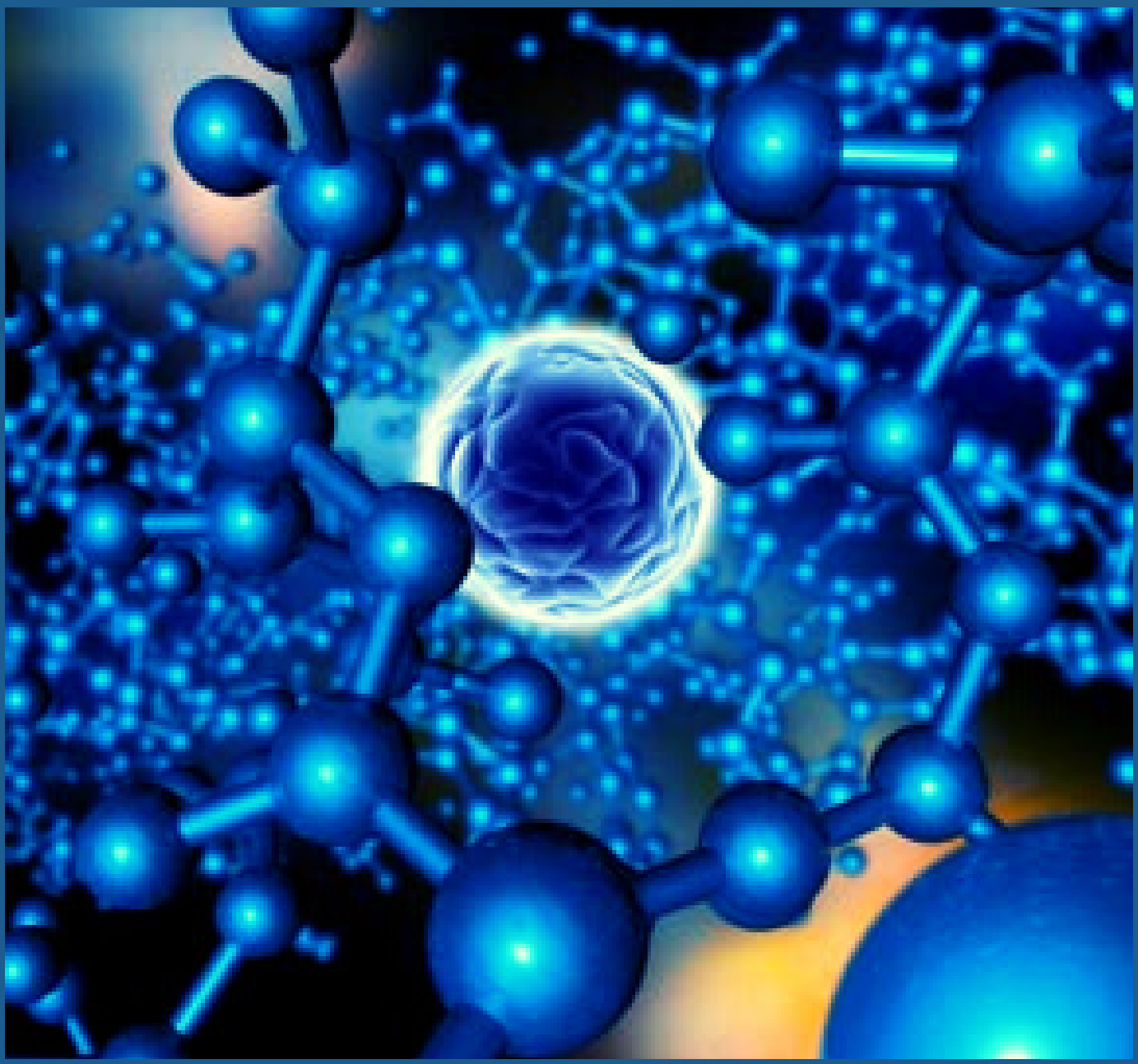
NIH Technology Transfer

Annual Report

FY 2020



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INTRODUCTION

FY2020 was an unprecedented year for the entire NIH Technology Transfer (TT) Community. Due to the COVID-19 pandemic, Technology Transfer Office (TTO) staff had to dramatically shift from working on-site to working from home. While that brought many challenges, I am amazed at how much the community was able to accomplish, including many COVID-19 related technology transfer efforts, described throughout this report.

Each IC TTO has detailed its activities from the past year including success stories, innovative collaborations, and awards; however, the Office of Technology Transfer (OTT) itself was busy as well. The first phase of the implementation of our new Enterprise Technology Transfer (ETT) data system was completed. ETT will replace multiple data systems at the ICs and at OTT, integrating processes and systems and providing a more comprehensive picture of technology transfer activities across NIH. OTT also led the implementation of twenty-four new NIH-wide Patent Legal Services contracts. Our Royalties Administration Unit administered $63.4 million in royalty income brought in from technology licenses. OTT also began work on a new Technology Transfer Community website to benefit all of the ICs as well as NIH's external stakeholders. Finally, we were excited to move to a beautifully remodeled office space – or at least, our furniture and equipment moved - and it will be waiting for us when we return to the workplace.

Another new item this past year was – me! I took over as Director of OTT in October from Karen Rogers, who had been graciously serving as Acting Director over an extended period of time. I have enjoyed coming "home" to OTT these past few months, although I am looking forward to the end of the pandemic so that I can see my colleagues in person.

OTT continues to provide key services and support functions for all of the NIH TTOs and the CDC, including management and oversight of royalty collection and disbursement, monitoring and enforcement of patent rights and licensing agreements, coordinating all patent annuity payments, communicating with existing and potential licensees, and providing patent docketing services. Additionally, OTT continues to support the TTOs through management of TechTracS, the current system of record for all patent and license information, and the OTT SharePoint site, which assists the community with the transfer, collaboration, and management of vital documents and other information.

The report laid out below provides insights into the achievements and scientific advancements made at the NIH and the CDC in FY2020 and reflects how the NIH TT Community was able to adapt to the challenges of working remotely in an uncertain time. The TT Community continues to impress me with their resilience and their ability to facilitate the collaboration and commercialization around NIH/CDC scientific discoveries to improve public health. I invite you to take some time to read about how each IC made an impact to NIH and to the public this past year.

Sincerely,

Tara Kirby

Director, Office of Technology Transfer

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.

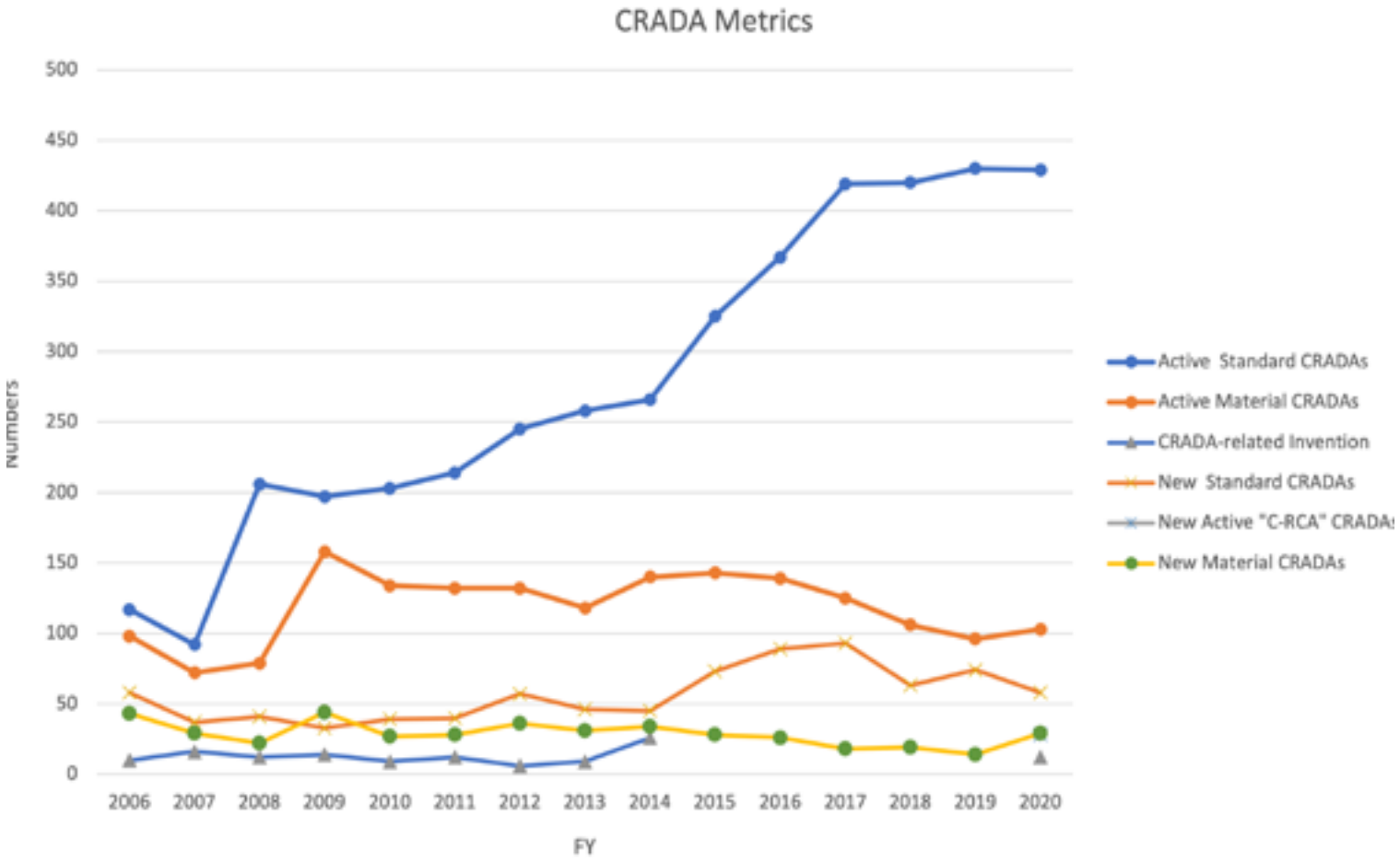
1 Please see the Appendix for a list of all the HHS Technology Transfer Offices within the NIH that contributed towards this report.

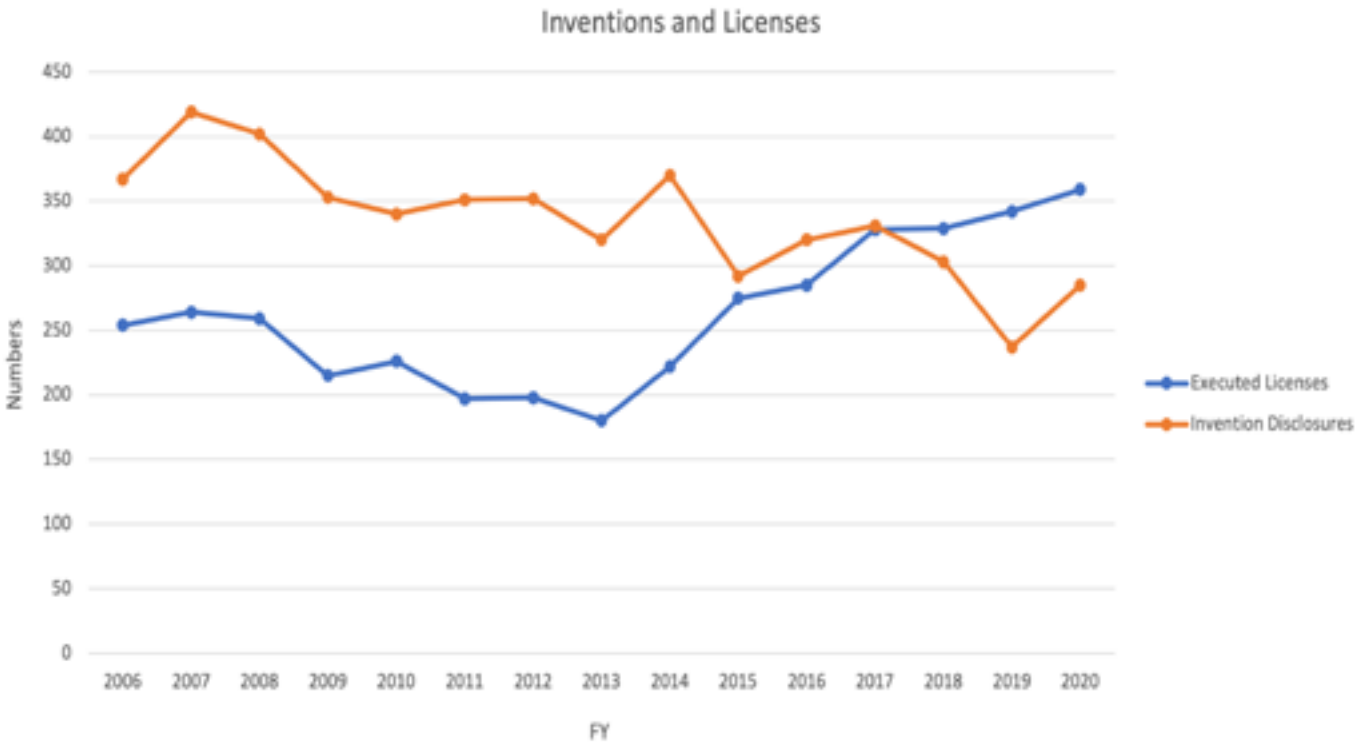
INVENTIONS AND AGREEMENTS

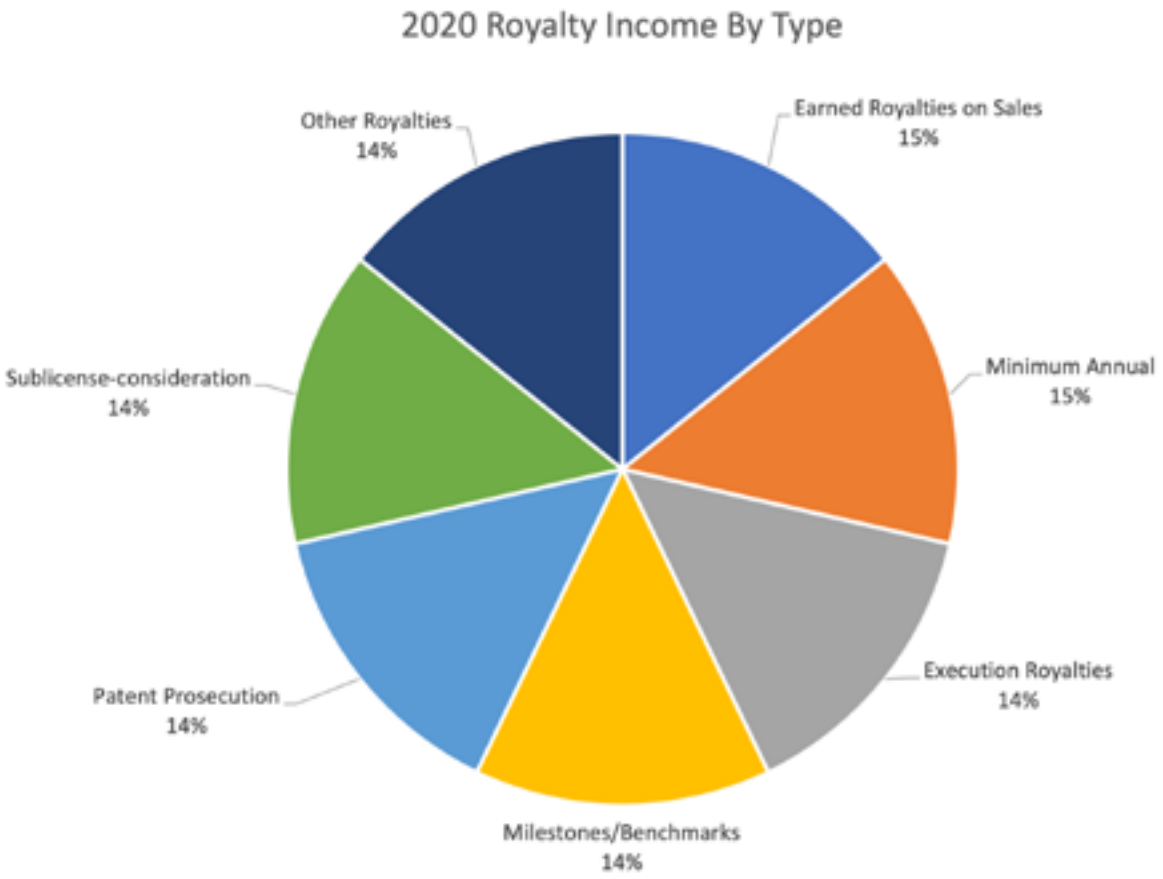
The TT Program at NIH is the focal point for implementation of the Federal Technology Transfer Act. Technology licensing specialists in the NIH ICs license patented inventions to pharmaceutical, medical device, and biotechnology companies in order to stimulate development of technologies into commercial products. These licensing specialists also transfer materials to non-profit research institutions and license for royalties 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.

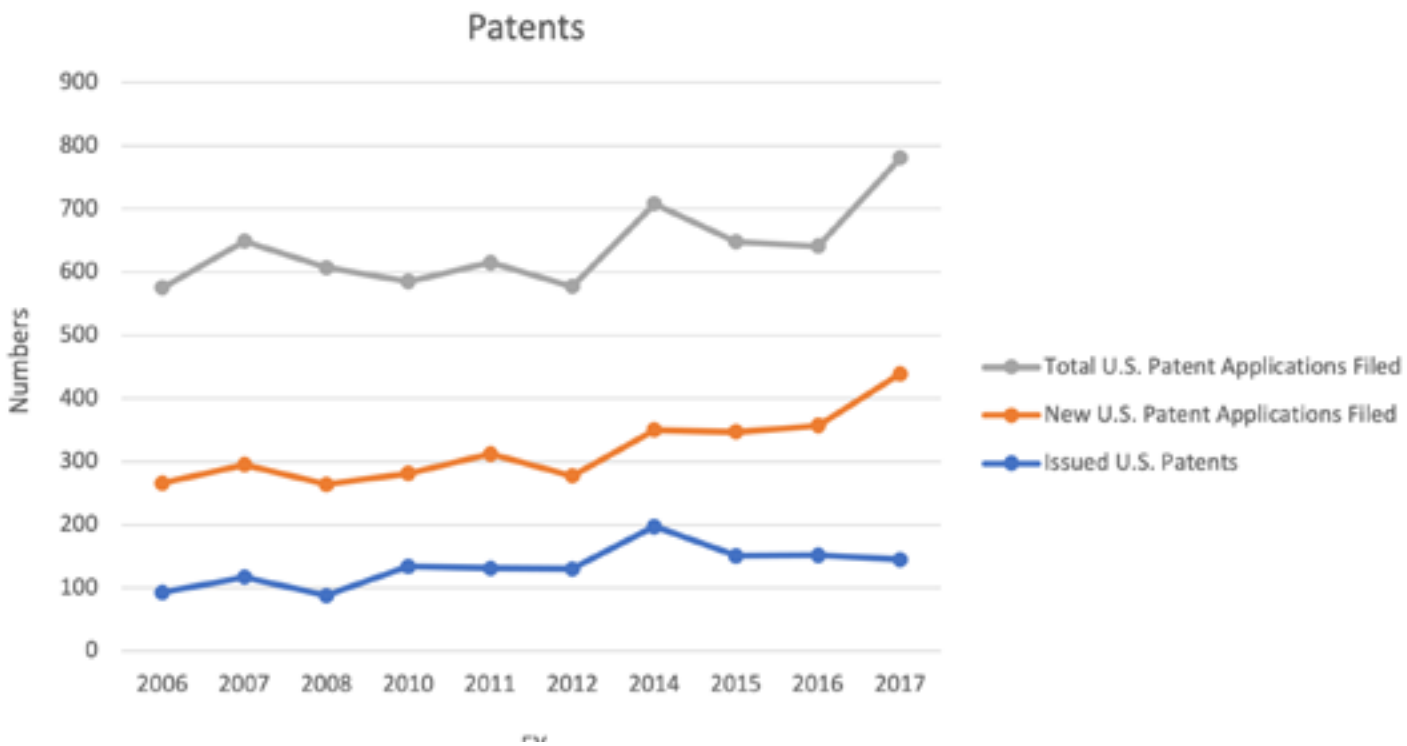
In addition, the TT Program negotiates terms for research collaborations between NIH and commercial and academic organizations. These collaborations leverage the strengths of each institution to advance basic and clinical research objectives. The TT Program also facilitates the transfer of thousands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

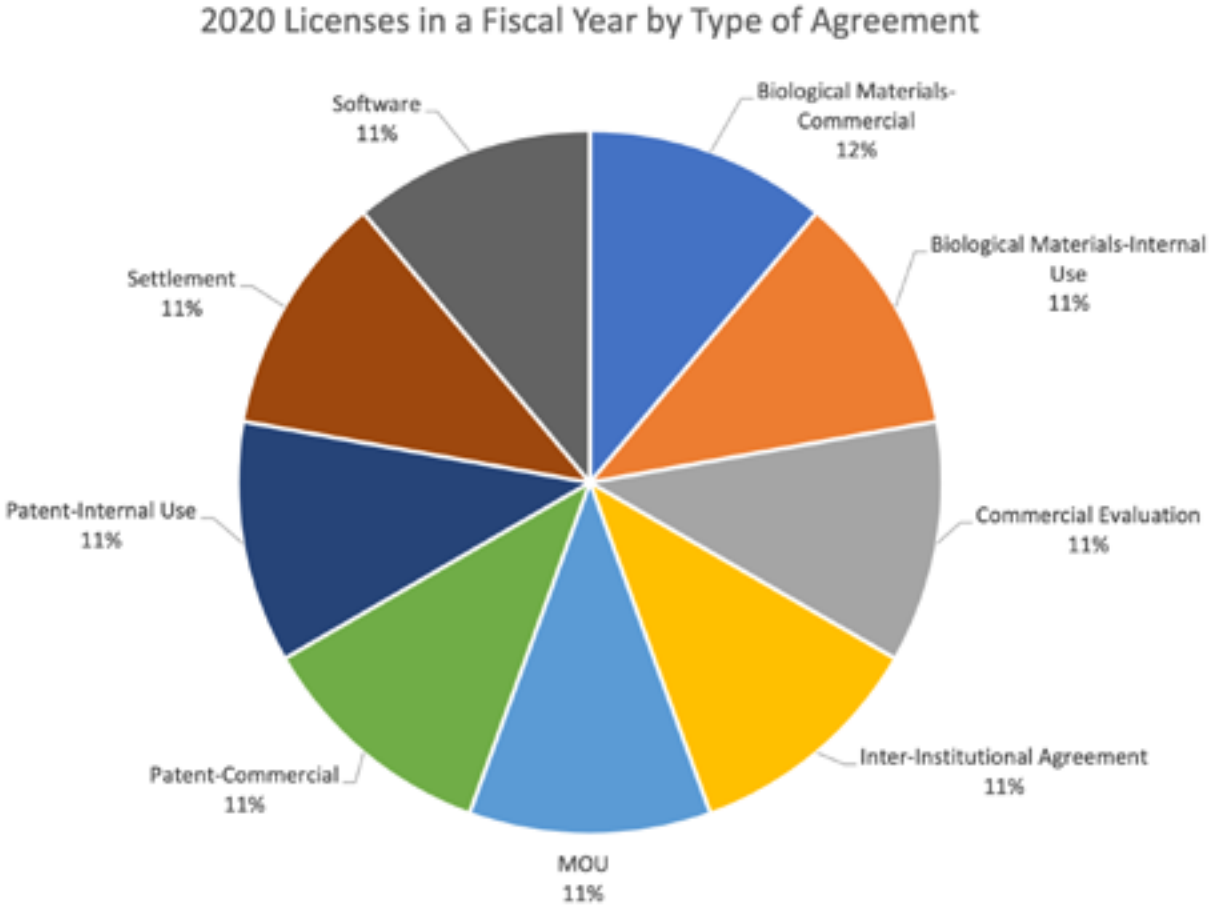
In FY2020 $63.4 million in royalty revenue was brought in. There were 285 invention disclosures, which is a 20% increase over the previous fiscal year. Patent applications filed increased by 47% to 265 and there were 107 U.S. patents issued. Executed licenses also had a slight bump, up to 359 for FY2020.




Inventions and Licenses
450
400
350
300
250
200
150
100
50
0
Numbers
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020
FY
Executed Licenses
Invention Disclosures


2020 Royalty Income By Type
Other Royalties
14%
Earned Royalties on Sales
15%
Sublicense-consideration
14%
Minimum Annual
15%
Patent Prosecution
14%
Execution Royalties
14%
Milestones/Benchmarks
14%


Patents
900
800
700
600
500
400
300
200
100
0
Numbers
2006
2007
2008
2010
2011
2012
2014
2015
2016
2017
Total U.S. Patent Applications Filed
New U.S. Patent Applications Filed
Issued U.S. Patents


2020 Licenses in a Fiscal Year by Type of Agreement
Biological Materials-Commercial 12%
Biological Materials-Internal Use 11%
Commercial Evaluation 11%
Inter-Institutional Agreement 11%
MOU 11%
Patent-Commercial 11%
Patent-Internal Use 11%
Settlement 11%
Software 11%

INSTITUTE AND CENTER UPDATES

NCATS - National Center for Advancing Translational Sciences

The success of The National Center for Advancing Translational Sciences (NCATS) in advancing translational sciences is built on effective management of three core pillars: **collaboration, innovation, and acceleration.** 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 accomplishment 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, 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 typically negotiates and annually executes on average a total of 300 agreements, in addition, there has been a concerted effort to assure that all agreements with term limits were either closed due to project completion or amended to enable the project to continue. While some of these executed agreements were built from institutional template agreements, many required customization as well as substantial unput of time for negotiations to terms acceptable to the NIH. Given the varied nature of NCATS' collaborations with industry, academia, patient groups, etc, many agreement negotiations require significant time and effort to educate our counterparts on the particulars and requirements of collaborating with the federal government, and in particular NCATS/NIH.

While implementing the mission-related programs and activities, NCATS has built and continuous to build a large and complex intellectual property (IP) portfolio. In numerical terms, NCATS portfolio includes more than 200 inventions, the majority of which (more than 150) are jointly owned with collaborators. These inventions have resulted in; 65 issued US patents; 150 issued foreign patents; and 150 pending patent applications.

Further, as a means for accelerating innovation and commercial development, NCATS has licensed many of its technologies (nearly 40 commercial licenses and over 60 Inter-Institutional license agreements). NCATS IP portfolio reflects the great strides being made in forming effective collaborations, which result in significant innovations in the form of new and novel IP, and further which culminate in accelerating development of diagnostics and therapeutics that will benefit patients.

NCATS COVID-19 Response

In early March 2020, NCATS OSA was confronted with a unique set of realities set in motion by the COVID-19 pandemic. With the entire NIH transitioning to a full and flexible telework environment, OSA was asked to support the Technology Transfer activities of NCATS remotely, a drastic change from being co-located with the NCATS Intramural Research Program (IRP). Rising to the occasion, NCATS staff shifted their research activities to address the pandemic. Knowing the urgency, OSA responded by expediting the onboarding, review, and execution of Technology Transfer requests, specifically those that were related in any way to COVID-19.

OSA participated in both NCATS' and NIH Leadership Initiatives, lending their expertise and experience to find creative approaches to solve problems created by this once-in-a lifetime pandemic. From drafting custom agreements, rapidly negotiating and executing Clinical Trial Agreements (CTAs), brainstorming in programmatic planning meetings and working with people across the NIH, OSA's involvement spans beyond the +450 agreements that were executed in FY20, representing an 80% increase above the number executed in fiscal year (FY) 2019.

NCATS
COLLABORATE. INNOVATE. ACCELERATE.

NCI - National Cancer Institute

Dr. Harvey Alter Honored with 2020 Nobel Prize in Physiology or Medicine

Congratulations to Dr. Harvey Alter who was awarded the 2020 Nobel Prize in Physiology or Medicine for his discovery of hepatitis C virus (transfusion-associated hepatitis not due to viral hepatitis type A or type B). Dr. Alter is a senior scholar at the NIH's Clinical Center (NIHCC), one of TTC's Client Institutes and Centers (ICs). Several TTC Staff members have supported Dr. Alter. For more than 20 years, TTC's Tedd Fenn, J.D., has managed patent filings on which Dr. Alter is an inventor. TTC Technology Development Coordinator Andrea Samari and TTM Dr. Kenneth Rose drafted and negotiated several agreements for Dr. Altar's laboratory. Ms. Samari assisted Dr. Alter by drafting and negotiating various Material Transfer Agreements (MTAs) including collaboration agreements, to assist with his lab's hepatitis-C-related research endeavors. Dr. Rose negotiated a clinical trial agreement to study a monoclonal antibody in hepatitis-C infected patients, and several MTAs to transfer hepatitis-C virus infected cell and blood samples to labs, universities, and companies for further study. TTC's long association with Dr. Alter has helped support these new therapeutics to fight this deadly disease.

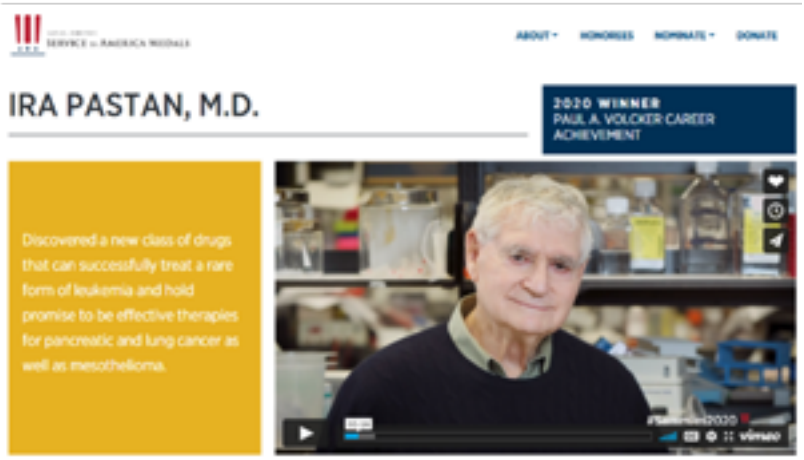
Dr. Harvey alter poses with Swedish ambassador Karin Olosfsdotter in the Nobel Laureates Hall at NIH on December 8, 2020 after a ceremonial presentation of the Nobel medal and diploma. Credit: NIH

NCI Licensee Granted Orphan Drug Designation and Rare Pediatric Disease Designation for Its Monoclonal Antibody Therapy for Pediatric Leukemia

In October 2020, Allterum Therapeutics announced that its monoclonal antibody therapy for pediatric leukemia was granted Rare Pediatric Disease Designation by the U.S. Federal Drug Administration. The therapy is based on a technology invented by NCI CCR's Scott Durum, Ph.D. a senior investigator in the Laboratory of Cancer Immunometabolism. The invention was exclusively licensed to Fannin Innovation, and its spin-out startup company, Allterum Therapeutics, continues to develop the technology and bring it to market. In December 2020, the company secured a $2.9 million product development award by the Cancer Research and Prevention Institute of Texas (CPRIT), a critical milestone to fund preclinical development including drug manufacturing and scale-up. Importantly, development of the technology has the potential to advance a new treatment option for patients with pediatric leukemia. TTC's Dr. Lauren Nguyen-Antczak, JD, TTM, negotiated the license.

NCI CCR's Dr. Ira Pastan Honored with 2020 "Sammie" Award

NIH Distinguished Investigator, Dr. Ira Pastan was honored in October with the Partnership for Public Service's 2020 Service to America Medal ("Sammie") award for discovering a new class of drugs that can successfully treat a rare form of leukemia and hold promise to be effective therapies for pancreatic cancer, lung cancer, and mesothelioma. The Sammie award recognizes federal employees who have led significant and sustained achievements over 20 or more years of government service.

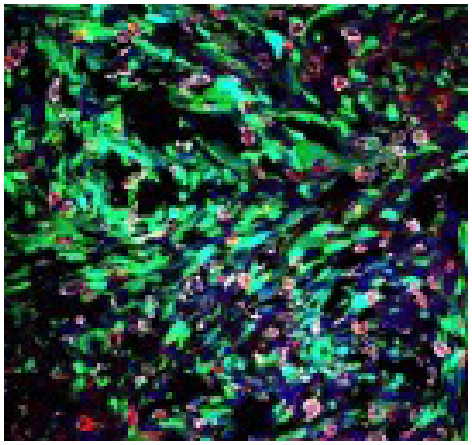


Click image to watch!

For many of these years, TTC's Drs. Dave Lambertson (13 years) and Laurie Whitney (18 years) worked together with Dr. Pastan's laboratory to advance this technology through extensive and complex technology transfer efforts. TTC played an important role in the development of the technology from 1989, when the first immunotoxin was created and patented, through clinical trials that began in 1999, and various improvements to the immunotoxin over the years, that created a large patent portfolio and required several CRADA and license partners. Ultimately, AstraZeneca took Lumoxiti to FDA approval for Hairy Cell Leukemia in 2018. To learn more about the development of Lumoxiti see CCR Milestones 2019.

FDA and EMA Grant Orphan Drug Designation to Zotiraciclib for the Treatment of Glioma

The U.S. Food and Drug Administration (FDA) and European Medicines Agency granted orphan drug status in December 2019 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. TTC's Michael Pollack, Ph.D., negotiated the clinical trial agreement with Tragara Pharmaceuticals (now Adastra Pharmaceuticals) toevaluate their agent, TG02, in the clinical trial. See: FDA Grants Orphan Drug Designation to Zotiraciclib for the Treatment of Glioma


Nanoparticles in the brain
Credit: NCI Visuals online

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 drug 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 one million natural product pre-fractionated extracts in five years for the use by the research community, with the goals 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 TTC. In January 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 CRADAs. In 2019, the first NPNPD CRADA was negotiated by the NCI TTC. Under the CRADA, the CRADA partner will use its assays and 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 the partner'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 natural resources. This first CRADA will become the template for future NPNPD CRADAs with commercial entities. The execution of this CRADA demonstrates that meeting the goals of NPNPD and the Cancer Moonshot initiative to reduce barriers to natural product drug discovery can result in renewed commercial interest in natural product discovery and development.

Spencer Trinh replicates the fraction library onto 384 well plates on the Hamilton Microlab Vantage Liquid Handler to be sent to screening centers around the world.

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, MBA negotiated the CRADA.

Pilot Project Demonstrates That Data Transfer and Use Agreement Streamlines Sharing of Research Data

Research data is frequently shared using a Data Transfer Agreement (DTA - also known as a data sharing agreement or data use agreement). The volume and complexity of these agreements are rapidly increasing. When data providers use different agreements, significant time must be spent reviewing widely varying agreement terms during negotiation. The Federal Demonstration Partnership (FDP) is a cooperative initiative among research institutions and federal agencies to reduce the administrative burdens associated with research grants and contracts. It recently initiated an effort to address the growing challenges associated with transfers of research data. As a first step towards creating greater consistency in terms and format and to improve efficiency of agreement negotiations through a universal template, an FDP working group created a data transfer and use agreement (DTUA) template. This template is intended for the one-way transfer of research data (non-human or human data) from the provider institution to a recipient institution for use in a research project at the recipient institution. NCI TTC's Lisa Finkelstein, Ph.D. participated in this working group and solicited feedback on the template from the entire NIH technology transfer community.

After releasing the DTUA template, the FDP launched a formal, year-long pilot of the template to gather feedback and metrics from institutions that were using it. An analysis of all DTAs executed by NCI during the pilot reveals that use of the FDP DTUA template reduced by half the time it takes to execute a DTA. Several pilot participants, including NCI, provided feedback recognizing the need for a collaborative, two-way template, and the FDP working group has now developed additional templates. Further support for the value of a universal DTA is evidenced by a January 2020 *Science* article where the FDP DTUA template project was recognized as a promising development in the effort to streamline data transfers. In addition, organizations have recently leveraged the FDP DTUA template for their own data transfer efforts including DTAs used for transfers of COVID-19 data. Each of the FDP DTUA templates is available for any institution to use and can be found on the FDP Data Stewardship subcommittee website. This site also contains guidance documents, tools, and FAQs to support its use.

The amount of time to execute Data Transfer Agreements when using the DTUA template for the NCI docket was reduced by half, according to an analysis conducted by TTC's Dr. Lisa Finkelstein who participated in the FDP working group.

Access to the UK's Clinical Practice Research Datalink (CPRD) is restored for multiple NCI investigators

The Clinical Practice Research Datalink (CPRD) is a cancer epidemiology and pharmacoepidemiology research database comprised of anonymized patient data from a network of medical practices across the United Kingdom. Since 2016, CPRD has been used by 10 different NCI investigators conducting cancer epidemiology and genetics research under a contract that included an attached license agreement which TTC, negotiated with input from NIH's Office of General Council and NCI's Office of Acquisitions (OA). Following implementation of the European Union General Data Protection Regulation (GDPR) in May 2018, NCI was asked to sign an updated license agreement (as part of the broader contract) to permit continued access to CPRD. Working closely with OGC, OA, and the Division of Epidemiology and Genetics' (DCEG) Dr. Shahinaz Gadalla, TTC's Dr. Lisa Finkelstein negotiated the terms of the license agreement language which was subsequently attached to the contract prepared by OA. The new contract allows full access to two primary care databases (~1600 clinics) with several linkages (inpatient and outpatient hospital registries through Hospital Episode Statistics, death records through the Office of National Statistics, and socio-economic status variables through the Index of Multiple Deprivation database). It also allows for access to the National Cancer Registry through Public Health England. The restoration of access to CPRD has allowed multiple NCI research projects to once again move forward.

NHGRI - National Human Genome Research Institute

FY2020 NHGRI CRADA information:

Executed Two (2) CRADAs, three (3) CRADA Amendments and one (1) CRADA Letter of Intent:

NHGRI received a total of $2,174,464 in CRADA funds during FY2020.

“A Multinational, randomized, double-blind, placebo-controlled study to assess the efficacy, pharmacodynamics, pharmacokinetics, and safety of venglustat in late-onset GM2 (AMETHIST)” (CRADA Number 2019-0157) effective June 2, 2020, with **Genzyme Corporation d/b/a Sanofi Genzyme**

“Clinical Development of Virtual Reality-based Interventions to Strengthen Cognitive Skillsets related to ADHD” (CRADA Number 2020-0079) effective May 13, 2020, with **Floreo, Inc.**

“Development of Gene Therapy for GM1 Gangliosidosis,” (**Amendment #1** to CRADA Number 2019-0042), signed on June 24, 2020 with **Sio Gene Therapies** (formerly **Axovant Sciences, Inc**.) and the **University of Massachusetts.**

“Identification of Novel Drug Discovery Targets for Underdiagnosed Diseases” (**Amendment #2** to CRADA Number 2017-0020), signed on December 6, 2019, with **Pfizer Inc.**

“Preclinical Development of Gene Therapy for Niemann-Pick Disease Type C” (**Amendment #1** to CRADA Number 2017-0214), signed on April 18, 2020 with **StrideBio, Inc.**

FY2020 License Information

Executed 7 license and license amendments; NHGRI currently has 44 active licenses.

FY2020 Conditional Gift Fund Agreements and Research Grants

The TTO negotiated and executed **five (5)** new conditional gift fund agreements and grants with various organizations.

The TTO submitted non-NIH research grants focused on the following human disease research topics: Parkinson’s disease, Gaucher’s disease, Tay-Sachs disease, methylmalonic acidemia and Salla disease. The NHGRI received in more than $500,000 in gift and research grant funds during FY 2020.

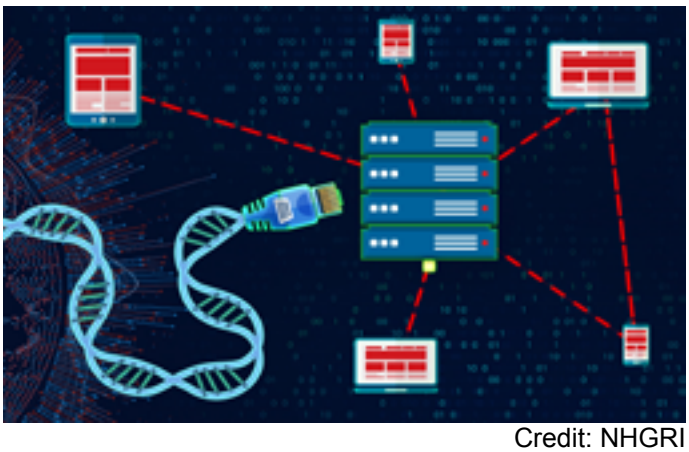
FY2020 Research Collaboration Agreements (RCAs) Information

In November 2019, the NHGRI signed an amendment to a Research Collaboration Agreement with NIAMS and Inova Translational Medicine Institute for a research project titled “The Genomic Ascertainment Cohort (TGAC) Project.”

In June 2020, NHGRI entered into a four-party, seven-PI Research Collaboration Agreement entitled “Preclinical development of potential gene editing therapy for Free Sialic Acid Storage Disorder.” The collaborating parties are: NHGRI, Yale University, Children’s Hospital of Orange County, and Albert Einstein College of Medicine.

In January 2020, NHGRI entered into a three-party Research Collaboration Agreement with the National Institute of Mental Health (NIMH) and the University of Pennsylvania. This project will involve modeling a form of Smith-Magenis Syndrome (SMS) in vitro using induced pluripotent stem cells (iPSCs) and genome editing.

In June 2020, NHGRI entered into a Research Collaboration Agreement with the University of Washington entitled “Identification of potentially-disease causing genetic variants in the Undiagnosed Diseases Program participants.”



Credit: NHGRI

In December 2020, the Research Collaboration Agreement between NHGRI and the National Center for Advanced Translational Sciences (NCATS) for a research project “Rare Disease Platform Vector Gene Therapy (PaVe-GT) Project: Methylmalonic Acidemia (MMA)” entered into an AAV pilot study involving the final synthetic Propionyl-Coa Carboxylase Alpha cassette with positive information regarding metabolites, expressions, and biodistribution of PCCA.

FY2020 Employee Invention Reports (EIRs), Patent Application Filings and Issued Patents

In FY 2020, NHGRI filed twenty-five (25) Employee Invention Reports (EIRs), of which 8 (eight) were biological materials, three (3) resulted in patent filings, one (1) was evaluated in a patentability opinion but the application has not yet been filed, three (3) were based on third-party collaboration where the collaborator is the lead, and ten (10) were CRADA Subject Inventions filed by a third-party collaborator. NHGRI filed 13 new patent applications and had 8 patents issue in FY2020. At the end of FY 2020, NHGRI had thirty-two (32) active patent families (including those with already issued but not abandoned patents), nineteen (19) issued U.S. patents (that were not abandoned nor had they expired), forty-nine (49) issued foreign patents (that were not abandoned nor had they expired), and fifty-eight (58) pending patent applications (U.S. and foreign).

NHLBI - National Heart Lung and Blood Institute

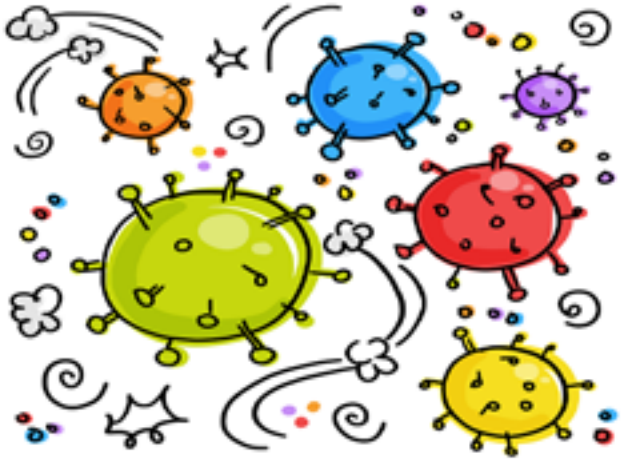
The National Heart, Lung, and Blood Institute investigates a particularly wide array of health areas, as the heart, the lungs, and the blood all play cross-cutting and interconnected roles in human diseases and conditions. The NHLBI stimulates basic discoveries about the causes of disease, enables the translation of basic discoveries into clinical practice, fosters the training and mentoring of emerging scientists and physicians, and communicates research advances to the public. The Institute collaborates with patients, families, health care professionals, scientists, professional societies, patient advocacy groups, community organizations, and the media to promote the application of research results and leverage resources to address public health needs.The NHLBI also collaborates with international organizations to help reduce the burden of heart, lung, and blood diseases worldwide. In doing so, it creates and supports a robust, collaborative research infrastructure in partnership with private and public organizations, including academic institutions, industry, and other government agencies.

The NHLBI Office of Technology Transfer and Development (OTTAD) directly supports the NHLBI mission by providing all tech-transfer services for the NHLBI's staff. Additionally, OTTAD operates a Service Center for the tech-transfer needs of six client ICs, specifically, NIAAA, NIAMS, NIBIB, NIDCD, NINR, and for patenting and licensing, NIEHS. Partnerships that were established, maintained, and updated in 2020 substantially impacted the research and product development arising from the research of these ICs.

In 2020, OTTAD successfully arranged for the NHLBI and its client ICs 120 material transfer agreements, 45 confidentiality agreements, twelve collaboration agreements (clinical and non-clinical), seven new CRADAs, and two commercialization licenses. Active licenses collected over $800,000 in royalties in 2020, up substantially from prior years.

RAPID INITIATION OF DISCOVERY OF THE BIOLOGICAL MECHANISMS AND DEVELOPMENT OF THERAPIES AGAINST COVID-19

The SARS-CoV-2 virus, which causes COVID-19, attacks all of the heart, lungs, and blood, so



while the NIAID focused on controlling infections, the NHLBI played the leadership role in researching how the virus works and what can be used to treat people afflicted with it. In February of 2020, Dr. Richard Childs, Rear Admiral in the Public Health Service and the NHLBI Clinical Director, coordinated the initiation of a major collaborative project with Inova Healthcare, in which the hospital in Fairfax, VA, would send to the NHLBI patient samples for use in various tests of interest to both parties. With herculean effort, Dr. Childs arranged for clinical evaluation to receive the approvals

of the NHLBI leadership, the IRB, and the FDA in two weeks. At the same time, OTTAD (Bruce Goldstein, Esq.) arranged a master collaboration agreement that specifically enabled adding parties and projects as needed.

Once the Inova project was underway, the collaboration expanded to a three-way CRADA (Denise Crooks, Ph.D.), which added Rigel Pharmaceuticals to investigate a first-in-class treatment with highly promising in vitro and in vivo test results. The CRADA project would test fostamatinib, Rigel's spleen tyrosine kinase inhibitor recently approved for treating thrombocytopenia, to see if it would ameliorate the clotting symptom associated with SARS-CoV-2. The CRADA anticipates using both in vitro samples and clinical trials at Inova and the NIH Clinical Center. The trial would be a multicenter, randomized, double-blind, placebo-controlled Phase I/II study of fostamatinib together with the current standard of care.

NOVEL IMMUNOTHERAPIES FOR HEAD AND NECK TUMORS

Immunotherapy for various tumor types is a relatively new and highly promising approach to treating cancer. Numerous studies have demonstrated that various types of products that target a specific tumor-associated antigen ("TAA") have great potential to attack tumor cells with less or no toxicity compared to standard-of-care chemotherapy and radiation, whether administered alone or in combination with other therapies.

The National Institute on Deafness and Other Communication Disorders (NIDCD) is charged with researching disorders involving hearing, balance, taste, smell, voice, speech, and language. Best estimates suggest that more than 46 million people in the United States have a disorder involving one or more of those disorders.The NIDCD Section on Translational Tumor Immunology has collected peripheral blood and tumor biopsies from patients with head and neck cancers (squamous-cell carcinomas), and are interested in investigating modulators of natural killer (NK) cells and tumor-infiltrating lymphocyte (TIL) cells.

The NIDCD recognized that certain investigational products made by ImmunityBio that held particular promise in treating the head and neck cancers of interest. ImmunityBio's next-generation anti-cancer products are designed to activate a patient's immune systems, both innate (NK and macrophage cells) and adaptive (TIL cells in particular), to fight the tumor directly. Additionally, these products are designed to be compatible with another immune-modulating strategy, engineering cells (called "chimeric antigen receptor T-cells," or "CAR-T") to recognize tumor cells among healthy cells, which is gaining momentum across the globe. ImmunoBio's products include antibody-cytokine fusion proteins, small-molecule synthetic compounds, extracts of natural products, viral-based delivery vehicles, nanoparticles, and monoclonal antibodies. Their lead compound, a novel fusion protein named Anktiva™ (interleukin-15 superagonist), has received "Breakthrough" designation from the US Food and Drug Administration, and is in late-stage trials for other cancer types. ImmunityBio

has also used its investigational products to develop an array of diagnostic tools.

The NIDCD and ImmunityBio intended to collaborate to see how well the latter's products perform in selected head and neck cancers. OTTAD (Dr. Brian Bailey) negotiated a CRADA to enable IND-directed preclinical studies, with the hope of extending the project into clinical trials. The project will first look at the diagnostics using patient samples already collected, and then will perform in vitro and in vivo (mouse) studies of the associated therapeutics, including Anktiva, cells engineered to express TAAs, and several proprietary antibodies.

CLINICAL CRADA TO EVALUATE A NOVEL TREATMENT FOR IMMUNE-MEDIATED NECROTIZING MYOPATHY

The mission of the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) research focuses on the causes, treatment, and prevention of arthritis and musculoskeletal and skin diseases. Among its strategic research goals, NIAMS seeks to advance breakthrough and first-in-class treatments for conditions that currently have none available, particularly where success depends on multidisciplinary and cross-cutting research, and where advancing a particular treatment may unlock deeper understandings of the underlying mechanisms of similar diseases.

Immune-mediated necrotizing myopathy (IMNM) is an ultra-rare condition (20 people per million) in which the patient's immune system destroys muscle tissue, causing increasingly severe muscle weakness. IMNM has no cure and no approved treatments; high-dose corticosteroids for several weeks may help some patients, but with substantial side effects. Its causes are not known, but it is associated with two known myositis auto-antibodies and certain anti-mitochondrial antibodies, along with more widespread diseases like certain types of cancer and types of connective tissue diseases. Learning how IMNM works may offer broader insight into those other conditions.

OTTAD (Brian Bailey, Ph.D.) arranged for NIAMS to enter a Clinical CRADA with Ra Pharmaceuticals (now a wholly owned subsidiary of UCB, a global pharmaceutical company) to test zilucoplan, the company's investigational drug, on IMNM patients. Zilucoplan is a synthetic, macrocyclic peptide that is in clinical development for treatment of disorders involving disruption of the innate immune system, Myasthenia Gravis in particular. Under this CRADA, NIAMS will operate as one site in a larger multisite, randomized, double-blind, placebo-controlled Phase-2 trial. With only about 6,000 patients in the US, the participation of NIAMS is critical to enable sufficient recruitment, and the potential impact of a successful project will be enormous for the afflicted patients, and success may reveal broad ramifications in other conditions of importance in the NIAMS research portfolio.

OTTAD SUPPORTS NEW NIBIB SECTION CHIEF WITH PURSUING PATENT PROTECTION FOR A NOVEL INHALED TREATMENT FOR SARS-COV-2

The National Institute of Biomedical Imaging and Bioengineering (NIBIB) is a world leader in integrating physical sciences into the research and development of its namesake technologies, accelerating the application of NIBIB researchers' discoveries to improve medical outcomes. Among the key strategic goals is to transform discoveries about cellular and molecular disease mechanisms into precise medical diagnostics and therapeutics.

OTTAD (Dr. Michael Davis) has begun prosecuting a patent application for an inhaled treatment for SARS-CoV-2 that uses a novel anti-SARS-CoV-2 IgA antibody, the first invention made by NIBIB's new Earl Stadtman Investigator, Dr. Kaitlyn Sadtler, Chief of the Section for Immuno-Engineering. Dr. Sadtler made this discovery while collaborating with Dr. Matthew Memoli (NIAID Laboratory of Infectious Diseases).

The immune response to viral respiratory infections includes a robust antibody production that can be detected systemically in blood sera (IgG and IgM antibodies) and at local sites of infection such as on the exposed mucosa of the sinus and lung (IgA antibodies). The strongest protection against a virus is incurred when the local immune response prevents its spread, which in the case of respiratory viral infections are neutralizing IgA antibodies in the nasal mucosa. Unfortunately, inducing natural IgA immunity against COVID-2 has proven particularly difficult, so work has focused on IgG and IgM types. The novel IgA antibody that Drs. Sadtler and Memoli created, however, displays high affinity binding of construct incorporating an SARS-CoV-2 Receptor Binding Domain, as well as to a full SARS-CoV-2 spike ectodomain trimer, supporting the premise that their IgA antibodies can effectively bind to active SARS-CoV-2 virus therapeutically when administered by intranasal or inhaled delivery – which is much less invasive and more comfortable for the patient than intramuscular injection delivery currently in use with the presently available vaccines.

NIAID - National Institute for Allergies and Infectious Diseases

NIAID Rapidly Shared SARS-CoV-2 Prefusion Stabilized Spike Proteins to Develop COVID-19 Vaccines

NIAID's Technology Transfer and Intellectual Property Office (TTIPO) negotiated agreements and licenses to enable rapid sharing of prefusion stabilized spike proteins and plasmids, developed at NIAID, for the development of coronavirus disease 2019 (COVID-19) diagnostics, vaccines, and treatments. COVID-19 is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The disease was first identified in December 2019 in Wuhan, China, and has since spread globally, resulting in the ongoing coronavirus pandemic. Like other coronaviruses, SARS-CoV-2 particles are spherical and have proteins called spikes protruding from their surface. These spikes latch onto human cells and then undergo a structural change that allows the viral membrane to fuse with the cell membrane. The viral genes can then enter the host cell to be copied, producing more viruses.

Based on knowledge gained from work on SARS (SARS-CoV) following the 2002-3 outbreak, Middle East respiratory syndrome (MERS)-CoV, and other coronaviruses, researchers at the National Institute of Allergy and Infectious Diseases (NIAID) Vaccine Research Center (VRC) and collaborators designed a SARS-CoV-2 prefusion stabilized spike protein quickly when the virus's genomic sequence became public on January 10, 2020.

They also learned early that, despite similarities in sequence and structure between the spike proteins of SARS-CoV and SARS-CoV-2, three different antibodies against the SARS-CoV spike protein did not bind to the SARS-CoV-2 spike protein. Potential vaccine and antibody-based treatments would need to be specific to SARS-CoV-2, making even more imperative the rapid sharing of specifically SARS-CoV-2 prefusion stabilized spike proteins and plasmids encoding them.

Dr. Anthony Fauci, Director of NIAID, receives the Moderna COVID-19 vaccine at the HHS/NIH COVID-19 Kick-Off event on December 22, 2020.

Therefore, NIAID and TTIPO worked diligently to share the spike proteins and plasmids for research use worldwide, as quickly as possible. By November 25, 2020, NIAID had signed 96 material transfer agreements (MTAs) with 75 academic organizations, non-profit entities, government agencies, and other entities to provide SARS-CoV-2 prefusion stabilized spike proteins or plasmids for their research projects, including approximately 20 international organizations. NIAID signed agreements

with Biodefense and Emerging Infections Research Resources Repository (BEI Resources) in June; BEI Resources has fulfilled an additional 55 requests for the plasmids that encode the SARS-CoV-2 spike proteins and 39 requests for its receptor ACE2 plasmid. NIAID also signed an agreement with the National Institute for Biological Standards and Control (NIBSC) in the United Kingdom in September 2020.

In addition to sharing these important materials with academic researchers, NIAID negotiated 21 licenses with biotechnology or pharmaceutical companies. Some plan to employ the SARS-CoV-2 prefusion stabilized spike plasmid to develop new diagnostics or to distribute the protein as a research reagent on a larger scale than NIAID laboratories can support. Most plan to develop SARS-CoV-2 vaccines, delivering prefusion stabilized spike protein constructs using their own vaccine platforms. This includes most of the vaccines in advanced clinical trials and several currently in use around the world.

In addition to materials transfers and licenses, NIAID has signed 16 agreements to collaborate on research projects, including six research collaboration agreements (RCAs) and four clinical trial agreements (CTAs) to develop SARS-CoV-2 vaccines.

One vaccine, mRNA-1273, was co-developed by Moderna, Inc., and the NIAID Vaccine Research Center (VRC). On December 18, 2020, the FDA issued an Emergency Use Authorization allowing Moderna to make the vaccine available for the prevention of COVID-19 in adults in the United States.

CDC's Low-cost Pneumococcal Vaccine Was Approved in India

NIAID's Technology Transfer and Intellectual Property Office (TTIPO) negotiated a license to support the commercialization of a low-cost vaccine that protects against pneumococcal infections. A collection of clinically relevant *S. pneumoniae* strains maintained by the Centers for Disease Control and Prevention (CDC) form the basis of the vaccine. According to the World Health Organization (WHO), globally, pneumonia is the number one killer of children under age five and *Streptococcus (S.) pneumoniae* is the most common cause of severe childhood pneumonia. The $29 to $50 cost per dose of existing pneumococcal conjugate vaccines (PCVs) in the private market has been a major barrier to sustainable and equitable access, especially in the developing world. Generally, there is little incentive beyond sheer goodwill for manufacturers to reduce pricing because that reduces profits.

In 2018, Serum Institute of India (SIL), one of the largest vaccine manufacturers in the world, negotiated a commercialization license through NIAID TTIPO to develop, manufacture, and distribute a vaccine (now called PNEUMOSIL) derived from 23 of the most common S. pneumoniae strains. In the license, NIAID included tiered royalty provisions as an incentive for the company to follow certain reduced pricing guidelines.

Credit: Pneumosil

In December 2019, PNEUMOSIL received WHO prequalification, certifying its quality and eligibility for global procurement. In June 2020, SIL agreed to supply UNICEF with 100 million doses over 10 years at only $2 per dose, a 30% savings over other available vaccines in low- and middle-income countries. On December 28, 2020, SIL announced the public market launch of PNEUMOSIL, starting in India, at only $3 per dose, a 90 to 95% savings versus competing products. SIL also reported that the Indian government is in the process of placing an order for 20 to 30 million doses of the vaccine. Even for upper-middle-income and high-income countries, PNEUMOSIL is expected to be far more affordable than other PCVs, which could help spark and sustain vaccination programs that would not otherwise be possible.

NIAID Conducted Rapid and Innovative Technology Transfer Activities to Enable ACTT Trial to Test COIVD-19 Treatments Including Remdesivir

NIAID TTIPO negotiated agreements to enable the Adaptive COVID-19 Treatment Trial (ACTT) to test COVID-19 treatments including the antiviral drug remdesivir. In response to the COVID-19 outbreak, the NIAID Division of Microbiology and Infectious Diseases (DMID) collaborated with companies to test existing therapeutics for effectiveness in treating COVID-19 through NIH-supported networks and at sites outside the funded networks.

Remdesivir, an investigational antiviral developed by Gilead Sciences Inc., emerged as a promising early therapeutic candidate for COVID-19 with broad spectrum antiviral activity in both in vitro and in vivo studies against multiple emerging viral pathogens. On February 21, 2020, DMID initiated ACTT, a randomized, controlled clinical trial to evaluate the safety and efficacy of remdesivir in hospitalized adults diagnosed with COVID-19. This NIAID-sponsored trial was the first clinical trial in the United States to evaluate an experimental treatment for COVID-19.

TTIPO and DMID collaborated to negotiate a clinical trial agreement (CTA) with Gilead to obtain remdesivir and generate letter of agreement (LOA) templates to be used to expand testing to many sites both within the United States and internationally. The creative technology transfer solutions and expeditiously negotiated agreements enabled initiation of the ACTT trial in late February, less than two months after determination that the Wuhan outbreak was caused by a novel coronavirus.

The Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) on May 1, 2020, for the use of remdesivir for the treatment of hospitalized patients with severe COVID-19 and expanded the EUA by no longer limiting its use to patients with severe disease on August 28, 2020. The FDA approved remdesivir for the treatment of COVID-19 patients on October 22, 2020; it is the first and only (to date) therapy to receive FDA approval for COVID-19.

ACTT has now progressed to test combination therapies. ACTT-2 began on May 8, 2020, to test remdesivir plus the anti-inflammatory drug baricitinib, developed by Eli Lilly and Company. ACTT-3 began on August 5, 2020, to test remdesivir along with Merck's immunomodulatory drug interferon-beta 1a in COVID-19 patients.

NIAID is pursuing testing of potential compounds in combination with remdesivir under NIH's Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) program, and successful therapeutics will be further evaluated in larger clinical trials, potentially leading to additional robust and effective therapies for COVID-19.

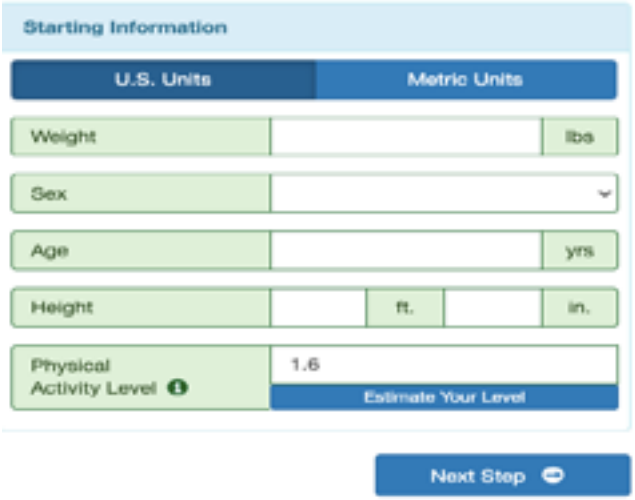
NIDDK - National Institute of Diabetes and Digestive Diseases

In 2020, in response to the CV-19 pandemic, NIDDK's Technology Advancement Office (TAO) implemented new DHHS/NIH administrative policies streamlining negotiation of CV-19 related agreements and material transfers. As a result, TAO expedited material transfers and collaboration agreements and nearly immediately initiated 19 new individual CV-19 research projects with collaborators outside NIH.

TAO was central to the efforts of the NIDDK Office of Clinical Research Support (OCRS) by participating in the development and preparation of a variety of policies, best practices, and training materials for both intramural and extramural clinical research programs governing data sharing, 3rd party collaboration agreements, copyright agreements, and FAR contract clauses protecting NIH rights in intellectual property.

TAO helped plan, fund, and implement a new NIDDK intramural research technology development project of a newly patented NIDDK peptide nucleic acid platform technology for custom design of diagnostics and therapeutics that directly interact with target RNA, and is especially applicable to targeting SARS-CoV-2. The project funds the production of a high quantity tool-kit of various GMP-quality oligomers to be used to expedite design and in vivo testing of anti-viral therapeutics and diagnostics. This technology also overcomes the inherent limitations of PCR and antibody-based diagnostics to provide increased sensitivity and accuracy. The project extends the most efficient use of NIDDK personnel time while optimizing production of high quality GMP tool-kit molecules in bulk and at lower costs. Thus, saving time and resources for the federal government to advance this promising technology and attract outside investment needed to implement these healthcare technologies.

TAO helped plan, fund, and implement a new updated version of the popular on-line NIDDK Body Weight Simulator. The new version incorporates an advanced NIDDK algorithm allowing iterative input of predicted daily changes in weight reflecting a more realistic approximation of variables and conditions discovered by NIDDK clinical researchers in the NIH Clinical Center.



The NIDDK Body Weight Simulator has attracted the interest of numerous academic researchers and private sector healthcare businesses looking to further advance the technology and bring new healthcare therapies and devices to those challenged with body weight health issues.

In 2020, NIDDK's Technology Advancement Office (TAO) expanded its capacity and reach to successfully take on all technology transfer services for NIDCR.

NIEHS - National Institute of Environmental Health Sciences

The National Institute of Environmental Health Sciences (NIEHS) uses state-of-the-art science and technology to investigate the interplay between environmental exposures, human biology, genetics, and common diseases to help prevent disease and improve human health.

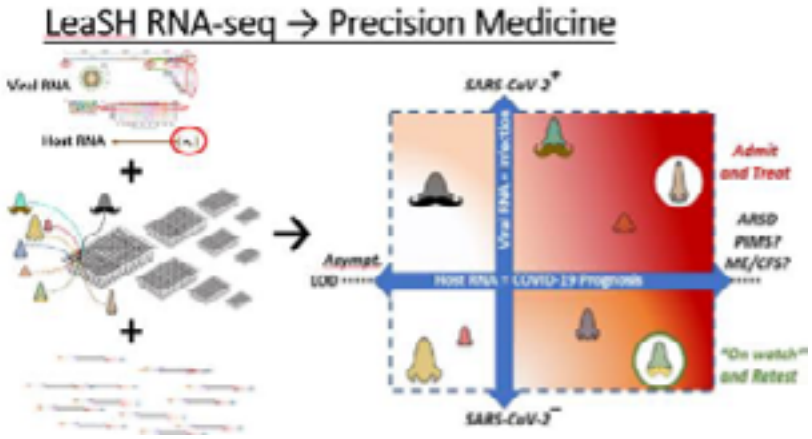
The Office of Technology Transfer (OTT) at NIEHS was established to support the development of emerging environmental health technologies. The mission of the Office of Technology Transfer is to facilitate partnerships that lead to the discovery of innovative technologies that improve human health.

NIEHS OTT successfully negotiated 502 agreements in FY2020 with 424 Material Transfer Agreements (273 of those are with Addgene), 17 Confidential Disclosure Agreements, 45 Data Transfer Agreements, and 16 Research Collaboration Agreements.

Success Stories Related to NIEHS' Response to COVID-19

Like other researchers at the National Institutes of Health, NIEHS scientists responded to the COVID-19 pandemic by adapting their research focus. The OTT implemented technology transfer strategies to incentivize rapid utilization of available technologies to prevent, diagnose, and treat COVID-19 infection during the pandemic.

Rapid Acceleration of Diagnostics Commercialization Path



As laboratories rapidly ramped up COVID-19 testing, a technology was born at NIEHS and nurtured by innovative funding at NIH to overcome the limitations of traditional nucleic acid-based diagnostic testing. NIEHS scientists received $1 million from the Rapid Acceleration of Diagnostics (RADx) program to develop a method to scale up COVID-19 diagnostic testing.

The LeaSH-RNA-seq method uses sample-specific barcoded indexes that detect both SARS-COV-2 virus and the host's transcriptional response to infection. This precision medicine focused method provides the capability for testing tens of thousands of patient samples in a large bolus, allowing accurate and fast-turnaround SARS-CoV-2 testing capacity at population scale while permitting massive scale monitoring of at-risk individuals with minimal processing delays.

The Office of Technology Transfer filed a provisional patent application on the diagnostic method to spur commercialization efforts and negotiated several CDAs, and eventually RCAs, to support clinical development of this technology.

NIEHS Joins the COPE Consortium

The rapid pace of the COVID-19 pandemic presents challenges to the real-time collection of population-scale data to inform urgent and evolving public health needs. The Coronavirus Pandemic Epidemiology (COPE) Consortium was formed to leverage the power of epidemiological cohort study data with new COVID-19 data provided by cohort study participants. The COPE Consortium developed a COVID Symptom Study mobile application as a common data collection tool for epidemiologic cohort studies with active study participants. The OTT swiftly negotiated a consortium agreement to ensure NIEHS had access to COVID-19 data obtained early in the pandemic. By linking NIEHS cohort data to data obtained from the COVID Symptom Study mobile application, NIEHS plans to identify health and environmental factors that affect the likelihood of developing COVID-19 and learn if the virus has any long-term health impacts.

CRADA Tests the Use of Hyaluronan to Prevent and Treat COVID-19

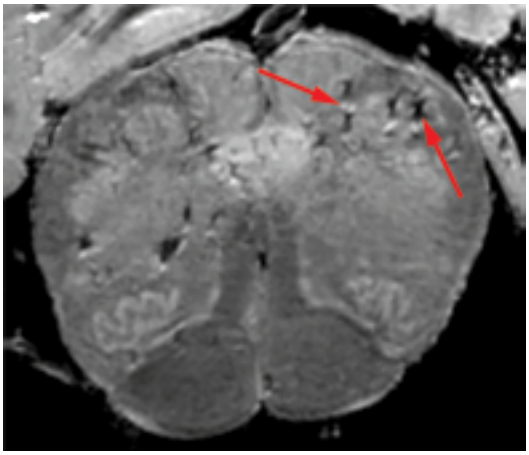
Hyaluronan is an abundant extracellular matrix component of the lung known to have anti-inflammatory properties. In May, researchers at NIEHS identified several hyaluronan binding domains in the spike protein of SARS-CoV-2. This prompted the investigators to ask whether hyaluronan could be used as a COVID-19 therapeutic. In July, the OTT negotiated and executed a Cooperative Research and Development Agreement (CRADA) with IBSA Institut Biochimique SA to test whether sodium hyaluronate can mitigate the pathophysiological effects of the novel coronavirus SARS-CoV-2.

NIMH - National Institute of Mental Health

The National Institute of Mental Health and Taisho Pharmaceuticals (Taisho) have entered into a Cooperative Research and Development Agreement (CRADA) to collaborate on the clinical development of Taisho's proprietary agent TS-161 and to determine its safety and efficacy in patients with treatment resistant depression.

NINDS - National Institute of Neurological Disorders and Stroke

Although COVID-19 is often thought of first as an infectious disease or lung disease, survivors continue to report lingering and highly concerning neurological effects. In response to the COVID-19 pandemic, researchers at NINDS (and elsewhere at NIH) pivoted from their normal scientific focuses. NINDS technology transfer executed approximately 25 agreements in support of COVID-19 research. These agreements covered a range of topics such as tissue samples, presentation forms, and testing and sharing potential therapeutics. One study (Lee et al., New England Journal of Medicine, December 30, 2020, DOI: 10.1056/NEJMc2033369) facilitate by these technology transfer agreements found blood vessel damage and inflammation in patient's brain but no direct infection in the brain. These results can help doctors understand the full scope of symptoms to aid in development of treatments. The publication's web page has been viewed over 60,000 times in less than two weeks since publication. More information can be found at here.



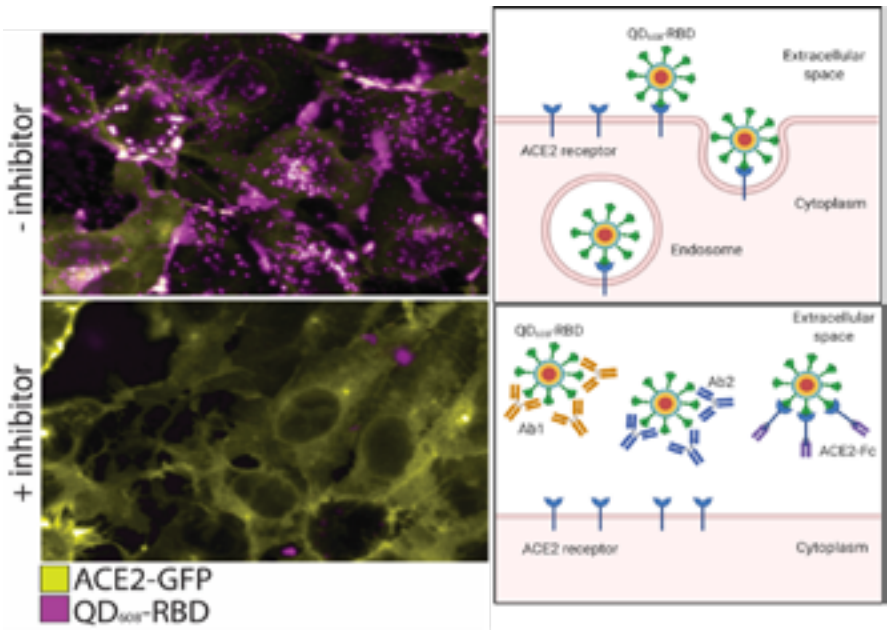
Arrows point to light and dark spots that are indicative of blood vessel damage observed in the study. Credit: NINDS

Under a Cooperative Research and Development Agreement (CRADA), the National Institute of Neurological Disorders and Stroke ("NINDS") of the National Institute of Health ("NIH") and TeraImmune, Inc., will work together to evaluate the therapeutic potential of autologous Foxp3+ T regulatory cells in multiple sclerosis (MS), that are functionally stabilized by oligonucleotides during an expansion process, using the ODNps25 method. MS is a neurodegenerative autoimmune disorder, in which pathogenic autoreactive T cells migrate into the central nervous system across the blood-brain barrier (BBB) and directly attack the myelin sheath. Expanded T regulatory cells (Tregs) have been used in clinical trials for some autoimmune diseases, but not for MS treatment due to the difficulty of obtaining large scale expansion of human Treg cells without their functional loss in vitro. This study aims to: (i) expand the MS patients-Treg cells in vitro for phenotype analysis by using multi-channel flow cytometry with multiple cell-surface/ intracellular markers; and (ii) test the specific phenotype, epigenotype, and immunosuppressive function in vitro against autologous T cells from the patients with MS.

"Pseudovirion"- A Quantum Dot decoy for SARS-CoV2

In March of 2020, NCATS' mission experienced a dramatic refocusing towards the COVID-19 pandemic. The Therapeutic Development Branch (TDB) laboratory at NCATS was tasked with developing assays for drug repurposing and high-throughput screening against the SARS-CoV-2 virus. Such assays did not exist and needed to be designed and executed to aid the public health crisis.

An idea that quickly gathered momentum was the development of SARS-CoV-2 viral spike protein quantum dots (QD) to measure binding to ACE2 receptors on human cells. Collaboration discussions between NCATS and the Naval Research Laboratory (NRL), where the quantum dots had been extensively developed, led to the execution of a Research Collaboration Agreement (RCA) and the realization that the approach of developing quantum dot virions had strong potential.



ACE2-GFP HEK293T cells (yellow) bind and internalize quantum dot-conjugated SARS-CoV-2 receptor binding domain (QD608-RBD, magenta) through receptor mediated endocytosis. Inhibitors such as anti-SARS-CoV-2 antibodies (Ab1, Ab2) and recombinant ACE2-Fc can prevent the binding of QD-RBD to ACE2 and their subsequent endocytosis.

The phenomenon related to virus binding to the cell surface and further internalization were observed microscopically using the artificial quantum dot "virions," suggesting that the proposed assay was capable of simulating viral infection using the QD-Receptor Binding Domain (RBD). The development of the tool, called a "pseudovirion" because of the size, shape, and function of the molecule, was published in ACS Nano where the article has ranked in the top 0.1% of all manuscripts for 2020.

As a further proof-of-principle for the "pseudovirion," NCATS scientists conducted high-throughput screening against the Center's 10,000-compound library and found several compounds that were able to inhibit the binding and internalization of the "pseudovirion." Follow up mechanistic studies on the "hit" compounds to understand the mechanism of action are being pursued. Licensing efforts are underway to commercialize this technology. This exciting development is also poised for rapid adaption into the field of COVID diagnostics.

“Innovation at NCATS” Patent Book

The innovation of NCATS’ scientists and their worldwide collaborators is hard to fully appreciate. One starting point would be to look at the patent filings and issued patents that originate in the NCATS labs. The NCATS Patent Book entitled, “Innovation at NCATS” is the first attempt at NCATS to document innovation, and to start a tradition that will continue to shine light on this subject. As NCATS approaches its Tenth Anniversary, “Innovation at NCATS” will be a wonderful way to showcase NCATS’ success stories.

“Innovation at NCATS” took shape over many conversations, many variables, design factors and technology vignette formats were created and subsequently fine-tuned. OSA compiled a list of patents issued to NCATS and verified the information via the United States Patent & Trademark Office patent database. OSA collaborated to gather design recommendations and compile abstracts along with other relevant information. The team used the services of the NIH Medical Arts group to typeset and print the book. As we are in the middle of the COVID-19 pandemic, a conscious decision was made to promote the electronic version of the publication and print only a limited number of hard copies.

“Innovation at NCATS” will be shared with all our audiences and can be used as a historical starting point for documenting NCATS innovation in the coming years and decades. This book will be a source of joy and pride for all the NCATS scientists.

For all of the above reasons, and the pride that “Innovation at NCATS” brings to the organization, the efforts described here deserve to be recognized.

TTC and NCI CCR Host the UK Northern Powerhouse Trade Mission’s Visit

Representatives from NCI CCR, TTC and the UK Northern PowerHouse trade commission at NIH’s Natcher Auditorium.

On March 2, 2020, NCI hosted a visit from 15 individuals and eight companies representing the first trade mission from the “UK Northern Powerhouse,” a 2019 initiative to foster collaboration and cooperation in the life science sector – as well as several other markets. The gathering took place at NIH’s Natcher Auditorium shortly before in-person gatherings were halted due to the pandemic. Companies and CCR PIs gave brief presentations. Company talks involved platform technologies for small or large molecule drug discovery as well as diagnostics and therapeutics.

NCI CCR participants included:

- Glen Merlino, Ph.D., NCI CCR Laboratory of Cancer Biology and Genetics
- Doug Figg, Pharm D., NCI CCR Genitourinary Malignancies Branch
- Gary Griffiths, Ph.D., Imaging Probe Development Center at NIH
- Bruce Shapiro, Ph.D., NCI CCR RNA Biology Laboratory
- Gary Robinson, Ph.D., NCI Office of Scientific Operations (CCR liaison)

TTC's Drs. Michael Salgaller and Joe Conrad, J.D. (IDMU) and Tom Clouse, J.D. (TTM) provided a brief overview of NCI licensing and partnering methods and opportunities. The trade mission led to several discussions with CCR personnel about collaborative and licensing opportunities. Trade missions are part of the TTC IDMU's international outreach strategy. The UK trade mission demonstrates the close bonds nurtured with the international community.

TTC's IDMU Pivots Outreach Strategy to Take Advantage of Virtual Events

One way that TTC's IDMU identifies potential partners and licensees is through engagement at industry events and conferences. Because of the Covid-19 pandemic, event organizers continued to make changes and adjustments in 2020, many pivoting to virtual events. The IDMU participated in multiple virtual conferences by taking advantage of one:one partnering meetings, participating on panel sessions, and even staffing virtual exhibit booths. Two notable examples include:

BIO Digital 2020

The BIO International Convention, typically one of the most widely attended biotechnology conferences in the world, pivoted to a virtual offering. To that end, BIO facilitated virtual one:one partnering – in 2019, the offering was noted as being one of the largest one:one partnering events in the world. In 2020, it included more than 7,000 participated from 64 countries across 28 time zones. IDMU Supervisor, Dr. Michael Salgaller, and Drs. Joe Conrad and Berna Uygur spoke with more than 40 companies to establish new partnering and licensing opportunities on behalf of NCI and the NIH ICs that TTC supports.

In addition, Dr. Salgaller organized and hosted a panel presentation entitled, Many Happy Returns: Federal Labs as Commercialization Partners, Turning Public Support into Marketed Innovations that included perspectives from various federal labs and a federal industry partner.

2020 BioInnovation Conference

The 2020 BioInnovation Conference was organized by the Maryland Life Sciences (MDLS), a division of the Maryland Tech Council. The October 5 – 6 conference connected more than 500 life sciences professionals from industry, academia, and government in the region with business leaders, venture capitalists and promising startups. IDMU created technology sheets and general information for interested visitors to their virtual booth. The conference offered the unique

opportunity to network through the BIO One-on-One Partnering System and dedicated networking time. Such events help to build a strong life sciences community within Maryland by supporting an environment where innovation can thrive.

49 Teams Selected for Innovate Children's Health Challenge (ICHC)

In October 2020, the Center for Advancing Innovation (CAI) selected 49 teams to participate in the Innovate Children's Health Challenge. NCI along with NCATS, NHGRI, NICHD, NHLBI, NIAID, and NIDCR each have inventions featured in the Challenge. Additional inventions from academic institutions and other entities are also part of the ICHC.

In the first phase of the competition, teams produced "elevator pitches" and executive summaries, which CAI and the public voted on October 3 – 8. In Phase 2 of the ICHC, semifinalists are working to produce comprehensive, 10-page business plans on how to commercialize promising inventions that are topics of the challenge; they will also produce financial models and a pitch deck. By January 2021, semifinalists will submit their business plans and financial models and pitch to a judging panel comprised of leaders from industry, academia, foundations, patient advocacy groups, and investor groups.

Earlier in 2020, TTC Associate Director, Richard Rodriguez worked closely with CAI to establish the latest challenge and coordinate involvement by NIH ICs. Through CAI, the Challenge is supported by Resonance Philanthropies, a donor-advised fund of the Silicon Valley Community Foundation. To conclude Phase 2 of the challenge, judges will select 15 winners. Winners will form start-up companies, pursue licensing agreements from institutions where promising inventions were sourced, and pitch for early-stage funding from CAI's network of investors. Challenge winners who selected an NIH invention will apply for a license through the standard NIH license process. Learn more: press release, Phase 1 Elevator pitches and ICHC.

Starting with the Breast Cancer Startup Challenge in 2014, TTC worked with CAI to establish several startup challenges — a strategic initiative to encourage licensing and collaborative development of NCI technologies, and encourage the formation of startups around those technologies. After the Breast Cancer Startup Challenge, the scope of the Neuro and Nano Startup Challenges expanded to include other NIH ICs and inventions from other organizations. A June 9th press release issued by CAI kicked off the ICHC.

INNOVATIVE COLLABORATIONS

National COVID Cohort Collaborative (N3C) Data Enclave

NCATS National COVID Cohort Collaborative (N3C) Data Enclave provides a safe and secure environment for electronic health information related to COVID-19, provided by participating institutions and health care providers. The N3C project created a novel, collaborative approach involving a Federal organization (NCATS), grantees funded under cooperative agreements to NCATS, diverse participating institutions and healthcare organizations to provide the electronic health record data, and a user community, where the majority of users do not have specific NCATS funds to conduct the research in a Federal data enclave. This created a unique set of policy, operational, and governance challenges that the N3C team navigated while aligning with community-driven objectives and activities, all with the urgency of addressing critical research and health needs unique to a pandemic.

OSA, as part of a multi-disciplinary team, facilitated the development and execution of formal contractual agreements (over 225), assessed the policy and regulatory implications contributing to operation of the Enclave, aligned National Center for Data to Health (CD2H) developed policies with NCATS/NIH Data Enclave policies and federal regulations and provided expertise in the review of licenses and contractual relationships. For this initiative alone, OSA has dedicated over 400 man-hours and continues to devote staff time for this important National COVID-19 resource.

Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) Program (ACTIV-1)

NIH's Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) program is a public-private partnership or initiative to speed development of the most promising treatments and vaccine candidates. ACTIV-1 Immune Modulators, is an adaptive Phase 3 clinical trial to evaluate the safety and efficacy of three immune modulator drugs in hospitalized adults with COVID-19. Three agents were selected based on several factors including their relevance to COVID-19, strong evidence for use against inflammatory reaction and availability for large-scale clinical studies. The initial agents are infliximab (REMICADE), developed by Janssen Research & Development, LLC, one of the Janssen Pharmaceutical Companies of Johnson & Johnson

Credit: NIH

(Janssen); abatacept (ORENCIA), developed by Bristol Myers Squibb (BMS); and Cenicriviroc (CVC), an investigational late-stage agent developed by AbbVie. (Janssen, BMS, and AbbVie will be collectively referred to as Pharma Partners.) COVID-19 would be a new use for these drugs, i.e. this is a drug repurposing effort. Gilead supplied the Remdesivir.

NCATS is coordinating and overseeing the trial with funding support from the Biomedical Advanced Research and Development Authority (BARDA) of the U.S. Department of Health and Human Services Office of the Assistant Secretary for Preparedness and Response, in support of the Trump administration's Operation Warp Speed (OWS) goals. The trial expects to have 60 sites in the United States and 30 sites in Latin America enroll participants in this trial. At least 30 sites in the United States are CTSA Program sites.

NCATS OSA launched into negotiations with the Pharma partners quickly. The National Institute of Allergy and Infectious Diseases (NIAID) collaborated and shared their ACTIV clinical templates, which provided helpful background as NCATS customized their own trial-related agreements. NCATS OSA and BARDA negotiated and executed a Memorandum of Understanding (MOU) to define the roles and responsibilities between the two parties. OSA quickly negotiated and executed the Confidential Disclosure Agreements (CDAs) with each Pharma Partner. The CDAs cover the scope of project and acknowledge that the information might be shared with others who are part of this ACTIV-1 program. CDAs were put in place to begin Investigational New Drug (IND) discussions. NCATS OSA also drafted and negotiated Clinical Trial Agreements (CTAs), and a Clinical Supply Agreement (CSA) all in parallel and with input from the entire team.

Acer Therapeutics – RCA Collaboration

Emetine was previously identified by NCATS and Johns Hopkins University as a broad-acting antiviral compound. Acer Therapeutics entered into a Research Collaboration Agreement (RCA) with NCATS Scientists to further explore emetine as a possible therapeutic treatment for SARS-CoV-2. Acer has taken the lead on filing two patent applications with NCATS since the RCA was executed.

BioIncept

Under a RCA, the NCATS Bridging Interventional Development Gaps (BriDGS) Program is collaborating with BioIncept to conduct toxicology (Tox) studies. BioIncept is currently preparing for a Phase I/IIa clinical trial at a leading US medical center to evaluate the safety and efficacy of sPIF in patients diagnosed with COVID-19. NCATS continues to collaborate and support Tox studies in BioIncept's submissions to the U.S. Food and Drug Administration (FDA).

Synthetic PreImplantation Factor (sPIF) Credit: BioIncept

Advancing Innovations through Mentorship (AIM) – Collaboration Between NCATS and NCI

Advancing Innovations through Mentorship (AIM) is a new short-course program that has been crafted to advance translational discovery and development arising from the NIH Intramural Research Program (IRP) and to empower NIH investigators in evaluating their technologies in the context of the commercial and healthcare landscape. AIM is based on the NIH Innovation Corps (I-Corps) program that has been further developed and fine-tuned for the NIH intramural program. Since 2018, leaders across the National Cancer Institute (NCI) Small Business in Research (SBIR) Development Center, the NCI Technology Transfer Center, and NCATS Office of Strategic Alliances (OSA) have been discussing expansion of the already successful NCI-led SBIR I-Corps program for the NIH IRP. In its current form, SBIR I-Corps at NIH is an entrepreneurial training program designed to help innovators - Phase I SBIR/STTR awardees - assess their technologies, recognize commercial opportunities, and build a scalable business model. This program has enormously increased the commercial awareness of SBIR/STTR awardees and has helped them to identify funding sources and finesse their commercialization plans.

The value of an I-Corps-like program for intramural scientists was soon recognized and led to the development of the pilot AIM program. Through this pilot program intramural investigators at NCI and NCATS would be able to translate their ideas from the bench to the bedside using the customer discovery process. In April 2020, the leadership at NCI and NCATS approved the pilot cohort of the AIM program. AIM's goal is to increase the likelihood that discoveries arising from NIH intramural research program are translated into products that can benefit patients and positively impact world health. Through a structured mentorship, the AIM program could help advance NIH-conceived inventions to the marketplace by leading the course participants to perform customer discovery, learn the methodologies behind a lean start-up, and incorporate agile development into their research. In May 2020, NCI and NCATS sponsored a total of seven teams for the initial pilot.

From August - September 2020, the first pilot cohort of teams completed the course. Through AIM, NCATS and NCI intramural scientists who applied and participated in the course worked in teams with their Technology Transfer Managers or OSA representatives and an entrepreneurial expert to advance their focus beyond the laboratory and to focus on the economic and societal benefits of public-funded basic-research projects.

The results of the pilot program have more than exceeded initial expectations. The course's exit questionnaire captured some striking data - see highlights of these statistics below. Many of the teams conducted close to 40 interviews, and these resulted in uncovering multiple new development paths. One team initiated two new collaborations, and another hired an outside instrument development group to make improvements to their prototype, to address customer

preferences, as told to them during the interviews:

- 95% of respondents said they would rate the course as good or very good.
- 85% of respondents said the course met or exceeded their expectations.
- 95% of respondents said all aspects of the course were valuable. (Pre-course assignments got the lowest response.)
- 75% of respondents said the course would change their approach to doing research.
- ~95% or respondents said the course would, even a little, impact their development pathway

Cooperative Research Collaboration Agreement (C-RCA)

NIH commonly utilizes Inter-Institutional Agreements (IIAs) to consolidate Intellectual Property (IP) rights for NIH inventions jointly developed with academic collaborators. IIAs enable NIH or the collaborator to take the lead for patent prosecution and licensing efforts for joint IP. Since the NIH Intramural Research Program (IRP) frequently collaborates with academic institutions with well-established IP Portfolios, the practice of executing IIAs that grant the collaborator an exclusive license for the management of the NIH's rights to the joint IP require the publication of a Notice of Intent to Grant Exclusive License in the Federal Register (FR). Since 60% of NCATS's current patent portfolio is co-owned with another institution (majority with academic partners), many of NCATS' collaborators already have background patents and are seeking to further develop their technologies towards commercialization through these collaborations with NCATS. It is therefore reasonable and desirable to have these collaborators take the lead in patenting and licensing the jointly developed IP to not delay IP management and stifle the transfer of the technology.

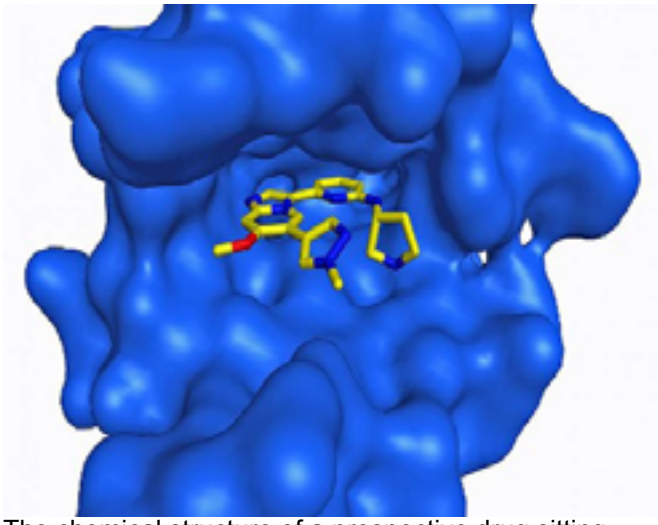
NCATS, working with various NIH Institutes/Centers (ICs) and Office of the Director (OD) Offices such as the NIH Office of General Counsel (OGC), the Office of Science Policy (OSP), as well as the NIH Cooperative Research and Development Agreements (CRADA) Subcommittee Chair, worked cooperatively and consensus emerged for the need to develop a new and simplified collaboration agreement that references CRADA statutory authority to transfer the joint IP management via an IIA. Drafted in consultation with OGC and OSP, the new agreement was called the "Cooperative Research Collaboration Agreement" (C-RCA). The C-RCA is entirely based on the Research Collaboration Agreement (RCA) template and references certain CRADA statutes to bring it within the purview of the CRADA authority. The new C-RCA requires a Research Plan which includes information on the Scope of the Project. Any invention developed under the C-RCA would be considered a CRADA Subject Invention and as such would be exempted from the FR Notice publication per the CRADA statutes.

The C-RCA has been extremely well received among NCATS' collaborators and has been used seven times in a short period of time. Other NIH Institutes/Centers (ICs) are also starting to adapt this model as they see enormous benefit from this innovative, streamlined CRADA mechanism.

Cincinnati Children's Hospital Medical Center (CCHMC)

NCATS and the Cincinnati Children's Hospital Medical Center (CCHMC) collaborated to develop small molecules for treating Myelodysplastic Syndrome (MDS) and Acute Myeloid Leukemia (AML). Interleukin-1 receptor-associated kinase (IRAK) and FLT3 kinase enzymes play key roles in driving the progression of AML and MDS. Small-molecule inhibitors of FLT3 have shown initial promise in treating AML. However, FLT3 inhibitors have not led to long-lasting remission, since FLT3 inhibition results in increased compensatory signaling through IRAK1/4. The new treatment co-developed by NCATS and CCHMC will have potential to provide long-term benefits for MDS and AML by inhibiting both IRAK and FLT3. Cincinnati Children's Innovation Ventures (CCIV) is a unit of CCHMC that facilitates the translation of discoveries into improved care for children. OSA worked closely with CCIV to explore pathways to support technology development through the late preclinical development phase, *i.e*. "valley of death".

NCATS entered into an Inter-Institutional Agreement (IIA) that allowed CCIV to take the lead in filing patent applications, marketing and exclusively licensing their joint Intellectual Property (IP) for the new IRAK/FLT3 inhibitors. CCIV filed and secured patents for the composition of matter and the methods of use for the inhibitors. CCIV facilitated to create a start-up, Kurome Therapeutics (Kurome), whose mission is dedicated specifically to the preclinical and clinical development of the novel IRAK/FLT3 inhibitors. CCIV facilitated series seed funding for Kurome from CCHMC and investment funds including CincyTech. CCIV also recruited an experienced entrepreneur-in-residence to manage the project operation and to coordinate product development by NCATS and CCHMC investigators. NCATS and CCIV worked together to enable CCHMC to enter into an exclusive license with Kurome for the IP covering novel IRAK/FLT3 inhibitors and for the treatment and diagnostic applications for AML, MDS and solid tumors. CCHMC, Kurome, and NCATS also entered into a Cooperative Research and Development Agreement (CRADA), providing Kurome with options to license future IP relevant to the inhibitors. The exclusive license agreement and the CRADA provide Kurome with a significant patent property portfolio.



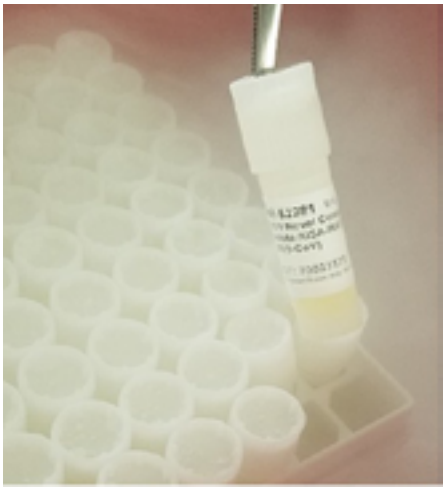
The chemical structure of a prospective drug sitting inside the protein kinase IRAK4. Credit: Cincinnati Children's Hospital Medical Center

NIAID, CDC, and HHS Cooperated to Rapidly Share SARS-CoV-2 Virus Specimens and Materials

SARS-CoV-2, the virus responsible for coronavirus disease (COVID-19), has wreaked havoc around the globe and caused substantial illness and death. As of January 28, 2021, more than 101 million COVID-19 cases were reported across 192 countries and territories, resulting in more than 2.1 million deaths, including more than 430,000 deaths in the United States.

As a novel virus in early 2020, little was known about the biology of, and medical countermeasures for SARS-CoV-2. Rapid sharing of SARS-CoV-2 materials, especially SARS-CoV-2 virus strains, was and remains an essential requirement for improving understanding of the virus and the development of effective diagnostics, vaccines, and therapeutics. Academic centers, U.S. government agencies, private companies, and the public health community requested specimens from NIAID to support SARS-CoV-2 research and development of medical countermeasures. Private companies were particularly eager to access SARS-CoV-2 materials with ease in coordinating shipments and without protracted legal negotiations or other constraints.

Technology transfer offices at NIAID, the Centers for Disease Control and Prevention (CDC), and the staff in the Department of Health and Human Services (HHS) Office of the Assistant Secretary for Preparedness and Response first tested a new approach to sharing materials during the Zika virus epidemic in 2016. Since that time, federal cross-agency partners including NIAID, CDC, and HHS Office of Global Affairs developed a more efficient and collaborative approach for sharing critical virus materials. The CDC reached out to its extensive global network of partner laboratories and sentinel surveillance sites to access SARS-CoV-2 specimens in early February 2020. Similarly, NIAID was able to access specimens from around the world by communicating through the Institute's grantee and contractor network.



A vial from Washington State SARS-CoV-2 isolate was shared through the Biodefense and Emerging Infections (BEI) Resources, a repository supported by NIAID. The first SARS-CoV-2 case in the U.S. was announced by the state of Washington on January 21, 2020. The isolate was received from CDC and appeared in the BEI catalog on February 6, 2020.

As of late 2020, the repository supported by NIAID received deposits of SARS-CoV-2 materials from 22 organizations, including CDC, NIAID, and three other U.S. federal agencies, and has fulfilled 8,441 requests for SARS-CoV-2 materials, all under emergency use simple letter agreements (EUSLA). Unlike traditional material transfer agreements, the EUSLA does not have a restriction on commercial use and does not prohibit subsequent transfer of the materials by a recipient. The team executed 4,108 agreements that allowed shipments of SARS-CoV-2 materials to 319 universities, hospitals, and research institutes; 509 biotech and pharmaceutical companies; 39 federal agencies and state public health departments; as well as 5 foreign governments. Materials have been distributed geographically to 49 U.S. states, Puerto Rico, and 43 countries.

The World Health Organization (WHO) in its Research and Development (R&D) Blueprint highlights the critical importance of transferring biological samples from one place to another during an outbreak. Progress in scientific methods, medical research, and the development and distribution of effective medical and behavioral measures are often tied to the availability of these biological samples and the willingness of governments and other partners to share samples. Movement of samples must be as simple, efficient, and transparent as possible. Efforts by WHO and its international partners to fully implement timely global specimen sharing of Zika virus, SARS-CoV-2, and other new and emerging infectious diseases continue to face significant challenges.

Annual Event Highlights NCI and FNL Technologies to Expanded Audience

The 2020 Technology Showcase on September 9th welcomed more than 400 viewers to a half day event to encourage collaboration and licensing of inventions from the NCI and the Frederick National Laboratory (FNL). The pivot to a virtual format presented an opportunity to expand to a new audience. Attendees logged in from all over the world, including the United Kingdom, Switzerland, Brazil, Malaysia, and China.

> "[The virtual format] allowed us to be accessible to everyone in the world," said Leonard Freedman, Ph.D., FNL chief science officer, in his opening remarks

In addition to presentations by six NCI and three FNL inventors, the 2020 Technology Showcase included keynote presentations by Maryland Commerce Secretary, Kelly Schultz and Kite Pharma Senior Director Supply Chain, Howard Bland. There were also four educational panels given by moderators and panelists from investment firms, industry, nonprofits, and various government laboratories and agencies. In addition, representatives from the NCI Technology Transfer Ambassadors Program presented 11 poster pitches highlighting the commercialization potential of additional NIH technologies.

In its fourth year, the Technology Showcase remains the only NCI event focused on attracting and informing industry licensees and partners. TTC's IDMU spearheads the planning of the annual event along with co-sponsors from the FNL, the Frederick County Office of Economic Development, the City of Frederick Department of Economic Development and TEDCO. The Annual Technology Showcase was the recipient of the 2020 NCI Director's Award. Dr. Michael Salgaller and Michele Newton of the TTC IDMU, along with TTC's Dr. Laura Prestia, again served on the Planning Committee. A hybrid in-person / virtual event is planned for 2021.

TTC Guides Fast-moving Collaboration with Immunotherapy Startup

In December 2019, Dr. James Yang, NCI CCR Surgery Branch, met with the vice president of research for Elicio Therapeutics, a start-up company formed to develop a technology licensed from MIT. Elicio is planning to use a novel approach to immunotherapy by harnessing its "Amphiphile Platform" to target a wide range of immunogens to the lymphatic system, the "brain center" of the immune response. Their Amphiphile platform is engineered to target immune-modulatory therapeutics and vaccines directly to the lymph nodes. By delivering these immunogens directly to immune cells in the lymph nodes, Amphiphiles can control immune signaling to stimulate and orchestrate the development of the immune response against cancer. The company's goal:

develop vaccines to “super-charge” CAR-Ts at the lymph nodes and improve immune responses to cancer. One of the company’s lead compounds, ELI-002, is an “AMP KRAS-vaccine” containing seven Amphiphile mKRAS peptides and a proprietary Amphiphile adjuvant.

A week after the initial meeting at a scientific conference, NCI initiated a CDA that was executed by January 2020. Preliminary discussions between Dr. Yang and Elicio led to NCI and Elicio entering into a Collaboration Agreement (CA) for non-human materials in April 2020 (Elicio press release). The research goal was to discover and evaluate mutant murine KRAS specific T cell Receptors (TCRs) for their potential to be used in engineered TCR-T cells for therapy of patients with KRAS-mutated tumors. This study would help monitor patient responses in the planned clinical study of ELI-002 and would set the stage for future clinical trials combining ELI-002 with KRAS-targeting T cells.

> “*This is a great example and case study of the evolution of technology transfer and how our office can help PI’s accomplish their scientific goals, all evolving from a first meeting and simple exchange of ideas, to a full blown clinical trial in less than one year!”* – Dr. Aida Cremesti, NCI TTC technology transfer manager for NCI Surgery Branch

The results of the initial CA were positive. In July, NCI and Elicio executed a second CA for human materials. In this CA, NCI and Elicio set out to collaborate on the development of a new biomarker assay. In addition, Elicio and NCI are developing an amphiphile vaccine to boost mEGFR specific T cell responses. In the meantime, Elicio completed preclinical validation, IND-enabling GLP toxicology studies, and a pre-IND meeting with the U.S. FDA for its lead candidate, ELI-002. As part of a plan to conduct multi-site Phase 1/2 trials, Elicio hired a Contract Research Organization (Icon). Icon reached out to NCI with a request to execute a CDA to allow them to share the clinical trial protocol with Dr. Yang in order to discuss next steps and a clinical trial agreement with NCI. Instead of a new CDA, TTC amended the existing CDA (with Elicio) to specifically add the clinical protocol. This enabled Icon to share the protocol with Dr. Yang who indicated interest in participating in Elicio’s multi-site clinical trial as one of the trial sites. TTC’s Dr. Aida Cremesti, TTM, supported these efforts.

AWARDS, PRESENTATIONS, AND PUBLICATIONS

FY2020 NHGRI Technology Transfer Office Accomplishments

Claire Driscoll, Director, and **Anna Solowiej**, Senior Licensing and Patenting Manager, received the 2020 NIH Director's Award in the category of Scientific/Medical Achievement for participation as part of the GM1 Therapy Group on September 23, 2020.

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 2020 and 2021 annual meetings and coordinating work of about 25 Committee members, with the 2021 meeting being planned as the first-ever fully virtual event.

Anna Solowiej volunteered on an NIH-wide Patent Legal Services (PLS) group to choose Biotechnology candidates for the new patent contract.

Anna Solowiej volunteered on an NIH-wide Patent Legal Services (PLS) group to coordinate implementation of the new patent services contract.

Eggerton Campbell, Senior Licensing and Patenting Manager, presented a virtual course titled "Transactional Agreements" at the Foundation for Advanced Education in the Sciences (FAES), April 9, 2020 in Bethesda, MD.

Claire Driscoll, Director, presented a talk at the invitation of Sethuraman (Panch) Panchanathan, Ph.D., Executive Vice President, ASU Knowledge Enterprise & Chief Research and Innovation Officer, Arizona State University on January 28, 2020 entitled "Technology Transfer at NIH: How a US Government Agency's Conventional Basic Research-Focused Endeavors Have Resulted in Innovative Public Health Breakthroughs" and visited with staff at SkySong (ASU's technology transfer office). *Dr. Panchanathan is now the Director of the U.S. National Science Foundation.

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 2020 annual conference in San Diego, CA (the event was cancelled due to the coronavirus pandemic) as well as the upcoming 2021 virtual annual conference (to be held in Feb 2021).

Claire Driscoll and **Eggerton Campbell** served as members of the NIH Platform Vector Gene Therapies (PaVe-GT) Project team; both were also listed as co-authors on a NIH PaVe-GT team paper published in Human Gene Therapy journal entitled "The Platform Vector Gene Therapies (PaVe-GT) Project: Increasing the efficiency of adeno-associated virus (AAV) gene therapy clinical trial startup".

Anna Solowiej and **Eggerton Campbell**, Senior Licensing and Patenting Managers, volunteered on an NIH-wide working group helping to review submissions for the PLS 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. During the Fiscal year 2020, Eggerton Campbell, served as the IC representative on the NIH Exclusive License Consultation Group (ELCG).

Sangeetha Raghavan moderated a panel for the virtual Licensing Executives Society Annual Meeting, 2020 on "Navigating the Data and Machine Learning Landscape in the Life and Physical Sciences". The panel shed light on the complexities associated with technologies involving data and machine learning, and the approaches involved with managing and commercializing such technologies. The panel occurred on October 18, 2020.

Eggerton Campbell moderated a virtual technology panel on the NIH Tuesday Licensing Forum, Negotiating Priority Review Voucher Licensing Terms: Monetizing Agreements That Won't Generate "Traditional" Royalties in April 2020.

2020 FLC National Award: CDC's Assay for Global Surveillance of Drug-resistant HIV-1 Was Commercialized

Researchers at the Centers for Disease Control and Prevention (CDC) developed a low-cost technology to rapidly detect HIV-1 drug resistance (HIVDR) in plasma and dried blood spot (DBS) samples with 95.8% genotyping sensitivity. CDC's partners at Life Technologies Corporation ("Life Tech") have licensed, further developed, and incorporated the technology into a commercialized product.

Life Tech's HIV-1 Genotyping Kit provides a cost-effective assay, scalable workflow, easy-to-read sequencing results, and robust test performance. The technology delivers high efficiency in genotyping diverse HIV-1 group M strains circulating globally from plasma samples and DBS with substantial reagent cost savings. The DBS testing capability removes a huge barrier for many resource-limited areas where the World Health Organization (WHO) recommends HIVDR surveillance and monitoring, but where storage and timely transportation of plasma samples from remote locations remain challenging.

Credit: CDC

The American Type Culture Collection (ATCC) first licensed CDC's technology in 2013 and partnered with Life Tech. CDC's Technology Transfer Office handled the first patent applications, agreements, and licensing. The CDC Team at the National Institute of Allergy and Infectious Diseases (NIAID) Technology Transfer and Intellectual Property Office (TTIPO) oversaw licensing and patenting on CDC's behalf beginning in October 2015. TTIPO

negotiated with Life Tech later and signed a non-exclusive patent license agreement in January 2017 for commercializing the technology. CDC researchers collaborated with partners and authored or co-authored 39 publications.

The elimination of HIV is one of CDC's "Winnable Battles," which are public health priorities in which CDC and its partners can make significant progress in a relatively short time. This technology transfer supports the Winnable Battle in monitoring HIVDR for optimal HIV treatment and viral load suppression.

As antiretroviral therapy (ART) scale-up continues, HIVDR surveillance is vital to ensuring sustained effectiveness of ART regimens and preventing transmission of drug-resistant HIV to newly infected persons. Importantly, in 2017, WHO issued guidelines recommending using alternative first-line regimens in countries for which pretreatment HIVDR to non-nucleoside reverse-transcriptase inhibitors exceed 10% of HIV-infected population initiating ART. Since 2017, the Thermo Fisher kit has been sold to 47 customers, including distributors in 27 countries. The kits are now in use at genotyping laboratories in Africa, the Americas, and Asia.

Maryland Innovation and Technology Series: Neurotechnology Conference

NIMH and NINDS participated in the 2019 Maryland Innovation and Technology Series: Neurotechnology conference sponsored by the Maryland Department of Commerce and the Federal Laboratory Consortium, held December 2019 on the NIH campus. This conference highlighted challenges in neurotechnology development as seen by regional neuroscience companies and federal opportunities available to help meet these challenges. Exemplary neuroscience technologies available for licensing and/or co-development were pitched by Federal scientists. Collectively, this conference aimed to facilitate connections and resources between local neuroscience companies, academic researchers and Federal labs to network with each other.

Credit: Maryland Department of Commerce

Both NIMH and NINDS heavily participated in the event. Dr. Amir Tamiz, Director of NINDS Division of Translational Research, was the keynote speaker and spoke about various partnership programs at NIH for the advancement of neurotechnologies. Dr. Sue Ano, NINDS Technology Development Coordinator, was a panelist on the Federal opportunities roundtable. Along with panelists from FDA, US Army, NIST, SBA, Dr. Ano fielded questions from audience members and the panel moderator about working with the Federal government for neurotechnology advancement. Major themes addressed in the panel session included education

of potential partners about neurotherapeutic-focused Government programs, tools utilized in the formation of partnerships, and distinctions about the experiences at different Government organizations.

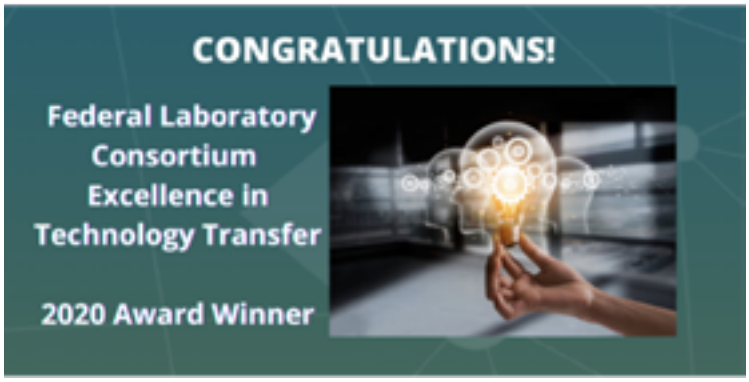
NIMH technology transfer recognized that participation of principal investigators in the partnering pitch session would increase exposure of a technology available for co-development and licensing as an example of what opportunities may exist at NIH. NIMH technology transfer identified Dr. Dietmar Plenz, NIMH's Chief of the Section of Critical Brain Dynamics, as a perfect candidate to fulfill this goal. Dr. Plenz was happy to participate and presented his research on a Neural Avalanche Signature (NAS) assay. NAS is a signature of healthy and optimal cognitive function. NAS abnormalities have been identified in key cortex region linked to major disease states and the assay has the potential to be an efficient high-throughput screen for antiepileptics, antipsychotics, cognitive enhancers and in general drug development for brain function and dysfunction.

The participation of NIMH and NINDS technology transfer in this conference advanced the NIH mission to see the outcome of scientific research and knowledge applied to enhance health, lengthen life, and reduce illness and disability. NIMH and NINDS had several conversation opportunities, both at the meeting and afterwards, to explore meeting topics further with interested parties. More information about the event can be found at here.

NCI Wins 2020 National FLC Excellence in Technology Transfer Award

The FLC honored NCI with two awards at its virtual 2020 national meeting, August 31 – Sept. 1. The FLC is a Congressionally mandated organization that educates, promotes, and facilitates federal technology transfer. The Excellence in TT Award recognizes employees of FLC member laboratories and non-laboratory staff who have accomplished outstanding work in the process of transferring federally developed technology.

Excellence in Technology Transfer Award Winner: "New, First-in-class Immunotherapy for Treatment of Recurrent, Metastatic Cervical Cancer"



In 2011, NCI and Iovance Biotherapeutics entered into a CRADA for the development of Adoptive Cell Therapy (ACT) using Tumor Infiltrating Lymphocytes (TIL). Technology licenses between NCI and Iovance were established to grant Iovance rights to the NIH's TIL patent estate. By 2019, Iovance began conducting two pivotal multi-center trials of TIL technology in advanced cervical cancer and metastatic melanoma and has achieved Breakthrough Therapy and Fast Track designations from the FDA in these indications, respectively. These are cancers for which patients have exhausted all other means of

treatment and have no options left. In June 2019, Iovance began construction of a state-of-the-art commercial-scale production facility in Philadelphia. The new TIL manufacturing facility is expected to create hundreds of jobs and meet demand.

This technology transfer outcome is rooted from discoveries by Dr. Steven Rosenberg, NCI Surgery Branch, a pioneer in cancer immunotherapy and individually designed "personalized" medicine. Importantly, the initial promise of Dr. Rosenberg's work to establish TIL technology for the treatment of metastatic melanoma is now being explored in additional TIL trials in other solid tumors that have been initiated by NCI, Iovance and its collaborators. Because of pioneering research and groundbreaking discoveries by NCI's Dr. Steven A. Rosenberg and his team, NCI's commitment to translational research, the formation of an effective partnership, the expertise and commitment by Iovance to develop an NCI-licensed technology, and courageous patients who participate in clinical trials, an unprecedented immunotherapy treatment was transferred and has advanced to late-stage clinical development. This innovative treatment has the potential to help thousands of patients a year with deadly and previously untreatable forms of cancer.

Award Recipients:

- **NCI Scientific Team:** Steven A. Rosenberg, M.D., Ph.D., Chief, NCI Surgery Branch; Christian Hinrichs, M.D., Investigator, formerly NCI Experimental Transplantation and Immunotherapy Branch
- **NCI TTC:** Aida Cremesti, Ph.D., Senior TTM; Andrew Burke, Ph.D., Senior TTM
- **Iovance Biotherapeutics:** Maria Fardis, Ph.D. MBA, CEO

NCI Technology Transfer Ambassadors Program (TTAP) Team Receives High Honors in 2020

In 2020, the NCI TTAP received an NIH Director's Award and the FLC National Meeting's first Innovation Award, a new award category launched in 2020. The FLC Innovation Award recognizes federal laboratories that successfully implemented innovative or unconventional technology transfer approaches that resulted in a significant increase in TT activities. TTAP received the NIH's Director's award in recognition of "Lab to Market Training for Post-doctoral Scientists Across the NIH."

In September 2016, to better engage and educate the scientific community, the NCI TTC launched the first federal TTAP. The program has significantly impacted TT efforts at the NCI and is now being offered across the NIH. TTAP is the first formal TT training and mentoring program open to NIH post-doctoral (post-docs) scientists and staff scientists/staff clinicians seeking professional development in invention analysis, commercialization, and entrepreneurship. The one-year program augments the scientist's current

research activities and boosts the impact of technology transfer at NIH.

TTAP results in a more entrepreneurial culture, stronger connections between technology transfer and the scientific community, and enhanced efficiency of NIH technology transfer efforts for commercialization. TTAP is a particularly unique opportunity for its range of subject matter; experience gained through training is valuable toward a wide variety of career paths. Previous Ambassadors have pursued careers such as: federal technology transfer managers, patent agents and technical specialists at law firms, health science analysts in the federal government, drug reviewers at the FDA, and staff scientists or senior scientists in the federal government or private sector. TTAP Ambassadors also add value to the annual NCI Technology Showcase by putting into practice their newly acquired TT skills and presenting pitches and posters about the commercialization potential of NIH technologies. Learn more: https://techtransfer.cancer.gov/abouttc/ambassadors

Award Recipients: **TTAP Team Leads, NCI TTC:**

- Laura Prestia, Ph.D., Communications & Strategic Initiatives Manager
- Rose Freel, Ph.D., Senior TTM
- Taryn Dick, Ph.D., M.B.A., TTM
- Abritee Dhal, Ph.D., TTM

Team Responsible for Annual Technology Showcase Receives 2020 NCI Director's Award

In 2016, TTC recognized the need for a new, unique event to encourage collaboration and licensing of inventions from the NCI and Frederick National Laboratory (FNL) to regional technology developers and stakeholders. By 2017, TTC, the NCI Frederick Office of Scientific Operations (OSO) and the FNL Partnership Development Office (PDO) proposed such an event that would also provide researchers a professional development opportunity to better understand how to move their research from bench to bedside to market. By hosting it at the FNL, they recognized an opportunity: they reached out to the economic development offices of the City and County of Frederick and TEDCO to leverage their regional knowledge, resources, relationships, and expertise. The organizations agreed on goals; under TTC leadership, they entered into a co-sponsorship agreement.

The event – going on its 5th year in 2021 – centers around NCI and FNL researchers who pitch their technologies to an audience of biotechnology development stakeholders (in contrast to traditional scientific presentations). In addition, representatives from the NCI TTAP – composed of post-doctoral scientists seeking unique professional/career education opportunities – develop and present posters highlighting the commercialization potential of additional NIH technologies. Importantly, the awareness and outreach provided by the annual Technology Showcase means

that regional stakeholders now understand they can turn to NCI and FNL when looking for a subject matter expert for collaboration to overcome a technology hurdle. They can engage NCI and FNL when looking for an innovation to license to bolster their pipeline.

Award Recipients:

- **NCI TTC:** Joseph Conrad, Ph.D., J.D., John Hewes, Ph.D., Michele Newton, Laura Prestia, Ph.D., Michael Salgaller, Ph.D.
- **FNL:** Victoria Brun, Maryellen Hackett, Vladimir Popov, Ph.D., Maggie Scully, Ph.D.
- **NCI Frederick Office of Scientific Operations:** Walter Hubert, Ph.D.

NCI Transition to Industry (T2I) Fellowship Initiative Receives 2020 NCI Director's Award

The NCI Transition to Industry (T2I) Fellowship is a first-of-its-kind training program launched in January 2020 that can support two fellows per year for a two-year term. The T2I Fellowship takes advantage of the strong NCI research and development expertise in its many laboratories and programs, and the training opportunities of the intramural program (Cancer Research Training Award [CRTA] and Research Fellowship) to provide an environment to incentivize champions of an intramural invention/patented technology with resources to support the technology's development toward a regulatory milestone (IND or IDE), clinical trials, and subsequent commercialization.

T2I was developed and implemented through the joint efforts of staff from the NCI CCR, TTC, Small Business Innovation and Research Development Center (SBIR), and Center for Cancer Training (CCT), to support post-doctoral career development while closing the "technology gap" toward commercializing an NCI invention. The team designed, developed, and successfully implemented this innovative new fellowship to accomplish two core goals. These goals were to increase the commercialization potential of NCI inventions and to support post-doctoral entrepreneurship and industry-focused research training. To learn more about T2I, visit: https://techtransfer.cancer.gov/transition-industry-fellowship-t2i

Award Recipients:

- **NCI TTC:** Sabarni Chatterjee, Ph.D., MBA, Eric Cheng, Ph.D., Abritee Dhal, Ph.D., Lauren Nguyen-Antczak, Ph.D., J.D., Laura Prestia, Ph.D., Thomas Stackhouse, Ph.D.
- **NCI CCR:** Tom Misteli, Ph.D., Joel Schneider, Ph.D.
- **CCT:** Erika Ginsburg, M.A., Jonathan Wiest, Ph.D.
- **SBIR:** Gregory Evans, Ph.D., Michael Weingarten, Ph.D.

TTC Staff Honored with National Eye Institute (NEI) Director's Award

TTC's Tedd Fenn, J.D. (TTM) and Andrea Samari (Technology Development Administrative Specialist) along with NEI's Technology Development Coordinator (TDC), Mala Dutta, Ph.D. were awarded the 2020 NEI Director's Award. This Administrative/Technical Excellence award was bestowed for "licensing NEI cell therapy intellectual properties to the right stakeholders for maximal return for the NEI." NEI's Dr. Kapil Bharti put forward the nomination.

TTC TTM Honored with NIH Clinical Center CEO Award

TTC's Tedd Fenn, J.D. and Ken Rose, J.D., Ph.D. were honored on December 18 with the 2020 NIH Clinical Center CEO Award as a part of the CT Artificial Intelligence in COVID-19 Team. This Making an Impact award was bestowed "for pivoting research towards multinational data and developing a CT scan artificial intelligence tool for detection of COVID-19, and differentiation from flu and other pneumonias."

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/os/technology/techtransfer/aboutus.htm

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

Service Center for:

- ORS - Office of Research Services

NIMH - National Institute of Mental Health

NIMH Office of Technology Transfer

https://www.nimh.nih.gov/research/research-conducted-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/