formed for each student, consisting of their mentor and at

least two other faculty members with similar research interests. These committees meet with the student twice a year to provide research guidance and to afford the student an opportunity to present their work throughout the internship. Each Advisory Committee reports back to the Supervisory Committee. The success of the initial Partner Program with Favorova and RSMU allowed for associations to be established with other high quality institutions in Russia. A program sponsored by Fox Chase and Moscow Engineering Physical Institute (MEPI) provides up to two students per year an opportunity to acquire skills in bioinformatics, software design, and protein modeling. A third affiliation with Smolensk State Medical Academy (SSMA) proved to be very fruitful in the past three years, and four students have already benefited from this partnership. We are also currently evaluating other institutions as prospective partners, including Kazan, Novosibirsk and Moscow State Universities. Several “pilot” students from these institutions are currently doing research at Fox Chase.

Currently, 7 students are working in research laboratories at Fox Chase, pursuing their Ph.D. degrees. Of the 42 students who have completed their internships, all have elected to further their education in biomedical research, and many of these students have gone on to Ph.D. programs in the U.S., Europe or Russia. Collectively, these students have contributed to over thirty peer-reviewed manuscripts, and have presented their work at multiple international meetings. We anticipate that the number of students and Fox Chase faculty who will benefit from this program will continue to increase.

- Fox Chase Cancer Center Partners is a select group of community hospitals in Pennsylvania and New Jersey linked with Fox Chase Cancer Center. This affiliation enables community cancer centers to develop or enhance community-based oncology programs. As part of the affiliation, medical staffs at Partner hospitals have access to innovative and unique research protocols developed at Fox Chase and can be administered to patients in the local community. FCCC and its affiliates have also joined forces in research, treatment, prevention and education efforts and work together to increase enrollment in clinical trials. More than 7,000 patients have been enrolled in clinical trials through this collaboration since 1986.

Commercial Research Development Training

- The ORDA meets individually with each new researcher that joins Fox Chase. During this meeting, the ORDA provides information on Fox Chase’s Intellectual Property Policy and procedures and the services provided by the ORDA. The researcher is asked about research projects, existing relationships with industry, and avenues of inquiry being pursued that have the potential to lead to discoveries with commercial potential. This initial meeting serves to introduce the ORDA staff to the researchers so that they are able to recognize each other by face, which greatly facilitates future informal interactions.
- ORDA staff regularly (weekly) schedules meetings with research staff to keep abreast of new developments in the laboratories. During these meetings, the ORDA advises researchers about the process of disclosing, protecting and commercializing intellectual property.

- The ORDA holds a seminar for research staff once per year, which discusses licensing and commercial development of research. Speakers are invited from outside Fox Chase and have included patent attorneys and entrepreneurs.
- Much of the investigator/inventor education takes place when a particular discovery is disclosed to the ORDA. When a new discovery is disclosed, a formal assessment of protectability and commercial potential is made, and is shared with the inventor. If it is decided that the discovery merits the investment of institutional resources to attract a commercial partner, there is an ongoing dialog with the researcher during patent filing and prosecution, as well as during the selection of companies to contact.
- The ORDA regularly presents updates to Fox Chase's Senior Leadership, Investment Committee and Board of Directors. These presentations inform leadership about the services provided by the ORDA and those senior administrators in turn assist the ORDA in the education of the researchers and staff. Additionally, several Fox Chase board members hold executive positions in life science or venture capital firms and are helpful in recommending others among their personal networks that may be interested in hearing about research at the Fox Chase.
- The ORDA maintains a webpage on Fox Chase's homepage that includes a Frequently Asked Questions section and other information intended to educate staff about the commercialization of research.
- Finally, the ORDA maintains an open-door policy and provides education to researchers at every opportunity.

Outreach to Businesses Regarding Recent Research Developments

- The ORDA has begun regularly hosting representatives of biotechnology and pharmaceutical companies at Fox Chase with the objective to learn about corporate development pipelines and preclinical research endeavors, and in turn, for companies to hear about Fox Chase preclinical research and Phase I clinical research programs.

Companies hosted at Fox Chase during the year included Amgen, Lockheed Martin, Roche Molecular Diagnostics, Bristol-Myers Squibb, Charles River Laboratories, MedImmune, Novartis, Microsoft, Abeome, Morphotek, Reaction Biology, Myriad Genetics, and ShanghaiBio.

- The Fox Chase Marketing and Public Affairs Department prepares press releases and notifies the media about significant research milestones achieved at Fox Chase, including the publication of papers and the filing and issuance of patents. These offices also propose stories to regional and national media outlets about research being conducted at Fox Chase.
- Researchers publish papers and present their work at conferences and are frequently contacted by their colleagues from industry. Researchers are encouraged to cultivate these relationships and inform the ORDA of potential collaborations that evolve therefrom.

- Technologies available for licensing are described in listings on the ORDA section of the Fox Chase homepage. Technologies are also listed with commercial websites that provide descriptions to subscribing life science companies and venture capital firms.
- The ORDA writes descriptions of technologies available for licensing which are strategically distributed to industry business development executives, venture capitalists and other potentially interested parties.
- Fox Chase prints publications that describe ongoing research projects being conducted by Fox Chase faculty and staff. These publications are widely distributed by Fox Chase staff to industry, venture capitalists, candidates for employment, etc.
- Members of the Fox Chase Board of Directors are kept informed through presentations at board meetings and in discussions with Fox Chase administration.
- When the ORDA receives an invention disclosure, the ORDA staff identifies those companies most likely to be interested in the technology. The appropriate individual at each company is then contacted by letter, email or phone to make them aware of the nature of the technology, its stage of development and its competitive advantages.
- The ORDA and Fox Chase researchers maintain a network of contacts that they regularly update about new developments in Fox Chase's laboratories.
- The ORDA staff regularly attends technology rich conferences including BIO, AUTM meetings, LES meetings, BioPharma America meetings, etc.
- All ORDA staff members are encouraged to play an active role in their respective professional organizations. The visibility created by this activity facilitates new relationships between the Fox Chase Cancer Center and industry.
- The ORDA created brochures that describe Fox Chase's Biosample Repository, R&D Facilities, The Institute for Personalized Medicine and the Phase I Clinical Trial Program. These brochures are being widely distributed to industry and have been the basis for initial discussions around research collaborations.

Research Development Collaboration

Fox Chase is a founding member of The Biotechnology Greenhouse of Southeastern Pennsylvania (BioAdvance). Fox Chase has submitted applications for BioAdvance's consideration for technologies that need further investment before commercialization can be achieved. Support was also solicited from existing companies, with first priority being given to companies in Pennsylvania.

Fox Chase has a history of establishing new firms around a platform technology, as it has demonstrated success in the creation of spin-off companies. One of its first spin-off companies

founded in 2005 with patented technologies discovered at the Center, NexusPharma is developing novel therapies based on small molecule protein-protein interaction inhibitors. The Center patents provide the basis for NexusPharma's platform technology, and enable the discovery and development of novel therapies by modulating protein-protein interactions with small molecules to advance the treatment of cancer through approaches based on non-cytotoxic mechanisms.

Another Fox Chase spin-off, Dynamis Therapeutics, focuses on the discovery and development of therapeutic pharmaceuticals for treatment of diabetic complications. Fox Chase Cancer Center granted Dynamis an exclusive world-wide license, including the right to grant sublicenses, to make, have made, use and sell products and processes related to metabolic pathways of fructoseamine-3-kinase and 3-deoxyglucosone (3DG), adversely reactive molecules that cause the formation of free radicals and advanced glycation end products. Today the company is focused on developing new pharmaceuticals to treat the effects of aging, to prevent or minimize the devastating effects of diabetes mellitus, and Dynamis has developed and introduced an anti-aging cream to the professional spa market with a distributor and sales team. These companies have been successful recipients of Ben Franklin funding, BioAdvance funding and federal SBIR funding.

The ORDA participates actively in regional trade organizations such as the Greater Philadelphia Venture Group, Women's Investment Network, and the Pennsylvania Biotechnology Association in an effort to identify Pennsylvania companies whose interests coincide with those of Fox Chase. The research interests of these companies are maintained in a database so that an appropriate group of companies can be contacted when a collaboration opportunity arises. The Assistant Vice President of The Office of Research and Development Alliances is a member of the Board of Directors of BioStrategy Partners, an organization and network of broad business, legal and scientific expertise, founded in 2004 to provide business coaching and mentoring, networking, nurturing and corporate development services to fledgling companies and budding entrepreneurs. Fox Chase Cancer Center and its inventors have been the beneficiaries of its services.