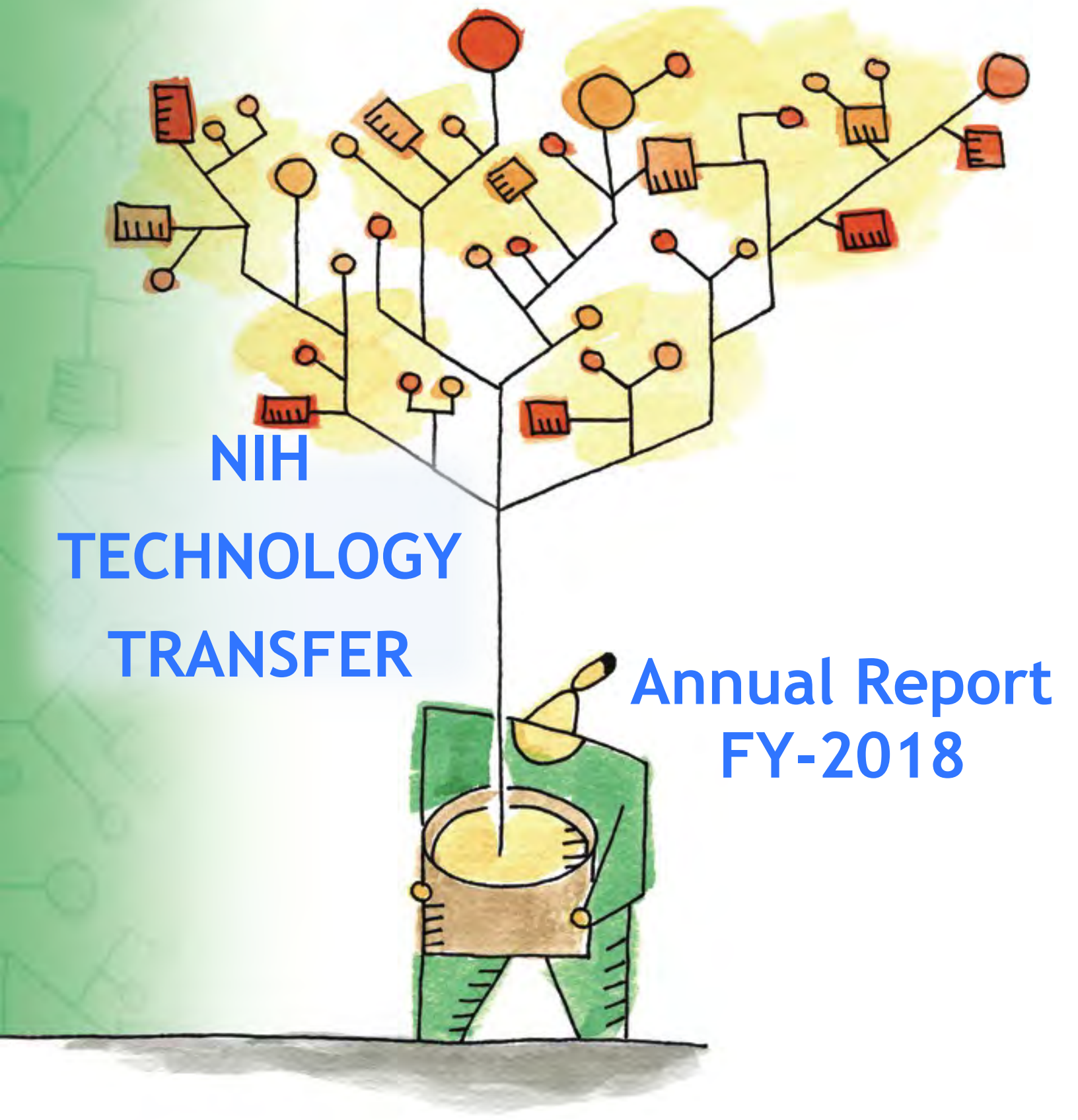


NIH TECHNOLOGY TRANSFER

Annual Report FY-2018

CONTENTS

MISSION STATEMENT

The mission of Technology Transfer at National Institutes of Health (NIH) is to facilitate partnerships with a wide array of stakeholders, and effectively manage the inventions conceived by scientists working at the NIH 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 technology transfer, the full potential of these inventions would not be realized, and the public would not receive the full benefit of these biomedical discoveries.
- Facilitates partnerships with outside parties to allow for collaboration.
- Negotiates licenses and collaborative agreements such as Cooperative Research and Development Agreements (CRADAs) to ensure the timely development of federal technologies that contribute to society by driving economic growth and productivity; These collaborations leverage the strengths of each institution to advance basic and clinical research objectives.
- Monitors the development of these technologies to ensure commercialization milestones are reached, products are brought to the market, and royalty fees are paid.
- Facilitates the transfer of thousands of research materials and data into and out of NIH.

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

INTRODUCTION

With the start of a new year, the NIH Technology Transfer (TT) Community can look back with pride at its activities and achievements during FY2018. Now three years out from a significant reorganization and patent and license decentralization, the NIH Institutes and Centers (ICs) have been able to build upon the long success and track record of the TT program at NIH that originally started in the late 1980s. Anchoring this effort again was the Office of Technology Transfer (OTT) now providing key service and support functions to the NIH Technology Transfer Offices (TTOs) and the CDC. Efforts by the entire community reflect another successful year, represented by the metrics, national awards and success stories presented in this report.

FY2018 also marked the start of preparations to review, renew and revitalize key systems that support the overall technology transfer effort across all the NIH Technology Transfer Offices – new Patent Legal Services Contracts and a new Enterprise Technology Transfer (ETT) Data System. During the year subject matter experts throughout the entire NIH TT Community contributed their time and effort to move both projects much closer to reality from earlier designs or concepts with launch of both anticipated in the coming year. In progressing these both forward, significant effort was made to analyze the complex interrelationship between the needs and goals of the various TT offices, intramural scientists and external stakeholders.

While overall the royalty income in FY2018 from the licensing portfolio continued its decline from historic heights due to expiring patents on major products, this decline was partially offset in FY2018 due to an extraordinarily active year in sublicensing related to both cyclodextrin and CAR-T based therapeutics by current licensees. Sublicensing remains a key component for ongoing product development in the biotech industry and an important part of the overall commercialization strategy for inventions arising from laboratory research at both the NIH and the CDC. At OTT, new sublicense agreements are carefully reviewed by staff in the Monitoring & Enforcement Unit with royalty invoicing and payment activities for such agreements expertly tracked by members of the Royalty Administration Unit.

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

While difficult to summarize in a single document, this report provides a glimpse into the technology transfer work at the NIH and CDC and provides a record of the community's ongoing commitment to meet the changing needs of stakeholders and facilitate the collaboration and the commercialization of NIH scientific discoveries to improve public health.

INVENTIONS AND AGREEMENTS

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

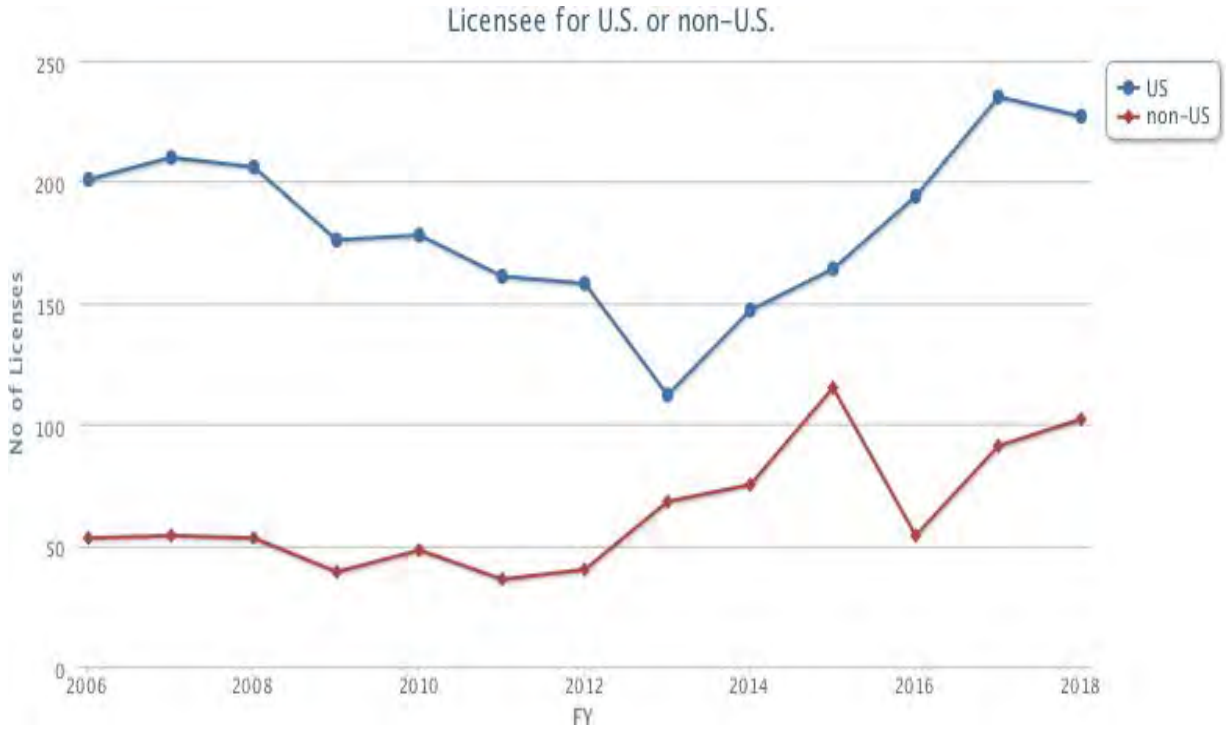
In addition, the Technology Transfer Program negotiates terms for research collaborations between NIH and commercial and academic organizations. These collaborations leverage the strengths of each institution to advance basic and clinical research objectives. Technology Transfer also facilitates the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

The Institutes in FY18 saw a jump of 6.2% in the number non-CRADA collaborations and transfer agreements; the numbers were up from 8,345 to 8,891. While the total number of active CRADAs executed in FY18 were almost the same as those active in FY17, the number of CRADA-related inventions went up by 6%.

IP-RELATED AGREEMENTS IN NUMBERS[2]

- 303 - Number of invention disclosures reported.
- 329 - License agreements executed.
- 94 - Small Business Licensees, up by 18% from FY17.

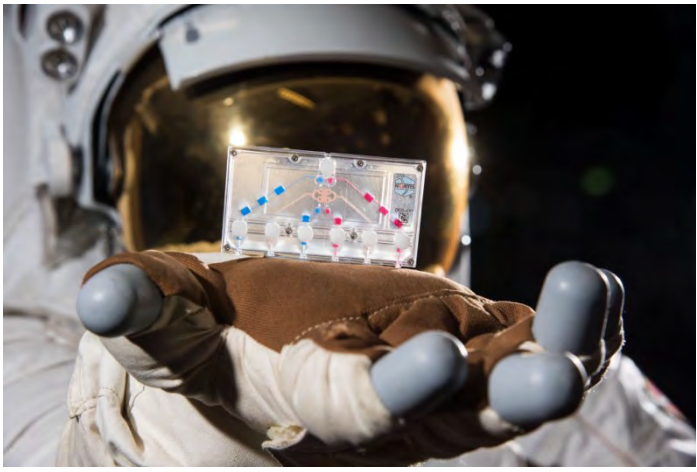
[2] includes NIH and CDC data



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

Institute and Center Updates

NCATS — National Center for Advancing Translational Sciences



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

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

The NCATS **Office of Strategic Alliances** (OSA) aims to make it easy for industry, small businesses and academia to interact and partner with NCATS scientists. 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 had a 59% increase in Research Collaboration Agreements (RCAs) and 17% increase in Confidentiality Disclosure Agreements (CDAs) executed from FY 2017 to FY 2018. In addition, there was a concerted effort to assure all agreements with term limits were either closed because the project had been completed or amended to enable the project to continue. While some of these were template agreements, many required ample time for negotiations to terms acceptable to the NIH. Given the varied nature of NCATS' collaborations with industry, academia, patient groups, et al., many agreement negotiations require significant time and effort to educate our counterparts on the particulars and requirements of collaborating with the federal government, and particularly NCATS/NIH.

NCATS Tissue Chip for Drug Screening Program – Tissue Chips in Space

A small device that contains human cells in a 3D matrix represents a giant leap in the ability of scientists to test how those cells respond to stresses, drugs and genetic changes. About the size of a thumb drive, the devices are known as tissue chips or organs on chips.

A series of investigations to test tissue chips in microgravity aboard the **International Space Station** (ISS) is planned through a collaboration between the NCATS and the ISS United States National Laboratory (ISS National Lab), formerly known as the Center for the Advancement of Science in Space (**CASIS**) in partnership with NASA. The **Tissue Chips in Space** initiative seeks to better understand the role of microgravity on human health and disease and to translate that understanding to improved human health on Earth. OSA helped negotiate the MOU and confidentiality agreement between NCATS and CASIS in order to send tissue chip experiments of NCATS grantees into space.

NCATS grantees researchers recently loaded a few dozen human tissue chips—tiny, 3D devices bioengineered to model different tissues and organs—onto a SpaceX Dragon cargo spacecraft that will ferry supplies to the International Space Station (ISS) U.S. National Laboratory, which is orbiting about 400 kilometers above Earth. SpaceX and its special biomedical cargo scheduled lift off from Cape Canaveral, FL was on Wednesday, December 5. The next set of tissue chips, scheduled to blast into space from Cape Canaveral in February 2019, will include a chip that models the blood-brain barrier. This blood vessel-tissue interface can prevent certain molecules —including some potentially beneficial therapies—from entering the brain. The third launch, from Wallops Island, VA, is set for April 2019.

NCATS New Therapeutic Uses (NTU Program)

NCATS' New Therapeutic Uses (NTU) program is an innovative effort that focuses on establishing public-private partnerships to advance the development of promising therapeutic candidates. It is designed to bring together partners from the pharmaceutical industry and academic institutions to crowdsource ideas for new uses of existing molecules. These molecules are proven to be safe in humans but were not effective against the diseases they were developed to treat. NCATS' goal is to repurpose these drugs and to speed the development of new therapies, and this year entered Round 4 of the NTU program.

NCATS knew that one major roadblock to success was time: It takes a significant time to set up a collaborative research agreement between the company that owns a molecule and the academic institution of the researchers that propose a new use. This legal agreement would describe how intellectual property such as patents will be handled in the project. Agreement negotiations can take a long time — sometimes a year or more — and a "new uses" project cannot start until they are completed. NCATS OSA recently reviewed and revised the template legal agreements between academic institutions and pharmaceutical companies that could be used as launching points for negotiations. OSA did these revisions of the templates to assure that new NTU program requirements were addressed in these agreements. The NTU template agreements continue to be some of the most downloaded content on the NCATS public website as universities and industry want to use similar agreement terms in their collaborations.

NCATS Stem Cell Translation Laboratory (SCTL)

The Stem Cell Translation Laboratory (SCTL) is a state-of-the-art research facility within NCATS' Division of Pre-Clinical Innovation that is dedicated to addressing the scientific and technological challenges in the induced pluripotent stem cell (iPSC) field.

As part of a collaborative network of scientists, the SCTL is leading multidisciplinary efforts for the scalable expansion, controlled differentiation and translational utilization of iPSCs. As one of its goals, the SCTL will develop efficient and standardized methods to produce mature cells from iPSCs meeting strict quality-control and reproducibility standards. Establishing advanced iPSC protocols will be guided by the discovery, validation and dissemination of small molecule reagents that can replace expensive recombinant proteins, xenogenic material and undefined media components in cell differentiation protocols. NCATS SCTL has collaborated with intramural and extramural scientists to help achieve common goals in iPSC biology in a faster and more coordinated fashion. NCATS OSA has helped negotiate research collaboration agreements and CRADAs with these extramural and intramural researcher's institutions.

NCATS Genetics and Rare Disease Information Center (GARD)

The GARD rare disease database was initially established in 2002, and then turned into a web-based resource in 2008. As a repository on rare disease, this valuable resource serves patients, doctors, researchers and drug developers. Through a series of Data Transfer Agreements (DTAs) developed by OSA, GARD has been able to enormously expand its data breadth and audience reach. Notable collaborators under the DTAs include the European based organizations Orphanet and FindZebra, and the Scripps Research Institute at San Diego. The Scripps collaboration would incorporate elements of Wikidata into the GARD information, and thus enrich the GARD database via crowd sourcing of information and patient experiences. On top of the enormous amount of standard data, genetic counsellors and information specialists add crucial contextual value to GARD. This has resulted in an average of 1.2 to 1.5 million visits to the GARD website, and more than 1,000 individual inquiry services per month. The DTAs established by NCATS OSA for GARD not only ensure the two-way exchange of data, but also promote synergies and community development among the rare disease community. These efforts can also point to future directions like the development of rare disease decision support tools.

3D Tissue Platforms for Drug Discovery

With the assistance and expertise of OSA, NCATS has executed agreements with Rockefeller University and Columbia University in New York City to develop 3-D printed skin tissues that can be used to investigate possible therapies for diseases such as cancer and psoriasis. Traditional drug development involves analyzing the effects of potential drugs in 2-D laboratory-grown cells or in laboratory animal models, both of which have limitations. Through these collaborations, NCATS intramural researchers and their collaborators are using the techniques of 3-D bioprinting to combine living cells with scaffolding materials, to create testing platforms of laboratory-grown human tissues that closely mimic natural tissues in human organs. Such 3-D tissue models will more closely mimic the complexity of tissues in the human body in a reproducible,

automated and scalable manner and can be used for compound testing and could accelerate drug development.

NCATS Therapeutics for Rare and Neglected Diseases (TRND) CRADA with Agilis Therapeutics

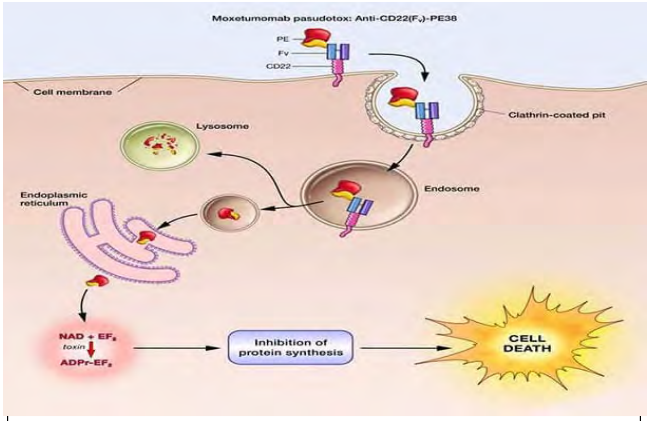
The aromatic L-amino acid decarboxylase (AADC) enzyme is necessary to produce important chemical messengers in the brain and other parts of the central nervous system. Children with AADC deficiency commonly experience severe developmental delays, weak muscle tone and involuntary movement of the limbs. There is no approved treatment for AADC deficiency, and patients with severe forms of the disorder usually die in the first decade of life. The gene therapy, called AGIL-AADC, can restore AADC enzyme production in the brain. In 2016, through a Cooperative Research and Development Agreement (CRADA) negotiated by OSA, Agilis was able to partner with the NCATS TRND Program to conduct pre-clinical safety studies and to produce AGIL-AADC in a way that met FDA requirements. In just over a year, these efforts led to a meeting with the FDA to review the pre-clinical, clinical and manufacturing data. In an unusual step, FDA reviewers determined that Agilis did not have to repeat clinical trials in the United States, clearing the path for the company to file a Biologics Licensing Application (BLA), which, if approved, would allow the company to market AGIL-AADC to this rare disease patient population.

NCI — National Cancer Institute

The National Cancer Institute is the Federal government's principal agency for cancer research and training. Various institutes and centers with NCI work to deliver on the NCI mission "leading, conducting, and supporting cancer research across the nation to advance scientific knowledge and help all people live longer, healthier lives." The *NCI Technology Transfer Center* supports technology development activities for the NCI and *nine NIH Institutes and Centers*. Highlights from 2018 exemplify potentially life-impacting outcomes of sustained technology transfer (TT) effort, as well as notable TT activities of FY18 that can make tomorrow's cancer research and patient treatments possible.

NCI Intramural Research-Conceived Technology, Moxetumomab (Lumoxiti™), Receives FDA Approval for Hairy Cell Leukemia

In September 2018, the Food and Drug Administration (FDA) approved moxetumomab pasudotox (Lumoxiti), a first-in-class, bacterial toxin-based drug, for the treatment of some patients with hairy cell leukemia (HCL). Technology Transfer played an important role in facilitating the development path of moxetumomab, which was originally discovered by Ira Pastan, M.D., and colleagues in NCI's CCR. NCI Technology Transfer negotiated the license for the technology with the commercial partner that further developed it into a



Moxetumomab pasudotox (Moxe) binds CD22 receptors on the surface of cancerous B cells, where it is internalized and processed to release its toxic payload. Credit: NCI

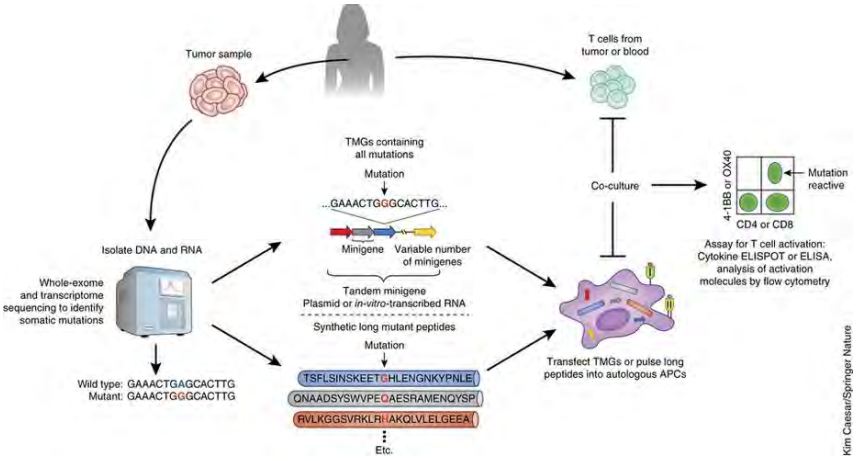
product, as well as the collaborative agreements necessary to support NCI-investigator-lead clinical trials. The development of moxetumomab is "an excellent example of the persistence in pursing research, believing in the potential of a technology, and giving a technology time to mature," commented David Lambertson, the Technology Transfer Manager (TTM) responsible for managing the multiple patents for the technology, as well as negotiating the license associated with the newly approved FDA therapy.

The first patent associated with moxetumomab was filed in 1986. Through the years, Dr. Pastan's commitment to study and develop immunotoxins involved filing multiple patents and collaborating with several industry partners to advance the technology. Adding complexity to the TT, the company to whom the technology was exclusively licensed in 2004 was sold and acquired multiple times. This required TTC to amend the license and CRADA several times. Ultimately, the long road from discovery to FDA approval resulted in a new treatment for some patients with Hairy Cell Leukemia (HCL), a rare disease. To learn more about moxetumomab, see: *Moxetumomab Approved by FDA for Hairy Cell Leukemia* and *Toxin-Based Drug Moxetumomab Pasudotox May Be New Option for Rare Leukemia*

NCI CRADA with Kite Pharma Allows Partners to Continue Adoptive Cell Therapy (ACT) Research

NCI and Kite Pharma, Inc. entered into a new CRADA that will allow the partners to continue and widen the scope of their joint research into ACT. NCI began to collaborate with Kite Pharma in 2012, and the partnership brought forth one of the first FDA-approved ACT treatments, YESCARTA®. The "personalized" therapy was granted FDA approval for the treatment of Non-Hodgkin's Lymphoma in the fall of 2017.

Looking ahead, NCI and Kite wanted to continue collaborating with the goal of increasing the application of cell therapy to other, more common types of cancer, and addressing the problem with solid tumors, which account for more than 90% of cancers. Kite proposed a new CRADA, and negotiations began while Kite was an independent company; however, its acquisition by Gilead Sciences in the fall of 2017 presented unique challenges to the negotiation: the need to include new counsel, scientists and a team from Gilead in the process. Despite this, the CRADA was executed in March 2018.



Under the new CRADA, the NCI and Kite Pharma Inc. will work on developing a personalized neo-antigen T cell receptor (neoAg TCR)-engineered autologous T-cell therapy using retroviral insertion of genes encoding neoAg-specific TCRs and using autologous engineered T cells. This represents a second, personalized cancer treatment with the potential to treat all solid tumor cancer types.

Kite announced plans to open new, worldwide facilities, including leasing a 26,000-square foot, FDA-approved GMP facility in Gaithersburg that would allow the company and NCI to develop GMP, cell-engineered cell products for clinical trials – potentially creating new jobs in Montgomery County, Maryland. The Maryland location will allow the NCI to be closely involved in the development of the novel, personalized cell therapy-based cancer treatment.

New CRADA with Apple and FDA Allows Assessment of Patient Symptomology Using Mobile Sensor Technologies

The wearable medical device market is forecasted to more than double in the next five years, according to ***ReportsNReports.com***. A new collaboration between NCI, Apple and the FDA exemplifies the research taking place to explore the potential patient benefits of mobile health technologies. The objective is a feasibility study in clinical trials utilizing Apple's proprietary mobile sensor technologies to assess behavioral and physiological symptomology of patients enrolled in NCI intramural protocols. A growing number of mobile health solutions are enabling the tracking, diagnosis, and management of various physiological processes and disease conditions. Many common devices such as smartphones (e.g., iPhone) have integrated robust sensors to collect and track data. This collaboration focuses on using a stream of sensor data that can augment clinical, imaging, and laboratory-based evaluations to provide a more accurate, detailed and quantitative picture of the patients' symptomology, functional status, response to therapy, and quality of life.

Current methods for evaluating cancer patients include clinical, laboratory, and imaging examinations in the physician's office – and primarily involve physical examinations and patient interviews. These evaluation methods are intermittent, providing a snapshot of the patients' status at the time of assessment. They are also largely subjective, relying on physician judgement and patients' ability to recall events and describe their symptoms and experience. Given these limitations, the use of remote sensor technologies could provide an objective, frequent, and near-real time stream of data in a machine-readable format. Data would be free of human bias, potentially enhancing the ability of both clinicians and patients to manage the complexities of cancer care. For example, continuous biometric data could provide actionable insights into fluctuations for patient activity level, as well as cognitive function and mood throughout treatment. It is theorized that biometric data could also empower patients to become active participants in their own care, by providing them with quantitative feedback on daily activities and status. TTC worked with FDA's Technology Transfer Office to negotiate the agreement.

CRADA Makes Possible Clinical Trial to Evaluate Therapy for Rare Brain Cancer

A CRADA allows NCI and Celgene to collaborate to conduct a Phase II clinical trial to evaluate Celgene's proprietary agent, Marizomib, in patients with recurrent, low-grade ependymomas. Ependymomas – a rare brain cancer that begins in the cells lining the spinal cord canal, ventricles, or choroid plexus – have a high rate of recurrence. The clinical outcome for patients with advanced ependymomas is generally poor, due to a lack of standard therapy options. Through this collaboration, NCI and Celgene will evaluate targeting of the constitutively

activated NF-κB signaling pathway via Marizomib in patients with recurrent ependymomas. Marizomib has the potential to quickly receive marketing approval because it was already granted orphan designation by the FDA for the treatment of malignant gliomas. Overall, this collaboration aims to provide better health care management and increased progression-free survival in patients with recurrent ependymomas.

CRADA Enables Three-Way Collaboration for Preclinical Research into Ovarian Cancer Prevention

A Materials CRADA between NCI's extramural Division of Cancer Prevention (DCP), the NCI CCR Center for Advanced Preclinical Research (CAPR), and Amgen, Inc. enables a three-way collaboration to conduct preclinical studies that will evaluate ovarian cancer prevention.

Specifically, in preclinical studies proposed and funded by DCP, the partners will utilize and evaluate Amgen's proprietary agent, mu-RANK-Fc recombinant fusion protein, in CAPR's proprietary genetically engineered mouse models to study the effects of pharmacological inhibition of the RANK/RANKL signaling pathway on the development of ovarian cancer. Potentially, the study results should provide data on the effects of RANKL inhibition on ovarian cancer development and progression. Under the terms of the Materials-Cooperative Research and Development Agreement (M-CRADA), the preclinical studies will utilize CAPR's GEM models to also study the impact of inhibition of the RANK/RANKL signaling pathways on the cellular proliferation of breast, ovary, and fallopian tubes.
Furthermore, it is hoped that these studies will complement a pre-surgical trial currently being developed by NCI DCP's Cancer Prevention Clinical Trials Consortia to investigate the effect of denosumab treatment on tubal/ovarian proliferation in BRCA1/2 mutation carriers.

TTC recommended an approach that streamlined the TT process by consolidating the agreements needed to support the study into one CRADA. To accomplish this, rather than establishing a separate agreement with CAPR, the CAPR investigator was named as a co-PI on the study because CAPR will be performing the research studies with funding provided by DCP.

TTC-Negotiated Collaborations Support Efforts for Single-Dose HPV Vaccine

Current human papillomavirus virus (HPV) vaccines on the market employ a two- or three-dose regimen. This can pose financial and logistical barriers to administration – especially in countries with limited resources, which often have high cervical cancer burden. Some research suggests that a single-dose of the HPV vaccine may confer sufficient protection. Notably, a single-dose vaccine regimen would be more cost effective – particularly in low- and middle-income countries – leading to greater adoption. NCI TTC recently executed two separate agreements to support use of a single-dose HPV vaccine.

- An agreement with PATH, a nonprofit global health organization, for NCI's participation in the Single-Dose HPV Vaccine Evaluation Consortium. This consortium, led by PATH, seeks to accelerate optimal use of HPV vaccines in low- and middle-income countries. To achieve this goal, the consortium will produce white papers providing evidence for the

use of HPV vaccines in one-dose or one-dose extended schedules to form the basis for global policy discussions and guidance. TTC's Kevin Chang, Ph.D. negotiated the agreement with PATH.

- A Memorandum of Understanding (MOU) between NCI and GlaxoSmithKline (GSK) for cooperation in engaging with the European Medicines Agency (EMA). NCI plans to conduct a formal non-inferiority trial of HPV vaccines to show that the immune response for one dose of the bivalent vaccine Cervarix is non-inferior to the immune response for three doses of the quadrivalent vaccine Gardasil, which has demonstrated efficacy. NCI, as the sponsor of this study, and GSK, as the Marketing Authorization Holder for Cervarix, concluded that cooperating for the purpose of seeking EMA feedback on the one-dose HPV vaccine study may eventually lead to an accepted one-dose administration for Cervarix. Such a change could have substantial public health effects including reducing the cost and logistical difficulties of vaccinating girls with the recommended multiple-dose administration. Cost and logistics are a significant impediment to high vaccine coverage in low resource and other settings. Under the MOU, NCI and GSK agree to cooperate as they separately seek input from the EMA.

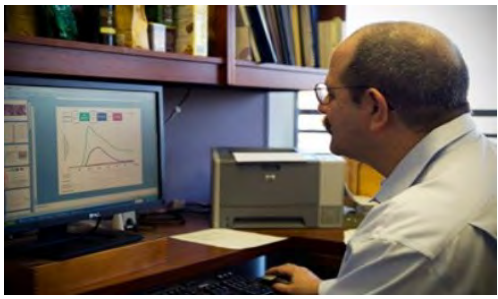
Agreements Aid in Development of Algorithms to Detect Cervical Precancers

TTC executed 14 Data Transfer Agreements (DTAs) with institutions worldwide for the development of algorithms for detection of cervical precancers based on cervical images. In its "Cervix Image Sharing Protocol (CISP)" study, the Clinical Genetics Branch of NCI's Division of Cancer Epidemiology and Genetics (DCEG) aims to develop better screening and diagnostic tools for cervical cancer, using machine learning algorithms to better guide treatment in low resource settings. Under the DTA developed by TTC, NCI provides institutions with digital cervical images and accompanying clinical data from large epidemiological studies on HPV and cervical cancer screening. These training sets are used to develop algorithms to detect cervical precancers. This effort supports DCEG's goal to foster development of cervical cancer prevention solutions for all kinds of settings – including low resource settings that rely on robust, low-cost screening and triage tools.

"Taking the Long View"

See video and article

Mark Schiffman, M.D., P.H.M., uses molecular epidemiology to predict and prevent cervical cancer.



TTC Implements New Process for NCI Human Material/Data Transfer Agreements — Improves Efficiency, Saves Time

NCI TTC handles agreements for the transfer of human materials (i.e. materials obtained from human subjects such as blood, tissue, and DNA) as well as agreements for the transfer of human data (i.e. data obtained from human subjects). The use of human materials and/or human data is critical for research projects that aim to increase knowledge about human diseases and

develop better methods for preventing, diagnosing, and treating these diseases. Ensuring the protection of data and personally identifiable information of the human subjects – those who participate in research conducted by the NCI Intramural Research Program – is also critical. Balancing these imperatives, while also facilitating a timely process that does not impede research, can be challenging.

In FY17, TTC executed 125 agreements involving the transfer of human materials and 91 human data transfer agreements for NCI investigators. When processing these agreements, TTC reviewed and confirmed that the NCI investigator obtained appropriate human subjects approval from the Institutional Review Board (IRB) or Office of Human Subjects Research Protection (*OHSRP*) prior to TTC signing the agreement. These steps increased agreement processing time. Exemplifying the consequences of lengthy processing times: at times, TTC finalized negotiations with the outside party but had to delay signature for weeks or longer waiting for IRB or OHSRP approval.

Beginning in Spring 2018, TTC implemented a new process. TTC provided NCI investigators a form to certify that the necessary human subjects approvals have been obtained or are being processed. As a result, TTC staff no longer needed to confirm IRB or OSHRP approval prior to signing these agreements. This change led to a rapid reduction in the number of these agreements pending at a given time – an indication that this streamlined approach improved efficiency and is saving time.

NHGRI — National Human Genome Research Institute

In October 2017, the NHGRI entered into a Collaboration Agreement with the University of Pittsburgh for a research project titled “Scleroderma Trios.”

In November 2017, the NHGRI entered into a Research Collaboration Agreement with NIAMS and Inova Translational Medicine Institute for a research project titled “The Genomic Ascertainment Cohort (TGAC) Project.”

On January 23, 2018, NHGRI secured a trademark for “The Forefront of Genomics.”

In February 2018, the NHGRI entered into a Research Collaboration Agreement with the National Urea Cycle Disorders Foundation for a research project titled “Algorithm on Common Metabolic Causes of Hyperammonemia (HA) and Recognizing/Identifying HA.”

In February 2018, the NHGRI entered into a Research Collaboration Agreement with Kyoto University for a research project titled “Characterization of SHARPIN Deficiency.”

In March 2018, the NHGRI entered into a Research Collaboration Agreement with the Uniformed Services University of the Health Sciences for a research project to study Staphylococcus aureus colonization and infection.

In May 2018, the NHGRI entered into a Research Collaboration Agreement with Cell Signaling Technology, Inc. for a research project titled "Development of an Antibody Against Glucocerebrosidase (GCase)."

In August 2018, the NHGRI entered into a Research Collaboration Agreement with Yale University for a research project titled "Whole Genome Sequencing of Individuals with GNE Myopathy and Their Family Members."

In FY 2018, the TTO staff reviewed **seven (7)** intramural EIRs and recommended that three (3) be marketed as unpatented research tools (cell lines and animal models); one (1) directed to patentable subject matter, and three (3) required addition data before filing.

In FY2018, the NHGRI TTO Staff negotiated and executed **thirteen (13)** licenses and amendments.

In FY2018, the NHGRI TTO Staff negotiated and executed **six (6)** CRADAs.

In FY2018, **two (2)** NHGRI patents were issued in the United States.

In FY2018, **six (6)** NHGRI patents were issued in foreign countries.

NIAID — National Institute of Allergy and Infectious Diseases

NIAID technology transfer staff received international recognition in 2018 for their contributions in bringing the following two products to market (more details are available in Awards section):

- low cost rotavirus vaccine in developing countries (derived from a NIAID invention), and
- mosquito trap for control and surveillance of mosquitoes including carriers of zika and other viruses (derived from a CDC invention).

Rapid Diagnostic Kits for Onchocerciasis and Lymphatic Filariasis (LF)

Onchocerciasis, commonly known as river blindness, is caused by the parasitic worm *Onchocerca volvulus* (Ov) and is transmitted to humans through the bite of the blackfly. It causes itching, skin disfiguration, and, with chronic exposure, permanent blindness. Worldwide, 169 million people are at risk of infection. Lymphatic filariasis (LF), commonly known as elephantiasis, is a painful and profoundly disfiguring disease, transmitted by mosquitos carrying parasitic worms. Of the three species known to cause LF, *Wuchereria bancrofti* (Wb) accounts for 90 percent of cases, including all cases on the African continent. Nearly 900 million people worldwide are at risk of infection.

The World Health Organization (WHO) has targeted LF for global elimination and onchocerciasis for elimination in select countries in Africa by 2020. Accurate surveillance data are required to inform program decisions around stopping treatment and detecting signs of reinfection.

Dr. Thomas Nutman and his colleagues at NIAID discovered Ov16, a recombinant antigen derived from Ov that can be used to detect Onchocerciasis before it is clinically apparent, and Wb123, an antigen specific to Wb with no cross reactivity against other closely related filariae.

These two innovations were licensed to PATH in 2013 and 2014 respectively. By April 2016, three rapid diagnostic kits became commercially available. They are: SD BIOLINE Onchocerciasis IgG4 rapid test, the Ov16 monoplex test for Oncoerciasis; SD BIOLINE Lymphatic Filariasis IgG4 rapid test, the Wb123 monoplex test for LF; and SD BIOLINE Onchocerciasis and Lymphatic Filariasis IgG4 rapid test, the Ov16/Wb123 biplex test for combined surveillance. As of mid-2018, more than half a million of these diagnostic tests have been used in 18 countries worldwide.

Research Reagents

In FY 2018, NIAID scientists continued to create novel and useful research materials and share them with the research community. Examples of these research reagents include an antibody against Chlamydial lipopolysaccharide and a monoclonal antibody that detects Norwalk Virus.

CRADA – Collaboration With Kineta Viral Hemorrhagic Fever, LLC To Develop Treatment For Lassa Fever

Lassa fever is an emerging infectious disease in West Africa with increasing case numbers and outbreaks over the past years. In 2018, Nigeria experienced an unusually large increase in Lassa fever cases leading the WHO to declare it an outbreak. From January 1 to October 14, 2018, there has been a total of 536 confirmed cases, with 137 deaths in confirmed cases and 16 in probable cases – giving a case fatality rate of 25.6%.

The causative agent is Lassa virus (LASV), a rodent-borne arenavirus. Humans get infected primarily through inhalation of contaminated excretions or secretions from infected rodents; human-to-human transmission may occur in hospital settings and households. Currently, there is no licensed vaccine or treatment for Lassa fever.

NIAID and Kineta Viral Hemorrhagic Fever, LLC have entered into a Cooperative Research and Development Agreement (CRADA) to evaluate the antiviral efficacy of Kineta's proprietary compound, LHF-535, in NIAID's non-human primate model of Lassa fever.

MTA – Transfer of Ebola mAB114 to THE Democratic Republic of the Congo (DRC) during 2018 Ebola outbreak

Ebola virus was first discovered in 1976 in the DRC (known then as Zaire) and has caused periodic outbreaks in the country ever since. The largest outbreak of Ebola occurred in 2014-

2016 in West Africa—a region with no recognized prior Ebola outbreaks—and caused more than 28,600 infections and more than 11,300 deaths.

In 2018, the DRC reported new outbreaks of Ebola virus disease. At the request of the DRC Minister of Health and in coordination with the WHO, NIAID has shipped treatment regimens of an experimental therapeutic, mAb114, to the National Institute of Biomedical Research (INRB) in Kinshasa, the lead research coordination group for the Ebola outbreak as designated by the Ministry of Health.

mAb114 is a human monoclonal antibody (mAb) isolated from a survivor of the 1995 Ebola epidemic in the DRC. This material transfer agreement (MTA) enabled the transfer of clinical grade mAb114, which the INRB is administering to Ebola patients under an expanded access protocol.

License - Ridgeback Biotherapeutics LP licenses Ebola mAb114 from NIAID

In December 2018 Ridgeback Biotherapeutics LP announced that it has entered into a patent license agreement with NIAID for intellectual property related to the mAb114. mAb114 has completed a Phase 1 safety study and is currently being administered to Ebola patients in the DRC under two separate protocols.

RCA – Collaboration with The Scripps Research Institute to characterize neutralizing antibody-hemagglutinin structure for Universal influenza vaccine development

A key focus of NIAID's influenza research program is developing a universal flu vaccine, a vaccine that provides robust, long-lasting protection against multiple subtypes of the influenza virus, rather than a select few. Such a vaccine would eliminate the need to update and administer the seasonal vaccine each year and could provide protection against newly emerging influenza strains, potentially including those that could cause a pandemic.

Influenza viruses are characterized by two proteins on the outer surface of the virus: hemagglutinin (H) and neuraminidase (N). There are 18 different H subtypes and 11 different N subtypes, and viruses can be further broken down into different strains within those subtypes. The H protein (also called HA) enables the flu virus to enter a human cell. It is made up of a head and a stem region. Seasonal flu vaccines fight infection by inducing antibodies that target the HA head. This region varies season to season, which is why flu vaccines must be updated each year. However, the stem typically remains well conserved, making it an ideal target for antibodies induced by a universal flu vaccine.

NIAID has isolated multiple HA stem-binding monoclonal antibodies (mAbs) capable of neutralizing a broad range of influenza subtypes. The Scripps Research Institute and the NIAID are collaborating to produce high-resolution crystal structures of these mAbs in complex with HA. This work will help define the critical contact points between broadly-neutralizing antibodies and the HA stem and inform structure-based immunogen design.

MARKETING NIH DISCOVERIES

The NCI Technology Transfer Center (TTC) manages technology transfer activities for the NCI and nine other NIH Institutes and Centers. TTC's Invention Development and Marketing Unit (IDMU), a specialized group within TTC, focuses on invention development strategies and outreach to potential licensees and collaborators.

NCI TTC Hosts Trade Mission of Scandinavian Cancer Companies

TTC hosted a trade mission of 23 people representing 11 Norwegian and Swedish cancer companies. TTC IDMU provided an overview of TTC and coordinated one-on-one meetings between NCI CCR PIs and various companies. CCR Director, Dr. Thomas Misteli (pictured below, left) provided a programmatic overview. Other presenters included Drs. Doug Figg (Co-Director, Office of Translational Services); Jeff Schlom (Chief, Laboratory of Tumor Immunology and Biology); and Ravi Madan, (Clinical Director, Genitourinary Malignancies Branch).

Exploratory CRADA and licensing discussions were initiated. Several follow-on discussions are underway between Scandinavian companies, various TTC Technology Transfer Managers and CCR PIs. While NCI is already working with several Norwegian companies, TTC hopes that the relationship between NCI and Scandinavian innovative companies will expand as a result of this effort. Such activities are part of IDMU's active international outreach – making connections with cancer stakeholders around the globe.

2018 Technology Showcase Spotlights NCI Intramural Inventions, Support of Industry Partnerships

National Cancer Institute and Frederick National Laboratory
TECHNOLOGY SHOWCASE

Commercially relevant technologies developed at the NCI and the Frederick National Laboratory for Cancer Research (FNLCR), their potential for patients and insights into how to partner with NCI were at the center of the second, annual Technology Showcase in Frederick, MD. The event, held at the FNLCR's Advanced Technology Research Facility (ATRF), drew attendance by biotechs, entrepreneurs, investors regional economic development stakeholders, and NCI staff. Through a partnership, the event was organized by TTC's IDMU, the FNLCR Partnership Office, the Technology Development Corporation of Maryland (TEDCO), and the economic development arms of the City and County of Frederick, MD.

Event highlights included:

- NCI Director, Dr. Ned Sharpless delivered the keynote address and reiterated NCI's commitment to encouraging development and licensing of NCI inventions. He shared three success stories of commercialized products arising from Industry partnerships.
- NCI and FNLCR inventors described the commercial and life-saving potential of 19 technologies.
- 12 additional NCI technologies were highlighted in posters presented by the NCI Technology Transfer Ambassador Program (TTAP).
- A success story roundtable featured scientist entrepreneurs and business leaders, who shared their perspective on NIH as a commercial development partner.

TTC Outreach at American Association for Cancer Research (AACR) Annual Meeting 2018

TTC's IDMU coordinated numerous activities at the 2018 AACR Annual Meeting to increase awareness of NCI, its investigators, staff and technologies.

In the NCI exhibit booth, the NCI designated a kiosk specifically for "Industry Partnerships" (photo). This helped facilitate interactions between TTC and prospective industry partners. Several of these interactions served to generate partnering interest and led to post-event follow up including several substantive discussions about CRADA and licensee opportunities. TTC also conducted in-the-booth "Meet the Experts" sessions entitled: "Licensing and Co-Development of NCI Intramural Research."

At the Meeting, TTC staff moderated sessions on "NCI as a Technology Development Partner" and "Intellectual Property and Technology Transfer as Career Opportunities for Scientists." Staff provided an overview of TTC, emphasizing TTC's ability to work with any size company either within or outside the US. This also generated several leads with potential CRADA and licensing partners.

TTC at 2018 American Society of Clinical Oncology (ASCO) Annual Meeting and 2018 BIO International Convention

At the BIO Convention, TTC discussions with potential licensees and CRADA partners contributed to setting a new Guinness Book of World Record for the largest business partnering event ever held – almost 50,000 meetings! Staff also devoted considerable time at the NIH exhibit booth to maximize outreach and awareness to the 18,000+ attendees. Other notable activities included:

- Delivering "Meet the Expert" sessions in the NIH booth to introduce companies, entrepreneurs, investors, and relevant stakeholders to licensing and collaborative opportunities.
- Participating in the "Business Development & Finance *Using America's Seed Fund (SBIR/STTR) and NIH Technology Transfer to Accelerate Technology Development and Secure Follow-On Investments*" panel discussion. This was the first time NIH Technology Transfer was represented at a BIO Conference Session.

- Representing TTC as invited speakers and panelists at several international forums associated with the conference. These outreach opportunities included a presentation on "NCI as a Technology Development and Commercialization Partner" at the "Spain Kicks off BIO" breakfast, and outreach opportunities at the France and European Union Exhibit Booths.

At the ASCO Annual Meeting TTC's IDMU engaged attendees representing small to mid-sized companies seeking insight and information on how to collaborate with, and license from NCI. Consistent with IDMU's experience, many were unaware that companies could in-license NCI technologies to expand their pipelines. IDMU again delivered in-the-booth "Meet the Expert" Sessions on how to work with NCI and leverage its technology assets through collaboration and licensing opportunities.

Follow up from these outreach activities include:

- Numerous conference calls to identify technologies and investigators aligning with the mutual interests of companies and investors, so businesses can explore collaborative and licensing opportunities
- Working with economic development entities and professional trade associations to organize "how to work with us" webinars to biotech regions both nationally and internationally
- Coordinating trade mission visits of companies and entrepreneurs to the NCI, so our PIs may pitch their inventions to several key stakeholders at one time.

Picture 1: IDMU Staff at Industry Partnerships Kiosk in the NIH booth at BIO 2018

Picture 2: IDMU conducts a "Meet the Expert" Session in NCI's booth at ASCO

INNOVATIVE COLLABORATIONS

Cancer Moonshot[SM] - TT Facilitates Collaboration to Enhance Cancer Immunotherapy Clinical Trials

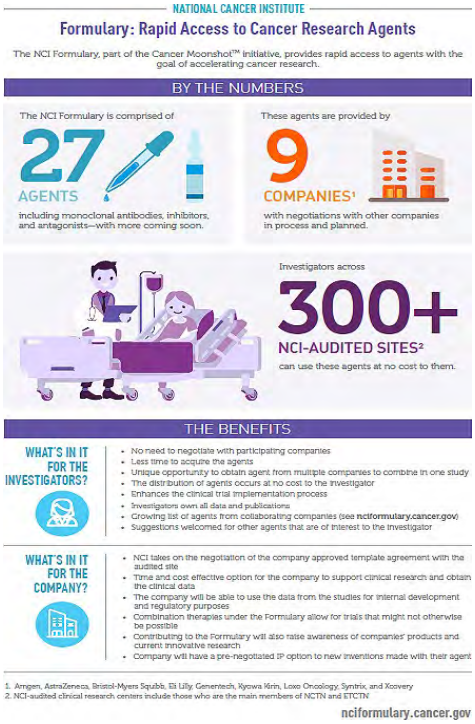
CIMAC-CIDC
Immuno-Oncology
Biomarkers Network

The Cancer Immune Monitoring and Analysis Centers (CIMACs) and Cancer Immunologic Data Commons (CIDC), jointly known as the CIMAC-CIDC Network, is an initiative of the NCI Cancer Moonshot that provides cutting-edge technology and expertise in genomic, proteomic, and functional molecular analysis to enhance clinical trials in cancer immune therapies.

Using the benefits acquired through collaborative efforts within four NCI-supported participating institutions, the CIMAC-CIDC Network has the capacity of furthering the integration and translation of a wide range of research findings to achieve the goal of dramatically improving the quality of immunotherapy for cancer patients.

To facilitate the collaboration of the CIMAC-CIDC Network institutions, DCTD negotiated a four-way research collaboration agreement. In addition, DCTD drafted a material transfer agreement template to enable transfer of materials and data to the CIMAC-CIDC from researchers interested in undertaking biomarker studies associated with NCI-supported clinical trials involving immunotherapy.

Cancer Moonshot: NCI Formulary Public-Private Partnership Initiative Advances Clinical Trial



The NCI agent formulary (NCI Formulary) is a public-private partnership between the NCI and pharmaceutical and biotechnology companies that provides NCI funded main-member Experimental Therapeutics Clinical Trial Network (ETCTN) and National Clinical Trials Network (NCTN) institutions and their investigators rapid access to agents for cancer clinical trial use or preclinical research. The NCI Formulary is particularly useful to investigators who would like to perform combination studies that focus on agents targeting molecular pathways from multiple collaborating pharmaceutical companies. The NCI Formulary CRADAs, negotiated by DCTD, provide NCI-audited academic institutions access to proprietary clinical agents, thereby eliminating the often-lengthy agent-access process that occurs between research institutions and pharmaceutical companies.

Exemplifying the desired outcome of this effort, Genentech, an NCI CRADA partner, approved the first NCI Formulary clinical trial: "A Phase I Trial of D2C7-IT in Combination with Atezolizumab in Recurrent WHO Grade IV Glioma;" the trial is expected to start in 2019.

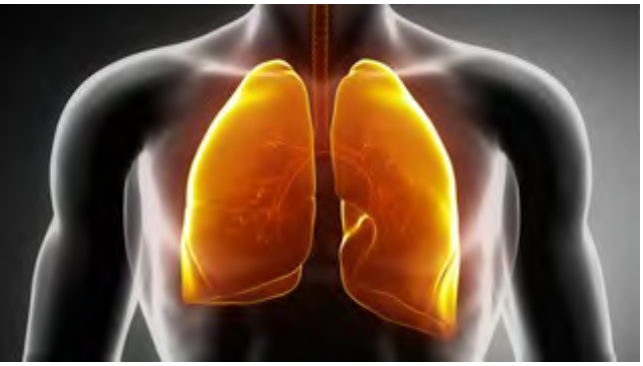
NCI-MATCH Trial – Genomic Analysis Correlative Study

Molecular Analysis for Therapy Choice or MATCH, is a precision medicine cancer treatment clinical trial. NCI MATCH is supported by NCI and is coordinated by ECOG-ACRIN Cancer Research Group. In this trial, adult patients are assigned to receive treatment, in NCI National Clinical Trials Network (NCTC) and National Community Oncology Research Program sites, based on the genetic changes found in their tumors through genomic sequencing and other tests. DCTD negotiated a research collaboration agreement (RCA) to allow ECOG-ACRIN and DCTD, through the NCI contractor Leidos Biomedical Research, to collaborate on a companion biomarker correlative study to the trial entitled, "*Comprehensive Genomic Analysis of NCI-MATCH.*" The trial will investigate additional underlying molecular factors associated with response or lack of response to a drug or class of drugs within the parent protocol.

NCTN Navigator: A Clinical Trials Specimen Resource

NCI's NCTN Navigator is a new resource for investigators who have typically conducted exploratory correlative analysis and are now seeking specimens to validate their hypotheses. Navigator currently holds a repository of 682,699 specimens from 59181 subjects over 107 clinical trials. DCTD was asked to coordinate with the five main clinical site groups that comprise the NCTN, in order to design a harmonized Material Transfer Agreement template that could be used in Navigator to allow efficient transfer of the specimens to requestors.

ALCHEMIST: Trials for Uncommon Types of Early-stage Lung Cancer



The Adjuvant Lung Cancer Enrichment Marker Identification and Sequencing Trials, or ALCHEMIST, were launched to identify early-stage lung cancer patients with tumors that harbor certain uncommon genetic changes and evaluate whether drug treatments targeted against those changes can lead to improved survival. ALCHEMIST involves substantial collaborations with biotechnology and pharmaceutical partners. DCTD was involved with negotiations more than 12 different agreements with these partners to facilitate access to drugs for the ALCHEMIST trials. One such trial is the "*ALK Treatment Trial (E4512)"* The trial is coordinated by ECOG-ACRIN to determine the value of adding therapy with specific agents targeted against genetic alterations or rearrangements to the ALK gene in the post-operative setting.

AWARDS, PRESENTATIONS AND PUBLICATIONS

NCATS Staff Highlights

The NCATS Office of Strategic Alliances (OSA) had a 59% increase in RCAs and 17% increase in CDAs executed from FY 2017 to FY 2018. In addition, there was a concerted effort to assure all agreements with term limits were either closed because the project had been completed or amended to enable the project to continue. While some of these were template agreements, many required ample time for negotiations to terms acceptable to the NIH. Given the varied nature of NCATS' collaborations with industry, academia, patient groups, et al., many agreement negotiations require significant time and effort to educate our counterparts on the particulars and requirements of collaborating with the federal government, and particularly NCATS/NIH.

NCI Staff Highlights

FEDERAL LABORATORY CONSORTIUM HONORS NCI WITH THREE NATIONAL AWARDS

The FLC presented NCI with three awards at its April 2018 national meeting in Philadelphia. The following teams received the Excellence in Technology Transfer award:

"Avelumab, New Therapy for Metastatic Merkel Cell and Urothelial Carcinomas"

NCI:

- **James Gulley, M.D., Ph.D.,** Branch Chief, Genitourinary Malignancies Branch, Center for Cancer Research (CCR)
- **Jeffrey Schlom, Ph.D.**, Chief, Laboratory of Tumor Immunology and Biology, (LTIB), CCR
- **John Greiner, Ph.D.,** Staff Scientist and Head of Cytokine Group, LTIB, CCR
- **Renee N. Donahue, Ph.D.,** Staff Scientist, Laboratory of Tumor Immunology and Biology, Center for Cancer Research, CCR
- **Ravi A. Madan, M.D.,** Associate Research Physician and Clinical Director, Genitourinary Malignancies Branch, CCR
- **Andrea B. Apolo, M.D.,** Investigator and Head of the Bladder Cancer Section, Genitourinary Malignancies Branch, CCR
- **Julius Strauss, M.D.**, Staff Clinician, LTIB, CCR
- **Isaac Brownell, M.D., Ph.D.**, Investigator, National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), formerly Investigator, Dermatology Branch, CCR

NCI TTC:

- **Michael Pollack, Ph.D.,** Supervisory Technology Transfer Manager (TTM), NCI Technology Transfer Center (TTC)
- **Kevin Brand, J.D.**, TTM, CDC, Formerly NCI TTC

Pictured left to right: James Gulley and Kevin Brand (award winners); Sabarni Chatterjee (NCI, FLC Award Committee); Thomas Stackhouse (NCI Associate Director); Michael Pollack and Julius Strauss (award winners); Anna Amar (NCI, FLC Rep.)

"FDA Approval: Personalized Cancer Treatment to Cure Deadly Blood Cancers"

NCI:

- **James Kochenderfer, M.D.** – Investigator, Experimental Transplantation and Immunology Branch, CCR
- Steven Rosenberg, M.D., Ph.D. – Chief, Surgery Branch, CCR

NCI TTC:

- **Andrew Burke, Ph.D.** – TTM
- **Aida Cremesti, Ph.D.** – Senior TTM

Pictured left to right: Anna Amar (NCI, FLC Rep.); Thomas Stackhouse (NCI Associate Director); Aida Cremesti (award winner)

PARTNERS:

- **Arie Bellegrun, M.D., FACS** – Founder & Strategic Advisor, Kite Pharma, a Gilead Company

- **David Chang, M.D., Ph.D.** – Executive VP and Chief Medical Officer, Kite Pharma

"Development of Large-Scale Production, Anti-HIV Microbicide in Soya Beans"

NCI SCIENTIFIC TEAM:

- **Barry R. O'Keefe, Ph.D.,** Deputy Chief, Molecular Targets Laboratory (MTL), CCR, and Chief, Natural Products Branch, Division of Cancer Treatment and Diagnosis (DCTD)
- **Michael R. Boyd, Ph.D., M.D.,** Chief, Laboratory of Drug Discovery, Research and Development, retired
- **James B. McMahon, Ph.D.,** Chief, MTL, CCR, retired

Pictured left to right: John Dement (Chair, FLC); Melissa Maderia and Barry O'Keefe (award winners); Anna Amar (NCI FLC Rep); Thomas Stackhouse (NCI Associate Director)

NCI TTC:

- **Bjarne Gabrielsen, Ph.D.,** TTM retired
- **Mike Currens, Ph.D.,** Special Assistant to Developmental Therapeutics Program Associate Director, Office of the Director, DCTD, formerly with TTC
- **Melissa Maderia, Ph.D.,** TTM, University of Illinois at Chicago, formerly with TTC

PARTNERS:

- **Elibio Rech, Ph.D.,** E Genetic Resources Department of EMBRAPA
- **Rachel Chikwamba, Ph.D.,** Council for Scientific and Industrial Research (CSIR Biosciences)

NHGRI Staff Highlights

NHGRI staff members organized, moderated, or served on the following panels at NIH, national and international technology transfer meetings:

- "High Volume, Low Margin Licensing of Unpatented Research Tools: Can an Academic Technology Transfer Office Make Money Selling Unpatented Biological Reagents?" at the Association of University Technology Managers 2017 Eastern Region Meeting.

- "Technology Transfer – an Alternative Legal Career?" for the University of Maryland School of Law students participating in an NIH externship course.
- "Technology Transfer Agreements for Sharing Human Materials and Data: Policies and Procedures" at the NIH Intramural Research Program Protocol Navigation Training Seminar series.
- "Government Labs are Different: NIH as a Research & Commercialization Partner" - webinar for the Center for Advancing Innovation's Freedom from Cancer Startup Challenge Teams.
- "Careers Outside Academics" at the NHGRI Research Training and Career Development Annual Meeting.
- "Career Development Forum" panel at the at the Association of University Technology Managers 2018 Annual Meeting.
- "The Current and Future State of Non-Profit Technology Transfer in the United States" at the Licensing Executives Society International (LESI) Annual Conference.
- "Diversity and Identity of the Licensing Profession: Career Development Discussion" at the Licensing Executives Society International (LESI) Annual Conference.

NHLBI Staff Highlights

In FY 2018, OTTAD successfully executed/processed 1,002 new technology transfer agreements on behalf of NHLBI & 6 Service Center client ICs serviced by OTTAD (NIAAA, NIAMS, NIBIB, NIDCD, NIEHS, & NINR). The executed/processed technology agreements include 4 CTAs, 31 RCAs, 96 CDAs, 761* MTAs (including OUTMTAs, UBMTAs, SLAs, Addgene Agreements), 5 CT-CRADAs, 1 M-CRADAs, 3 S-CRADAs, 25 CRADA amendments, 25 MTA amendments, & 51 other agreements, of which 82 were complex agreements.

Some of the highlights from the agreements executed by OTTAD include:

- An NHLBI S-CRADA with Children's Hospital of Philadelphia to evaluate lentiviral vector (LV)-ZF-Ldb1 SA to be used in autologous transplant of hematopoietic stem cells (HSPC) for the treatment of sickle cell anemia (SCD) and beta-thalassemia (BT).
- An NHLBI M-CRADA with ChromaDex to study the use of nicotinamide riboside chloride (NR) as a nutritional supplement to improve mitochondrial health.
- An NHLBI CT-CRADA with Novartis Pharma Corp. to study Eltrombopag for patients with Fanconi anemia.
- An NHLBI CT-CRADA with Merck Sharp & Dome Corporation which will conduct a Phase II study of Ibrutinib, Fludarabine, and Pembrolizumab in high-risk or relapsed/refractory chronic lymphocytic leukemia/small lymphocytic lymphoma.

- A NIAAA S-CRADA with Vital Sparks, Inc. to study a hybrid inhibitor of peripheral cannabinoid-1 receptors (CB1R) and inducible nitric oxide synthase (iNOS) for the treatment of scleroderma (systemic scleroris).
- A NIAMS S-CRADA with Bristol-Myers-Squibb to study the characterization of the role of BMS peptidylarginine deminase (PAD) inhibitors in animal models of lupus and in modulation of neutrophil extracellular traps (NET) formation and cargo in neutrophils from individuals with autoimmune diseases.
- A NIAMS CT-CRADA with Incyte under which it will lead a Phase II clinical study to examine the safety, tolerability and efficacy of topically applied ruxolitinib cream to treat cutaneus chornic graft-versus-host disease (cGVHD).
- An NIDCD/NEI collaboration with MPI Research, Inc., now a subsidiary of Charles River Laboratories, to examine the transduction efficiency of certain adeno-associated virus vectors carrying an EGFP reporter gene and the human terinoschisin gene. Positive results in this study could lead to new options for gene therapy to correct inherited opthalmological disorders.

NIAID Staff Highlights

Low Cost Rotavirus Vaccine in Developing Countries

ROTASIIL, a heat stable rotavirus vaccine, was approved by the Drug General Controller of India in 2017. The Government of India subsequently ordered 3.8 million doses of ROTASIIL for its Universal Immunization Program. ROTASIIL is based on a human-bovine reassortant rotavirus vaccine invented by the late Dr. Albert Kapikian and his colleagues at the National Institute of Allergy and Infectious Diseases (NIAID) and has been developed and manufactured by Serum Institute of India.

In August 2018, NIAID/NIH and Serum Institute of India were recognized for this low-cost, temperature tolerant rotavirus vaccine for developing countries, both by the U.S. Patent and Trademark Office with a "Patents for Humanity" award and by the Licensing Executives Society (LES) with a "Deals of Distinction™ Award".

CDC - Mosquito Trap For Control And Surveillance Of Mosquitoes Including Carriers Of Zika And Other Viruses

An autocidal gravid ovitrap (AGO trap) was developed by researchers within the Division of Vector-Borne Diseases at the Centers for Disease Control and Prevention (CDC) as a low-cost, pesticide-free method for controlling mosquito

populations. The AGO trap requires no power and is economical to manufacture. It has shown efficacy for at least two months without replacement of its inexpensive consumable components, in marked contrast to weekly application of pesticides that can be unsafe for use around children, pets, and livestock.

In August 2018, the U.S. Patent and Trademark Office recognized the CDC with a "Patents for Humanity Honorable Mention" for this low-cost, simple-to-assemble, and easy-to-maintain mosquito trap to reduce the spread of disease in resource limited settings.

NIMH & NINDS Staff Highlights

Special Initiatives

The NIMH/NINDS Technology Transfer Core consists of technology transfer staff from both institutes and was designed to take advantage of the common neuroscience underpinnings that form the foundation of each IC. Among the key accomplishments of 2018 was the implementation of Technology Assessment Group (TAG) comprised of NIMH/NINDS investigators to assist technology transfer staff in the review of technologies at various stages of the patent process. 2018 marked the commencement of monthly meetings to review NIMH/NINDS technologies. The initiative has involved significant collaboration between intramural-extramural programs and has resulted in a more robust patent portfolio for both NIMH and NINDS with technologies that have a high likelihood of being licensed. One of the primary benefits of the group is the ability to take advantage of the wide variety of expertise from TAG members, with members specializing in mental and neurological disorders, imaging, clinical trial practice, engineering, physics, law, and technology transfer.

Additional initiatives of the group

Continued efforts to develop content for a new Technology Transfer Core Group website that focuses not only on technology transfer, but all NIMH and NINDS resources that are available and of interest to the scientific community.

Continued efforts related to the planning of a one-day neuroscience partnership seminar involving companies, universities, government agencies, and research organizations engaged in neuroscience research. The meeting will be designed to showcase a diverse array of neuroscience-related research, services, programs, and technologies available for licensing from the various sectors.

NINDS Technology Transfer Office negotiated agreements with Pfizer, UCB, GSK and Eisai for the transfer of large epilepsy datasets from previous clinical studies performed independently by these entities. The central goal of the meta-analysis is to study the influence of natural variability of seizures on study outcome. This research will provide clarity on whether the variability in seizure frequency is predictable. The study will also provide insight that can guide future clinical studies on epilepsy and the treatment of the disorder.

Under a clinical CRADA negotiated by NINDS Technology Transfer Office and executed in FY17, the National Institute of Neurological Disorders and Stroke (NINDS), an institute of the National Institutes of Health (NIH), part of the U.S. Department of Health and Human Services, is collaborating with Audentes Therapeutics, Inc. as one site in a multi-site pre-Phase 1 prospective, non-interventional clinical assessment study in X-linked Myotubular Myopathy (XLMTM) subjects aged 3 years and younger (INCEPTUS).

NINDS Technology Transfer Office piloted a six-month agreement lifecycle assessment. This effort required documenting an agreement's movement through every step in the negotiation process and analyzing the data. Through these efforts, the office has established an average agreement lifecycle as the basis on which to assess the effectiveness of future initiatives to improve efficiencies. Additionally, this effort led to the identification of one process element that was changed to increase overall efficiency. The office had a nearly 90% resolution rate for agreements initiated in FY17.

APPENDIX

DHHS Technology Transfer Offices

NIH OTT - NIH Office of Technology Transfer

https://www.ott.nih.gov

CDC - Centers for Disease Control and Prevention

CDC Office of Technology and Innovation

https://www.cdc.gov/od/science/technology

NCATS - National Center for Advancing Translational Sciences

NCATS Office of Strategic Alliances

https://ncats.nih.gov/alliances/about

NCI - National Cancer Institute

NCI Technology Transfer Center

https://techtransfer.cancer.gov

Service Center for:

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

NHGRI - National Human Genome Research Institute

NHGRI Technology Transfer Office

https://www.genome.gov/techtransfer

NHLBI - National Heart, Lung, and Blood Institute

NHLBI Office of Technology Transfer and Development

https://www.nhlbi.nih.gov/research/tt

- Service Center for:
- NIAAA - National Institute on Alcohol Abuse and Alcoholism
- NIAMS - National Institute of Arthritis and Musculoskeletal and Skin Diseases
- NIBIB - National Institute of Biomedical Imaging and Bioengineering
- NIDCD - National Institute on Deafness and Other Communication Disorders
- NIEHS - National Institute of Environmental Health Sciences
- NINR - National Institute of Nursing Research

NIAID - National Institute of Allergy and Infectious Diseases

NIAID Technology Transfer and Intellectual Property Office

https://www.niaid.nih.gov/research/technology-transfer-and-intellectual-property-office

Service Center for:

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

NIDCR - National Institute of Dental and Craniofacial Research

NIDCR Office of Technology Transfer and Innovation Access

https://www.nidcr.nih.gov/research/NIDCRLaboratories/Intramural_Technology_Transfer_Office

NIDDK - National Institute of Diabetes and Digestive and Kidney Diseases

NIDDK Technology Advancement Office

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

Service Center for:

- ORS - Office of Research Services

NIMH - National Institute of Mental Health

NIMH Office of Technology Transfer

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

NINDS - National Institute of Neurological Disorders and Stroke

NINDS Technology Transfer Office

https://tto.ninds.nih.gov