ANNUAL REPORT

FY 2016

NIH Technology Transfer Activities

Contents

MISSION STATEMENT

The mission of Technology Transfer at National Institutes of Health (NIH) is to facilitate partnerships with a wide array of stakeholders, and effectively manage the inventions conceived by scientists working at the NIH, Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC). In doing so, NIH Technology Transfer supports the larger NIH mission to enhance public health and safety, lengthen life, reduce illness and disability, and expand the worldwide biomedical knowledge base.

Working on behalf of the NIH, the FDA and the CDC – all agencies of the Department of Health and Human Services (HHS), Technology Transfer offices[1] across the NIH apply responsive, and sometimes creative approaches to meet the needs of all parties involved, operating with a goal of moving scientific research and discovery forward for the benefit of public health. Technology Transfer at NIH:

- Protects U.S. intellectual property and the discoveries conceived by NIH, FDA and CDC intramural researchers. This includes working with researchers to determine if an invention warrants patent protection, overseeing the filing of Employee Invention Reports (EIRs), and coordinating the patenting filing and prosecution process.
- Serves as a bridge through marketing and communications, connecting the inventive discoveries made by scientists in the NIH, FDA, and CDC research programs to commercial partners with the capability of developing these technologies into products and services to benefit public health. Without technology transfer, the full potential of these inventions would not be realized, and the public would not receive the full benefit of these biomedical discoveries.
- Facilitates partnerships with outside parties to allow for joint collaboration.
- Negotiates licenses and collaborative agreements such as Cooperative Research and Development Agreements (CRADAS) to ensure the timely development of federal technologies, that contribute to society by driving economic growth and productivity; These collaborations leverage the strengths of each institution to advance basic and clinical research objectives.
- Monitors the development of these technologies to ensure commercialization milestones are reached, products are brought to the market, and royalty fees are paid.
- Facilitates the transfer of thousands of research materials and data into and out of NIH.

[1] Please see Appendix A for a list of all the HHS Technology Offices within the NIH that contributed towards this report.

INTRODUCTION

In FY2016, the NIH Technology Transfer community completed the first full year of patent and license decentralization, with the NIH Institutes and Centers (ICs) in control of patenting and licensing decisions, and the Office of Technology Transfer (OTT) serving a purely service and support function to the NIH Technology Transfer Offices (TTOs), the FDA and the CDC. The DHHS Technology Transfer community has worked collaboratively to ensure a smooth transition of authority and process. In FY2016, the community reported 320 new invention disclosures and 285 executed licenses, both increases over FY2015. We are thrilled that our community is successfully settling into this new environment.

Our community completed a significant amount of work in FY2016. The OTT worked diligently on IT systems in support of the community and made available to the TTOs TechTracS, the system of record for all patent and license data and information, and the OTT SharePoint site, which aids the community with transfer and management of vital documents and information. This was no small feat, as the design and build of these systems was for single-office use and access. System design and security enhancements were required to ensure appropriate system access and data stability. By the close of FY2016, there were 175 TechTracS users and 225 SharePoint site users from the community, with access points from across the country. Additionally, OTT staff scanned into electronic format, more than 1.8 million paper documents for TTO availability in the TechTracS system.

These information systems are aging and not dynamic. For this reason, our Technology Transfer community worked diligently with OTT to complete a "Fit-Gap Analysis" of the community's technology transfer agreement needs (for all types of agreements). The information provided by the community in the Fit-Gap Analysis was included in a jointly submitted proposal to the NIH Capital Investment Fund to request funding for a new, trans-NIH enterprise technology transfer system. We look forward to working on requirements for this new IT system in FY2017.

In FY2017, the FDA will assume responsibility for its own technology transfer services (patenting, licensing, royalties administration, monitoring and enforcement of agreements, marketing, patent docketing, etc.) through its Technology Transfer Office. The OTT and our Technology Transfer community have begun collaborating closely with our FDA colleagues to ensure a smooth transition of data and support services; our communities welcome the opportunity to working closely in support of DHHS goals and missions.

Our technology transfer professionals promoted the development and commercialization of many notable scientific advancements in FY2016. This report reflects the accomplishment of technology transfer at the NIH, FDA and CDC, and demonstrates the community's commitment to meeting the changing needs of our stakeholders and facilitating the collaboration and the commercialization of NIH scientific discoveries.

INVENTIONS & AGREEMENTS

The Technology Transfer Program at the National Institutes of Health is the focal point for implementation of the Federal Technology Transfer Act. Technology licensing specialists in the NIH Institutes and Centers license patented inventions to pharmaceutical, medical device and biotechnology companies in order to stimulate development of technologies into commercial products. These licensing specialists also transfer materials to non-profit research institutions and license for a fee to commercial entities unpatented research tools to increase their availability to the scientific community. These activities support the NIH's mission to benefit the public health and to provide a financial return on public investment.

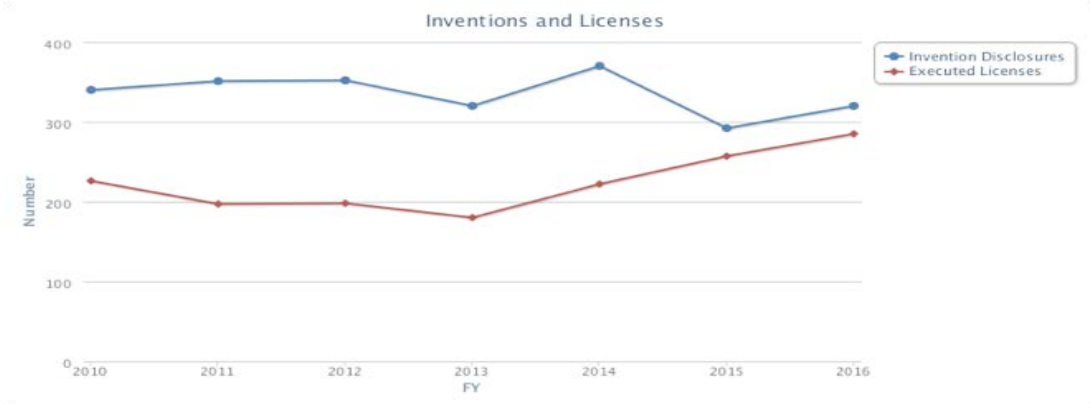
In addition, the Technology Transfer Program negotiates terms for research collaborations between NIH and commercial and academic organizations. These collaborations leverage the strengths of each institution to advance basic and clinical research objectives. Technology Transfer also facilitates the transfer of thousands of research materials and data into and out of NIH.

In FY16, NIH Institutes executed 8,323 of these collaboration and transfer agreements, including 115 new Cooperative Research and Development Agreements (CRADAs). CRADAs are an important mechanism used by NIH for many of the collaborations with industry. The new CRADAs combined with those active from prior years brought the total active CRADAs to 523, an 8% increase from FY15.

IP-Related Agreements in Numbers*

(*includes NIH, FDA and CDC data)

- **320** - Number of **invention disclosures** reported.
- **279** - **License agreements executed**, **44** were **exclusive**.



- **-36%** - **Decrease** in the number of **non-US licenses executed** compared to FY15.
- **55%** - **Increase** in the number of **US licenses executed** compared to FY15.

Additional Stats:

- **112** - **Licenses** issued to **small, US-based businesses.**
- **95** - **Licenses** issued to **large, US based businesses.**
- **5%** - **Increase** in number of **US Patents filed** from FY15.
- **-6%** - **Decrease in royalties received at the NIH** from FY15.

All technology-licensing activities led to a total royalty income of $138 million, which is a 6% decrease from FY2015. After inventors are paid their portion of the royalties, NIH institutes use royalties income to offset the operational costs associated with patenting and licensing programs, and when available, to support mission-related activities. As reported in the FY2015 annual report, NIH is projecting that royalties will decline in FY18 – FY20 when certain licensed patents expire, and the downward trend is in evidence in FY16.

Readers of this report interested in more details on the above metrics, or who would like to learn more about yearly benchmarks tracked at the NIH such as Exclusive Licensing, breakdown of Licensees by Type of Business, First Time Licensees, number of Active CRADAs, etc., are encouraged to visit the NIH OTT website Metrics section at https://www.ott.nih.gov/tt-metrics. Charts displayed at this website are interactive. Viewers can zoom in, highlight, or disable certain metrics to gain greater insight.

In addition, readers can also interactively view the stories highlighted here along with all the various advances made in the Intramural Research Program (IRP) at the NIH. For viewing these, and other success stories, please visit https://www.irp.nih.gov.

DHHS AGENCIES & NIH INSTITUTES AND CENTERS

CC - NIH Clinical Center

CDC - Centers for Disease Control and Prevention

CIT - Center for Information Technology

FDA – Food and Drug Administration

NCATS - National Center for Advancing Translational Sciences

NCCIH - National Center for Complementary and Integrative Health

NCI - National Cancer Institute

NEI - National Eye Institute

NHGRI - National Human Genome Research Institute

NHLBI - National Heart, Lung, and Blood Institute

NIA - National Institute on Aging

NIAAA - National Institute on Alcohol Abuse and Alcoholism

NIAID - National Institute of Allergy and Infectious Diseases

NIAMS - National Institute of Arthritis and Musculoskeletal and Skin Diseases

NIBIB - National Institute of Biomedical Imaging and Bioengineering

NICHD - Eunice Kennedy Shriver National Institute on Child Health and Human Development

NIDA - National Institute on Drug Abuse

NIDCD - National Institute on Deafness and Other Communication Disorders

NIDCR - National Institute of Dental and Craniofacial Research

NIDDK - National Institute of Diabetes and Digestive and Kidney Diseases

NIEHS - National Institute of Environmental Health Sciences

NIMH - National Institute of Mental Health

NIMHD - National Institute on Minority Health and Health Disparities

NINDS - National Institute of Neurological Disorders and Stroke

NINR - National Institute of Nursing Research

NLM - National Library of Medicine

ORS - Office of Research Services

INSTITUTIONAL HIGHLIGHTS

Fighting Infectious Diseases

► Progress on Zika (NIAID and CDC)

Fighting Zika (NIAID): Zika dominated the news in FY 2016. The Zika virus is a mosquito-borne flavivirus that was identified in humans in 1952 in Uganda and the United Republic of Tanzania. From the 1960s to 1980s, human infections were found across Africa and Asia, typically accompanied by mild illness. In October 2015, Brazil reported an association between Zika virus infection and microcephaly. By late spring 2016, it was confirmed that Zika virus infection during pregnancy is a cause of congenital brain abnormalities, including microcephaly; and that Zika virus is a trigger of Guillain-Barré syndrome.

The urgent need for diagnostics, vaccines, and treatments for Zika virus infection led to a surge in NIAID's related research and partnership activities, and NIAID's Technology Transfer and Intellectual Property Office (TTIPO) rose to the challenge. During FY 2016 NIAID TTIPO completed 33 agreements and filed 2 patent applications to help advance NIAID research and development on the Zika virus.

Rapid Sharing of Zika Clinical Samples (NIAID): One of the first barriers to advancing research and developing diagnostics, vaccines, and treatments for Zika virus infection was rapid access to Zika samples such as virus isolates and patient sera. TTIPO coordinated with the Office of General Counsel (OGC) and the Office of the Assistant Secretary for Preparedness and Response (ASPR) – both of the Department of Health and Human Services (DHHS), the Centers for Disease Control and Prevention (CDC), and the NIAID Division of Microbiology and Infectious Diseases (DMID), to develop a strategy and framework using the existing infrastructure to quickly share Zika clinical samples.

The team developed an Emergency Use Simple Letter Agreement (EUSLA) to memorialize exchanges of Zika samples during this emergency. NIAID leveraged its Biodefense and Emerging Infections Research Resources Repository (BEI Resources), to expand capacity to store and distribute these critical research samples. Under NIAID's direction, BEI Resources sent Zika samples and materials to over 250 entities in 35 states in the US and 13 foreign countries in FY 2016 to encourage the development of countermeasures to this emerging health threat.

Zika Vaccine Development with the Walter Reed Army Institute of Research (WRAIR) (NIAID): NIAID and the Walter Reed Army Institute of Research (WRAIR) of the United States Army Medical Research and Materiel Command (USAMRMC) have been collaborating to develop an effective and safe vaccine for the prevention of Zika virus infection. In FY2016, NIAID, WRAIR, and the Biomedical Advanced Research and Development Authority (BARDA) entered into a

Memorandum of Understanding (MOU) to define and delineate roles and responsibilities in support of the development of Zika Purified Inactivated Vaccine ("ZPIV") candidates.

Interagency Collaborations to Combat Zika (CDC): While utilizing CDC expertise in addressing infectious disease public health challenges, CDC's Technology Transfer Office (TTO) realizes that leveraging the strengths of outside partners and successful interagency collaborations confers great benefits to the public we serve. In the midst of developing the Zika Simple Letter Agreement (a Zika "SLA" modified from a longer Material Transfer Agreement) for rapid sharing, TTO worked with other agencies such as Biomedical Advanced Research and Development Authority, National Institute of Allergy and Infectious Diseases (NIAID) and the Department of Health and Human Services to partner with two specimen and research tool repositories to expedite the distribution of Zika virus specimens and related laboratory research materials such as reagents. This reduced potential backlogs and delays for sharing these items in light of the numerous requests from academia/industry to access such materials to support Zika research for diagnostic tests and vaccine candidate development.

Use of this multi-pronged approach to advance CDC's research to develop products that meet public health needs through technology transfer has proven scalable for use during the Zika outbreak. To date, CDC has shared Zika research specimens and related materials with 158 organizations using the Zika SLA. Four short-term, no-fee licenses were structured to address the immediate public health need to expand use of CDC's Zika MAC-ELISA antibody assay for patient testing. Components of the Zika ELISA test with virus-like particle (VLP) technology are in the process of being licensed to a fifth company, which will then mass manufacture and sell these materials to commercial diagnostic testing organizations. These licensing efforts were accomplished with our partner, the NIAID Technology Transfer and Intellectual Property Office, which is responsible for patenting and licensing CDC technologies. Numerous industry partnerships are now in place to advance CDC's Zika research. Lastly, use of the Zika SLA with other United States government agencies has led to depositing Zika reagents with two repositories, where 296 added requests have been shipped out to partners in 38 states and 12 other countries.

Leveraging industry to help address public health challenges has been part of the CDC TTO's key functions. This takes on great significance in the context of addressing an emerging challenge like the Zika virus outbreak. CDC's successful partnering with industry has helped in three ways: developing vaccine candidates and diagnostic tests, testing new insecticide and mosquito repellents, and developing and deploying a new mosquito trap. In conjunction with the NIAID Technology Transfer and Intellectual Property Office, which is responsible for patenting and licensing CDC technologies, TTO has used CDC patents with commercial partners to: 1) file two patent applications for Zika vaccine candidates (a dengue/Zika chimera and VLP technology), subject of two CRADAs to develop Zika vaccines; 2) commercially license a VLP (part of a CDC-developed Zika MAC-ELISA antibody test); 3) issue three US patents for a compound that is also the subject of a CRADA and patent license agreement to develop and register a natural mosquito insecticide and repellent; 4) award a Small Business Innovation and Research (SBIR) Program and other innovation grants for CDC's Autocidal Gravid Ovitrap (AGO) mosquito trap.

At the onset of the Zika outbreak, CDC was the only reference testing facility in the United States. In order to establish national Zika virus testing capacity, TTO worked to expand private industry partnerships. The results are commercial Zika virus diagnostic testing options through CDC TTOs having executed four short-term, no-fee licenses with four clinical testing reference laboratories.

Autocidal Gravid Ovitrap (CDC): CDC's Autocidal Gravid Ovitrap (AGO) mosquito trap has been successfully used by mosquito control programs for mosquito surveillance and control. The patented AGO attracts and catches female *Aedes aegypti* mosquitoes looking for a place to lay eggs. Field trials in which the AGO trap has been installed in most homes in a community have shown it reduces mosquito populations AND rates of infection. Smaller scale field trials were so successful that CDC and the Puerto Rico Department of Health are implementing large-scale installation of AGO traps throughout several communities to help reduce mosquito populations and the viruses they spread.

CDC TTO and CDC staff are working with an outside partner to mass produce the trap and use it further in Puerto Rico. Upon successful completion of its Phase I SBIR award, the partner received Phase II SBIR funding to pursue continued work on the trap. CDC TTO is renegotiating a research collaboration agreement (RCA) because the partner wishes to collaborate further with CDC. Our colleagues at the NIAID Technology Transfer and Intellectual Property Office, who are responsible for patenting and licensing CDC technologies, have also negotiated a non-exclusive license with another commercial partner to bring this trap to the marketplace.

▶ Sharing of Databases to Help Fight Antibiotic Resistance in Microorganisms (CC)

The execution of multiple agreements for the NIH Clinical Center's (CC) Department of Laboratory Medicine are facilitating the transfer of databases of antibiotic resistant organisms to hospitals and health care recipients around the U.S. The spread of antibiotic resistance in disease-associated microorganisms is an area of growing health concern worldwide. The CC developed databases of such microorganisms. These databases are made available for use by treating physicians to identify microorganisms and assist in the diagnosis of infectious diseases in patients at their hospitals.

▶ Enhancing Commercialization of Dengue Vaccine (NIAID)

Dengue virus is a mosquito-borne flavivirus present worldwide in tropical and semitropical regions. It is estimated that 500 million infections occur annually, resulting in more than 2 million cases of severe dengue and 21,000 deaths. An effective vaccine is a public health priority. Dr. Stephen Whitehead and others at NIAID's Laboratory of Infectious Diseases (LID) have developed a tetravalent live attenuated dengue virus vaccine, TV003, which was shown to elicit a robust antibody and cellular immune response after just one dose.

In 2016, TV003 protected all 21 volunteers who received the vaccine from Dengue infection in a virus challenge study, while all 20 placebo recipients developed infection. The Butantan Institute, a non-profit producer of immunobiologic products for Brazil, is sponsoring a placebo-controlled, multi-center Phase 3 trial. This technology was licensed to five licensees, including the Butantan Institute, covering worldwide development and commercialization. In FY 2016, TTIPO continued to market this technology and added two more non-exclusive licensees, enhancing the commercialization in Taiwan, India, South East Asia, Middle East, Australia and New Zealand.

► Clinical Trials on the Use of Encochleated Drugs to Treat Infections (NIAID, NHLBI, Clinical Center)

This CRADA was the first of what is anticipated to be several clinical trial CRADAs between NIH and Matinas BioPharma Holdings using a new Matinas-specific CRADA template (umbrella agreement) to examine safety, efficacy and pharmacokinetics of a proprietary encochleated delivery platform for orally administered drugs. Encochleated drugs are resistant to premature enzyme degradation and can targeted, thereby reducing effective dosages and toxicity. Under this CRADA encochleated amphotericin B and amikacin are being studied to treat fungal, bacterial, and viral infections. Matinas is providing $600,000 over three years to NIH in support of this important research objective.

► Ebola Vaccine Development (NIAID)

A collaboration between Dr. Nancy Sullivan at the NIAID Vaccine Research Center (VRC) and Okairos, initiated in 2008, was very productive. NIAID filed patent applications claiming the co-invented cAd3-EBOV technology in 2010. Ebola vaccine candidate cAd3-EBOV is a chimpanzee adenoviral vector vaccine expressing Ebola virus glycoproteins. As the 2014 Ebola Virus outbreak began to reach historic proportions, the VRC decided to expedite its clinical trial plans. GlaxoSmithKline (GSK), which acquired Okairos in 2013, and other clinical trial partners quickly joined the VRC in its plan to accelerate development efforts. This made it necessary for the technology transfer team to apply creative and pragmatic solutions to quickly enable the start of clinical trials.

Within two months, all agreements enabling the start of clinical trials were negotiated and executed for the conduct of Phase I trials in the U.S. (Baltimore, Bethesda, and Atlanta), the U.K., Switzerland, and Mali. In many cases, unique agreements were drafted to circumvent anticipated delays. For example, early on a special material transfer agreement (MTA) was used to send the cAd3-EBOV through customs to the U.K. This allowed the clinical trial to begin within hours of the execution of the clinical trial agreement. When GSK agreed to have more cAd3-EBOV clinical product manufactured through a contract research organization, a specialized MTA was used for VRC to transfer the necessary materials for cGMP manufacturing. A “Quality Agreement” between GSK and the VRC was signed to ensure that the clinical product was make to the proper standards before vialed and labelled at the VRC’s Vaccine Production Plant.

▶ Vaccine Development Against Human Respiratory Syncytial Virus (NIAID)

Human Respiratory Syncytial Virus (RSV) is the leading viral agent of severe pediatric respiratory tract disease worldwide. RSV has been estimated to be responsible each year for 34 million cases of lower respiratory tract disease, over 3.5 million hospitalizations, and 66,000- 200,000 pediatric deaths worldwide. There are no available vaccines for RSV.

NIAID and Sanofi Pasteur, Inc. have entered into a CRADA to identify and/or test live attenuated RSV vaccine candidates for pediatric use in preclinical and clinical studies. Under the CRADA, Sanofi Pasteur, Inc. will provide significant research support to Dr. Peter Collins and his colleagues at LID, DIR.

▶ Repurposing Approved Drugs (NIDDK)

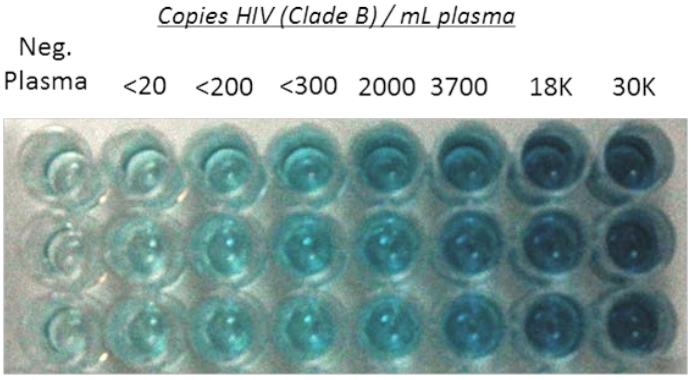
Chlorcyclizine, an antihistamine available over-the-counter, was found to have activity against hepatitis C in lab models. The method of use patent has been licensed and a small clinical trial using the maximum approved dose is underway at NIDDK. The effect against the virus is believed to be host-mediated.

▶ Global Disease Vaccines (NIDDK)

A conjugate cholera vaccine with intellectual contribution from NIDDK, FDA in conjunction with the infectious diseases department of a major university hospital progressed through engineering scale-up, characterization assays, and generation of cGMP cell banks for both the polysaccharide and antigen components. Additional funding to produce the cGMP vaccine for a clinical trial is being sought by the university partner.

▶ Point of Care Diagnostic Platform (NIDDK)

A diagnostic platform that uses peptide nucleic acids to bind the target RNA or single strand DNA has been developed. The proof of concept test was targeted to HIV viral load measurement. License applications were received from four companies, each planning to incorporate the NIDDK technology with own proprietary operating system. The technology may be deployable in minimally resourced areas as well as developed countries.



Combating Neurodegenerative and Neuropsychiatric Disorders

▶ Non-opioid Pain Medication (NIDDK)

NIDDK out-licensed a lead and two back-up compounds that are agonists to the adenosine 3 receptors. The investigators showed in animal models that this g-coupled protein receptor is part of the neuropathic pain pathway. Of particular interest is that these compounds do not induce tolerance and reverse tolerance to opioids in animal models. Preclinical testing in vitro and non-GLP testing in animal models was completed by NIDDK before the license was negotiated.

▶ Enhancing the Use of Positron Emission Tomography (NIMH)

NIMH and Pfizer, Inc. are collaborating under a clinical CRADA to study Pfizer's proprietary positron emission tomography (PET) radiotracer to image abnormalities in patients with neuropsychiatric disorders.

▶ Approval of Daclizumab (Zinbryta) to Treat Multiple Sclerosis (NINDS)

In May 2016, the FDA approved daclizumab for treating adults with relapsing forms of multiple sclerosis (MS). First approved for organ transplant rejection, daclizumab's use as a MS treatment involved both collaboration and licensing technology transfer efforts. In 2010, NINDS established a CRADA with Biogen Idec and Facet Biotech/PDL for conducting phase I studies. These initial studies demonstrated the potential of the treatment for MS. The technology is exclusively licensed to AbbVie (acquired Facet Biotech/PDL), which in collaboration with Biogen conducted the further clinical trials leading to the product's eventual regulatory approval in the US as well as Europe (July 2016).

▶ Evaluating Potential Therapeutics for Parkinson's Disease (NINDS)

NINDS technology transfer negotiated and executed a CRADA with Mitokinin, LLC to evaluate twenty-five (25) kinetin analogs to identify the most promising molecules that optimally stimulate the catalytic activity of PTEN Induced Kinase 1 (PINK1). PINK1 is found to be mutated in individuals with Parkinson's disease. The most clinically relevant PINK1 mutations are those that impact the catalytic activity of the kinase. PINK1 utilizes kinetin analogs catalytically better than ATP. The identification of the most promising kinetin analogs can lead to the development of novel therapies for Parkinson's disease.

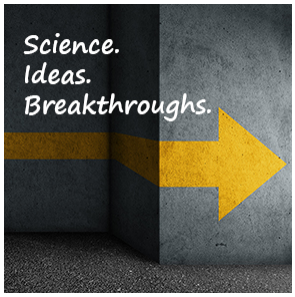
▶ Therapeutics for Amyotrophic Lateral Sclerosis (NINDS)

In late September 2015, Dr. Avindra Nath and his research group at NINDS published studies demonstrating that the pathogenic activity of envelope protein from the family of endogenous retroviruses (HERV-K) is involved in amyotrophic lateral sclerosis (ALS) and developed cellular and transgenic mouse models that can be used to evaluate various therapeutic candidates to treat ALS, including anti-HERV-K antibodies. To facilitate collaborations or utilization of this technology with commercial partners, NINDS technology transfer initiated pursuit of patent

protection for this technology prior to disclosure and has filed a Patent Cooperation Treaty (PCT) application in FY16.

This strategy proved effective as GeNeuro, a biopharmaceutical company developing new treatments for neurological disorders and autoimmune diseases, approached NINDS to discuss potential development novel therapeutic antibodies for the treatment of amyotrophic lateral sclerosis (ALS). NINDS negotiated a confidentiality disclosure agreement to facilitate discussions of a potential collaboration, and CRADA negotiations began in FY16. Under the CRADA (executed in FY17), GeNeuro will provide antibodies designed to block the activity of HERV-K envelope protein. These candidate antibodies will be tested in cellular and animal models of HERV-K associated ALS by the NINDS with the aim to achieve preclinical proof-of-concept of this novel therapeutic avenue addressing ALS pathogenesis. With this partnership, NINDS and GeNeuro aim to show that blocking the pathogenic HERV protein could lead to a novel ALS treatment and, in time, expand into novel treatments for additional neurological disorders.

Race Against Rare Diseases



► Treating Fibrodysplasia Ossificans Progressiva (FOP) (NCATS)

The original CRADA between NCATS and Partners Healthcare envisioned the development of small molecule therapeutics for FOP, a debilitating rare disease that leaves the sufferers with increasing morbidity, disability and eventually death. The CRADA allowed Partners to take the lead on patenting and licensing the CRADA inventions. As the project team made significant advances in identifying a lead drug candidate, a group of investors developed interest in the technology, and established a new company Keros that then secured an exclusive license to the patent estate. Further impressed by the ongoing collaboration between NCATS and Partners, Keros wanted to support the CRADA and join the group as an active lead optimization and development partner. Subsequently, Keros has invested heavily in the project, and is providing a set of useful synergistic studies and developmental efforts.

► Treating Pulmonary Alveolar Proteinosis (NCATS)

In collaboration with Genzyme and NCATS, Dr. Bruce Trapnell of Cincinnati Children's Hospital Medical Center (CCHMC), began the approval process for Granulocyte-macrophage Colony-Stimulating Factor (GM-CSF) to treat the rare lung disease Pulmonary Alveolar Proteinosis (PAP). In collaboration with the NCATS Clinical Translational Science Award (CTSA) program, we were able to find the requisite funding for Phase1 clinical trials for using an inhaled version of GMCSF to treat PAP. The CTSA supplemental funding would support a limited safety study of the drug at two sites – CCHMC and University of California, Los Angeles (UCLA). The NCATS Office of Strategic Alliances (OSA) negotiated a Clinical Trial Agreement (CTA) that made this collaboration possible.

▶ Slowing the Progression of Fuchs Dystrophy (NCATS)

Fuchs Dystrophy is characterized by a loss of endothelial cells from the posterior cornea, leading to the loss of optical quality of the cornea, and impaired vision. The only treatment option for severe cases is transplantation of the cornea. Trefoil Therapeutics is developing an engineered form of fibroblast growth factor 1 (eFGF-1), which has been shown to stimulate the proliferation and migration of human corneal endothelial cells in vitro and has the potential to be regenerative in vivo. The CRADA between NCATS and Trefoil would allow the company to overcome a number of preclinical challenges including drug scale up, toxicology testing and the development of bio-analytical methods. Once the CRADA negotiations were negotiated, Trefoil successfully raised additional funds from private investors to get eFGF-1 to the next stage of drug development.

▶ Studying Waldenström Macroglobulinemia (NCI)

A collaboration agreement with a French research institute will facilitate international studies on Waldenström Macroglobulinemia (WM), a rare lymphoproliferative disorder originating in B cells. No genes have been identified as contributing to WM susceptibility – despite promising genome-wide linkage analysis and candidate gene association studies. Negotiation of this complex collaboration agreement was complicated by the French institution requiring inclusion of unmodifiable European Union (EU) Data Protection Directive clauses. The National Cancer Institute's Technology Transfer Center (TTC) arrived at a solution to these problematic clauses by drafting language in the collaboration agreement to address the provisions in the EU Directive clauses. This approach was accepted by the outside institution, and may be useful for future data transfer agreement negotiations with EU institutions. As a result of this agreement, NCI was able to obtain genomic samples and associated data to understand and analyze the diagnostic, therapeutic, phenotypic and genotypic associations of this rare disorder. TTC's initiative to find a way to meet the needs of the parties resulted in: establishing a new framework for agreements with EU institutions, allowing NCI researchers access of needed samples and data, and contributing to the understanding of a rare disease.

▶ Collaborations to Fight Neimann-Pick Disease (NHGRI)

The NHGRI entered into a Research Collaboration Agreement with the University of Pennsylvania for a project titled "Design and Testing in Animal Models of Adeno-Associated Virus (AAV) Gene Therapy Constructs to Treat Niemann-Pick Type C1 (NPC1)."

The NHGRI entered into a Research Collaboration Agreement with the California Institute of Technology for a project titled "Analysis of the Efficacy of Two AAV Serotypes in Gene Therapy," for Neimann Pick Disease Type C (NPC). With this partnership, NHGRI and CalTech aim to show that an AAV-based gene therapy approach may be feasible as a treatment for NPC, a rare genetic disorder for which there is no effective therapy.

▶ Using Statistical Modeling to Understand UDP-N-acetylglucosamine 2-epimerase/N-acetylmannosamine (GNE) Myopathy (NHGRI)

In April 2016, the NHGRI entered into a Research Collaboration Agreement with Berry Consultants, LLC to build statistical models for disease progression for GNE kinase myopathy. Utilization of this novel disease progression model will allow for more accurate tracking and monitoring of patients who are enrolled in both natural history and interventional drug clinical studies.

▶ Clinical Trial for Treatment for Cockayne Syndrome (NIA)

A CRADA executed between NIA and Chromadex allowed for NIA to conduct a clinical trial to investigate the ability of ChromaDex's proprietary Nicotinamide Riboside ("NIAGENTM"), a form of Vitamin B3, to mitigate certain symptoms of Cockayne Syndrome in children. Cockayne Syndrome is a rare and fatal autosomal recessive neurodegenerative disorder characterized by growth failure, impaired development of the nervous system, photosensitivity, eye disorders and premature aging.

▶ Using Gene Therapy to Help Xerostomia Patients (NIDCR)

Using a CRADA agreement, NIDCR partnered with MeiraGTx, LLC to investigate the use of gene therapy to restore saliva flow to radiation induced xerostomia patients. Transferred to the new partner under a second amendment was a NIDCR Orphan Drug Designation, which classified radiation induced xerostomia for the first time as a rare disease and identifying NIDCR's gene therapy vector as a potential therapeutic. This was the first time an Orphan Drug Designation was transferred through a CRADA mechanism at the NIH, which ensured continued development of the Orphan Drug for this rare disease as well as NIDCR participation in and oversight over the clinical trial.

▶ Successful Completion of Clinical Trial to Help Patients with Hypocalcemia (NIDCR)

A clinical trial, funded through a CRADA agreement with NIDCR's partner Shire plc, was successfully completed. The trial objective was to determine the effects of NPSP795 on calcium-sensing receptors in Autosomal Dominant Hypocalcemia patients. An abstract was published and a manuscript is in preparation.

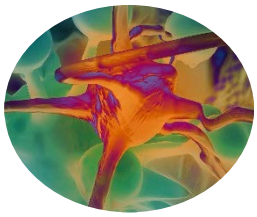
▶ Towards a Cure for Dermatomyositis (NIEHS)

Juvenile and adult dermatomyositis are inflammatory muscle diseases that can also have severe non-muscular complications. Calcinosis, which is the development of ectopic soft tissue calcification, is difficult to treat and can severely limit people to the point of becoming bed bound. There is no generally accepted method for assessing or monitoring changes in calcinosis.

A CRADA was executed in FY16 between NIEHS and Hope Pharmaceuticals of Scottsdale, Arizona, entitled "An Open-label Study of Sodium Thiosulfate for Treatment of Calcinosis

Associated with Juvenile and Adult Dermatomyositis." Principal Investigator, Frederick Miller, MD, PhD, and staff clinician Adam Schiffenbauer, MD, seek to determine the efficacy of sodium thiosulfate in the treatment of adult and juvenile dermatomyositis patients with calcinosis and to establish an evaluation tool for changes in calcinosis. This CRADA supports the piloting of a new assessment tool based on patient response and incorporating novel imaging modalities.

Combating Cancer



▶ Development of Bromodomain and Extra-Terminal Inhibitors (NCATS)

NCATS Office of Strategic Alliances (OSA) has successfully negotiated an exclusive license agreement with ConverGene for the rights to commercialize jointly developed small molecule Bromodomain and Extra-Terminal (BET) inhibitors that have a unique core structure as compared to other cancer therapeutics currently in clinical trials. Acute Myelogenous Leukemia (AML) is an orphan disease and about 20,000 new cases will be diagnosed in the U.S. in 2017. Treatment of patients with AML has changed little over the last two decades and currently, only 25% of adults with AML are expected to survive three or more years. Thus, new classes of targeted AML therapy that intervene on cancer-specific pathways are desperately needed to improve the quality of life and survival rate in this patient population. The first focus of ConverGene will be in the hematology oncology space followed by solid tumors. Via press release on the ConverGene website, ConverGene CEO Dr. Jeff Strovel commented, *"We are delighted to be working with NCATS and see a bright future for this compound in treating a variety of diseases for which patients currently have no treatment options."*

▶ Development of Screening Methods for Cervical Pre-cancer in Low-Resource Settings (NCI)

Multiple collaboration agreements negotiated in FY16 with external partners (for-profit and not-for-profit) will facilitate the development of low-cost human papillomavirus (HPV) screening and triage tools for the detection of cervical pre-cancer and human papillomavirus (HPV) management protocols for implementation in low-resource settings. Since persistent infections with HPV can lead to cervical carcinomas, the development of HPV vaccination and HPV testing is leading to major changes in cervical cancer prevention programs worldwide. These agreements involve NCI's Division of Cancer Epidemiology & Genetics and include the transfer of cervical specimens from large epidemiological studies.

▶ Working with American Cancer Society (NCI)

An Omnibus Collaboration Agreement with the American Cancer Society (ACS) allows for the updating and consolidation of six previously executed agreements between American Cancer Society (ACS) and NCI's Division of Cancer Epidemiology and Genetics (DCEG). The projects under the Omnibus agreement continue ongoing Genome-Wide Association Studies (GWAS) in

various cancers – bladder, lung, kidney, glioma, non-Hodgkin lymphoma, pancreas, upper gastrointestinal, breast, prostate and detectable mosaicism. The agreement simplifies the tracking and documentation to facilitate ongoing studies of the role of germ-line genetic variation, including single nucleotide polymorphism (SNP) genotype and copy number variation (CNV) in the etiology of cancers and other diseases.

Preclinical and Clinical Studies Critical to Advance Immunotherapies (NCI)

Immunotherapy is a type of cancer treatment that helps the immune system fight cancer. A series of CRADAs executed on behalf of NCI's Laboratory of Tumor Immunology and Biology (LTIB), are helping to advance combination studies that are critical to developing and improving the efficacy of immunotherapies. The CRADAs include:

- Clinical CRADA, "Evaluation of Altor Bioscience Corporation's Proprietary Interleukin-15 Superagonist ALT-803, IL-2 Fusion Protein ALT-801, and TxM Product Candidates"
- Clinical CRADA "The Use of NantBioScience, Inc.'s and its Affiliates' Proprietary Recombinant NK Cells and Monoclonal Antibodies in Monotherapy and in Combination Immunotherapies"
- Clinical CRADA "Evaluation of Syndax Pharmaceuticals Inc.'s Proprietary Entinostat (a Histone Deacetylase Inhibitor) and SNDX-6352 (an Anti-CSF-1R Monoclonal Antibody)"

Why are they significant?

- Under these CRADAs, each CRADA Collaborator's proprietary agents will be evaluated both as single agents and/or in combination therapies for the treatment of cancer in preclinical and clinical studies. The emerging data from the preclinical studies will guide the design of the clinical studies.
- These CRADAs are leading to multiple research collaborations between CCR Labs and Branches, specifically, the Laboratory of Tumor Immunology and Biology (LTIB), the Genitourinary Malignancies Branch (GMB), and the Urologic Oncology Branch (UOB).

▶ Using Nano-particles (NIDCD)

Under a CRADA agreement, the Van Waes laboratory at NIDCD will work with a small company, miRecule, Inc., to evaluate proprietary nanoparticle-formulated mimetics with the hope of advancing novel microRNA replacement cancer treatments that mitigate intrinsic or acquired resistance that occur through the use of selective small molecule or biological therapies that target a single oncogene or pathway. This approach if successful would open up a whole new approach to treatment of a wide range of diseases and medical conditions.

▶ Startup to Work Exclusively on Cancer Pain Management (NIDCR)

NIDCR's licensing partner Sorrento Therapeutics split off its resiniferatoxin (RTX) human therapeutics division to its current-majority owned subsidiary Scintilla Pharmaceutical, Inc. Scintilla's lead program is resiniferatoxin ("RTX") for the treatment of intractable cancer pain, licensed from NIDCR. Scintilla announced an acquisition of Semnur Pharmaceuticals, Inc. in

FY2016. The acquisition will lead to operation of Scintilla as a stand-alone company focused on non-opiate pain treatment such as RTX.

▶ Development of Pipeline Software to Look for Tumor Signatures (NIEHS)

Drs. Steven Roberts and Dmitry Gordenin from the NIEHS Chromosome Stability Group, along with Dr. Les Klimczak at Integrative Bioinformatics (NIEHS contractor) have created a user-configurable, data processing pipeline which has been requested by several groups in the extramural community. Scaling and automating the analytical work performed by biologists is difficult and frequently unsuccessful because it most often involves very fragmented ad hoc operations in multiple poorly structured Excel files that do not lend themselves easily to standardization and automation. The APOBEC Pipeline Software represents a rare example of a successful migration from individual analytical operations developed step-by-step and bottom-up by the biologists themselves in Excel to a fully automated "single-click" multistep pipeline operating on multiple large files and implemented in R. The pipeline performs analyses of sequence motifs in the vicinity of mutation calls collected in Mutation Annotation Format (MAF) files generated by Next Generation Sequencing (exome or whole genome) projects and, while it could be generalized to any type of mutation in any type of data, it focuses on detecting the overrepresentation of the APOBEC signature in tumor samples. The operations were developed bottom-up by the biologists in Excel and were later generalized and scaled up in R scripts corresponding to the individual steps and coordinated by a controller script written in R as well. This required a disciplined focus on standardizing the data sets and operations that is rarely achievable in a biological lab. In addition to a number of simple parameters that can be provided to the pipeline using a GUI interface or configuration files, there are several complex modifications that have been designed to be defined by the biologists and to be easily "pluggable" as code modules without major rewriting of the scripts. The application of the pipeline to detecting the overrepresentation of the APOBEC signature in various tumors has been published (Nature Genetics: 45, 970-976, 2013). The developers are currently collaborating with several cancer consortia to include the pipeline results in their analyses and are working with the bioinformatics group of the Broad Institute to incorporate the pipeline into their Firehose platform. Simple Letter Agreements have been negotiated with Beijing Institute of Genomics at the Chinese Academy of Sciences, the Institute for Systems Biology at the University of Washington, the University of Minnesota, The University of California-San Francisco, University of North Carolina-Chapel Hill, and the National Cancer Institute.

Immune Function Disorders

▶ Marching Against Diabetes and Other Immune Function Disorders (NHGRI)

The NHGRI entered into a Research Collaboration Agreement with Exosome Diagnostics, Inc. to identify pharmacoepigenetic signals of diabetes and obesity drugs by profiling changes in circulating nucleic acid. Being able to easily and quickly identify people who are, for example, either responding well or not responding well to standard drugs using a simple, non-invasive biomarker test (analysis is of exosomal RNA from a blood or urine sample) should allow these

individuals and their physicians to take various active steps to avoid that predicted future negative health outcome.

NHGRI also entered into two other Collaborative Research Agreements involving immune function disorders. The first was with Gilead Sciences, Inc. for a project titled "Reverse Transcriptase Inhibitors in Aicardi Goutières Syndrome (AGS)." Currently there is no treatment for AGS and this drug repurposing study aims to test two FDA-approved drugs to treat HIV in patients with this rare genetic disease. The second was with Merck Sharp & Dohme Corp. to identify and validate genes involved in immune function and regulations through next generation sequencing.

▶ Advancing the Understanding of Rheumatoid Arthritis and Inflammatory Bowel Disease (NIAMS)

Dr. Richard Siegel's Laboratory at NIAMS is collaborating with MedImmune to assay and quantify expression levels and anatomical distribution of TNF-like ligand 1A to study ways of blocking its interactions with its receptor, DR3. This research aims to provide an increased understanding of an important inflammatory pathway associated with rheumatoid arthritis and inflammatory bowel disease that could potentially be targeted therapeutically.

Health Technologies

▶ Development of Tissue- and Organ-on-a-Chip Platform (NCATS)

NCATS Office of Strategic Alliances (OSA) developed and negotiated a custom Memorandum of Understanding (MOU) with the Center for the Advancement of Science in Space (CASIS) on its Tissue Chips in Space initiative. Through this initiative, NCATS and CASIS will collaborate to refine tissue- and organ-on-chip platforms for on-flight experiments at the International Space Station U.S. National Laboratory so that scientists can better understand diseases and translate those findings to improve human health on Earth.

▶ Transferring New Software Technology to Non-profits and Industry (NCI)

NCI TTC developed a new Software Transfer Agreement (STA) that will allow non-profit researchers access to a research tool developed by Choonsik Lee, Ph.D., NCI Division of Cancer Epidemiology and Genetics, Radiation Epidemiology Branch. The National Cancer Institute dosimetry system for Computed Tomography (NCICT) is a novel computer program with graphical user interface (GUI) that can interactively estimate radiation dose to the organs of patients undergoing computed tomography (CT) examinations. Although CT provides great benefits to patients, there are concerns about the potential risk of radiation exposure to pediatric patients who are more sensitive. In order to estimate risks and make an informed decision in clinical practice, better understanding of the magnitude of radiation doses delivered to patients during CT examinations is crucial.

With input from NCI TTC, Lee developed a website that will provide non-profit investigators access to the NCICT program following execution of the newly developed STA. TTC is also consulting with Lee on expanding the technology to include a NCI dosimetry system for Nuclear Medicine (NCINM) and NCI dosimetry system for X-Ray (NCIXR). It is anticipated that this growing suite of computer programs will be available via the website and STA. To date, 19 STAs have been executed between NCI and research organizations worldwide for NCICT. In addition, a non-exclusive license was executed with a for-profit company for this technology.

▶ Using Technology to Improve Personalized Medicine and Informed Consents (NHGRI)

The NHGRI entered into a Research Collaboration Agreement with Public Democracy America for a project titled "Functionalities of Informed Consent Interface," to develop and test a multimedia interface/platform to perform and study informed consent process.

The NHGRI entered into a Research Collaboration Agreement with Samuel Merritt University for a project titled "Personalized Medicine Decision Making in a Virtual Clinical Setting."

▶ Development of Mobile Health Technology (NIDA)

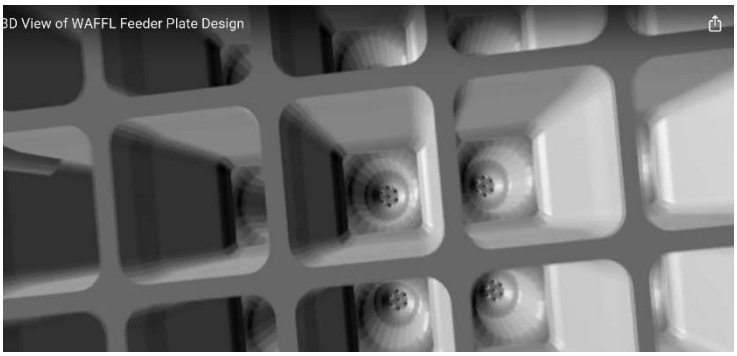
The execution of multiple agreements for NIDA is facilitating meetings with several companies to discuss the development of NIDA's mobile health technology for monitoring and predicting a user's psychological status and for delivery of an automated drug overdose intervention when needed. This smartphone technology monitors the user's location and asks questions about psychological status throughout the day. The mobile data are combined with geospatial risk maps to quantify exposure to risk and predict a future psychological state. The future predictions are used to warn the user when he or she is at especially high risk of experiencing a negative event that might lead to an unwanted outcome (e.g., lapse to drug use in a recovering addict).

▶ The Whole Animal Feeding Flat (NIDDK)

Hours of time are spent monitoring the food, water and cage conditions of laboratory mice. An innovative system was built from NIDDK designed parts that were 3-D printed and combined with commercially available parts plus open-source software that allows remote monitoring and food consumption. This technology was not patented, rather a bill of materials has been packaged with assembly instruction for free download from the Investigator's NIDDK webpage.

Drosophila melanogaster, commonly called fruit flies, are often used in genetic studies and may be a suitable replacement of laboratory animals for some drug or chemical toxicity studies. The flies are small and hard to manipulate. An NIDDK biologist-engineer tackled the problem and developed the Whole Animal Feeding Flat (WAFFL), a 96-well system for housing and feeding 96 fruit flies. Each well can contain a different chemical or the wells can present a gradient of exposures to a single chemical. The housing tray, below, sits on the plate containing the wells of

treatment. The food plus test compound comes into the bottom of the tray through the tiny holes so the fly can feed but not get wet. An image of the WAFFL feeder plate appears below.



Collaborations

▶ Managing the Ketamine Patent and License Portfolio (NCATS/NIA/NIMH)

This past year, the NCATS Office of Strategic Alliances (OSA) took the lead in developing a Memorandum of Understanding (MOU) between the National Institute on Aging (NIA), the National Institute on Mental Health (NIMH) and the National Center for Advancing Translational Sciences (NCATS), for the development of 2R, 6R-hydroxynorketamine as a therapeutic and filed several patent applications claiming this technology. Since NIA, NIMH and NCATS have contributed to the development of 2R, 6R-hydroxynorketamine as a therapeutic for major depressive disorder, treatment-resistant depressive disorder and suicide ideation, it was critical to develop an agreement on how the technology would be developed at the ICs and which IC would have the lead on negotiations for all the involved NIH ICs. This technology also was co-developed with other outside institutions. NCATS took the lead in advertising the technologies and as a result of these efforts, several companies expressed interest in licensing some of these technologies.

Additionally, NCATS completed multiple Material Transfer Agreements (MTAs) for the compounds which allowed distribution of the material to promote research. In an effort to alleviate processing research use MTAs of the material, NCATS negotiated and executed a non-exclusive license with Tocris Bioscience in the U.K., in accordance with an MOU with two other ICs (NIA, NIMH). This will allow Tocris to distribute ketamine related materials to the research community.

▶ Clinical Trial to Combat Age-Associated Macular Degeneration (NCI/NEI)

NCI TTC's Competitive Service Center continued to provide technology transfer support for a multi-year project for NEI that aims to perform the first clinical trial of human induced pluripotent stem cell (iPSC)-derived retinal pigment epithelium (RPE) transplants as potential therapeutics for age-associated macular degeneration (AMD). AMD is a leading cause of vision

loss among elderly in the United States. This comprehensive project involves a number of interactions and collaborations with outside parties regarding various aspects of the IND-enabling studies. Multiple agreements supporting this project were executed in FY16 including eight CDAs, eight MTAs, three CRADAs, and invention reports. Under one of the CRADAs, NEI is working with a commercial entity on preclinical studies to advance clinical-grade iPSC-derived RPE cell products for treating retinal degenerative disease, in particular AMD. Under this CRADA, the Collaborator will provide funding over three years to offset the costs incurred by NEI.

▶ Reducing Animal Testing in Toxicology Studies (NIEHS)

The National Toxicology Program (NTP) at the NIHES, as part of the US Toxicology in the 21st Century (Tox21) initiative, participated in the initiation of collaborative activities with the EU-ToxRisk project. The collaboration is an effort to reduce the use of animals and achieve more efficient chemical safety assessments. A total of 28 representatives from both projects gathered in a workshop held in Mainz (Germany) on the 12th-14th September 2016 to initiate collaboration across areas of mutual interest within the field of risk assessment. The following areas were agreed upon for areas of mutual practical cooperation.

- Develop practices of cross-consortium data sharing with particular emphasis on the ongoing EU-ToxRisk case studies
- Develop core methodology in read-across and the application of high-throughput transcriptomics for safety assessment
- Create synergies across overlapping chemical subsets
- Utilize ongoing developments of in vitro tissue models and computer-based predictions of drug concentrations for risk assessment
- Develop joint case studies focused on innovations in the application of alternative approaches

In one of the first partnerships, Richard Paules (NIEHS NTP) entered into a collaboration with Dr. Bob van de Water, at the University of Leiden and Principal Investigator for the EU-ToxRisk program, with a Data Transfer Agreement to jointly analyze data produced from gene expression analysis of 50 unique human liver cell cultures exposed to chemicals representing four major mechanisms implicated in injury processes. This study will better define cellular responses to changes in theses pathways and will investigate inter-individual variations in those responses.

▶ Neuroscience Collaboration (NIMH/NINDS)

Implemented a Technology Transfer Core group consisting of NIMH and NINDS technology transfer staff designed to take advantage of the common neuroscience underpinnings that form the foundation of each IC. Among the key accomplishments of 2016 were working to establish, implement, and improve an integrated technology transfer database that captures information about negotiated agreements to facilitate the coordinated efforts between the ICs. Additional accomplishments of the group include:

- Establishing the framework for a Technology Assessment Group comprised of NIMH/NINDS investigators to assist technology transfer staff in the review of technologies at various stages of the patent process.
- Establishing the framework for a one-day neuroscience collaboration seminar designed to facilitate partnerships between industry, academic, and government organizations. The seminar will feature NIMH and NINDS technologies available for licensing/collaboration, scientific presentations, poster sessions, and networking opportunities.
- Establishing the framework for developing a new Technology Transfer Core Group website.
- Streamlining the agreement negotiation process by establishing standardized templates between the ICs and drafting Standard Operating Procedures for the various agreement types.

New Technology Transfer Strategies Move Science Forward

► Launch of New Online Tool Streamlines NIH CRADA Process (Multiple)

In 2013, with seed money from the NCI and the Centers for Disease control (CDC), a project team comprised of staff from the National Institutes of Health (NIH), the Centers for Disease Control (CDC), and the Federal Drug Administration (FDA) worked with a Center for Biomedical Informatics & Information Technology (CBIIT) contractor to create an online, automated agreement builder that allows technology transfer staff to create custom draft agreements tailored to the specific needs of the collaboration. At the same time, a working group refreshed the template CRADA language with more clearly stated, concise language, which in turn is used to populate the CRADA Builder system. As a result of this enterprise effort, CRADA Builder was launched in September 2015.

As of early February 2017, the NIH CRADA Subcommittee has approved six (6) CRADAs generated from CRADA Builder, as submitted by three institutes. The tech transfer specialists who have used the tool report it to be more efficient than beginning a CRADA with a model template and expressed that having a customized draft agreement streamlines negotiations. CRADA Builder saves the specialist time, provides a standardized method of building a CRADA, and minimizes problems with version control.

CRADA Builder is currently available for use by specialists at the NIH, FDA and CDC. The NCI shared the code with the National Institute of Standards and Technology (NIST). NIST, via its contractor, is developing an improved version of the tool for use by the Federal Laboratory Consortium on a secure platform that will be made available to other Federal agencies.

▶ MTA Template for the NCATS CANVASS Program

NCATS Office of Strategic Alliances (OSA) drafted a unique Material Transfer Agreement (MTA) template for use in the Pilot CANVASS program. This MTA has facilitated NCATS' ability to screen over 1,500 natural products against more than 30 biological assays. The resultant biological footprint data will be shared back with the original providers. The hope is that data and information generated will be further shared and will help the research community about novel and unknown uses for these natural products and lead to new discoveries. Over 50 agreements were executed using this custom MTA template.

▶ Facilitating the Helicobacter pylori Genome Project May Result in New Way to Provide Early Cancer Diagnosis (NCI)

Helicobacter pylori (*H. pylori*), a Gram-negative bacterium associated with a spectrum of benign and malignant gastric conditions, is one of the most genetically variable pathogens. Variations in a few genes have been associated with risk of inflammation and carcinogenesis, the process by which normal cells are transformed into cancer cells, but no systematic study has evaluated the entire bacterial genome. NCI investigators devised a multi-country study to establish and analyze an informative, international collection of *H. pylori* clinical isolates from residents of defined geographic areas. Molecular characterization will be conducted at the Frederick National Laboratory for Cancer Research (FNLCR). Findings from this study may help to characterize the differential virulence among *H. pylori* isolates and suggest predictive biomarkers for early diagnosis of cancer. The bacterial isolates and databases from this study will also provide a foundation for further elucidation of *H. pylori* pathogenesis.

NCI's TTC developed an MTA specifically for incoming human materials for the new *Helicobacter pylori* Genome Project (HpGP). Lead by researchers from NCI's Division of Cancer Epidemiology and Genetics, Infections and Immunoepidemiology Branch. The MTA allows NCI to: (1) receive human specimens from around the world, (2) perform molecular characterization, (3) establish a resource repository of multi-dimensional data and well-characterized *H. pylori* strains for utilization by the scientific community, and (4) further transfer human specimens to other researchers to promote collaborative research projects. To date, nine MTAs have been executed for receipt of human specimens for the HpGP.

▶ Access to Experimental Models from NICHD's Zebrafish Program Furthers Study of Basic Biological and Human Disease Mechanisms

Specific types of zebrafish have been developed for researchers to use as experimental models for studying basic biology and human diseases mechanisms. NICHD considers it a high priority to make its zebrafish experimental models available to researchers studying basic biology and human disease mechanisms. In FY16, 18 technology transfer agreements were executed providing zebrafish models to researchers around the world. This includes a collaboration between NICHD and a local research hospital to provide access to NICHD's Zebrafish Core for a major screening project to identify putative therapeutic candidates for mitigating human

hyperammonemia, a metabolic disturbance characterized by an excess of ammonia in the blood. In addition, a master deposit agreement with the Zebrafish International Resource Center is allowing for NICHD researchers to deposit published zebrafish models for distribution.

▶ Human Brain Collection Core (NIMH)

NIMH modified the existing MTA template for the Human Brain Collection Core to streamline programmatic operations. This new MTA template contains monitoring and annual reporting provisions to more effectively capture metrics and distribution language that minimizes the burden associated with recipients' transfer of materials to other research organizations.

▶ Streamlining Availability of Plasmids (NINDS)

NINDS TTO has streamlined the process by which its researchers obtain materials from a major plasmid repository by pre-approving transfers associated with established terms and conditions known to be acceptable. Previously, the technology transfer office confirmed the accuracy of orders with researchers prior to approving the associated agreement, which was manually accomplished through the repository's website. These two steps introduced a variable delay into the overall process. After consulting with and receiving concurrence from NINDS researchers responsible for a majority of repository orders, these steps were eliminated. Utilizing the new process resulted in a time savings for technology transfer staff of near a week in a four-month trial, faster receipt of the reagents by the scientists, and zero incorrectly processed orders. NINDS TTO provides the researchers with bi-annual reminders of the terms and conditions of the pre-approved agreements.

Proactive Approaches to Facilitate External Partnerships and Invention Commercialization

▶ Nanotechnology Startup Challenge Winners Announced (NCI)

The NCI partnered with the Center for Advancing Innovation (CAI) to launch the Nanotechnology Startup Challenge in Cancer or NSC2. The Challenge was centered on commercially viable, nanotechnology cancer-related inventions conceived by the NCI. Once accepted into the Challenge, international teams competed by selecting one of these intramural inventions, and creating a business plan to launch a startup. Alternatively, teams could elect to bring other commercially viable, nanotechnology cancer-related inventions into the challenge that are not from NCI. The primary goal was to stimulate the creation of start-up businesses to advance development and commercialization of these nanotechnology inventions. NSC2 launched in October 2015, and winners were announced in July 2016. The winners are now in various phases of launching their startups, including incorporation, negotiating a license to the technology and raising funding. The NSC2 was the third NIH Startup Challenge and is based upon the award-winning model created by the Breast Cancer Startup Challenge, followed by the Neuro Startup Challenge

▶ Increased Focus on Invention Commercialization at NCI

TTC's Invention Development and Marketing Unit (IDMU) was formed as a new unit within NCI TTC dedicated to developing, facilitating, and executing more effective strategies to increase licensing and partnership agreement transactions. It is active – regularly engaging directly with the medical research ecosystem – rather than passive. The IDMU is crafting focused awareness, education, and marketing initiatives to advance the development and commercialization of the NCI and Client Institutes invention portfolios.

"Overall, the IDMU has greatly increased pro-active outreach by seeking out companies, investors, and foundations to discuss how our medical solutions could be utilized to benefit their patients, loved ones, and customers," commented IDMU's new Supervisor, Michael Salgaller, Ph.D. "Creating awareness of the NCI and Client Institutes patent portfolio is being enhanced through outlets such as webinars, digital media (LinkedIn, Twitter, etc.), and a greater emphasis on face-to-face interactions at more business-oriented technology conferences."

▶ Techtransfer.cancer.gov — NCI TTC's New Platform to Market NIH Inventions

TTC launched techtransfer.cancer.gov, a new, visually engaging website that provides organizational information and exposure for inventions originating from the intramural labs of NCI and the nine NIH Institutes and Centers it serves. The new web site provides an excellent platform for TTC to foster licensing and research collaborations between the research laboratories of NIH and companies, universities, and non-profits seeking new technologies. This site provides partners a simplified navigation and improved search capabilities to find technologies of interest. Its open source platform allows the TTC to keep information updated, and provides more information to NIH scientists to help them through the patent process.

▶ Extending Tech Transfer Reach (NCI)

The NCI Technology Transfer Ambassadors Program (TTAP) was conceived and initiated in September 2016 by NCI Technology Transfer Center (TTC) post-doctoral fellows, Rob Sons, Ph.D., Alan Alfano, Ph.D. and Laura Prestia, Ph.D. The NCI TTAP provides a unique training opportunity for NCI post-doctoral fellows seeking to augment their current activities with hands-on training in biomedical invention development, commercialization, and entrepreneurship. NCI TTAP ambassadors also gain experience in networking and communication as they extend technology transfer awareness to the scientific networks with which they are already engaged. During the 2016-2017 program, the NCI TTAP ambassadors (11 in Bethesda, MD; 4 in Frederick, MD), have been exposed to a wide range of concepts, including collaborative research agreements, invention identification, intellectual property analysis, marketing, and licensing, in a series of monthly workshops. They are now applying these concepts through the submission of new invention reports, marketing & patenting projects with TTC staff, matching industry partners with potential scientific collaborators, and developing commercialization development plans around NCI technologies (in collaboration with Johns Hopkins Carey Business School's Discovery to Market program). Through these high impact

projects, the NCI TTAP offers NCI post-doctoral fellows the ability to develop a first-hand understanding of NIH technology transfer tools and commercialization strategies.

► NCI Invention Development Program (IDP) Bridges Gaps, Facilitates Commercialization

As part of NCI TTC's effort to increase invention commercialization, it created the IDP, a program piloted in 2014 to facilitate further development of NCI inventions needing specific data to increase commercial interest for licensing or collaboration. In two years of operation, investigators with inventions selected for the program receive the benefit of feedback from the IDP Review Committee Transferee for insight on commercial development. The IDP funds were used for proof-of-concept and validation testing. IDP funded a range of study areas that included biologics, small molecule therapeutics, and instrumentation to facilitate PET imaging of small animals. Data from IDP studies have contributed to a range of technology transfer outcomes. For some inventions the study results attracted new interest from companies in collaboration and licensing.

Awards

► Federal Laboratory Consortium (FLC) Mid-Atlantic Region (MAR) Honors (NCI)

The FLC MAR selected NCI TTC's Andrew Burke, Ph.D. for its "Rookie of the Year" award. The award recognizes "the efforts of an FLC laboratory technology transfer professional who has demonstrated outstanding work in the field of technology transfer in a manner significantly over and above what was called for in the normal course of their work during the past year. The nominee must be new to technology transfer with three years (or less) experience in a technology transfer position," according to the FLC MAR award criteria. Burke was selected for the award, in part, because of his "positive attitude and commitment to public service and continued management of a wide-range of projects that exemplify how T2 is critical to the NCI mission." Burke joined TTC as a fellow in 2013, and accepted a licensing and patenting manager position in 2015. To learn more, see: FLC MAR 2016 Awards Gallery.

► TTIPO Director Receives NIAID Merit Award (NIAID)

Michael R. Mowatt, Ph.D., received a NIAID Merit Award "for exceptional leadership in implementing the reorganization of the NIAID Technology Transfer and Intellectual Property Office. The complex reorganization, part of the NIH-wide effort to restructure the NIH Technology Transfer Program, accommodated many changes, including a substantial increase in personnel, increased office space, and new patent and licensing capabilities.

▶ TTIPO Zika Response Team Receives NIAID Merit Award (NIAID)

TTIPO staff were recognized for the design and implementation of NIAID's immediate response to the Zika threat to global health. The TTIPO recipients were: S. Dana Hsu, J.D., M.S., Tara Kirby, Ph.D., Christopher Kornak, J.D., Haiqing Li, M.D., Ph.D., Michael R. Mowatt, Ph.D., Jenish Patel, Ph.D., Amy Petrik, Ph.D., Maryann Puglielli, Ph.D., J.D., Mukul Ranjan, Ph.D. and Jeffrey Thruston, J.D., M.S. These individuals worked diligently to react quickly, resolve complicated issues, and move forward with a large number of often complex collaborative agreements. In fiscal year 2016 alone, TTIPO negotiated over thirty Zika related agreements and through NIAID's efforts Zika samples and related materials were sent to over two hundred fifty entities in thirty-five states and thirteen foreign countries to encourage the development of countermeasures to the Zika threat.

▶ DHHS Secretary's Award for Distinguished Service (NIAID)

Michael Piziali, J.D., received the DHHS Secretary's Award for Distinguished Service as part of the Ebola Clinical Research Response Team for work related to the Ebola outbreak. The TTIPO recipient was Michael Piziali, J.D., M.S.

▶ NIAID Awarded a Federal Laboratory Consortium (FLC) Excellence in Technology Transfer Award

TTIPO staff were recognized for their technology transfer efforts related to "Ebola Vaccine Development from Basic Research to the Clinic: Partnering for Public Health". TTIPO awardees included Vincent Feliccia, Ph.D., J.D., Carol Salata, Ph.D., and Amy Petrik, Ph.D. The unique agreements and the speed at which TTIPO negotiated them demonstrated excellence in technology transfer. Agreements enabling the start of clinical trials were negotiated and executed within two months for the conduct of Phase I trials in the U.S. (Baltimore, Bethesda, Atlanta), the U.K., Switzerland, and Mali.

▶ NIMH Director's "Rookie-of-the-Year" Award

Both members of the NIMH technology transfer staff, Jennifer Wong, MS and Charles Salahuddin, JD, MS, were recognized with NIMH Director's Award "Rookie of the Year" honors for forward-thinking ideas for expanding collaborations, including establishing the framework for a research tool catalogue designed to showcase all NIMH research tools available for licensing in a single space. 2016 efforts related to establishing the research tool catalogue included meeting with numerous NIMH investigators about research tools developed in each lab and working with the inventors to create material descriptions and properly document each material.

► FDA Receives a Patents for Humanity Award from the United States Patent and Trademark Office (USPTO)

FDA and its Center for Biologics Evaluation and Research (CBER) were recognized by the USPTO for developing an improved meningitis vaccine production process that has been used to immunize over 235 million people in high-risk Africa countries. The Patents for Humanity Program was launched in February 2012 to showcase the meritorious work of patent owners to address 21st century humanitarian challenges. To make the FDA invention became part of a vaccine that provided a real public health solution for Africa, agreements to carry out the research, development, and commercialization were established by technology transfer staff at both NIH and FDA. FDA staff who received this honor at the Patents for Humanity award ceremony were inventors Carl Frasch, Ph.D., and Robert Lee, Ph.D., along with Carolyn Wilson, Ph.D., Associate Director for Research for CBER, and Alice Welch, Ph.D., Director, FDA Technology Transfer Program.

Appendix

DHHS Technology Transfer Offices

NIH OTT - NIH Office of Technology Transfer

https://www.ott.nih.gov/

CDC - Centers for Disease Control and Prevention

CDC Office of Technology and Innovation
https://www.cdc.gov/od/science/technology/

NCATS - National Center for Advancing Translational Sciences

NCATS Office of Strategic Alliances
https://ncats.nih.gov/alliances/about

NCI - National Cancer Institute

NCI Technology Transfer Center
https://techtransfer.cancer.gov/

Service Center for:

- CC - NIH Clinical Center
- CIT - Center for Information Technology
- NCCIH - National Center for Complementary and Integrative Health
- NEI - National Eye Institute
- NIA - National Institute on Aging
- NIDA - National Institute on Drug Abuse
- NICHD - Eunice Kennedy Shriver National Institute on Child Health and Human Development
- NIMHD - National Institute on Minority Health and Health Disparities
- NLM - National Library of Medicine

NHGRI - National Human Genome Research Institute

NHGRI Technology Transfer Office
https://www.genome.gov/techtransfer

NHLBI - National Heart, Lung, and Blood Institute

NHLBI Office of Technology Transfer and Development
https://www.nhlbi.nih.gov/research/tt

Service Center for:

- NIAMS - National Institute of Arthritis and Musculoskeletal and Skin Diseases
- NIBIB - National Institute of Biomedical Imaging and Bioengineering
- NIDCD - National Institute on Deafness and Other Communication Disorders
- NIEHS - National Institute of Environmental Health Sciences
- NINR - National Institute of Nursing Research

NIAID - National Institute of Allergy and Infectious Diseases

NIAID Technology Transfer and Intellectual Property Office
https://www.niaid.nih.gov/research/technology-transfer-and-intellectual-property-office

Service Center for:

- CDC - Centers for Disease Control and Prevention (CDC)

NIDCR - National Institute of Dental and Craniofacial Research

NIDCR Office of Technology Transfer and Innovation Access
https://www.nidcr.nih.gov/research/NIDCRLaboratories/Intramural_Technology_Transfer_Office/

NIDDK - National Institute of Diabetes and Digestive and Kidney Diseases

NIDDK Technology Advancement Office
https://www.niddk.nih.gov/about-niddk/offices-divisions/technology-advancement-office/Pages/default.aspx

Service Center for:

- NIAAA - National Institute on Alcohol Abuse and Alcoholism
- ORS - Office of Research Services

NIMH - National Institute of Mental Health

NIMH Office of Technology Transfer
https://www.nimh.nih.gov/labs-at-nimh/scientific-director/office-of-technology-transfer/index.shtml

NINDS - National Institute of Neurological Disorders and Stroke

NINDS Technology Transfer Office
https://tto.ninds.nih.gov/