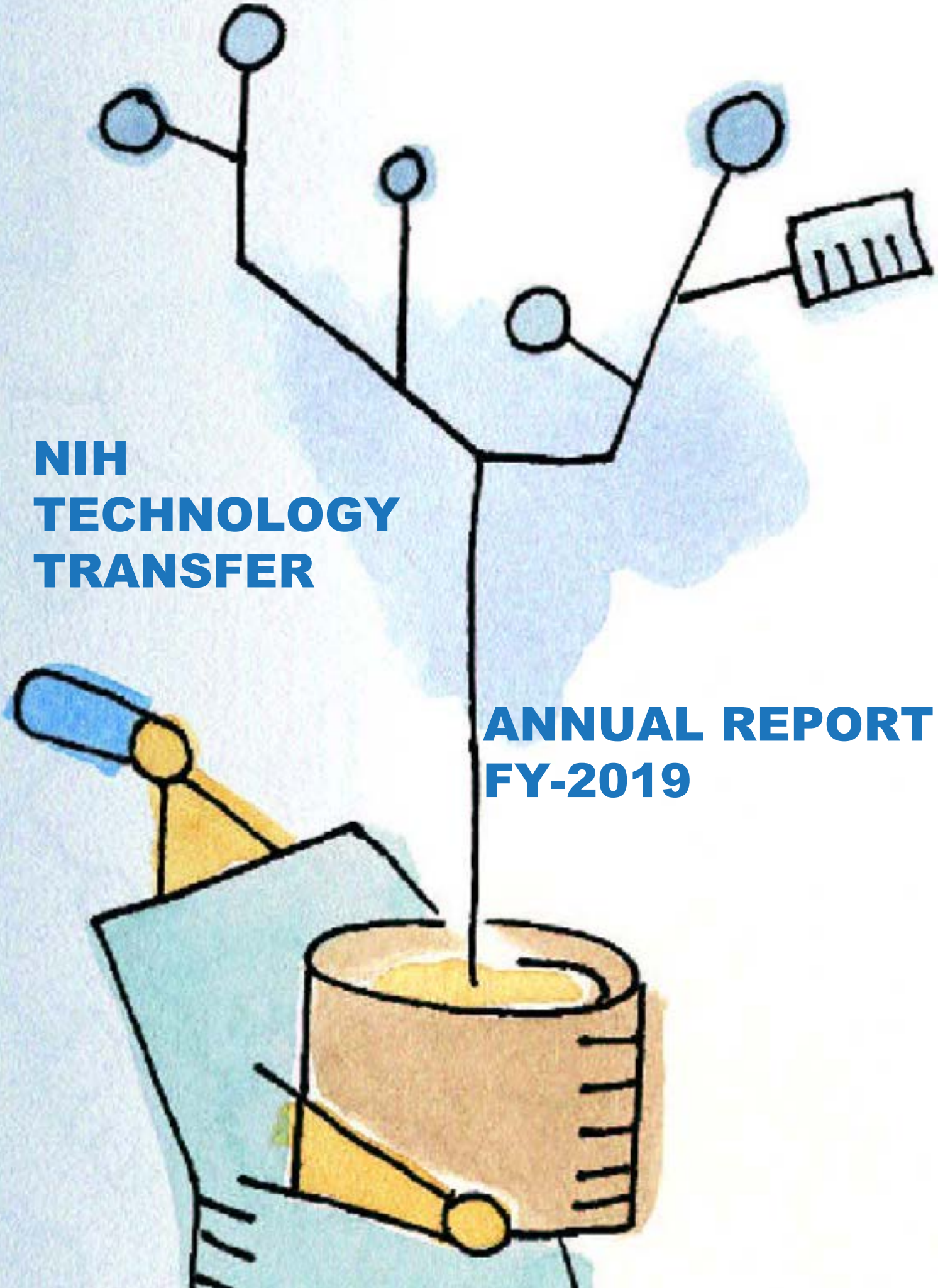
NIH TECHNOLOGY TRANSFER

ANNUAL REPORT FY-2019



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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 and the Centers for Disease Control and Prevention (CDC). In doing so, NIH Technology Transfer supports the larger NIH mission to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability.

Working on behalf of the NIH 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 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 patent filing and prosecution process.

- Serves as a bridge through marketing and communications, connecting the inventive discoveries made by scientists in the NIH and CDC research programs to commercial partners with the capability of developing these technologies into products and services to benefit public health. Without TT, 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 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

As we move forward in FY2020, the NIH Technology Transfer (TT) Community should take time to reflect on what was achieved during FY2019. After the significant reorganization and patent and license decentralization that took place now four years ago, the Office of Technology Transfer (OTT) continues to provide key service and support functions to the NIH Technology Transfer Offices (TTOs) and the CDC. This has allowed the NIH Institutes and Centers (ICs) to build upon the long success and track record of the TT program at NIH that originally started in the late 1980s. The TT Community had a very successful year, and this report serves to highlight that through the national awards, success stories, and metrics presented.

A key feature of NIH's TT Program in FY2019 was the foundational work that took place for the future implementation of a new agency-wide Enterprise Technology Transfer (ETT) Data System and new agency-wide Patent Legal Services (PLS) contracts. The expected benefits of the new ETT System will be improved responsiveness in the implementation of system changes, reduced cost of ownership, and improved integration of processes and systems between ICs. FY2019 saw the procurement of the software platform that will be the basis of the ETT system and the customization of the system from its vendor. The NIH ETT team facilitated stakeholder engagement across the NIH ICs, migrated data, and conducted gap analyses for a planned launch in FY20. Similarly, the NIH PLS team, worked diligently to set up the new infrastructure to handle a new PLS contract system for de-centralized patent work across NIH as well as start the process for selecting new PLS providers for a new series of contracts to replace the ones expiring in FY20.

Looking at the commonly tracked metrics at NIH OTT shows the significant breadth and depth of activities by the NIH TTOs in FY2019. Royalty income was $78.1M. Active CRADAs increased from the previous year, as well as executed licenses and exclusive licenses, reflecting the ever-expanding relevance and role of technology transfer in programs at the NIH and CDC

OTT continues to provide management and oversight of the collection and disbursement of royalties, monitor and enforce patent rights/licensing agreements, coordinate the payment of all patent annuities, market and communicate with existing and potential licensees, and provide legal docketing services. In addition, OTT continues to support the TT community through management of the NIH TechTracS, which is the existing system of record for all patent and license data and information, and the OTT SharePoint site, which assists the community with the transfer, collaboration and management of vital documents and information.

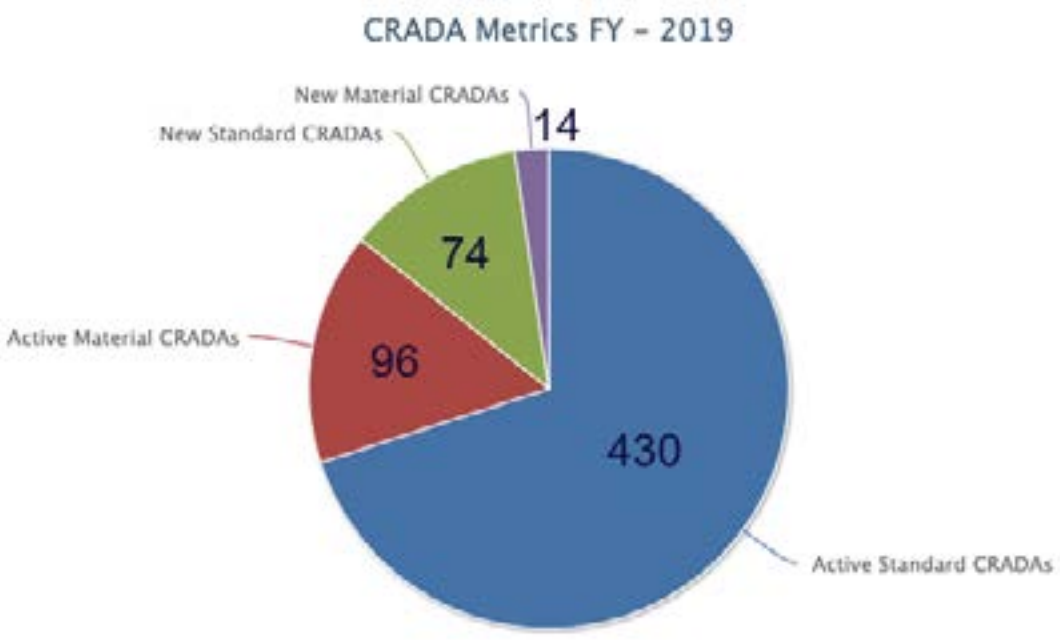
The following report provides insight into numerous TT achievements and scientific advancements in FY2019 and reflects the accomplishments of TT at the NIH and CDC. It also demonstrates the TT Community's commitment to meeting changing stakeholders needs with the goal of facilitating the collaboration and commercialization around NIH/CDC scientific discoveries to improve public health.

INVENTIONS AND AGREEMENTS

The TT 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.

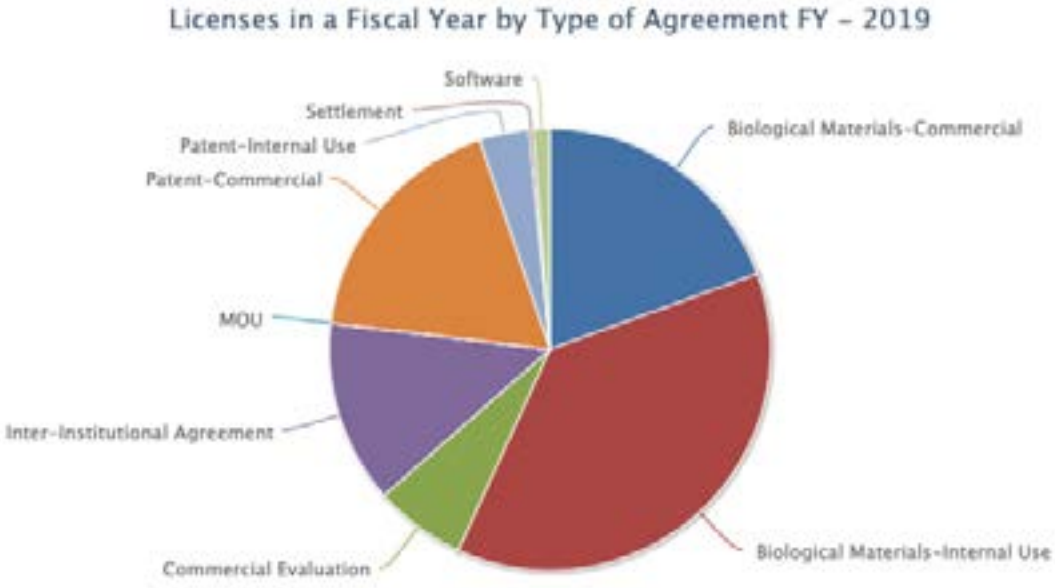
In addition, the TT Program negotiates terms for research collaborations between NIH and commercial and academic organizations. These collaborations leverage the strengths of each institution to advance basic and clinical research objectives. TT also facilitates the transfer of thousands of research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

The Institutes in FY2019 saw roughly the same amount of non-CRADA agreements as the past few years, with a total of 8,267. The number of active CRADAs executed in FY2019 rose 2.3% from the previous year. The pie chart below shows the CRADA metrics for FY2019.



IP - Related Agreements in Numbers

- 237 - Number of invention related disclosures reported
- 342 - License agreements executed
- 128 - Small business licenses



For a deeper look at the various technology transfer-related metrics, please visit the OTT Web Site -- https://www.ott.nih.gov/reportsstats/ott-statistics.

INSTITUTE AND CENTER UPDATES

NCATS — NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES

The expertise, capabilities and resources required to successfully advance a drug, device, or intervention resides in different groups as these efforts progress through the translational science spectrum. Partnerships and collaborations across individuals, organizations and sectors are essential to efficient progress. The creation of productive and mutually beneficial collaborations depends not only on individual excellence, but on teamwork, coordination, cooperation and communication.

Traditional professional incentive structures focus on individual accomplishments and make teamwork difficult to navigate. Embracing patients and communities as research partners also holds great potential for the development treatments with meaningful outcomes for the populations affected by disease. With these needs in mind, the National Center for Advancing Translational Sciences (NCATS) tests novel partnership structures that cut across traditionally siloed scientific disciplines, organizations and sectors.

The NCATS Office of Strategic Alliances (OSA) aims to make it easy for industry, small businesses and academia to interact and partner with NCATS scientists. OSA staff help develop formal partnerships that proactively address complex issues, such as intellectual property and project management roles to make for smoother, more effective collaborations.

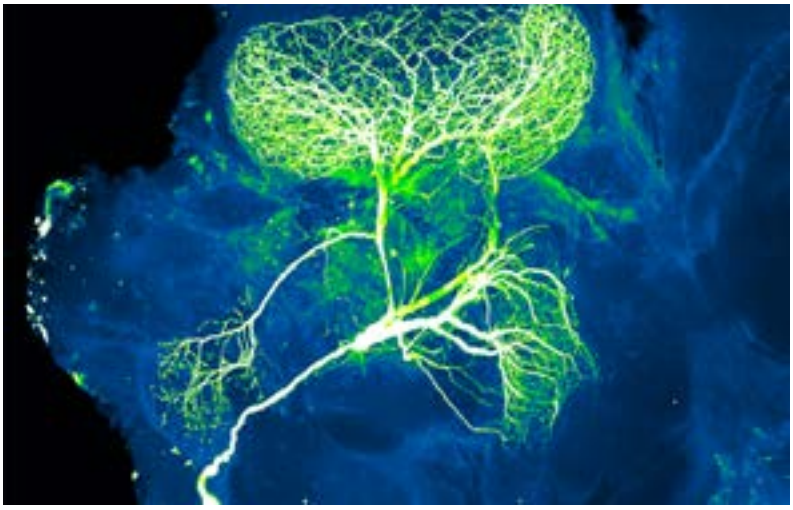
NCATS OSA negotiates and executes on average a total of 300 agreements, in addition, there was a concerted effort to assure all agreements with term limits were either closed, due to project completion, or amended to enable the project to continue. While some of these were template agreements, many required customization as well as ample time for negotiations to terms acceptable to the NIH. Given the varied nature of NCATS' collaborations with industry, academia, patient groups, et al., many agreement negotiations require significant time and effort to educate our counterparts on the particulars and requirements of collaborating with the federal government, and particularly NCATS/NIH.

NCATS ROLE IN THE NIH HEAL (HELPING TO END ADDICTION TO LONG-TERM) INITIATIVE

NCATS is playing a major role in the National Institutes of Health (NIH) HEAL (Helping to End Addiction Long-term) Initiative, a trans-agency effort focused on improving prevention and treatment strategies for opioid misuse and addiction, and enhancing pain management. Launched in April 2018 with funding from Congress, the HEAL Initiative brings new hope for people, families, and communities affected by the national opioid public health crisis.

With NIH HEAL Initiative support, NCATS is providing a suite of translational science resources and expertise to investigators working on opioid and pain research.

HEAL – COOPERATIVE RESEARCH AND DEVELOPMENT AGREEMENT (CRADA): BRAEBURN PHARMACEUTICALS AND NCATS



As part of the HEAL initiative, with the assistance of OSA, NCATS and the National Institute on Drug Abuse (NIDA) have executed a CRADA with Braeburn Pharmaceuticals to develop a Dopamine D3 Antagonist for Opioid Use Disorder (OUD). OUD includes both addiction and overdose as well as other disorders related to drug use.

The CRADA collaboration will use the combined resources and expertise of NCATS, NIDA and Braeburn to conduct IND enabling preclinical development studies with VK4-116 as a treatment for OUD. If VK4-116 is found to be unacceptable for development, this CRADA would also cover the IND-enabling studies for an additional identified backup compound.

This project represents the first of several projects that will be supported by NCATS under HEAL special funding.

A SPECIALIZED PLATFORM FOR INNOVATIVE RESEARCH EXPLORATION (ASPIRE)

NCATS proposes to transform chemistry from an individualized craft to a modern, information-based science through A Specialized Platform for Innovative Research Exploration (ASPIRE). By addressing long-standing challenges in the field of chemistry, including lack of standardization, low reproducibility and an inability to predict how new chemicals will behave, ASPIRE is designed to bring novel, safe and effective treatments to more patients more quickly at a lower cost.

ASPIRE aims to address two challenges of the current era in biomedical research: to harness new technologies to accelerate understanding of living systems and to fulfill the promise of science to improve the lives of the many patients with untreatable or poorly treatable diseases. As such, it could complement current NIH efforts in unexplored therapeutic space such as the NIH Illuminating the Druggable Genome program.

NCATS scientists are using the ASPIRE platform in preclinical drug discovery to help

study/map unexplored biologically active chemical space through integrating automated synthetic chemistry, high-throughput biology and artificial intelligence technologies to accelerate the drug discovery process.

This initiative promotes multidisciplinary collaborations among government, academic and pharmaceutical researchers; funders; professional societies; scientific publishers; and other stakeholders. ASPIRE supports NCATS' work to develop, demonstrate and disseminate innovative technologies that will bring diagnosis and treatments to patients and will deliver on NIH's efforts to increase reproducibility and scientific rigor. OSA supports the ASPIRE initiative in a number of ways by managing any new inventions, collaborations or commercial outcomes that may result from these activities.

ASPIRE – CRADA: STRATEOS, INC. AND NCATS

As part of the ASPIRE initiative, OSA has negotiated the execution of the CRADA between NCATS and Strateos, Inc. to develop medicinal chemical synthesis workflows. This collaboration will encompass the delivery of the reactor to be deployed at the automated synthetic chemistry laboratory operated by Strateos, Inc. in San Diego, CA. NCATS will embed a scientist at the facility to work alongside Strateos, Inc. personnel while the Site Acceptance Testing (SAT) for the automated reactor is being performed by the manufacturer. The main goal of this CRADA is the transfer of knowledge between NCATS and Strateos, Inc. to advance the automated medicinal chemistry field.

NCATS COLLABORATIVE RARE DISEASE PLATFORM VECTOR GENE THERAPY TRIAL (PAVE-GT)

Advances in gene delivery and gene editing have recently re-invigorated gene therapy as a potential approach to treating genetically-based diseases. The current approach to gene therapy clinical trials is still "one disease at a time," which does not maximize the inherent platform capacity of viral vectors. This results in duplication of effort and delay in trial startup. To address this roadblock, NCATS proposes a novel public-private partnership model for explicitly platform-based gene therapy clinical trials. The approach involves using well-characterized viral vectors as gene delivery vehicles for the treatment of at least three rare genetic diseases that share the same therapeutic target tissue or cell type. To maximize efficiency, therapeutic vectors for all diseases in a platform trial will be produced in the same manufacturing facility and will undergo Investigational New Drug (IND)-enabling (toxicity and biodistribution) studies in parallel, using processes developed by the NCATS Division of Pre-Clinical Innovation (DPI). This initiative involves three different divisions/offices of NCATS (i.e., Office of Rare Disease Research (ORDR), DPI, and OSA), as well as the involvement of academic investigators, rare disease patient groups and biotech partners. If successful, NCATS will expand this strategy to provide rare diseases researchers with a palette of vectors to treat many, and potentially all, rare genetic diseases.

OSA will play a key role in creating agreements and managing interactions and partnerships between NCATS, academia and industry partners. Currently, OSA has negotiated and executed research collaboration agreements (RCAs) with both the National Human Genome Research Institute (NHGRI) and the National Institute of Neurological Disorders and Stroke (NINDS) to expedite the pilot programs. These RCAs are specifically crafted to achieve the primary program objective of making the regulatory package (IND submission, Food and Drug Administration (FDA) responses, and all preclinical data) publicly available and include specific provisions to enable fair and quick dissemination of the knowledge. OSA, along with scientific teams and collaborators, is also coordinating the IP due diligence requirements such as Freedom To Operate analysis for this project and advising the program officers to proactively facilitate smooth implementation of the projects.

CRADA: ALAGILLE SYNDROME ALLIANCE (ALGSA), RETHROPHIN, INC. AND NCATS

OSA has negotiated the execution of the CRADA between The Alagille Syndrome Alliance (ALGSA) patient foundation, along with biopharmaceutical company Retrophin, Inc. and NCATS, Therapeutics for Rare and Neglected Diseases (TRND) Biology Laboratory, for the development of potentially novel therapeutics for patients suffering from Alagille Syndrome (ALGS). The scope of this collaborative project is potential validation of an identified drug repurposing target, and assay development, high-throughput screening (HTS) and hit validation to identify chemical matter on novel mechanisms. The plan outlines assay development in relevant cell types of hepatic lineage, HTS, and hit validation to identify compounds that potentially can be advanced into hit-to-lead. Retrophin is interested in the continued development of any hit compounds identified through this collaboration, with the goal of delivering a new, novel therapeutic options to patients suffering from Alagille Syndrome.

MEMORANDUM OF UNDERSTANDING (MOU) – NCATS, CDRD, EATRIS, TIA, AMED AND LIFEARC

With the expertise and guidance of OSA, an MOU has been executed between NCATS, The Centre for Drug Research and Development (CDRD), The European Advanced Translational Research Infrastructure in Medicine (EATRIS), Therapeutic Innovation Australia Pty Ltd (TIA), Japan Agency for Medical Research and Development (AMED), and LifeArc (LifeArc). This MOU provides a platform on which the Collaborators decide to collaborate on joint studies among United States (US), Canadian (CA), European Union (EU), Australian (AU), Japanese (JP) and UK research scientists affiliated with universities, research institutes and other organizations and centers engaged in translational research.

NCI – THE NATIONAL CANCER INSTITUTE

The National Cancer Institute is the Federal government's principal agency for cancer research and training. Various institutes and centers with NCI work to deliver on the NCI mission "leading, conducting, and supporting cancer research across the nation to advance scientific knowledge and help all people live longer, healthier lives." The NCI Technology Transfer Center (TTC) supports technology development activities for the NCI and nine NIH Institutes and Centers. Highlights from 2019 exemplify potentially life-impacting outcomes of sustained TT effort, as well as notable TT activities of FY2019 that can make tomorrow's cancer research and patient treatments possible.

AI APPROACH OUTPERFORMED HUMAN EXPERTS IN IDENTIFYING CERVICAL PRECANCER

"A research team led by investigators from the NIH and Global Good has developed a computer algorithm that can analyze digital images of a woman's cervix and accurately identify precancerous changes that require medical attention. This artificial intelligence (AI) approach, called automated visual evaluation, has the potential to revolutionize cervical cancer screening, particularly in low-resource settings" stated a January 2019 NCI press release.

These TT agreements have advanced the capabilities of PRO-CTCAE™, its use around the world, and have resulted in over $2M worth of translation and linguistic validation work.

The collaborative work that led to the development of this AI approach was made possible by a Collaboration Agreement executed by TTC (Yogi Prabhu, Ph.D.) in 2016 between NCI and Global Good. Since that time, TTC has executed several other agreements with institutions worldwide for the development of algorithms for detection of cervical precancers based on cervical images. In Fall 2018, the Collaboration Agreement with Global Good was amended by TTC's Michelle Favila, Ph.D. to expand the project to include additional cervical images. These agreements will hopefully lead to the development of more algorithms which can become part of cervical cancer prevention solutions for all kinds of settings, including low-resource settings that rely on development of robust, low-cost screening and triage tools. Learn more: NIH Director's blog

TECH TRANSFER EFFORT SUPPORTS LANGUAGE TRANSLATION AND VALIDATION OF CLINICAL TRIAL REPORTING TOOL

The NCI PRO-CTCAE™ (Patient Reported Outcomes-Common Terminology Criteria for Adverse Events) is a new measurement system that aids in evaluating and capturing the symptomatic adverse events in patients on cancer clinical trials. TTC executed several TT agreements with multiple collaborators, such as GlaxoSmithKline, AstraZeneca, Johnson & Johnson and Genentech/Roche, for PRO-CTCAE™ projects. In these projects, the collaborators translate and linguistically validate the PRO-CTCAE questionnaire into foreign languages for use in the collaborator's clinical study. Sandra A. Mitchell, Ph.D., and her team in the Healthcare Delivery Research Program (HDRP) of the Division of Cancer Control and Population Sciences (DCCPS), work together with the collaborator and its contractor to prospectively monitor the study conduct and to analyze the data. Importantly, the translated and linguistically validated PRO-CTCAE™ questionnaires are provided back to NCI for NCI's use and public dissemination. Through these collaborations, many new languages versions of PRO-CTCAE™ are being made available to the public, including Czech, Korean, Portuguese,

Malay, Romanian and Turkish. According to Dr. Mitchell, “PRO-CTCAE integrates the patient perspective into adverse event reporting and may ultimately prove useful as an outcome measure in comparative effectiveness research and to profile the severity and impact of therapy-related symptom burden in patients undergoing treatment for cancer.” TTC’s Benfeard Williams, Ph.D. negotiated the agreements.

NCI DCP COLLABORATES WITH AMGEN ON A MULTI-SITE CLINICAL STUDY FOR THE PREVENTION OF OVARIAN CANCER

NCI Division of Cancer Prevention (DCP) and Amgen, an international biotech company, are collaborating under a clinical trial CRADA to investigate the use of Amgen’s proprietary agent, denosumab, for the prevention of ovarian cancers in BRCA1/2 mutation carriers. Under this CRADA, NCI is acting as a coordinator for a multi-site, prevention clinical trial that will be conducted at six U.S clinical and one international site. NCI is providing funding and support for the clinical trials to be conducted at these sites. TTC coordinated with Amgen to establish its first collaboration with DCP through this CRADA, and worked with the NCI contracting office to align the terms of NCI’s contracts with the clinical sites and NCI’s agreement with Amgen. After careful coordination of multiple components, the CRADA, negotiated by TTC’s Sidra Ahsan, Ph.D was executed in January 2019.

There is a large unmet need for an ovarian cancer chemopreventive agent: BRCA1/2 mutation carriers are at high risk for ovarian cancer, there is a high mortality associated with diagnosis, and limited options exist for ovarian cancer prevention and screening. This clinical study’s primary objective is to determine whether treatment with denosumab affects the growth and spread of ovarian cancer cells in premenopausal BRCA1/2 mutation carriers undergoing risk-reducing bilateral sphingo-oophorectomy (BSO). Importantly, this study will assess whether denosumab alters cellular proliferation in the fimbrial end of the fallopian tube, the presumed site of origin of the most common and fatal ovarian cancer histologic subtype, in BRCA1/2 mutation carriers. Denosumab is a monoclonal antibody that inhibits Receptor Activator of NF-κB (RANK) ligand (RANKL). Denosumab treatment showed promising results in the prevention of breast cancer in BRCA1/2 mutation carriers. Nonetheless, there is no published data on the effect of denosumab on gynecologic tissues that play a key role in the development and progression of ovarian cancer. The results of this clinical study may have implications for the development of new preventative strategies for BRCA1/2 mutation carriers at risk of developing ovarian cancer.

COLLABORATION TO EVALUATE USE OF IMMERSIVE VIRTUAL REALITY FOR SCANXIETY IN ONCOLOGY

A collaboration between NCI and AppliedVR will study a Virtual Reality solution to address the anxiety many cancer patients experience when they undergo diagnostic imaging testing for their cancer. While this distress can be attributed to cancer progression and treatment-related toxicity, it also can correlate to the diagnostic scans that patients undergo to determine the status of their disease. Termed “scanxiety,” researchers from the NCI Neuro-Oncology Branch are working to develop and evaluate the use of an immersive environment virtual reality (VR) system in which VR technology facilitates patient-directed essential skills and techniques to reduce scan-related distress. These skills include breathing techniques, mindfulness, and psycho-education positive thinking to improve scanxiety management. NCI’s main hypothesis is that with use of this platform, patients will develop skills to escape from the distress of the procedure and facilitate positive coping related to the uncertainty of the disease.

Under a Collaboration Agreement, NCI will utilize the Neuro-Oncology Branch (NOB) Natural History Protocol, a longitudinal study in which patients with primary brain tumors are followed for clinical course, imaging studies, and patient-reported outcomes (PROs). The research partners outlined a three-part study. The Collaboration Agreement will allow the partners to conduct part one: "development and evaluation of feasibility and effect of 'NOB-RESCUE' on a neuro-onology patient and caregiver in an outpatient clinic." Amendments to the agreement may be needed to facilitate subsequent studies. TTC's Michael Pollack, Ph.D. negotiated the agreement.

CRADA ALLOWS FIRST-IN-HUMAN STUDY OF A RADIOLABELED CONJUGATE IN PATIENTS WITH TUMORS KNOWN TO EXPRESS MESOTHELIN

A CRADA between NCI and Bayer HealthCare Pharmaceuticals Inc. (Bayer) was recently executed for investigators to conduct a multi-center, first-in-human Phase I clinical study of Bayer's proprietary agent, BAY 2287411, a mesothelin targeted Thorium-227 conjugate. Mesothelin is a tumor differentiation antigen whose expression in normal human tissues is limited to mesothelial cells lining the pleura, peritoneum and pericardium. However, mesothelin is highly expressed in several cancers such as mesothelioma and ovarian cancer. Available treatments do not show a favorable response. BAY 2287411 demonstrated potent, targeted anti-cancer activity against mesothelin-expressing tumors in preclinical models. The radioactive conjugate is designed to target and bind to tumor cells that express mesothelin, exposing the tumor cells to a lethal dose of radiation. Using the resources and expertise of the NCI and Bayer, this collaboration will evaluate the efficacy, safety and pharmacokinetics of BAY 2287411 in patients with solid tumors known to express mesothelin. TTC's Ricquita Pollard, Ph.D. negotiated the CRADA.

TECHNOLOGY TRANSFER AS A PARTNER TO ADVANCE DCEG MISSION

"Discovering the causes of cancer and the means of prevention" is the mission of NCI's Division of Cancer Epidemiology & Genetics (DCEG). One way that DCEG accomplishes that mission is through strategic national and international partnerships/consortia for conducting Genome-wide Association Studies (GWAS). Technology Transfer provides the framework to facilitate these important partnerships. In the past several months, TTC's Virginia DeSeau and Michelle Favila, Ph.D. have updated and expanded agreements for several consortia representing research in many different types of cancer, including:

- Testicular Cancer Consortium (TECAC);
- Genome-Wide Association Study (GWAS) Analysis of Gastric Cancer in Hispanic Populations
- International Barrett's and Esophageal Adenocarcinoma Consortium (BEACON)
- NCI GWAS of Lymphoid Malignancies and Related Disorders (LM).

NCI DCEG is also a partner in the international GWAS consortium, the Breast Cancer Association Consortium (BCAC) managed at Cambridge University in the United Kingdom. To enhance and expand BCAC's impact on the research community, DCEG and TTC are working to establish a template data sharing agreement for a rich cloud-based data resource that will involve this >100-member consortium. Through the negotiated agreements and amendments for these collaborations, TTC serves a vital role in moving this type of research forward.

CLINICAL TRIAL TO EVALUATE BMS'S NIVOLUMAB, IN COMBINATION WITH VANCOMYCIN AND TADALAFIL, TO TREAT LIVER CANCER

A CRADA between NCI and Bristol-Myers Squibb (BMS) was recently executed for a new Phase II clinical trial to investigate the use of BMS' nivolumab, in combination with tadalafil and oral vancomycin, in liver cancer patients. Nivolumab is an immunotherapy that works by blocking PD-1 on T cells, a receptor that can prevent activated T cells from attacking cancer cells. Tadalafil suppresses tumor growth by reducing the amount of myeloid-derived suppressor cells, and vancomycin is an antibiotic that kills Gram-positive bacteria in the gut. Previous studies have shown that the gut microbiome can directly influence the host's immune system. Vancomycin will be used to manipulate the gut microbiome, which can potentially enhance the ability of the immune system to fight cancer. The rationale is based on an invention disclosure by Drs. Tim Greten and Chi Ma that the use of vancomycin and tadalafil can provide a synergistic anti-tumor effect with nivolumab. A PCT patent application for the invention was filed last October.

Under the terms of the CRADA, the Phase II study led by Dr. Tim Greten will be conducted at the NIH Clinical Center. The study will determine the best overall response to the combined treatment and will evaluate the relationship between the immune system, tumor, and the gut microbe composition. No similar treatment strategy has been developed. The trial can potentially lead to a novel approach to enhance the effectiveness of immunotherapies and to treat cancer. TTC's Douglas Cheung, Ph.D. and Sabarni Chatterjee, Ph.D. negotiated the CRADA.

A MEMORANDUM OF UNDERSTANDING BETWEEN NCI AND CANCER RESEARCH UK TO SUPPORT NCI'S PRIMAVERA TRIAL

The current Human Papillomavirus Virus (HPV) vaccines on the market employ a two- or three-dose regimen which can pose financial and logistical barriers to administration, especially in countries with limited resources, which often have high cervical cancer burden. There have been some research findings that suggest that a single dose of the HPV vaccine may confer sufficient protection. A single-dose regimen would be more cost effective, particularly in low and middle- income countries, and could lead to greater adoption of these vaccines. NCI and Cancer Research UK (CRUK) entered into a Memorandum of Understanding (MOU) for cooperation in support of the PRIMAVERA Trial. The objective of the PRIMAVERA Trial is to show that the immune response for a single dose of the bivalent vaccine Cervarix is non-inferior to the immune response for three doses of the quadrivalent vaccine Gardasil. The trial will be financially supported in part by funds from CRUK (via the gift mechanism). The MOU describes the CRUK funding as well as relevant scientific and fiscal progress information that NCI will share with CRUK. The PRIMAVERA Trial may eventually lead to an accepted one-dose administration for the HPV vaccine and such a change could have substantial public health impact including reducing the cost and logistical difficulties of vaccinating girls with the recommended multiple-dose administration, which has been a significant impediment to high vaccine coverage in low resource and other settings. TTC's Lisa Finkelstein, Ph.D. negotiated the MOU with CRUK.

NHGRI – NATIONAL HUMAN GENOME RESEARCH INSTITUTE

A few notable activities involving NHGRI collaborations with industry or the commercialization of NHGRI technologies include:

January 2019, the NHGRI entered into a Data Use Agreement as a member of the Clinical Sequencing Evidence-Generating Research (CSER) Consortium. The primary goal of the CSER Consortium is to study the effectiveness of integrating genome sequencing into the clinical care of diverse and medically underserved individuals.

February 2019, the NHGRI entered into a Data Use Agreement as a member of the Consortium for Refractive Error and Myopia ("CREAM") to identify genes that confer susceptibility to refractive error.

May 2019, the NHGRI entered into a Professional Practice Agreement with Johns Hopkins University to perform ELTA-MS to identify ADP-ribosylated proteins from five cell lines coming from NIH.

May 2019, the NHGRI entered into a Clinical Trial Agreement with Arqule, Inc. to conduct a clinical study of ARQ 092 for the treatment of Proteus Syndrome.

June 2019, the NHGRI entered into a Research Collaboration Agreement with the National Center for Advanced Translational Sciences (NCATS) for a research project "Rare Disease Platform Vector Gene Therapy (PaVe-GT) Project: Methylmalonic Acidemia (MMA)."

July 2019, the NHGRI entered into a Research Collaboration Agreement with Oregon Health & Science University for a research project titled "Discordant ADHD Twins Whole Genome Sequencing."

August 2019, the NHGRI entered into a Collaboration Agreement with the University of Pittsburgh for a research project titled "Propionic Acidemia Study."

September 2019, the NHGRI entered into a Collaboration Agreement with the University of Pittsburgh for a research project titled "Methylmalonic Acidemia Study."

September 2019, the NHGRI entered into a Collaborative Research Agreement with the University of Tennessee and Samford University for a research project to identify the susceptibility of single nucleotide polymorphisms to breast cancer (cases) in AA women with breast cancer (controls) and without breast cancer.

CRADAs Entered

"Clinical Development of EPI-743 for Treatment of Pediatric Metabolic Disease of Oxidation/ Reduction or a Mitochondrial Disorder" (Amendment No. 4 to CRADA 2015-0098), dated March 25, 2019.

"Clinical Development of N-acetyl-D-mannosamine (ManNAc) to Treat GNE Myopathy" (Amendment No. 1 to CRADA 2017-0216), dated April 5, 2019.

“Development of Gene Therapy for GM1 Gangliosidosis” (CRADA No. 2019-0042) dated May 9, 2019.

• Under this clinical three-party Agreement, NHGRI Investigator, Cynthia J. Tifft, M.D., Ph.D., Axovant Sciences, Inc., and the University of Massachusetts will collaborate on developing gene therapy for GM1 gangliosidosis, an extremely rare lysosomal storage disorder, whose current care is limited to symptomatic medical treatment.

“Treatment of Methylmalonic Acidemia by GeneRide” (Amendment No. 1 to CRADA 2016-0181) dated June 26, 2019.

• Under pre-clinical three-party Agreement, NHGRI Investigator, Charles Venditti, M.D., Ph.D. and LogicBio Therapeutics will collaborate on the development of a gene therapy protocol (GeneRideTM treatment for Methylmalonic Acidemia) and testing the therapeutic efficacy and neonatal genotoxicity in mouse models.

• Collaboration resulted in a CRADA Subject Invention (NIH Ref. No: E-034-2019)

“Clinical Development of N-acetyl-D-mannosamine (ManNAc) to Treat GNE Myopathy” (Amendment No. 2 to CRADA 2017-0216), dated April 5, 2019.

“Development of Assays for Discovery of Small Molecules to Treat Gaucher Disease and Parkinson Disease” (CRADA No. 2019-0097) dated August 26, 2019.

• Under this pre-clinical three-party Agreement, NHGRI Investigator, Ellen Sidransky, M.D., will collaborate with F. Hoffman-LaRoche and the National Center for Advancing Translational Sciences (NCATS) to develop new generation assays for the identification of compounds that would be able to ameliorate symptoms of Parkinson Disease and Gaucher Disease.

“Preclinical Development of Gene Therapy for Niemann-Pick Disease Type C” (CRADA No. 2018-0120) dated August 26, 2019.

• Under this pre-clinical Agreement, NHGRI Investigator William J. Pavan, Ph.D., will collaborate with Chameleon Biosciences, Inc. on evaluating potential gene therapy to treat Niemann-Pick Disease, Type C, a potentially devastating rare disease with frequent pediatric onset.

NIAID – NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

DEVELOPING EBOLA TREATMENTS

NIAID supported a historic clinical trial of investigational Ebola treatments in the Democratic Republic of the Congo (DRC). TTIPO negotiated multiple agreements that underpinned critical studies and enabled this historic achievement. In addition to the material transfer agreement (MTA) to transfer mAb114 to DRC for use to treat patients under an Expanded Access Protocol and a license with Ridgeback Biotherapeutics LP as described in the FY 2018 report, TTIPO negotiated three Clinical Trial Agreements (CTAs), three confidential disclosure agreements (CDAs), three MTAs and one memorandum of understanding (MOU) in support of this groundbreaking clinical trial..

The clinical trial, known as PALM (short for "Pamoja Tulinde Maisha," a Swahili phrase which translates to "together save lives"), is a randomized, controlled trial of four investigational agents (ZMapp, remdesivir, mAb114 and REGN-EB3) for the treatment of patients with Ebola virus disease. The trial is organized by an international research consortium coordinated by the World Health Organization (WHO). It is led and funded by the DRC's INRB and Ministry of Health, and the National Institute of Allergy and Infectious Diseases (NIAID).

The trial is monitored by an independent Data and Safety Monitoring Board (DSMB) that meets periodically to review interim safety and efficacy data and to make recommendations to the study team and the sponsors. As a result of their August 9, 2019 review, the DSMB recommended that the study be stopped and that all future patients be randomized to receive either REGN-EB3 or mAb114. The preliminary results in 499 study participants indicated that those individuals receiving REGN-EB3 or mAb114 had a greater chance of survival compared to those participants in the other two arms. After a comprehensive analysis of the full dataset from nearly 200 additional patients, the results of this study were published in The New England Journal of Medicine in November 2019. The investigational therapeutics mAb114 and REGN-EB3 offer patients a greater chance of surviving Ebola virus disease (EVD) compared to the investigational treatment ZMapp.

"Response teams have faced unprecedented challenges in ongoing efforts to save lives and control the outbreak of Ebola in a highly insecure region of the Democratic Republic of the Congo," said NIAID Director Anthony S. Fauci, M.D. "Although effective treatments alone will not end this outbreak, the PALM study findings identify the first efficacious treatments for Ebola virus disease and therefore mark a significant step forward in improving care for Ebola patients. We thank the study team for their extraordinary efforts to conduct this landmark trial."

The Ebola treatment center (ETC) in Beni, DRC (Pictured to the left). Operated by The Alliance for International Medical Action (ALIMA) and Doctors Without Borders (MSF), the Beni ETC enrolled patients in the PALM study of Ebola therapeutics. Credit: ALIMA

CHANGING LIVES IN PASLI PATIENTS, DISEASE DISCOVERY, AND TREATMENT

TTIPO negotiated a CRADA that yielded a new treatment option for a debilitating immune deficiency disease in children. Primary immune deficiency diseases (PIDDs) are rare, genetic disorders that impair the immune system. In 2013, NIAID researchers and their collaborators identified a novel PIDD called PASLI disease, named after the mutated gene and its symptoms (p110 delta-activating mutation causing senescent T cells, lymphadenopathy and immunodeficiency).

There are slightly over 200 patients identified with this disease to date. These patients experience recurring infections beginning in childhood, including bacterial infections of the respiratory system and chronic viral infections with Epstein-Barr virus (EBV), and a subset of PASLI patients go on to develop EBV-associated lymphoma. The genetic basis of the disease was discovered by NIAID scientists, and independently by investigators at Cambridge University, and was linked to mutations in the PI3 Kinase delta gene encoding p110 delta, a protein highly expressed in the immune system. Additional mutations in the PI3 Kinase gene were identified in the cohort of PASLI patients and their families under NIAID's collaboration with Merck under a CRADA negotiated by TTIPO, further supporting the role of PI3 Kinase mutations in PALSI disease.

Novartis Pharmaceuticals Corporation (Novartis) has designed an oral PI3 kinase-delta inhibitor, CDZ173 (leniolisib) to treat autoimmune diseases which has shown promising outcomes in early clinical trials. Given the specificity of CDZ173 to selectively inhibit the p110 delta subunit of PI3 kinase and the potential to treat the disease, TTIPO negotiated the CRADA between Novartis and NIAID in 2015 to test Novartis's proprietary CDZ173/leniolisib in PASLI patients.

Interim data from this trial indicated that leniolisib treatment was well tolerated and improved laboratory and clinical parameters in PASLI patients (PASLI/APDS-CDZ173 trial publication in 2017). Following the success of the Phase II trial, TTIPO amended the CRADA with Novartis in 2018 to launch a Phase III trial to increase patient enrollment as well as to initiate an extension study testing long term safety and efficacy of leniolisib treatment in PASLI patients. This study provides an effective treatment opportunity for PASLI, fulfils an unmet medical need and exemplifies the power of precision medicine therapy in a rare disease.

MEDICINES FOR COMPASSIONATE USE

Each year, TTIPO negotiates agreements to obtain compassionate use medicines from biopharma and biotech companies to enable treatment of severely ill patients who were not responding to standard therapies. With these TTIPO-negotiated agreements in place, NIAID's Laboratory of Clinical Immunology and Microbiology (LCIM) physicians are able to treat these severely ill patients under emergency INDs, which permit the use of investigational drugs for these emergency situations. In FY 2019, TTIPO negotiated agreements to enable treatment of patients with cryptococcal meningitis, CANDLE (Chronic Atypical Neutrophilic Dermatosis) and NTM (Non-Tuberculous Mycobacterial infection), respectively.

Cryptococcal meningitis: Cryptococcal meningitis is a serious infection of the brain and spinal column that can occur in people with suppressed immunity (e.g. cancer or HIV). It is caused by a fungus called Cryptococcus neoformans. If it is not treated correctly, cryptococcal meningitis can be fatal. A letter of agreement allowed Dr. Peter Williamson, an expert on cryptococcal meningitis to use Biogen's Tysabri (a monoclonal antibody that acts as an immunosuppressant) under an emergency IND for a comatose patient flown by medevac from Washington state. Emergency treatment with the Biogen drug suppressed the patient's brain inflammation, allowing the patient to slowly recover from the infection.

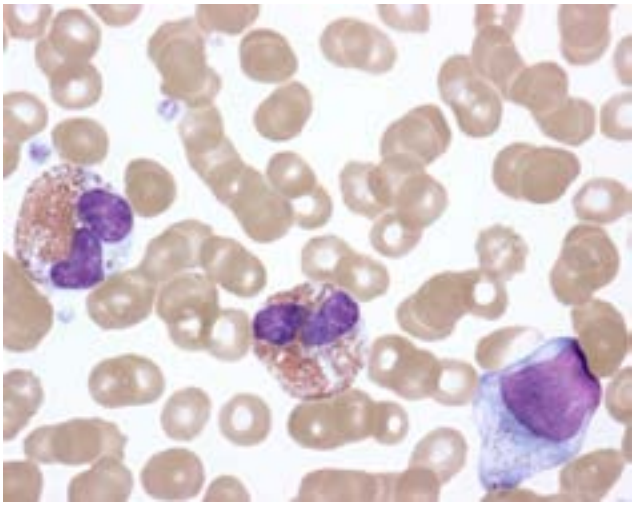
CANDLE: Chronic Atypical Neutrophilic Dermatosis with Lipodystrophy and Elevated Temperature (CANDLE) syndrome was first named and classified in March 2010 and manifests as various autoinflammatory responses throughout the body, multiple types of skin lesions and recurrent long-term fever symptoms. CANDLE is an autosomal recessive disorder; the current known cause is a mutation in the proteasome subunit beta type 8 (PSMB8) gene or mutations in other closely related genes. Eli Lilly provided Olumiant (baricitinib) on an expanded access basis allowing Dr. Goldbach-Mansky to treat patients with severe CANDLE. The continued drug supply enabled by the agreements allowed effective disease management and improved patients' quality of life.

Non-tuberculous mycobacterial infection: Nontuberculous mycobacteria (NTM) are mycobacteria which do not cause tuberculosis but do cause pulmonary diseases that resemble tuberculosis. NTM are present in the environment with different species preferring different types of environment. Human disease is acquired from environmental exposures, animal-to-human or human-to-human transmission of NTM rarely occurs. NTM infections are commonly found in patients individuals with autoimmune disorders. Under a letter of agreement, Novartis provided Lamprene (clofazimine), an antimycobacterial drug for leprosy to Dr. Steven Holland, for the off-label treatment of an NTM patient. The patient has been receiving the drug treatment since October 2018 and is doing well.

TREATING HYPEREOSINOPHILIC SYNDROMES (HES)

TTIPO negotiated and executed a CRADA to explore the safety and efficacy of new treatment for Hypereosinophilic syndromes (HES). HES are a group of rare chronic immune disorders characterized by elevated levels of white blood cells called eosinophils in the blood, tissues or both, and by evidence of eosinophil-associated tissue damage. The symptoms of HES vary widely from one patient to the next and can affect the heart, lungs, skin, gastrointestinal tract, central nervous system and other organ systems. HES is difficult to diagnose and treat because it is pleomorphic (i.e., occurring in various distinct forms), it can be idiopathic (i.e., arises spontaneously or has no known cause) or it can be associated with a variety of underlying conditions.

The Human Eosinophil Section of the Laboratory of Parasitic Diseases (LPD) at NIAID focuses its efforts on this challenge. TTIPO negotiated and executed a CRADA with MedImmune, LLC (now d.b.a. AstraZeneca) in 2014 to explore the safety and efficacy of benralizumab in the treatment of HES. Benralizumab consists of an antibody that binds to a protein, called IL-5 receptor α, found on the surface of eosinophils. Scientists hypothesize that once this binding takes place, immune cells called natural killer cells approach and destroy the eosinophils. Under this CRADA, AstraZeneca provided benralizumab to NIAID for a HES phase 2 trial.



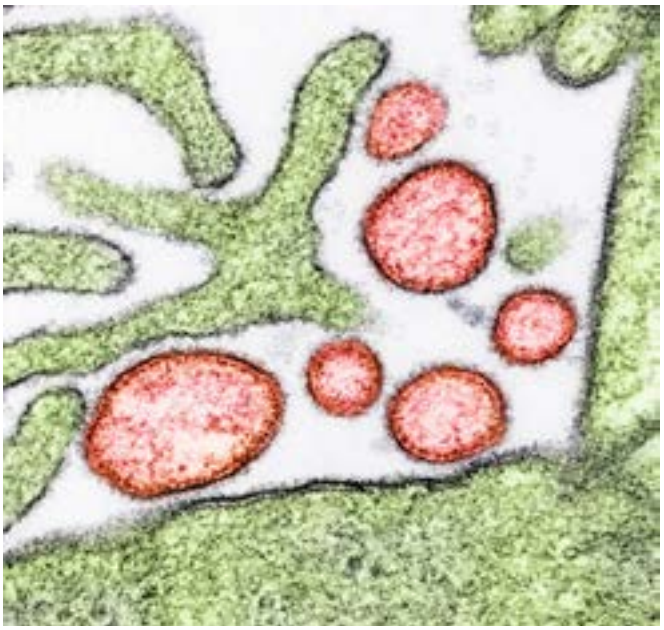
The results of the trial were published in the New England Journal of Medicine in April 2019. This study was only the second randomized, placebo-controlled trial—the gold standard of medical research—to test the effectiveness of a drug specifically for treating HES. After at least 12 weeks of benralizumab therapy, 17 of 19 participants had undetectable levels of eosinophils in the blood and a reduction in HES-related symptoms, with few or no side effects.

Left: Activated eosinophils in the peripheral blood of a patient with idiopathic hypereosinophilic syndrome. Credit: NIAID

“People living with a rare disease often have few, if any, effective treatment options,” said NIAID Director Anthony S. Fauci, M.D. “This promising treatment advance for people with hypereosinophilic syndromes is just one example of how NIH research responds to the unique medical needs of individuals with rare diseases.”

PARTNERING WITH CEPI TO DEVELOP VACCINES AGAINST DEADLY INFECTIOUS DISEASES

TTIPO negotiated and executed four CRADAs and one license to support the development of vaccines against Nipah virus, Middle East Respiratory Syndrome Coronavirus (MERS-CoV), and Lassa virus (LASV) with the Coalition for Epidemic Preparedness Innovations (CEPI) and its collaborators. CEPI is a global alliance between public, private, philanthropic, and civil society organizations launched in 2017 to develop vaccines against infectious diseases. CEPI’s mission is to stimulate and accelerate the development of vaccines against emerging infectious diseases and enable access to these vaccines during outbreaks. CEPI’s priority diseases include deadly diseases for which no licensed vaccines are currently available, such as MERS-CoV, Lassa virus and Nipah virus. Research with either Lassa virus or Nipah virus requires a maximum containment laboratory that meet
biosafety level 4 (BSL-4) standards.



Colorized transmission electron micrograph of mature extracellular Nipah Virus particles (red) near the periphery of an infected VERO cell (green). Credit: NIAID

NIAID’s Laboratory of Virology (LV) conducts innovative scientific research on viral agents requiring high or maximum containment (BSL-2 to BSL-4) to develop diagnostics, vaccines, and therapeutics against these agents. TTIPO has worked extensively with CEPI and its collaborators to execute four CRADAs and one license to support the development of vaccines against Nipah virus, MERS-CoV, and Lassa virus.

The non-exclusive license with Public Health Vaccines, LLC. (PHV) is for a Nipah vaccine candidate developed by Dr. Heinz Feldmann and his lab at NIAID’s LV. It uses a weakened version of the recombinant vesicular stomatitis virus (rVSV) that expresses a type of Nipah-virus protein (known as glycoprotein G) on its surface (rVSV-Nipah), which can induce protection against the virus. Dr. Feldmann and his group have demonstrated the protective efficacy of the rVSV-Nipah vaccine candidate in preclinical studies. CEPI will fund PHV up to $43.6 million for pre-clinical, clinical advancement through Phase 2, and the establishment of an investigational stockpile of this vaccine candidate.

The CRADAs with CEPI partners support the following projects:

- Challenge study evaluation of the protective efficacy of Inovio Pharmaceuticals, Inc. ‘s proprietary vaccine, INO-4700, in NIAID’s non-human primate model of MERS-CoV,
- Challenge study evaluation of the protective efficacy of proprietary chimpanzee adenoviral vectored vaccines against Nipah virus and Lassa virus developed by the Jenner Institute and Oxford

University in NIAID's non-human primate models of Nipah virus and Lassa virus, and in NIAID's guinea pig model of Lassa virus,

• Challenge study evaluation of the protective efficacy of CureVac AG's proprietary Lassa virus vaccine candidates in NIAID's guinea pig and non-human primate models of Lassa virus,

• Challenge study evaluation of the protective efficacy of Inovio Pharmaceuticals, Inc. 's proprietary vaccine, INO-4500, in NIAID's non-human primate model of Lassa fever.

With the execution of the license and these CRADAs, NIAID will be able to leverage CEPI's financial and other resources in the development of vaccine candidates against MER-CoV, Lassa and Nipah viruses.

A TECHNOLOGY TRANSFER OVEVIEW OF THE LAD2 CELL LINE, A HIGHLY VALUED TOOL FOR ALLERGY RESEARCH AND DEVELOPMENT

Since its availability in 2001, TTIPO negotiated more than 400 MTAs to make immortalized mast cell line LAD2 widely available to research community, resulting in more than 60 publications from academic laboratories worldwide. This cell line has also had an incredible impact on commercial use by NIAID licensees in compound screening, expression studies and degranulation assays. TTIPO negotiated nearly 70 licenses with biotechnology and pharmaceutical companies, making this important tool available to support commercial development of proprietary products by these companies and bringing in more than $3.5 million of royalty income to NIAID.

Reactive mast cells are the culprit in allergic diseases and are also implicated in other diseases ranging from autoimmune disorders to cancer to atherosclerosis. These immune sentinel cells normally defend against parasites and bacteria, but sometimes they overreact to harmless intruders, such as pollens or plant oils, releasing granules loaded with inflammation-inciting molecules, such as histamine, as well as various proteases and cytokines that cause allergic and inflammatory reactions. During routine study of cells from bone marrow aspirates from a patient with mast cell sarcoma/leukemia, the Laboratory of Allergic Diseases (LAD), Drs. Dean Metcalfe and Arnold Kirshenbaum at NIAID observed cultures of mast cells with functional FcεRI and FcRI receptors, which continued to proliferate. These unique cell lines, designated as LAD 1 and LAD2, most closely resembles primary human mast cell cultures due to (1) functional FcεRI receptors and the ability to degranulate to immunologic stimuli, and (2) growth dependence on the presence of stem cell factor (SCF).

The availability of this immortalized mast cell line ensures a continuous supply of human mast cells, yielding reproducible data that is more easily compared between different labs. Additionally, this cell line ensures that scientists can save time, effort, and expense to advance allergy and inflammation research.


Material Transfer Agreements
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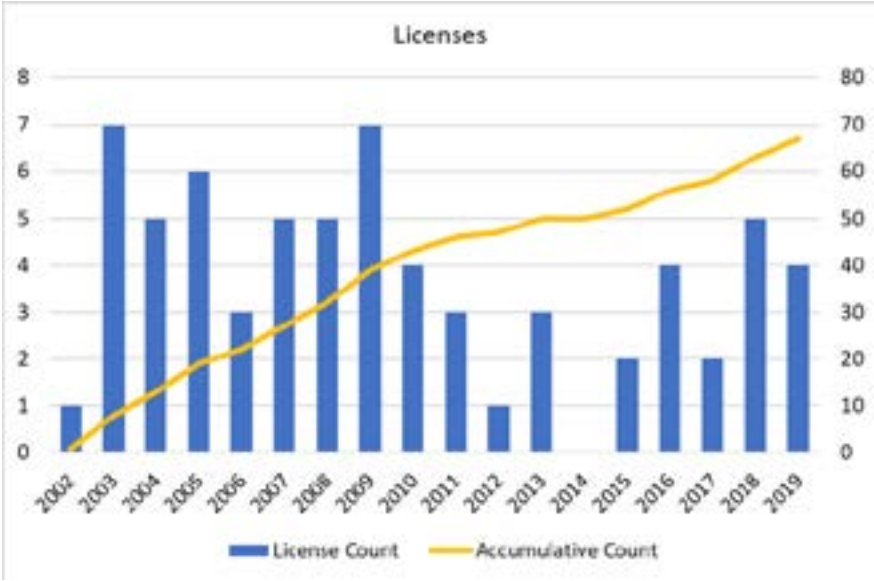
Licenses
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NIDDK – NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

NIDDK entered into an MOU with NIDCR for the NIDDK Technology Advancement Office (TAO) to serve as the service center for NIDCR patenting and licensing activities beginning August 2019. NIDDK licensee BioIntervene Inc. announced a successful $30 million Series A financing to develop and advance first-in-class small molecule A3 adenosine receptor agonists developed at NIDDK by Dr. Ken Jacobson for treating pain, and as a long-sought-for needed replacement for misused and deadly opioids and pain drugs. The proceeds of the financing will be used to advance the Company's lead program, BIO-205, through human proof-of-concept studies in neuropathic pain as well as to advance its portfolio of A3AR agonists for a potentially broad range of chronic inflammatory and neurodegenerative indications. BIO-205 is anticipated to enter Phase 1 clinical trials in the second half of 2020.

Working closely with NIDDK's extensive extramural programs for clinical networks and consortia, NIDDK TAO in its support role within the virtual NIDDK Office of Clinical Research Support (OCRS) helped update funding opportunity announcement language and terms and conditions of award for NIDDK's U01 collaborative agreements. These updates implemented best practices for NIDDK program staff to fully manage their clinical networks, consortia programs, and outside U01 collaborators consistent with NIH policies for data & biospecimen sample sharing, confidentiality, publications, intellectual property, and interactions with 3rd party partners. In addition, TAO provides regular presentations, guidelines, and training materials for NIDDK extramural programs regarding consortium best practices, data and biospecimen sample sharing and repository decisions, U01 ancillary study policies, and managing 3rd party agreements so they remain consistent with NIH policy. TAO also provides presentations and training materials for NIDDK intramural clinical staff regarding clinical research agreement planning, human data and material transfers, IRB functions, agreement negotiation, and trial funding and implementation.

NIDDK TAO strategically designed and implemented separately awarded technology development projects to further advance NIDDK research discoveries and technologies, including:

Software design and coding of an improved iterative algorithm for version 2.0 of NIDDK Dr. Kevin Hall's popular and publicly available bodyweight simulator computer program. NIDDK's bodyweight simulator web site is the most visited site at NIDDK. The new version's updated iterative algorithm will permit a more accurate weight model by incorporating calculated daily weight changes which more closely models the day-to-day data NIDDK has resolved from human weight trials in the NIH clinical center.

Prototype production of NIDDK Dr. William Simonds low-cost easy use "Puri-Fast" protein purification apparatus for use in schools or underserved communities. Typical protein purification using chromatography and column gels may cost upwards of $50,000 or more. This simple apparatus is only about $200, allowing wide distribution for STEM education purposes. Training materials and hands-on tutorials with students are planned as next steps for advancement to encourage more students to pursue an education in the biomedical sciences.

Production of a specialized laboratory instrument for NIDDK Dr. Rob Star's kidney disease branch

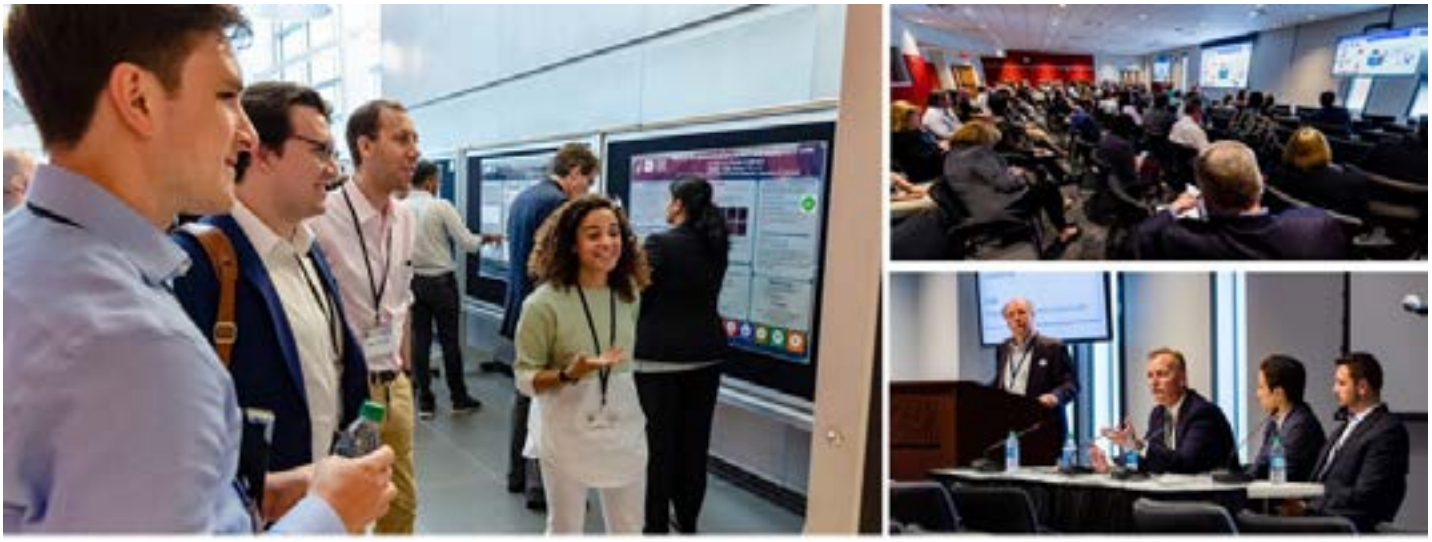
research laboratory to enable simultaneous in vitro measurement of two key kidney function markers in a single sample: glomerular filtration rate (GFR) and GI barrier integrity (GIBI). This new instrument with dual-channel fluorescence and independent dye markers for GFR and GIBI is an important technological advancement for monitoring kidney function in preclinical and human trials, enabling monitoring and diagnosing kidney injury status and the differential effect of various kidney function stressors.

The Employee Viewpoint Survey Analysis & Results Tool (EVS ART) was developed within the NIDDK Office of the Director (OD) to enable rapid and impactful analysis of results from the annual Federal Employee Viewpoint Survey (FEVS). Prior to EVS ART, raw data was provided back to the agencies from the initial EVS survey and analysts would often require many weeks to analyze and identify meaningful results. EVS ART allowed raw data to be analyzed and heat-mapped reports generated within minutes! NIDDK wanted to widely disseminate this method of generating meaningful EVS information and to make EVS ART available for use by all U.S. federal government agencies at no cost. NIDDK TAO designed and implemented an overall strategy and transfer agreement language to protect and track the use of EVS ART to ensure it was publicized and properly distributed for free to other government agencies (and not sold back to the government by outside contractors). By 2019, the EVS-ART had been successfully disseminated throughout all agencies within the US Government.

MARKETING NIH DISCOVERIES

2019 TECHNOLOGY SHOWCASE SPOTLIGHTS NCI AND FNLCR INTRAMURAL INVENTIONS, SUPPORT OF INDUSTRY PARTNERSHIPS

The 2019 Technology Showcase provided scientists from NCI and the Frederick National Laboratory for Cancer Research (FNLCR) a platform to highlight the commercial and life-saving potential of their discoveries to an audience of potential collaborators and licensees. The third annual conference took place at the FNLCR Advanced Research and Development Facility, and drew over 200 attendees from companies, entrepreneurs, investors, regional economic development stakeholders, and NCI/FNLCR staff. Major organizers included TTC's Invention Development and Marketing Unit (IDMU), FNLCR's Partnership Development Office, Frederick County and City, and the Maryland Technology Development Corporation (TEDCO).



Event highlights included:

- A panel poster session highlighting additional NCI technologies presented by the NCI Technology Transfer Ambassador Program
- Keynote presentation by Richard Bendis, President and CEO of BioHealth Innovation
- Panel sessions focused on technology commercialization such as "How to partner with the NCI and FNLCR," "Non-dilutive sources of funding for commercializing technology," "The Role of Incubators and Accelerators" and "Making Your Company Attractive to Equity Investors"
- Networking opportunities

During the course of the half-day event, researchers and business professionals learned a little of each other's language - and how they need one another to create the next generation of medical solutions. They interacted with potential partners and investors, laying the foundation to commercialize future life-changing treatments and cures for cancer patients. TTC is following up on several of the leads generated by the event. The 2020 Technology Showcase will tbe a virtual event to take place on September 9th.

NCI MICRO-DOSE CALIBRATOR FOR PRE-CLINICAL RADIOTRACER ASSAYS

An IDMU-produced video highlighting a technology invented by the Frederick National Laboratory's Dr. Stephen Adler, Clinical Monitoring Research Program was a useful and important aspect of IDMU's strategy to proactively market the technology. The IDMU leveraged the video as part of a marketing campaign that also included targeted, direct outreach, and consistent marketing of the tech at various outreach events the Unit attended in 2019. Dr. Adler also utilized the video to market his technology with connections he made attending various conferences. The IDMU-organized 2018 Technology Showcase also provided a platform for Dr. Adler to pitch the "Micro-dose Calibrator for Pre-clinical Radiotracer Assays" to potential partners and licensees.

The video project was led by Karthik Mosur-Krishna, Ph.D., a special volunteer in TTC's IDMU.

IDMU PROMOTES INDUSTRY PARTNERSHIPS AT KEY 2019 CONFERENCE

TTC's IDMU promoted NCI as a potential collaboration and licensing partner at several events in 2019. In April – June 2019, TTC's IDMU staffed the exhibit booth, organized and participated in panel sessions and met individually with nearly 100 companies

HIGHLIGHTS:

World Vaccine and Immunotherapy Congress West (WVC) 2018
In November, IDMU's Dr. Michael Salgaller attended WVC in San Diego. He developed and participated in a panel on NCI commercialization activities. In a continuing effort to facilitate licensing and collaborations across NIH I/Cs and federal labs, IDMU asked Mike Mowatt (Director, NIAID) and Barry Datlof (Director, USArmy OTT) to participate in the panel, "How Federal Labs Bring Value to Your Company's Pipeline and Bottom Line." One-on-one partnering meetings were held with several companies.

American Association for Cancer Research Annual Meeting 2019 - represented Industry partnerships in the NCI booth. Organized and led a panel session that highlighted "NCI Innovations as a Key Driver of Company Formation and Early-Stage Technologies." Scheduled several in-person meetings with relevant stakeholders.

American Society of Clinical Oncology Annual Meeting 2019 - represented Industry partnerships in the NCI booth. Scheduled several in-person meetings with relevant stakeholders. Provided “Meet the Expert” seminars.

BIO International Convention 2019 - represented Industry partnerships in a high-traffic NIH booth. Michael Salgaller was an invited speaker and panelist at several international forums associated with the conference. He put together a presentation forum with Barry Datlof, Chief, Bus. Dev. and Commercialization in the Office of Medical Technology Transfer, U.S. Army; they spoke about “How to Collaborate with NIH and DoD for Technology Commercialization with the Support of European Initiatives” at the European Commission and Enterprise Europe Network Pavilion. Also, presented at the Scandinavian Cancer Cluster Showcase. Scheduled >50 in-person meetings.

MD Tech Council Roundtable – Dr. Joseph Conrad represented NIH and TTC on “Doing Business with the Federal Government” panel.

INNOVATIVE COLLABORATIONS

FDA AND EMA GRANT ORPHAN DRUG DESIGNATION TO ZOTIRACICLIB FOR THE TREATMENT OF GLIOMA

The U.S. Food and Drug Administration and European Medicines Agency granted orphan drug status in December to zotiraciclib for use in patients with glioma, a cancer of the brain that begins in glial cells (cells that surround and support nerve cells). Gliomas comprise about 30 percent of all brain and central nervous system tumors and 80 percent of all malignant brain tumors, and the types of gliomas include astrocytoma, ependymoma, and oligodendroglioma. This designation is based on results from an ongoing NCI-sponsored phase 1 trial at the NIH Clinical Center. Jing Wu, M.D., Ph.D., Investigator in the Neuro-Oncology Branch, led the trial to evaluate zotiraciclib plus temozolomide for the treatment of recurrent anaplastic astrocytoma and glioblastoma.

Wu's team is now working with Mark Gilbert, M.D., to open the phase II study of zotiraciclib plus temozolomide versus temozolomide alone in recurrent high-grade glioma patients through the Brain Tumor Trials Collaborative. TTC's Michael Pollack, Ph.D., negotiated the clinical trial agreement with Tragara Pharmaceuticals (now Adastra Pharmaceuticals) to evaluate their agent, TG02, in the clinical trial. TTC is working closely with the collaborator to facilitate the phase II clinical trialLearn more.

FDA Grants Orphan Drug Designation to Zotiraciclib for the Treatment of Glioma

TUMOR-INFILTRATING LYMPHOCYTE (TIL) THERAPY ADVANCES FROM LAB TO PATIENTS

In May 2019, the FDA granted breakthrough therapy designation for advanced cervical cancer to Iovance Biotherapeutics, an NCI CRADA partner, for their promising tumor-infiltrating lymphocyte therapy (LN-145) technology. This milestone is an important step in advancing tumor-infiltrating lymphocytes (TIL) research conceived by NCI's Dr. Steven Rosenberg and moving this breakthrough type of cancer treatment from the lab to clinical trials and ultimately, to patients with recurrent, metastatic, or persistent cervical cancer who have progressed on or after chemotherapy. This type of cancer is very aggressive and the prognosis for patients after metastases is very bleak. Following the FDA breakthrough therapy designation announcement, Iovance announced that it will open a new manufacturing facility to support manufacturing of TIL technologies. The new 136,000 square foot production facility is anticipated to "ultimately create employment opportunities for several hundred individuals in Philadelphia once at full capacity. Iovance expects to invest approximately $75 million over three years for equipment and construction of the manufacturing suites."

In 2011, NCI formed a CRADA partnership with Lion Technologies, a startup company strongly committed to moving this new class of treatment through FDA approval and commercialization. The technology from the Rosenberg lab of the NCI Center for Cancer Research (CCR) Surgery Branch, uses T cells that are naturally found in a patient's tumor, called TILs. TILs that best recognize the patient's tumor cells in laboratory tests are identified and selected, isolated and grown to large numbers in the laboratory. The tumor recognizing cells are then activated by treatment with immune system signaling proteins called cytokines and infused into the patient's bloodstream. This treatment is a "live therapy" consisting of a single infusion of TIL. The complex collaboration with Iovance is managed by NCI TTC Technology Transfer Managers, Drs. Aida Cremesti and Andrew Burke.

BREAKTHROUGH THERAPY DESIGNATION FOR POMALIDOMIDE FOR THE TREATMENT OF HIV-POSITIVE KAPOSI SARCOMA

In May 2019, the FDA granted Breakthrough Therapy designation to POMALYST® (pomalidomide) for the treatment of patients with human immunodeficiency virus (HIV)-positive Kaposi sarcoma who have previously received systemic chemotherapy, as well as patients with HIV-negative Kaposi sarcoma. More details in this press release.

NCI entered into a CRADA with Celgene in 2011 to study Celgene's proprietary compound pomalidomide as a potential therapeutic for Kaposi sarcoma. The Breakthrough Therapy designation was granted by the FDA on the basis of the results of a clinical study performed under the CRADA by a team led by Dr. Robert Yarchoan, of the HIV and AIDS Malignancy Branch within NCI's Center for Cancer Research. Pomalidomide is a therapeutic drug that can treat cancer through several mechanisms. Pomalidomide can help treat cancer by blocking certain factors that promote tumor growth or by stimulating the immune system to attack tumor cells. It also prevents the growth of new blood vessels that help cancer grow. In clinical trials, researchers wanted to see if pomalidomide could treat Kaposi sarcoma, a rare and potentially fatal skin cancer. Because Kaposi sarcoma may be associated with HIV infection, researchers wanted to determine if pomalidomide was a safe and effective treatment for Kaposi sarcoma in people with or without HIV. TTC's Wendy Patterson, J.D. manages the ongoing CRADA with Celgene.

REVITALIZING NATURAL PRODUCTS DRUGS DISCOVERY

The NCI Natural Product Repository is one of the world's largest, most diverse international collections of natural products and includes over 230,000 unique extracts derived from plant, marine, and microbial organisms. Successes in deriving drugs from natural products include the cancer drugs Eribulin which originates from a marine sponge and paclitaxel which originates from the Pacific yew tree's bark. Recognizing the potential and the challenges of natural product drug discovery, the NCI invested in a new Cancer Moonshot program, the NCI Program for Natural Product Discovery ("NPNPD") and has created state-of-the-art laboratories for the pre-fractionation of crude extracts and the high-throughput isolation and chemical characterization of biologically active natural products.

The NPNPD plans to generate a library of 1 million natural product pre-fractionated extracts in five years for the use by the research community, with the goal of overcoming the hurdles of working with the complex crude extracts and reinvigorating scientific interest in natural products research. In January 2019, when an initial library of 150,000 pre-fractionated extracts was made available, NPNPD began providing the library free-of-charge under a specially crafted NPNPD Material Transfer Agreement ("MTA") developed with NCI's Technology Transfer Center ("TTC"). In January of 2020 a second set of 176,000 additional fractions was released.

The NPNPD can also share its extensive expertise and resources in isolating and determining the precise chemical structure of active compounds through collaborations with partners under CRADA and in 2019, the first NPNPD CRADA was negotiated by the NCI TTC.

The CRADA is with AstraZeneca UK Limited and under the CRADA, AstraZeneca will use its assays and will work with NPNPD to identify, isolate and investigate compounds with anti-cancer activity derived from the natural products pre-fractionated library. Like the NPNPD MTA, the CRADA was crafted to meet the NCI's and AstraZeneca's obligations to the source country providing the natural product to ensure the equitable sharing of research and development results and the benefits

arising from the commercial utilization of a source country's genetic resources. This first CRADA will become the template for future NPNPD CRADAs with commercial entities. Also significantly, the execution of this CRADA demonstrates that meeting the goals of NPNPD and the Cancer Moonshot initiative to reduce the barriers to natural product drug discovery will result in renewed commercial interest in natural product discovery and development.

The NCI, Developmental Therapeutics Program ("DTP"), Natural Products Branch ("NPB") maintains the Natural Products Repository. Dr. Barry O'Keefe is Chief of the Natural Products Branch and Principle Investigator on the CRADA. Dr. Jeff Thomas and Kathy Higinbotham negotiated the CRADA.

TTC ORGANIZES FIRST SITE VISIT BY US PATENT AND TRADEMARK OFFICE (USPTO) AT NCI

NCI TTC's Michael Pollack (second from left) hosts delegation of nine USPTO examiners at the NIH Clinical Center.

On June 19, NCI hosted nine patent examiners from the USPTO as part of a first-ever NCI-USPTO Site Experience Education trip. The agenda included inventors from the NCI Surgery Branch who spoke about their immunotherapy technologies (Drs. Steven Rosenberg, James Yang and Douglas Palmer), followed by a tour of the Surgery Branch labs. Later that day, inventors (Drs. Peter Choyke, Noriko Sato and Stephen Adler) spoke about their Molecular Imaging Program technologies. The well-received training program was part of the USPTO's Site Experience Program (SEE) "designed to provide patent examiners with an opportunity to visit organizations and learn about state-of-the-art technology developments."

The event was organized and attended by NCI TTC (Drs. Michael Pollack, Aida Cremesti, Andrew Burke, and Tom Stackhouse). "TTC is grateful to all the inventors who so generously shared their time. This was a great opportunity for our inventors to showcase their technologies to some of the examiners responsible for assessing patentability of some of NCI's most promising inventions," commented TTC's Michael Pollack.

NCI INVESTIGATOR-LED STUDIES FACILITATE FDA ORPHAN DRUG DESIGNATION FOR IMMUNOTHERAPY FOR BILIARY TRACT CANCER

In 2010, TTC negotiated a CRADA between NCI and EMD Serono (the U.S. arm of Merck-KGaA Darmstadt, Germany) to allow for preclinical and clinical studies of several EMD Serono proprietary agents. One of the agents studied under this CRADA is M7824, "an investigational bifunctional immunotherapy that combines a TGF-β trap with the anti-PD-L1 mechanism in one fusion protein. Designed to combine co-localized blocking of the two immunosuppressive pathways, M7824 is thought to control tumor growth by potentially restoring and enhancing antitumor responses" (Merck press release). NCI facilitated FDA orphan drug designation of M7824 for biliary tract cancer by conducting important preclinical studies of M7824 as well as the first-in-human Phase 1 clinical trial of M7824. Dr. Gulley, the coordinating PI of the international study, serves on the safety monitoring committee. TTC's Dr. Michael Pollack manages the complex technology transfer activity under the CRADA. The CRADA was amended several times to allow for additional areas of study, including funding for a new Immunotherapy Fellowship in Cancer.

VISION FOR NCI IMMUNOTHERAPY FELLOWSHIP PROGRAM COMES FULL CIRCLE

NCI CCR's Dr. Gulley identified the need to train the next generation of physicians developing and conducting immunotherapy clinical trials. He recognized that for today's up-and-coming oncologists, the basics of immunotherapy taught to them in medical schools does not provide the in-depth preparation needed to meet the demanding and rapid advancements of this high-technology field. In addition, the breadth and depth of opportunities for training in clinical immunotherapy at the NCI CCR are unsurpassed. This spurred Dr. Gulley to create the NCI Immunotherapy Fellowship.

ENGAGED PARTNERSHIPS HELP TO OVERCOME HURDLES

A major hurdle in creating the new training opportunity concerned finding funds to support the fellowship. By working closely with TTC, a solution was found though the novel use of the CRADA mechanism, forming a partnership with the Society of Immunotherapy in Cancer (SITC), and financial support by an existing CRADA partner. To date, three fellows, participated in the NCI Immunotherapy Fellowship. During his fellowship, Dr. Strauss was involved in the Phase 1 study of EMD Serono's agent, M7824.These studies led to a recent FDA orphan drug approval for a rare cancer (story above). Dr. Julius Strauss is now a co-director of the NCI Clinical Trials Group in the Laboratory of Tumor Immunology and Biology, The 2018 NCI Immunotherapy Fellowship recipient, Jason Redman, M.D., completed the fellowship and is now "treating patients with combinations of immunotherapy and chemotherapy" as an assistant research physician at the Genitourinary Malignancies Branch. Lekha Mikkilineni, M.D. was awarded the 2019 fellowship and began working on Dr. James N. Kochenderfer's team at the NCI Surgery Branch in July 2019.

CRADA – USE OF KYMAB MOUSE MODEL FOR VACCINE DEVELOPMENT

Scientific researchers often use mouse models as an early means to assess vaccine candidates ahead of human clinical trials.However, promising results in mice do not necessarily indicate that the vaccine candidate will be effective in humans due to differences in the immune systems of mice and that of humans.

For this reason, NIAID researchers have long sought access to a mouse model with an immune system that is humanized (commonly termed "humanized mice"). Accessing such humanized mice has not been possible because many of these models are tightly controlled by commercial entities that require the retention of ownership rights to any new inventions realized through use of their humanized mice. Such ownership is not consistent with laws, regulations and policies applicable to NIH.

Kymab Limited (Kymab) has developed a humanized mouse model by inserting the entire human immunoglobulin variable-gene repertoire into the mouse genome to engineer Kymouse™ mice. In 2016, the Bill & Melinda Gates Foundation ("BMGF") funded Kymab to develop vaccines and therapeutic antibodies to pathogens of infectious diseases.

As a UK-based company, Kymab had no experience working with the U.S. government or with the statutes and regulations that govern NIAID's activities. To overcome this obstacle, TTIPO negotiated three CRADAs in 2018 that enabled the use of Kymouse™ model to evaluate and develop new vaccine candidates against influenza, HIV and Respiratory Syncytial Virus (RSV), with agreement terms consistent with Federal laws and regulations as well as NIH policies.

CTA – CONTROLLING AND PREVENTING ASTHMA PROGRESSION AND SEVERITY IN CHILDREN WITH OMALIZUMAB

TTIPO negotiated a complex, three-party CTA to receive omalizumab (Xolair) from Genentech, Inc., and the rescue medications Flovent and Ventolin from GlaxoSmithKline LLC (GSK) without cost. This CTA will not only advance NIAID's research interest in asthma, but also yield significant research-cost savings. In addition, TTIPO negotiated and executed a Clinical Material Transfer Agreement (CMTA) with Kaleo, Inc., to receive free Auvi-Q autoinjectors worth over $2 million for use in the clinical trial. These agreements will ensure consistent understanding of different roles in a study titled "Preventing Asthma in High Risk Kids (PARK)" among the companies, DAIT, and clinical research sites.

Asthma is a chronic lung disease characterized by episodes of airway narrowing and obstruction, causing wheezing, coughing, chest tightness, and shortness of breath. NIH issued the first set of guidelines for the diagnosis and management of asthma in 1991. Since then, NIAID has sponsored a series of research programs to reduce the public health burden of asthma in low-income urban environments, where asthma is more prevalent and severe. NIAID-supported research has established that decreasing exposures to household allergens—such as those from dust mites and cockroaches—and implementing guidelines-based asthma therapy can reduce asthma symptoms and healthcare visits.

NIAID's Division of Allergy, Immunology, and Transplantation (DAIT) is sponsoring the PARK study that is being conducted at Boston Children's Hospital. The PARK study is a randomized, double-blind, placebo-controlled trial designed to test whether treating preschool children aged 2 to 3 years at high risk for asthma with omalizumab for two years will prevent the progression to childhood asthma. Omalizumab targets and reduces levels of an antibody called immunoglobulin E, which is central to the allergic response. The drug currently is approved in the United States for patients ages 6 years and older with moderate to severe persistent allergic asthma.

GIFT AND RCA – DEVELOPMENT OF MALARIA TRANSMISSION BLOCKING VACCINES

The Laboratory of Malaria Immunology and Vaccinology (LMIV) has been developing Malaria Transmission Blocking Vaccines (TBVs) to help eliminate malaria transmission in low-endemic areas and to reduce disease burden in moderate to high endemic areas by blocking infection of mosquitoes with antibodies taken up in the blood meal. The use of the vaccines is meant to compliment conventional malaria control programs, such as insecticide use and insecticide-treated bed nets.

Vaccine development by LMIV is focused on two proteins: Pfs25, a member of the P25 family of ookinete surface proteins synthesized by malaria parasites in the mosquito midgut, and Pfs230, part of the Pfs230 antigens expressed on the surface of gametes after being released from red blood cells ingested by the mosquito. Antibodies to these proteins are highly effective in killing parasites through mechanisms not yet fully understood.

TTIPO negotiated several agreements this year to enable and facilitate the development of these TBV candidates. They include:

• Conditional gift agreements with PATH Malaria Vaccine Initiative (PATH MVI) to support a phase 1 clinical trial currently underway in Mali, to test the safety, immunogenicity, and functional

activity of the two leading Pfs25 and Pfs230 vaccine candidates. This trial was enabled by a CRADA between NIAID and GlaxoSmithKline Biologicals S.A.

• Conditional gift agreements with PATH MVI to further develop Pfs230 vaccine candidates by assessing a series of adjuvants and alternate conjugation approaches and evaluating new expression clones to improve production yield.

• An RCA with Novavax Inc. to evaluate the effect of Novavax's Matrix M™ adjuvant on the immunogenicity of these TBV candidates.

• A consortium agreement for NIAID to participate in a consortium of eight institutions across Africa, America and Europe to rapidly evaluate malaria TBV candidates through enhanced African Resource Centers to facilitate their integration into malaria control and elimination efforts.

NIMH ASK SUICIDE-SCREENING QUESTIONS TOOLKIT

The National Institute of Mental Health (NIMH) is the lead federal agency for research on mental disorders and its mission is to transform the understanding and treatment of mental illnesses through basic and clinical research, paving the way for prevention, recovery, and cure.

Suicide is a global public health problem and the second leading cause of death for young people ages 10-24 worldwide. Suicide is also a major public health concern in the United States. According to the Centers for Disease Control and Prevention (CDC), more than 5,900 youths killed themselves in 2015. Even more common than death by suicide are suicide attempts and suicidal thoughts. NIMH is working on two fronts to address this public health issue: early detection and rapid-acting treatments.

The Indian Health Service (IHS) in partnership with NIMH are collaborating to promote and implement universal suicide screening in IHS emergency departments, using NIMH's Ask Suicide Question (ASQ) toolkit and will be working to develop further training and specific educational materials for IHS/Tribal/Urban providers in the near future.

The Indian Health Service, an agency within the Department of Health and Human Services, is responsible for providing federal health services to American Indians and Alaska Natives. Its mission is to raise their health status to the highest possible level. The IHS provides a comprehensive health service delivery system for American Indians and Alaska Natives.

The ASQ toolkit is a free resource for medical settings (emergency department, inpatient medical/surgical units, outpatient clinics/primary care) that can help nurses or physicians successfully identify youth at risk for suicide. The ASQ is a set of four screening questions that takes 20 seconds to administer. In an NIMH study, a "yes" response to one or more of the four questions identified 97% of youth (aged 10 to 21 years) at risk for suicide. By enabling early identification and assessment of young patients at high risk for suicide, the ASQ toolkit can play a key role in suicide prevention.

Esketamine Receives FDA Approval For Treatment Of Depression

A recent breakthrough from research funded by NIMH is the development of a fast-acting medication for treatment-resistant depression (TRD) based on ketamine. In 2006, for the first time in patients, NIMH investigators and their collaborators found that ketamine produced rapid, robust, and relatively sustained antidepressant effects in patients with TRD. These findings led to the development of esketamine, the S-enantiomer of ketamine, as a treatment for TRD and in 2019, it received FDA approval. Delivered intranasally in a doctor's office, clinic, or hospital, esketamine acts rapidly – within a couple of hours – to relieve depression symptoms in approximately half patients with TRD.

AWARDS, PRESENTATIONS AND PUBLICATIONS

FOUNDATION FOR THE NIH AWARDS 2019 TRAILBLAZER PRIZE FOR CLINICIAN-SCIENTISTS TO DR. JAMES KOCHENDERFER

The Foundation for the National Institutes of Health (FNIH) bestowed the 2nd annual Trailblazer Prize for Clinician-Scientists (Trailblazer Prize) to James Kochenderfer, M.D., of the National Cancer Institute (NCI) in October 2019. Dr. Kochenderfer received the Trailblazer Prize and a $10,000 honorarium for pioneering the development of immunotherapies that leverage chimeric antigen receptor (CAR) T-cells to treat blood cancers. The Trailblazer Prize is made possible by a generous donation from John I. Gallin, M.D., and Elaine Gallin, Ph.D., to the FNIH. The Trailblazer Prize recognizes the outstanding contributions of early career clinician-scientists whose work has the potential to or has led to innovations in patient care and seeks to raise awareness of the critical role the clinician-scientist plays in biomedical research and clinical care. Dr. Kochenderfer is in NCI Surgery Branch, and his tech transfer work is managed by TTC's Drs. Abritee Dhal and David Lambertson.

NCI RECIPIENT OF 2018 "EDUCATIONAL INSTITUTION AND FEDERAL LABORATORY PARTNERSHIP AWARD"

NCI received the "Educational Institution and Federal Laboratory Partnership Award" at the Federal Laboratory Consortium 2018 Mid-Atlantic meeting for the establishment of the "NCI Immunotherapy Fellowship Co-sponsored by Society for Immunotherapy of Cancer." "The award exemplifies what is possible through engaged partnerships, in this case, TTC, investigators from NCI's Center for Cancer Research, a CRADA partner and a non-profit," commented Dr. Michael Pollack, the NCI TTC Technology Transfer Manager who was part of the team that helped develop a creative solution to make establishment of the fellowship possible.

Pictured from the left: Kathleen Carroll, Michael Pollack (NCI TTC); Howard Kaufman (SITC)

Award Recipients:
NCI Scientific Team:
Drs. James Gulley, Marijo Bilusic, Ravi Madan, and Christian Hinrichs
NCI TTC and NCI Ethics:
Drs. Michael Pollack, Laura Hennueller, Kathleen Carroll and Mr. Eric Hale
SITC:
Dr. Howard Kaufman

TTC FELLOW RECEIVES 2018 "ROOKIE OF THE YEAR" HONORS FROM THE FLC MAR

Sidra Ahsan (pictured to the right), Ph.D., a fellow at the NCI TTC, received the "Rookie of the Year" award from the FLC MAR. The award recognizes the efforts of an FLC laboratory technology transfer professional who has demonstrated "outstanding work in the field of TT 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 have three years or less experience in a TT position.

TTC TECHNOLOGY TRANSFER MANAGER RECEIVES 2019 NEI DIRECTOR'S AWARD

TTC's Alan Hubbs, Ph.D. received the NEI Director's Award in December. NEI's Ocular and Stem Cell Translational Research Unit is focused on translational research to address degenerative eye diseases using induced pluripotent stem (iPS) cell technology. Age Related macular Degeneration (AMD) is estimated to eventually affect over 65 million persons in the United States. A large number of genes have been linked to a potential risk of developing AMD. In order to accelerate development of therapies for AMD, NEI sought to make an "AMD-Risk Ranked" set of iPS cell lines available to the research community. The NEI goal was: to design the set of cell lines based upon selected human cells with known genetic changes; to have the cell lines manufactured under an acquisition contract; and to separately deposit the lines in a repository; and to distribute them widely at a low cost under a standardized technology transfer agreement that ensures that recipients retain control of their own inventions.

Related to this effort, Dr. Hubbs received the NEI Director's Award as a member of NEI's "New York Stem Cell Foundation (NYSCF) Contract Development Group." His contribution was to establish a collaboration agreement under which NEI and NYSCF would collaborate on the development of the lines, and once developed, to make them available for distribution from the NYSCF repository. The agreement established terms under which the cell lines were to be distributed and it included a distribution Material Transfer Agreement for use by NYSCF in making the distributions. He advised the contracting officer in areas related to the manufacture from human subject materials, such as the need for the contract to include a provision requiring the manufacturer to destroy left-over human materials, and on other matters.

NHGRI STAFF HIGHLIGHTS:

Anna Solowiej, Senior Licensing and Patenting Manager, served as the Chair of AUTM (formerly known as the Association of University Technology Managers) Annual Meeting Planning Committee, helping to organize the 2019 and 2020 annual meetings and coordinating work of about 25 Committee members.

Eggerton Campbell, Senior Licensing and Patenting Manager, presented a course titled "Introduction to Technology Transfer" at the Foundation for Advanced Education in the Sciences (FAES), March 28, 2019 in Bethesda, MD.

Claire Driscoll, Director, presented two talks (Licensing: Types of Licenses, Terms and Considerations session; and Negotiation: Principles and Strategies session) at the U.S. Patent and Trademark Office (PTO) Workshop on Technology Transfer and Management of Government Intellectual Property, July 25, 2019 in Alexandria, VA.

Claire Driscoll served as a member of the AUTM (formerly known as the Association of University Technology Managers) Annual Meeting Planning Committee, helping to organize the sessions and line up speakers for the organization's annual conference and she attended the 2019 AUTM Annual Meeting in Austin, Texas on February 10-13.

Anna Solowiej, Senior Licensing and Patenting Manager attended the 2019 Annual Meeting of AUTM in Austin, Texas on February 10-13 and moderated a four-person panel discussion on "Artificial Intelligence: Impact on Technology Transfer" on February 11, 2019.

Anna Solowiej, Senior Licensing and Patenting Manager received an AUTM Volunteer Service Award at the Annual Meeting in Austin, Texas, on February 11, 2019, "In Recognition of Outstanding Volunteer Service to the AUTM Meetings Portfolio Annual Meeting Planning Committee."

Anna Solowiej, Senior Licensing and Patenting Manager moderated an AUTM webinar on "Artificial Intelligence: Impact on Technology Transfer" on November 7, 2019.

Anna Solowiej and Eggerton Campbell, Senior Licensing and Patenting Managers, volunteered on an NIH-wide working group helping to review submissions for the Patent Legal Services Contract.

Anna Solowiej and Eggerton Campbell, Senior Licensing and Patenting Managers, volunteered on an NIH-wide Technology Transfer User Group (TTUG), helping to coordinate technology transfer transition to a new database system and its related services.

Claire Driscoll served as a member of the NIH-wide Enterprise Technology Transfer (ETT) governance board and several of the ETT work groups helping to coordinate technology transfer transition to a new database system and ensure a smooth transition from our current IT systems.

Claire Driscoll served on the NeuroNext (NN) 109 study team (GNE myopathy Phase 2/3 clinical trial which is being carried under a NN extramural cooperative agreement in conjunction with a 4-party CRADA which involves NHGRI, NINDS, NIAMS and a company, Leadiant Biosciences).

Claire Driscoll served on the NHGRI extramural division's Third Party Engagement workgroup and helped to develop an internal guidance document to be used by extramural program directors and program officers.

In FY2019 Claire Driscoll celebrated twenty (20) years as a NHGRI employee and a total of thirty (30) years of federal service (29 of which was spent at NIH).

Anna Solowiej and Eggerton Campbell, Senior Licensing and Patenting Managers, received a 2019 Genome Recognition of Employee Accomplishments and Talents (GREAT) Award in the Administrative category for service on the Patent Legal Services Contract workgroup on November 25, 2019.

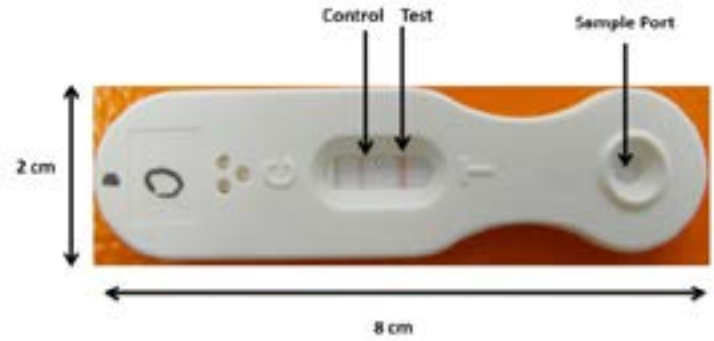
During the Fiscal year 2019, Eggerton Campbell, served as the IC representative on the NIH Exclusive License Consultation Group (ELCG).

Eggerton Campbell volunteered as a mentor to complete a capstone project in the NIH Tech Transfer (FAES Class TECH 607).

PROTECTING HEALTHCARE WORKERS BY DETECTING CONTAMINATION FROM HAZARDOUS ANTINEOPLASTIC DRUGS

2019 Federal Laboratory Consortium (FLC) National Award: Excellence in Technology Transfer

2019 FLC Southeast Regional Award: Excellence in Technology Transfer Project of the Year



CDC NIOSH early technology to detect surface contamination by hazardous antineoplastic drugs. (Photo credit: CDC NIOSH)

Antineoplastic drugs, also known as anti-cancer drugs or chemotherapy, are used in the treatment of many types of cancer. While these drugs are lifesaving to patients, they must be handled with care by healthcare workers. Exposure from contaminated surfaces and drug vials can cause skin problems, birth defects, reproductive issues, and increased risk of various cancers. NIAID TTIPO has helped to improve the handling of these drugs by leveraging patenting and licensing expertise to advance the development and commercialization of new rapid detection kits.

Currently, an estimated 8 million U.S. healthcare workers are potentially exposed to antineoplastic drugs. Traditional sampling methods to test for surface contamination produce results in several weeks, involve significant expense, and require analysis in a laboratory.

Centers for Disease Control and Prevention (CDC) researchers at the National Institute for Occupational Safety and Health (NIOSH) developed technology to rapidly detect three commonly used antineoplastic drugs. (The technology is applicable to many types of antineoplastic drugs.) CDC initially developed the lateral flow immunoassay that allows sampling of surfaces to assess drug contamination.

CDC NIOSH's Research to Practice (r2p) Office, CDC's Technology Transfer Office (TTO), and the CDC Team at NIAID Technology Transfer and Intellectual Property Office (TTIPO) leveraged multiple mechanisms, resources, and activities to successfully transfer this technology, including patent protection, a conference presentation, marketing at additional conferences and via websites, multiple agreements and two licenses.

CDC NIOSH's partners at Becton, Dickinson, and Company (BD) licensed, further developed, and incorporated the technology into a portable device. The resulting tool, the BD™ HD Check system, can analyze samples for doxorubicin and methotrexate (two common chemotherapy drugs) and provide reliable results in less than 10 minutes. It empowers healthcare workers to test surfaces when and where needed — and quickly determine the level of contamination in areas where hazardous antineoplastic drugs are present.

In April 2018, BD launched the HD Check system in the U.S. to strong interest from the pharmacy and nursing communities. BD expects to make the product commercially available in Europe, Japan, Canada, and Australia. NIOSH and BD are continuing research to incorporate additional hazardous drugs in the rapid detection kits.

BD launched the BD™ HD Check system, the first and only rapid hazardous drug detection system, in the U.S. in April 2018. The commercial product reflects a successful transfer of a CDC NIOSH technology.

Credit: BD

APPENDIX

HHS 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 T echnology
- 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:

- NIAAA - National Institute on Alcohol Abuse and Alcoholism
- 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:

- 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