Commercial Development of Research

While the economic landscape as a whole continues to improve, new challenges to research in academic institutions have appeared with sequestration and the consequent lessening of Federal funds available for research. Scientists at Magee-Womens Research Institute and Foundation (MWRIF) continue to make strong efforts to deepen our partnership with the pharmaceutical and biotechnology industries. These efforts include the licensure and commercial development of new discoveries supported by Health Research Formula funds. Our current research support from industrial sources remains approximately five percent, which is similar to the level of support from industrial sources for other U.S. universities, hospitals, and research institutions.

Several areas of research are naturally more appropriate for commercial development. In the field of infections and prevention of microbial diseases in the female reproductive tract, Charlene Dezzutti, PhD, is working with Mapp Biopharmaceutical and the International AIDS Vaccine Initiative to evaluate monoclonal antibodies for use in HIV prevention. She and Lisa Rohan, PhD, who collaborate on the Microbicide Trials Network, are involved with ImQuest Biosciences on separate, but related, projects exploring the potential of pyrimidinedione gels or films as topical microbicidal agents against HIV. Dr. Rohan is also working with Universal Stabilization Technologies on vaginal probiotic microbicides. Richard Beigi, MD, is conducting a study on maternal immunization in cooperation with Novartis. Ian McGowan, MD, PhD, extends his expertise in HIV prevention technologies to Merck as a consultant on a proposed intravaginal ring.

In the field of contraceptives, Beatrice Chen, MD, MPH, recently completed a study, as Site Principal Investigator (PI), for Bayer. She was assessing the safety and efficacy of ultra-low dose levonorgestrel contraceptive intrauterine systems. Dr. Chen is also Site PI on a study of comparative contraceptive efficacy being undertaken for Evofem.

Is other areas, Health Research Formula funds recipient Xin Huang, PhD, is working with OncoGene Oncology on a study of circulating microRNAs for use as biomarkers in ovarian cancer; Tony Plant, PhD, is working with the Belgian company Euroscreen in a study of NK3 receptor signaling in the control of luteinizing hormone secretion; and James Roberts, MD, serves on the advisory board of Pluristem, a company involved in the development of cell therapies for a variety of human diseases. Pluristem’s products are derived from human placentas, traditionally treated as medical waste after delivery. Lastly, in the area of pregnancy, which has traditionally not been a most attractive area for commercial development, Robin
Gandley, PhD, studies the clinical utility of a device (Alere Triage PLGF) to test placental growth factor levels as a prognostic indicator of preterm delivery, and Steve Caritis, MD, is working with the ProStraken Group to determine the pharmacokinetics and bioavailability of granisetron in a transdermal delivery system for use in pregnancy.

**Research Licensing Agreements**

Researchers at MWRIF are served by the University of Pittsburgh’s Office of Technology Management (OTM) through a subcontract agreement. The OTM is responsible for the protection, management, and commercialization of intellectual property for the University of Pittsburgh, including all standard licensing agreements. MWRIF’s investigators are a primary source of intellectual property, either through the invention of new products or processes or through unique expertise. The OTM employs intellectual property experts, specialized licensing managers, business development and technology marketing professionals, outreach teams, and reporting and compliance personnel. Our scientists interact closely with the OTM to ensure compliance to regulations and adherence to standard agreements. The OTM provides support, documentation, and forms for patent assignment, copyright assignment, confidential disclosure agreements, one-way confidentiality agreements, mutual confidentiality agreements, and materials transfer agreements.

On the basis of work done with the support of the 2011 Health Research Formula Grant, Yoel Sadovsky, MD, Scientific Director of MWRIF, in collaboration with Dr. Carolyn Coyne from the Department of Microbiology and Molecular Genetics at the University of Pittsburgh, submitted a patent application, in the previous reporting period, entitled “Use of the chromosome 19 miRNA cluster (C19MC) for treating microbial disease and promoting autophagy” (USPTO Application number 61/607,899). That patent is currently pending, and the development has gained more interest with the recent publication of this line of research.

MWRIF researchers and Health Research Formula Grant recipients Anda Vlad, MD, PhD, and Xin Huang, PhD, filed patent applications for plasma miRNAs as biomarkers for endometriosis and endometriosis-related ovarian cancer. Dr. Huang filed an international application, through the OTM, under the Patent Cooperation Treaty.

William Walker, PhD, filed a patent application on animal sterilization using inhibitors of the SHP2 tyrosine phosphatase, based on work done with the assistance of Health Research Formula funds. Yaacov Barak, PhD, filed an invention disclosure, “Hybrid mouse embryonic stem cells,” on May 16. It is currently under OTM review.

**Training Students and Health Professionals**

One of the prime missions of MWRIF is the training of the next generation of scholars in the area of reproductive sciences and women’s health. Indeed, our training programs are some of our crown jewels, and include scholars at all levels of academic development. For faculty, we now have two NIH-funded K12 programs that center on early faculty career development in women’s health and the reproductive sciences. These are Building Interdisciplinary Research Careers in Women's Health (BIRCWH), recently renewed, with four new trainees, and the Women's
Reproductive Health Research (WRHR) Career Development Program for three trainees. Together, seven junior faculty members are currently supported by these rich and intense 2- to 4-year training programs.

We continue to fund trainees at other levels who seek to acquire expertise in our field. MWRIF provides research infrastructure and support for postdoctoral scholars, supporting 2-3 trainees in basic, translational, or clinical research in reproduction, development, and women’s health. Each of our trainees is supported by $50,000 per year for up to 2 years. Graduates of our programs have generally been very successful in career advancement and in securing NIH funds for subsequent research.

At the graduate level, we have increased the number of positions available. A course in reproductive biology and development for students at the University of Pittsburgh is now in its third year, and has been a tremendous success. Our Clinical Research Training Award is designed to assist three or four OB/GYN residents or clinical fellows in pursuing clinical or translational research. This year, three trainees received $3,500 each to pursue their research.

Finally, we offer two types of summer programs, supported with stipends from MWRIF and community donors. The first is designed for undergraduate college students; 8–10 students are mentored in our laboratories for eight weeks. The second summer program provides 10 stipends for high school students undergoing four weeks of reproductive biology research training, which includes discussions, seminars, and formal instruction. All MWRIF programs support the recruitment of women, minorities, and disadvantaged or disabled scholars.

Commercial Research Development Training

We continue to educate our trainees in commercial research development, and the application of research advances to products. Training in this area is available for students, residents, clinical and postdoctoral fellows, and faculty, and includes recommended formal courses and hands-on training. We highlight that formal training in the commercial application of research is available through the University of Pittsburgh. For example, the University’s Office of Enterprise Development acts as a resource for health sciences faculty, including MWRIF faculty pursuing entrepreneurship and interaction with industry. The office acts as a catalyst to stimulate academic-industry collaboration and foster closer ties to industry and assists in the development of new start-up companies in and around Pittsburgh and, consequently, promotes economic growth in Western Pennsylvania. We specifically encourage our faculty trainees in the BIRCWH and WRHR programs to take courses in this area as part of their training.

An ongoing T32 grant provides training in basic and clinical pharmacology for postdoctoral fellows. This grant is critical to our mission because research into diseases that affect some of the most vulnerable members of our society, pregnant women (and their fetuses), has been sidelined by the pharmaceutical industry through fear of litigation. Therefore, the development of drugs designed for pregnant women has been limited, and these women receive limited scientific information or guidance about the medications they are prescribed. There are few investigators at academic institutions working in this area. Additional training in the fields of obstetrics and pharmacology are sorely needed, and we expect our program to address some of these needs.
Jerry Schatten, PhD, now has two R25 training grants (1R25CA163168 “Frontiers in Stem Cells in Cancer,” and 1R25AG043365, Frontiers in Aging and Regenerative Medicine), which are designed to train promising physician-scientists and other scientists from predominately underrepresented communities in sophisticated technologies using pluripotent stem cells for clinically relevant discoveries in cancer and in aging research. These grants include courses at diverse locations, including Howard University in Washington, DC, Ponce School of Medicine in Puerto Rico, Xavier University, Morehouse School of Medicine, and Meharry Medical College. Some of the didactic training include the biology of aging and cancer, related diseases, epigenetics, and the like. These training venues emphasize elimination of barriers to the recruitment and retention of our most talented researchers and training in responsible conduct of research, ethical, legal and societal implications, and especially problems of minority health disparities in research. They encourage and empower trainees and alumni by guiding them through the graduate application and matriculation processes.

An important component of training in research aimed at commercial development is education in the basic concepts, values, and policies related to the conduct of research. Topics available through courses and online modules include informed consent, the design and justification of randomized trials, doing research with vulnerable populations, and the ethical aspects of research. Our training also emphasizes conflicts of interest (COIs). Financial COIs are discussed, as are the underlying ethical principles associated with COI, and the risks of unmanaged COIs. The program includes important management tools, policies related to researchers, consulting agreements, the commercialization of inventions, required disclosure of outside interests, COIs related to technology transfer and start-up companies, and sanctions that apply for violations of COI policies. In addition to lectures, hands-on training is provided. Such topics have been discussed by the University of Pittsburgh’s OTM at MWRI faculty meetings.

**Outreach to Businesses Regarding Recent Research Developments**

In reaching out to businesses on recent research developments, we have submitted registration information on several innovations to the Office for Technology Management at the University of Pittsburgh School of Medicine. In addition, investigational new drug (IND) applications are submitted to the FDA. These are developed with the long-term intention of stimulating the potential for commercialization of these products through partnerships with industry. IND applications for new antimicrobial agents were submitted in the current fiscal year by Drs. Lisa Rohan and Ian McGowan.

A critically important way to stimulate interest in our projects involves scientific presentations at national academic meetings, which are also attended by industry. The MWRIF Web site ([www.mwrif.org](http://www.mwrif.org)) offers another venue, on which we place details of our research, making this information available to potential business partners. We also make faculty research interests and project results available through the Faculty Research Interests Project of the University of Pittsburgh, which is regularly reviewed by businesses.
Research Development Collaboration

Our scientists recognize the importance of sharing expertise between researchers and among institutions. Such collaborations foster new ideas, confer abilities beyond what either party alone could bring to bear, and offer savings in cost and time, moving scientific and clinical understanding ahead to the benefit of women and society. As is always the case, too, each step forward offers new opportunities for commercial development, scientific exploration, and therapeutic application. Our researchers strive to lay the foundations for new transdisciplinary research in partnership with academic and nonacademic entities alike. Such collaborations may lead to synergies, and accelerate the pace of discovery and the translation of knowledge to care and wellness.

We outline here active collaborations in research development.

- In the field of reproductive development and fertility, Kyle Orwig, PhD, is collaborating with Renee Reijo Pera of Stanford University to test the function of germ cells generated from induced pluripotent stem cells (IPSCs), with Amander Clark of UCLA in a study of fertility restoration via transplantation of patient-specific IPSCs to the testes of infertile male monkeys, and with Marvin Meistrich and Gunapal Shetty of MD Anderson Cancer Center to test the potential of stem cell transplantation to restore fertility in nonhuman primates rendered infertile by chemotherapy or radiation. Studies in this area are strengthened by working with Miles Wilkinson of UC San Diego to test the function of spermatogonial stem cells in a mouse model, and with Makoto Nagano of McGill University to explore optimal conditions for maintaining human spermatogonial stem cells in culture. Judith Yanowitz, PhD, is collaborating with Verena Jantsch of the Universitat Wien to investigate crossover points in homologous chromosome pairs during meiosis.

- In the field of pelvic health, Halina Zyczynski, MD, is collaborating with investigators from the Cleveland Clinic, the University of Pennsylvania, Brown University, the University of Alabama, Duke University, UC San Diego, the University of New Mexico, and the National Institute of Child Health and Human Development in research on female pelvic floor disorders and their treatment.

- In the field of Infections and Antimicrobial drugs, Charlene Dezzutti, PhD, studies innovative drug delivery systems as well as anti-HIV drugs with investigators at Loma Linda University, Scripps Research Institute, the University of Manitoba, the University of Louisville and CONRAD. Lisa Rohan, PhD, collaborates with researchers from both academia and industry in the area of pharmaceutical drug development. These include Janssen Pharmaceuticals, Advanced BioScience Laboratories, Merck Pharmaceuticals, CONRAD, and the International Partnership for Microbicides Dr. Phalguni Gupta in the Department of Infectious Diseases and Microbiology of the University of Pittsburgh’s School of Public Health. Other collaborators are at Johns Hopkins, Brown University, the University of Central Florida, the University of Washington, and the University of Louisville.

- In the field of contraceptives, Beatrice Chen, MD, is the Site PI for several studies sponsored by the Contraceptive Clinical Trials Network, the Society of Family Planning, and CONRAD.
In the field of Cancer, Francesmary Modugno, PhD, MPH, and Robert Edwards, MD, began working on a multicenter study with investigators from Roswell Park Cancer Institute, Dana-Farber Cancer Center, and Memorial Sloan-Kettering Cancer Center to investigate factors associated with molecular signatures in female cancers. The goal of the study is to identify preventive and risk-reducing interventions and to gain insight into the biology of cancer development.

In the field of Pregnancy, James Roberts, MD, a former recipient of Health Research Formula funds, heads a Bill and Melinda Gates Foundation program designed to facilitate worldwide collaboration in monitoring, preventing, and treating adverse pregnancy outcomes. Currently, 22 centers are involved in these high impact collaborations, with information and/or biological samples from 300,000 pregnancies. Carl Hubel, PhD, a current Health Research Formula Grant awardee, has a collaboration agreement with Susan Fisher of UC San Francisco to investigate placental vascular function as part of his investigation of the mechanisms of preeclampsia. Janet Catov, PhD, is collaborating with Claudia Holzman, Professor of Epidemiology at the University of Michigan on Dr. Catov’s Health Research Formula Grant, “Maternal lipids and placental function.” She also works with investigators from the Coronary Artery Risk Development in Young Adults (CARDIA) study and with Erica Gunderson of Kaiser Permanente’s Research Division. Richard Chaillet, MD, PhD, has established a collaboration with the laboratory of Jacquetta Trasler of McGill University for a genetic study of mouse embryonic stem cells and placenta.

In the field of patient wellness and family health, Judy Chang, MD, MPH, works with community advocates from the Women’s Center and Shelter of Greater Pittsburgh on projects to foster mother-child communication between victims of intimate partner violence and their children, and to educate healthcare providers about intimate partner violence and train them to communicate more effectively on this subject with their patients.