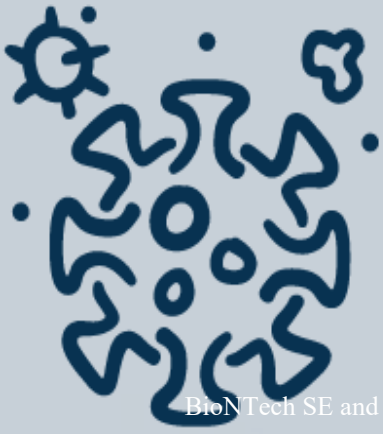
NIH Technology Transfer

ANNUAL REPORT

FY 2021



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INTRODUCTION

FY2021 marked a full year of continued remote work by NIH Technology Transfer Office (TTO) staff during the COVID-19 pandemic, but even in the face of this challenge our community was able to accomplish an amazing amount of work, described throughout this report, including many COVID-19 related technology transfer successes. This report provides insights into the achievements and scientific advancements made at the NIH and the CDC in FY2021, and each IC TTO has detailed its activities from the past year including success stories, innovative collaborations, and awards.

The Office of Technology Transfer (OTT) was busy as well. In FY2021, OTT entered the second phase of implementation of our new Enterprise Technology Transfer (ETT) data system, with the third and final phase rapidly approaching. ETT is a centralized system that will replace nine IC and OTT legacy database systems, resulting in integrated and streamlined processes and systems, and providing a more comprehensive picture of technology transfer activities across NIH. Our Royalties Administration Unit administered $127.6 million in royalty income brought in from technology licenses; a large portion of this income was due to COVID-related technologies, including a non-exclusive license for the BioNTech/Pfizer “Comirnaty” vaccine. OTT also led the implementation of twenty-four new NIH-wide Patent Legal Services contracts. Additionally, OTT launched a new Technology Transfer Community Website to benefit all of the ICs as well as NIH’s external stakeholders. This new site features easier to navigate menus, a prominent search bar with enhanced search functionality, and fresh content to keep prospective licensees interested.

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 licenses, coordination of all patent annuity payments, communications with existing and potential licensees, and patent docketing services. Additionally, OTT supports the TTOs through management of TechTracS, the current system of record for all patent and license information, and the OTT SharePoint site, which facilitates the transfer, collaboration, and management of vital documents and other information for the TTOs.

The TT community continues to impress me with their resilience and their ability to facilitate the collaboration and commercialization of NIH/CDC scientific discoveries to improve public health throughout the pandemic. 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

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MISSION STATEMENT

The mission of Technology Transfer at National Institutes of Health (NIH) is to facilitate partnerships with a wide array of stakeholders, and effectively manage the inventions conceived by scientists working at the NIH and the Centers for Disease Control and Prevention (CDC). In doing so, NIH Technology Transfer supports the larger NIH mission to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability.

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

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

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

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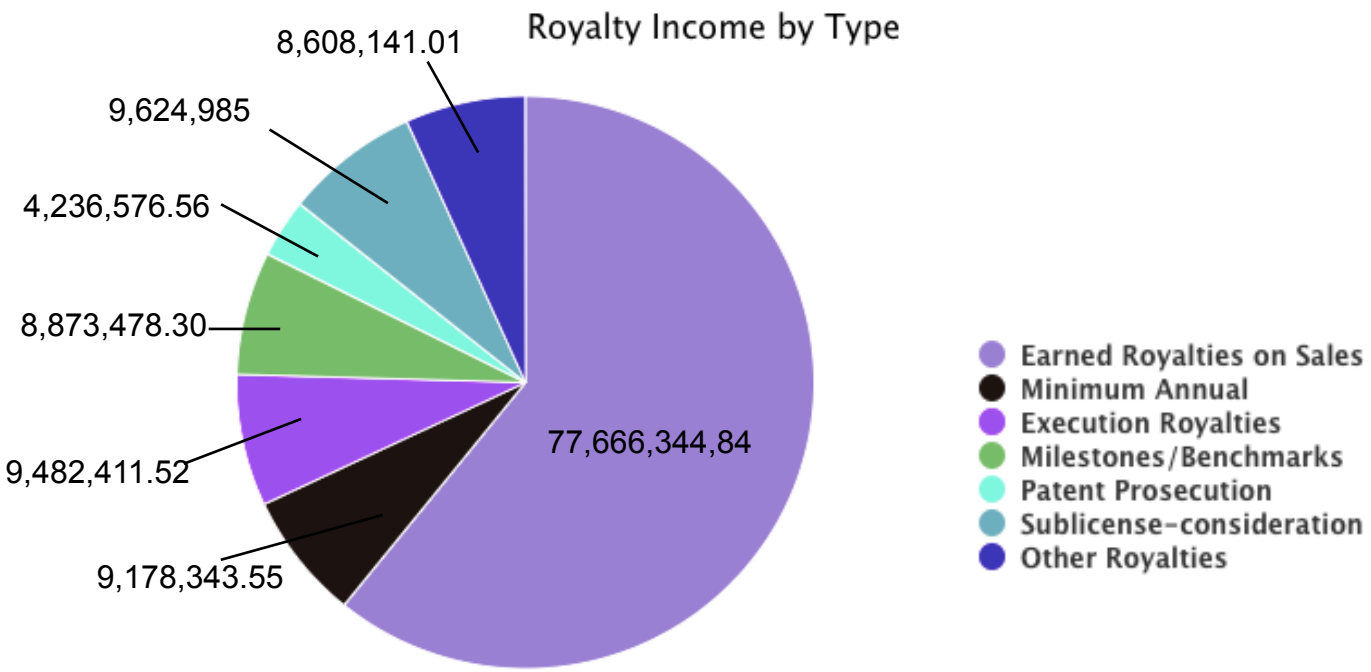
INVENTIONS AND AGREEMENTS

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 FY2021 there was $127.6 million in royalty revenue brought in. There were 253 invention disclosures, 185 patent applications filed, 106 U.S. patents issued, and 334 executed licenses. A graphical breakdown of these numbers is provided on the following pages.



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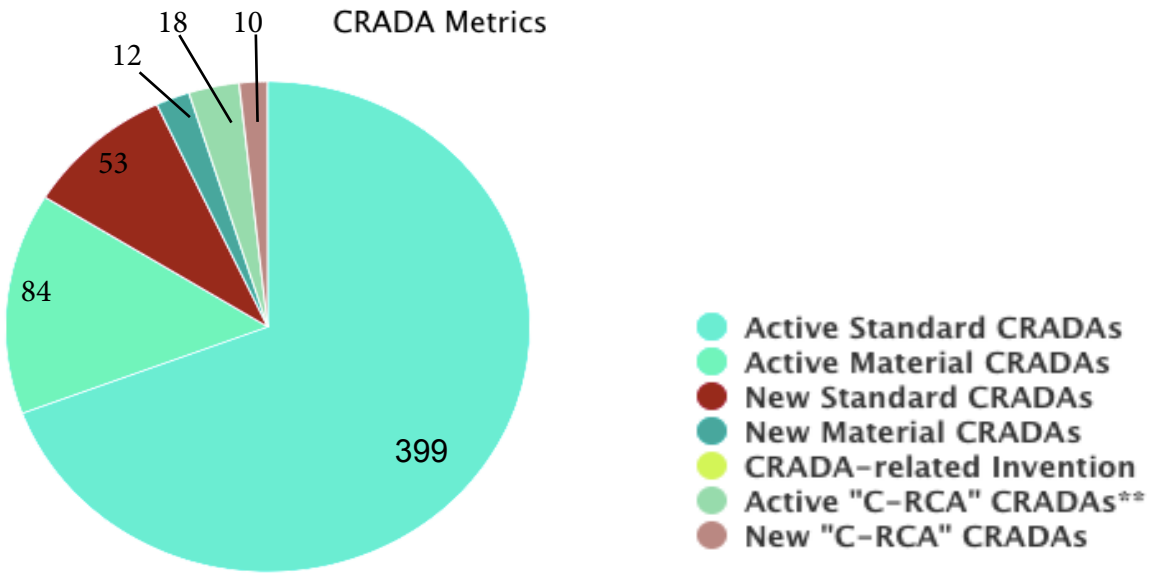

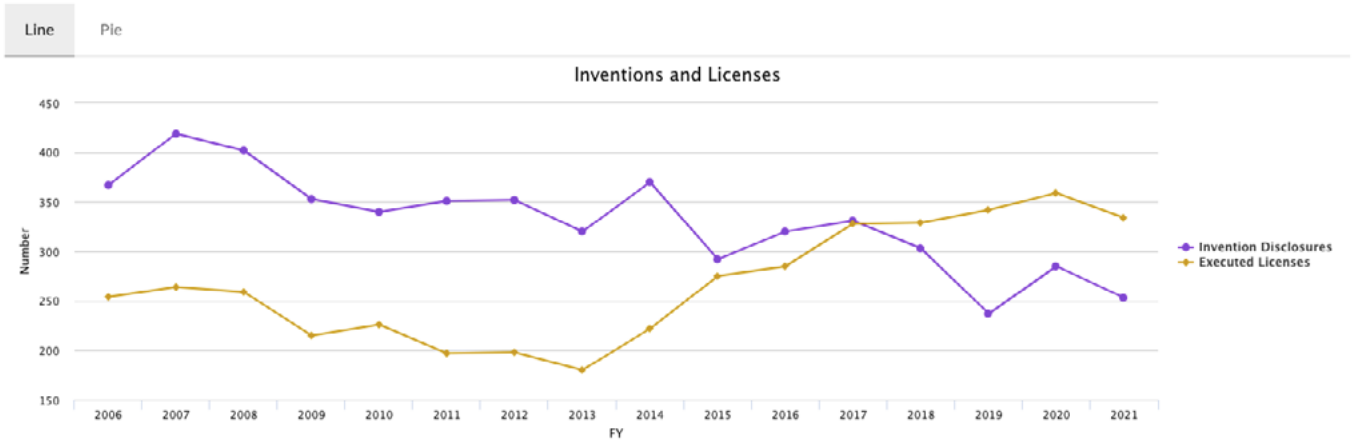

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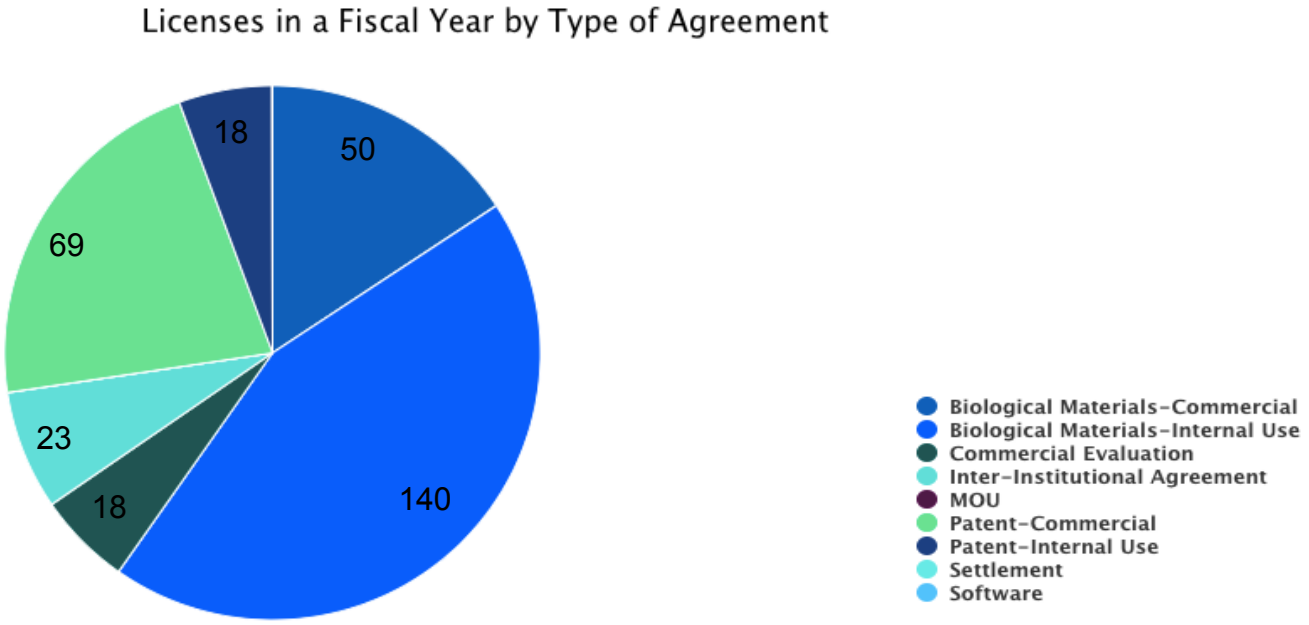

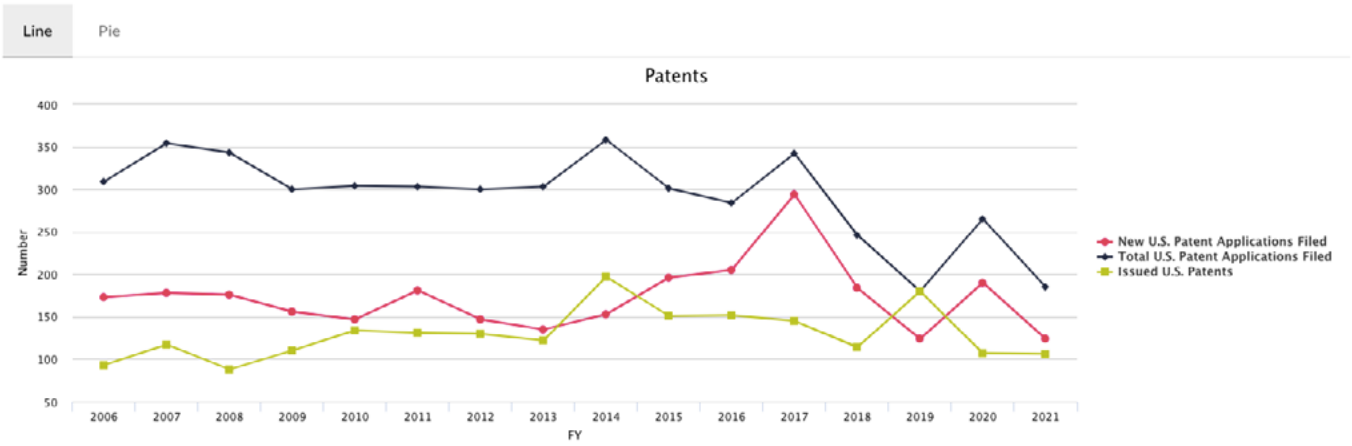

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INSTITUTE AND CENTER UPDATES

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.

MORE TREATMENTS, MORE QUICKLY. That's the goal of translational science.

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, most required customization as well as substantial input of time for negotiation of 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 continues to build a large and complex intellectual property (IP) portfolio. In numerical terms, the 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.

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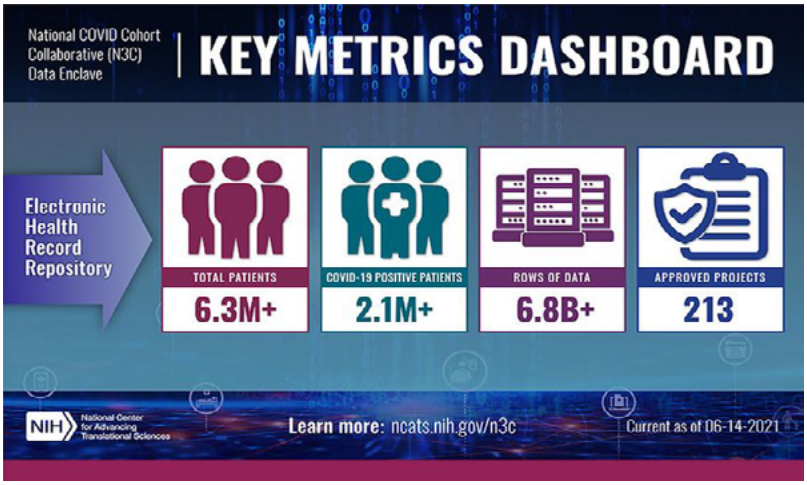
Further, as a means for accelerating innovation and commercial development, NCATS has licensed many of its technologies (nearly 40 commercial licenses and over 60 Inter-Institutional license agreements). The NCATS IP portfolio reflects the great strides being made in forming effective collaborations,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

Privacy Preserving Record Linkage (PPRL)

Privacy Preserving Record Linkage (PPRL) is a means of connecting records using secure, pseudonymization processes in a data set that refers to the same individual across different data sources while maintaining the individual's privacy. NCATS is piloting PPRL technology to determine if linking multiple data sets enhances COVID-19 real-word data research in the NCATS National COVID Cohort Collaborative (N3C) Data Enclave. The N3C Data Enclave is a centralized, secure, national clinical data resource with powerful analytics capabilities that the research community can use to study COVID-19, including potential risk factors, protective factors, and long-term health consequences.

All organizations contributing data to the N3C Data Enclave must have an approved Data Transfer Agreement (DTA). In addition to the DTA, these organizations have the option of signing the Linkage Honest Broker Agreement (LHBA) to participate in the PPRL pilot. NCATS' OSA lead the effort in developing both the DTA and LHBA. The output of extensive communication with internal and external stakeholders was a DTA that has been executed over 90 times without edits. On the other hand, the LHBA posed OSA with a unique challenge. PPRL is at the cutting edge of innovation and the LHBA facilitates N3C to run PPRL across the DTA signee's data with the hopes of enriching the research value of the whole N3C dataset. Although most sites have heard of PPRL, they often don't link data outside their site. With that said, PPRL is a very new technology to the NIH, so extensive feedback from the Office of Science Policy (OSP) and the Office of General Counsel (OGC) were needed to formulate an agreeable document. To date, OSA has executed over 25 LHBAs without edits.



To clarify what the LHBA is, the LHBA is an agreement between the organization, NCATS, and The Regenstrief Institute, which serves as the linkage honest broker. A linkage honest broker in the PPRL's infrastructure is a party that holds de-identified tokens and operates a service that matches tokens generated across disparate data sets to formulate a single Match ID for a specific use case. PPRL enables three functions within N3C: Deduplication of patient records, linkage of a patient's records from different sources, and cohort discovery. NCATS was eager to lead the effort to bring this technology to the N3C and familiarize the research community with its potential and OSA is always ready to facilitate NCATS vision with unique and custom agreement that push research into the future.

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NCI - National Cancer Institute

FDA Approval of idecabtagene vicleucel (Abecma) for People with Multiple Myeloma

On March 26, 2021, the Food and Drug Administration (FDA) approved idecabtagene vicleucel (Abecma), a BCMA-targeted chimeric antigen receptor (CAR), for people with multiple myeloma that has not responded to or has returned after at least four different prior cancer treatments. "I'm very excited about this [approval]. This work builds on earlier work conducted by my group at NCI that showed CAR T cells could be an effective treatment for multiple myeloma," commented James Kochenderfer, M.D., senior investigator in NCI CCR's Surgery Branch in an April 2021 *Cancer Currents* blog.

Manufactured CAR T cells ready for infusion into a patient.
Credit: Penn Medicine

Dr. Kochenderfer and NCI colleagues designed and created the first BCMA-targeted CAR T cells for multiple myeloma in 2013. Two years later, the technology was exclusively licensed by Bluebird Bio and developed under a CRADA between NCI, Bluebird Bio, and Bristol Myers Squibb. The NCI TTC supported this technology transfer through many phases. In 2013, TTC's James Knabb, Ph.D. negotiated the CRADA with bluebird bio and, in 2015, NIH OTT negotiated the exclusive license for the technology. The CRADA was amended twice since its execution to progress development of the technology.

Belzutifan Approved to Treat Tumors Linked to Inherited Disorder von Hippel-Lindau Disease (VHL)

A new drug approved in August 2021 by the Food and Drug Administration (FDA) may help people with a rare inherited disorder called von Hippel-Lindau disease VHL), avoid or delay surgery by shrinking their tumors.

The FDA approved belzutifan (Welireg) to treat adults who have several tumors associated with VHL. Specifically, the drug is approved to treat VHL-associated renal cell carcinoma (a type of kidney cancer), central nervous system hemangioblastomas (a type of noncancerous tumor that forms in the brain or spinal cord), and pancreatic neuroendocrine tumors (a rare type of cancer in the pancreas) that don't require immediate surgery.

The approval is based on results from a small clinical trial that tested belzutifan in people with VHL-associated renal cell carcinoma, all of whom also had other VHL-associated primary tumors. The clinical trial was facilitated through a National Cancer Institute (NCI) TTC-negotiated Clinical CRADA between NCI and Peleton (later acquired by Merck).

After 18 months, nearly half of the participants had kidney tumor shrinkage of at least 30% (a partial response), and a majority of those patient's tumors were still responding to treatment after

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one year. Belzutifan also shrank VHL-associated brain, pancreatic, and eye tumors.
"When we first started seeing responses in patients, my knees got weak. I couldn't believe it," said W. Marston Linehan, M.D., chief of the Urologic Oncology Branch in NCI's Center for Cancer Research, who was part of the team that conducted the phase 2 study. "This drug has real potential to revolutionize the management of these patients."

"This is the first time we have an FDA-approved agent for the treatment of patients with VHL-associated tumors," said the study's principal investigator, Ramaprasad Srinivasan, M.D., Ph.D., also of the Urologic Oncology Branch. "Now we can say to some patients, 'We can give you a drug that may help you avoid surgery.'""

In addition to a CRADA, TTC also negotiated a Data Transfer Agreement that supported sharing information necessary for FDA approval. TTC's James Knabb, Ph.D. negotiated these agreements.

The above is excerpted from NCI's *Cancer Currents* blog. Visit this link which also details belzutifan's pathway of discovery to treatment.

Data Transfer Agreements (DTAs) for the Helicobacter Pylori Genome Project

TTC Unit Supervisor, Lisa Finkelstein, Ph.D. negotiated 17 separate DTAs for the Helicobacter pylori Genome Project (HpGP). H. pylori infects half the world's population and is the primary cause of gastric cancer. The HpGP will describe the worldwide genomic and epigenomic variation of H. pylori to identify molecular determinants of carcinogenicity. NCI DCEG investigators are sequencing 1000 H. pylori strains from individuals with and without gastric cancer residing in 40 different countries. Since 2016, Dr. Finkelstein's unit has negotiated over 70 MTAs to receive materials for this effort. In spring 2021, the DCEG investigators needed to send out H. pylori data sets to collaborators for various analyses. Dr. Finkelstein drafted the agreements and executed them in a short period of time to meet the program's deadlines. These DTAs will allow NCI to further enhance the HpGP data set making it a more robust resource for the research community.

DTAs Support Registry Linkage and Cohort Study of Cancer Risks in U.S. Radiologic Technologists

TTC Technology Transfer Manager, Ramona Bhattacharya, Ph.D. executed multiple Data Transfer Agreements for the Registry Linkage and Cohort Study of Cancer Risks in U.S. Radiologic Technologists (USRT), a project aimed at identifying all incident cancers diagnosed in members of the USRT for as many years as possible during 1985-2015 for dose-response occupational and personal medical radiation-related risk assessment and survival analyses. The USRT project required negotiation with state departments of health with each department having its own specific template agreement and requirements for project documentation. Due to the number of states

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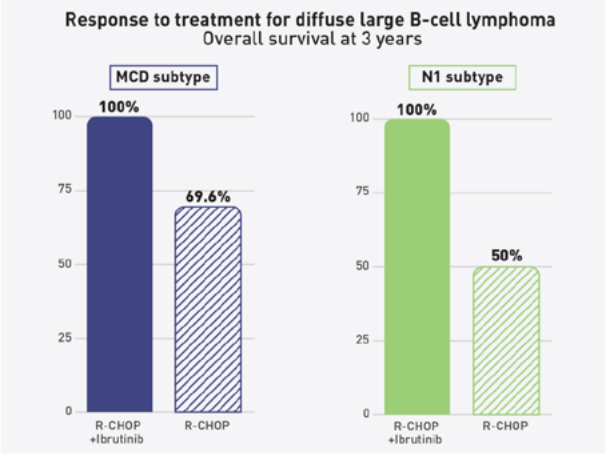
involved in this project and the amount of paperwork involved, a spreadsheet tracking system was developed that allowed Dr. Bhattacharya and other TTC staff to coordinate with the investigators and program specialists to track progress of agreements toward execution. The spreadsheet tracking system has since been utilized by other TTC staff who oversee NCI DCEG projects that require agreements with multiple outside organizations.

Clinical Trial Agreement and Data Transfer Agreement Support NCI's New Diffuse Large B-Cell Lymphoma Findings

New evidence from NCI suggests that adding the targeted therapy, ibrutinib (Imbruvica) to a standard chemotherapy regimen can improve how long some younger patients with a specific form of diffuse large B-cell lymphoma (DLBCL) live. DLBCL is the most common type of lymphoma, accounting for 40% of lymphoma cases worldwide. People with DLBCL are typically treated with a chemotherapy regimen known as R-CHOP that includes cyclophosphamide, doxorubicin, vincristine, prednisone, and the monoclonal antibody- rituximab. Unfortunately, R-CHOP is not effective for all patients with DLBCL. Ibrutinib was the first targeted therapy evaluated for the treatment of DLBCL and works by blocking the activity of a protein involved in the growth and survival of B cells.



NCI participated in the phase III clinical trial, called the PHOENIX trial, to evaluate the impact of adding ibrutinib to R-CHOP in patients with newly diagnosed non-germinal center B-cell-like (GCB) DLBCL. Initial results from the trial showed that combining ibrutinib with the standard chemotherapy regimen did not help patients with non-GCB DLBCL to live longer overall. However, by analyzing tumor biopsy samples from patients across the trial sites, NCI researchers and their collaborators have shown that younger patients with specific genetic subtypes of non-GCB DLBCL, called MCD and N1, had an exceptional response to the treatment combination, with all such patients alive without disease three years after diagnosis. *(See graph)*

"For years we have only had chemotherapy and rituximab to offer these patients," said Louis M. Staudt, M.D., Ph.D., chief of the Lymphoid Malignancies Branch in the Cancer for Cancer Research at NCI. "Now, we hope that adding ibrutinib to current therapy may give younger patients a better chance of surviving this aggressive cancer."

NCI's participation in the PHOENIX trial was supported by a clinical trial agreement and the further analysis and interpretation of DNA/RNA sequencing data from the clinical trial was supported by a data transfer agreement. Both agreements were negotiated by TTC Technology Transfer Manager, Ramona Bhattacharya. Ph.D.

The above is excerpted from a Nov. 4, 2021, NCI press release, *Ibrutinib improves survival for younger people with diffuse large B-cell lymphoma.*

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Series of International Material and Data Transfer Agreements Support NCI's Sherlock-Lung Project

NCI's Sherlock-Lung Project is a comprehensive study that aims to investigate the etiology and progression of lung cancer in never smokers (LCINS). Through genomic analysis of tumors and surrounding lung tissue, NCI Division of Cancer Epidemiology & Genetics (DCEG) investigators are characterizing the genomic landscape of LCINS and identifying the exogenous and endogenous processes involved in lung tumorigenesis. Overall, Sherlock-Lung aims to refine classification of LCINS and provide insights into prognosis and treatment strategies. In FY21,

TTC Unit Supervisor, Lisa Finkelstein, Ph.D. and Technology Transfer Manager, Michaela McCrary, Ph.D. negotiated and executed seven separate DTAs and MTAs with institutions from five countries for NCI's Sherlock-Lung Project. Since 2018, Dr. Finkelstein and her team have negotiated over 30 MTAs and DTAs from institutions from over 11 different countries to facilitate this large-scale research effort. These MTAs and DTAs allow for NCI to study lung cancer in thousands of never smokers worldwide, including some populations with special exposures, such as indoor/outdoor air pollution, radon, and asbestos exposure. Learn more: NCI press release, Nature Genetics, Sept. 2021

TTC Negotiates Agreement with Clinigen to Obtain IL-2 for Combination Study for Melanoma and Renal Cancer Patients

Clinigen is the only company that has rights to clinical-grade Interleukin-2 (IL-2), or Proleukin®. In 2019, Clinigen provided the NCI Surgery Branch (SB), free of cost, the IL-2 necessary for the SB to grow patient-derived T cells for treatment of patients under various SB protocols at NCI's CCR IL-2 enables T cells to grow faster and produce a more robust cytokine response when used in cancer immunotherapy. This aids in making NCI's personalized cell therapy more efficient and anti-tumor response more robust. In these studies, after cells are extracted from patients, they are grown in the presence of IL-2 and expanded. The T cell Receptor constructs are inserted, and then the engineered cells are grown in large quantities and re-infused back into the patients. Another clinical study led by Stephanie Goff, MD, NCI CCR SB, in 2021, proposed treatment of melanoma and renal cancer patients with a combination of IL-2 and Pembrolizumab (humanized anti-PD1 antibody) to determine if the combination improves patient immune response.The planned study requires a large amount of IL-2 that will be directly injected to patients instead of treating and growing T cells ex vivo as in the first study. IL-2 is costly. From a technology transfer perspective, NCI TTC needed to find the appropriate type of agreement that would allow Clinigen to provide IL-2 to NCI free of charge.

After reviewing the clinical trial protocol, Clinigen understood that the combination therapy could ultimately provide cancer patients a valuable, new therapeutic option. After understanding the perspective of both parties, TTC proposed and executed a unique Agreement which incorporated terms from an MTA and clinical terms from a Clinical Trial Agreement. Aida Cremesti, Ph.D., the Technology Transfer Manager, supporting NCI's SB, negotiated the Agreement.

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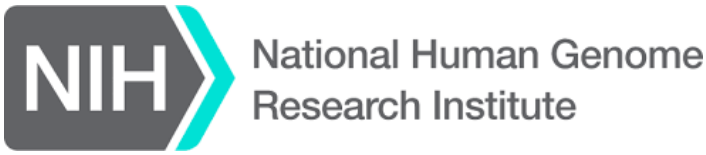
NHGRI - National Human Genome Research Institute



During FY21, all NHGRI staff have been teleworking 100%. The transition from office work (with partial telework) to a fully remote environment has been seamless, and the TTO has continued to be efficient, productive, and effective under these new complex circumstances. The volume and complexity of projects continues to trend ever upward even in this new virtual environment (with most labs being only partially open/functional). This work has included:

NHGRI EIRs and Patents

In FY 2021 three new employee invention reports (EIRs) were evaluated by the NHGRI TTO, filed with the NIH OTT, assigned an official record number, and classified as biological materials (non-patentable).

In the entire active patent portfolio seven new patent application were filed, based on NHGRI EIRs in FY2021.

At the end of FY 2021, three patents were issued in the NHGRI portfolio.

The titles of the issued patents were: “Cancer Detection Methods,” “Synthetic Methylmalonyl-CoA Mutase Transgene for the Treatment of MUT Class Methylmalonic acidemia (MMA),” and “N-Acetyl Mannosamine as a Therapeutic Agent.” All three issued patent were U.S. patents.

At the end of FY 2021, NHGRI had thirty-two active patent families, sixty issued U.S. patents (including abandoned, expired and filed by third parties), one hundred and sixty-eight issued foreign patents (including abandoned, expired and filed by third parties), and fifty-five pending patent applications (U.S. and foreign), including third party leads.

NHGRI has received a royalty payment for the sale of a Priority Review Voucher (PRV) linked to NIH License No: L-175-2020 (Farnesyltransferase Inhibitors for Treatment of Laminopathies, Cellular Aging and Atherosclerosis).

In total, NHGRI currently has 44 active licenses, including Biological Material License Agreements (BMLAs) and Patent License Agreements (PLAs). 10 new NHGRI licenses were executed in FY2021.

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NHGRI CRADAs:

Three new CRADAs, four CRADA Amendments and one CRADA Letter of Intent were executed during FY2021. The new CRADAs are:

1. "Pre-Clinical Development of AAV9-based Gene Therapy to Treat Niemann-Pick Disease Type C" (CRADA Number 2020-0099), effective December 4, 2020 with Novartis Gene Therapies, Inc.

2. "Analyses of Methylmalonic Acidemia (MMA) Natural History Study Data and MMA Patient Samples to Enable a Future MMA Gene Therapy Clinical Trial" (CRADA Number 2020-0172) effective December 17, 2020, with Asklepios BioPharmaceutical, Inc. ("Ask Bio").

3. "Preclinical Studies of Mmut-Specific Gene Therapy for Methylmalonic Acidemia (MMA)" NHGRI CRADA Reference No.: 2020-0167 is a 2nd CRADA with Asklepios BioPharmaceutical, Inc. ("Ask Bio") executed in October, 2020.

NHGRI Heavily Participated in Planning of Annual AUTM Meeting

Claire Driscoll, Director, 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 2022 annual conference to be held in New Orleans, LA in February 2022.

Anna Solowiej, Senior Licensing and Patenting Manager served as the Program Chair of AUTM (formerly known as the Association of University Technology Managers) Annual Meeting Planning Committee, helping to organize the 2021 and 2022 annual meetings and coordinating work of about 25 Committee members, with the 2021 meeting being the first-ever fully virtual event.

Eggerton Campbell, Senior Licensing and Patenting Manager, organized an AUTM panel for the 2021 AUTM annual conference (which became a virtual meeting and some panels, like this, had to be cancelled) on the topic of licensing terms for priority review vouchers for rare diseases (this session is now scheduled to take place at the 2022 AUTM annual conference).

Sangeetha Raghavan, Senior Licensing and Patenting Manager, moderated a panel on "The Dilemma of Software Inventions and Associated Data in the Age of AI" during the virtual 2021 Annual Meeting of the Association of Technology Managers (AUTM) organized on March 17, 2021.

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NHGRI Has Strong Participation in Technology Transfer Community Volunteer Positions

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 (Inteum's Minuet system) and ensure a smooth transition from our current IT systems (Wellspring's Sophia and TechTracs).

Claire Driscoll served on the NeuroNext (NN) 109 study team (GNE myopathy Phase 2/3 clinical trial which is being carried under a NN extramural cooperative agreement in conjunction with a 4-party CRADA which involves NHGRI, NINDS, NIAMS and a company, Leadiant Biosciences and will start enrolling patients in 2022).

Claire Driscoll served on the NHGRI extramural division's Third-Party Engagement workgroup and previously helped to develop an internal as well as external publicly available guidance documents to be used by NHGRI extramural program directors and program officers as well as used by NHGRI grantees.

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

Sangeetha Raghavan volunteered as a member of the Enterprise Technology Transfer (ETT) group for purpose of evaluating the process for tagging and classifying technologies to be listed within the soon-to-be established Inteum Minuet database which will store Technology Transfer related documents and agreements.

During the Fiscal year 2021, Eggerton Campbell, served as the IC representative on the NIH Exclusive License Consultation Group (ELCG).

Eggerton Campbell served as a member of the NIH Platform Vector Gene Therapies (PaVe-GT) Project team. In September 2021, the PaVe-GT team successfully obtained an Orphan Drug Designation (ODD) from the FDA for their lead AAV9-based propionic acidemia gene therapy vector.

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NHGRI Prioritizes Continued Learning

NHGRI has shown their commitment this past year to continued learning through attending trainings, presenting at forums, and writing scientific papers.

Anna Solowiej began NIH Senior Leadership Training on August 9, 2021.

Eggerton Campbell presented a talk at the NIH Licensing Forum on the spring of 2021 entitled “Negotiating Priority Review Vouchers Licensing Terms: Monetizing Agreements that Won’t Generate “Traditional” Royalties.”

Sangeetha Raghavan participated in the Management Seminar Series (MSS) for FY2021. The MSS provides administrative and scientific staff an opportunity to obtain and/or enhance management and leadership skills through presentations, interactive activities, and open discussions to address core leadership and management issues and NIH-related matters. In FY2021, a total of seven seminars were offered which includes the introduction to this program, and six specific topics.

Sangeetha Raghavan participated in the courses offered by the Technology Transfer University program at the NIH for Technology Transfer professionals.

Claire Driscoll was a co-author on a NHGRI scientific paper: Nuria Carrillo, May C. Malicdan, Petcharat Leoyklang, Joseph A Shrader, Galen Joe, Christina Slota, John Perreault, John D. Heiss,Bradley Class, Chia-Ying Liu, Kennan Bradley, Colleen Jodarski, Carla Ciccone, Claire Driscoll, Rebecca Parks, Scott Van Wart, Levent Bayman, Christopher S. Coffey, Melanie Quintana, Scott M Berry, Marjan Huizing, William A. Gahl, “*Safety and efficacy of N-acetylmannosamine (ManNAc) in patients with GNE myopathy: an open-label phase 2 study,*” Genetics in Medicine (2021).

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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 Fiscal Year 2021, the NHLBI Office of Technology Transfer and Development (OTTAD) successfully executed/processed 356 new technology transfer agreements on behalf of on behalf of NHLBI & 6 Service Center client ICs serviced by OTTAD (NIAAA, NIAMS, NIBIB, NIDCD, NIEHS, & NINR).

The executed/processed technology agreements include 24 RCAs, 92 CDAs, 180* Material and Data Transfer Agreements (including MTAs, DTAs, UBMTAs, SLAs), 2 CT-CRADAs, 5 S-CRADAs, 20 CRADA amendments, and 45 other agreements, of which 38 were considered to be complex agreements.

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NIAID - National Institute for Allergies and Infectious Diseases

NIAID Technology Transfer Facilitated Many Critical Clinical Trials that Supported Emergency Use Authorization (EUA) and Continued Development of Vaccines to Combat COVID-19

NIAID technology transfer efforts played a pivotal role to facilitate key COVID-19 vaccine clinical trials in response to the COVID-19 outbreak. The Technology Transfer and Intellectual Property Office (TTIPO) worked closely with the NIAID's Division of Microbiology and Infectious Diseases (DMID) to ensure that the trials described below were conducted under a harmonized umbrella of agreements and in compliance with federal statute, regulations, and local policies. To date, these efforts have led to an EUA for the mRNA-1273 vaccine.

COVID-19 and the pandemic response continue to evolve, making scientific and technology transfer efforts critical and urgent. Success was possible due to the unprecedented pace of vaccine and therapeutic research and development throughout 2020 and 2021. With regard to vaccines, once the sequence of SARS-CoV-2 was available, the vaccine's mRNA sequence finalized, and appropriate pre-clinical data obtained, DMID took the lead as the sponsor of the "first-in-human" clinical study just 63 days after the viral sequence was published. After the Phase I trial demonstrated safety of the vaccine, subsequent Phase II and Phase III trials demonstrated that two doses of the vaccine were more than 94% effective at preventing COVID-19. The outcome of these trials led the Food and Drug Administration (FDA) to issue an EUA for the use of the mRNA-1273 vaccine for the prevention on COVID-19 in individuals 18 and older.

TTIPO continues to play a crucial role in supporting DMID to facilitate negotiations of compliant agreements to ensure each trial can be activated in an expedited and timely manner while ensuring that each organization and clinical site abides by harmonized terms and restrictions. While COVID-19 vaccines receiving EUAs is a huge achievement, there are still areas of significant unmet need. For instance, under the active EUA, the mRNA-1273 vaccine cannot be administered to individuals under the age of 18. In addition, new variants of SARS-CoV-2 continue to emerge, which may reduce the efficacy of the current COVID-19 vaccines. To this end, DMID is also supporting a pediatric trial (KidCOVE study) to test mRNA1273 in children from ages 6 months to up to 12 years. An analysis of preliminary data generated by KidCOVE suggest that mRNA1273 is safe and allows kids from 6 months to 12 years old to generate an immune response against the SARS-CoV-2 spike protein. DMID also sponsored a Phase I clinical trial to evaluate an investigational vaccine, mRNA 1273.351 that may provide protection against infection with the B.1.351 variant.

Another area of unmet need relates to logistical issues with vaccine delivery, which may mean that two doses of the same vaccine cannot be administered on a pre-defined time scale to the same individual. Because there is also clinical evidence suggesting that administration of different vaccines for the 'prime' and 'booster' shots can generate an effective immune response, DMID has initiated an adaptive protocol for the 'mix and match' vaccine trial, which is evaluating the safety and immunogenicity of different heterologous delayed doses (boosts) in individuals who received

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one of the three EUA vaccine regimens. Under the study, various combinations of vaccines from different companies starting with EUA vaccines from Moderna, Janssen, and Pfizer have been tested and show that using different vaccines for a booster shot can boost the immune response. As new vaccines enter late-stage clinical trials and are shown to be safe and effective, their efficacy as boosters will also be tested separately under the study.

NIAID Technology Transfer Enabled Rapid Development of bamlanivimab, a COVID-19 Therapeutic Monoclonal Antibody

For COVID-19 patients exhibiting mild or moderate symptoms, healthcare providers can administer one of several antibody-based treatments. One of those antibodies, bamlanivimab, was developed by NIAID and a collaborator on an accelerated timetable, beginning in January 2020 and culminating in a ”first in human” trial initiated during June 2020. The NIAID Technology Transfer Intellectual Property Office (TTIPO) negotiated critical research collaboration and license agreements that memorialized and advanced this highly productive and successful partnership. 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. This process is necessary for viral infection and ultimately leads to COVID-19. When SARS-CoV-2 infects an individual, the immune system responds in several ways, including generation of antibodies to SARS-CoV-2. These antibodies bind to the virus which can interrupt the viral infection cycle and spread of viral particles by preventing viral entry into human cells.

For this reason, the blood of recovered COVID-19 patients is fertile ground for novel antibodies that are highly effective at neutralizing SARS-CoV-2 infection. The monoclonal antibody bamlanivimab was discovered by using an engineered version of the SARS-CoV-2 spike protein as ”bait” to search for antibody producing B cells from the blood of patients who recovered from COVID-19 infection that target the spike protein.

Credit: Eli Lilly

SARS-CoV-2 or isolated un-engineered SARS-CoV-2 spike protein cannot be used effectively to identify and isolate neutralizing antibodies. Instead, Dr. Barney Graham, Deputy Director of NIAID’s Vaccine Research Center and his team introduced specific mutations to increase the stability of a prefusion conformation of coronavirus spike proteins and have shown that introducing these mutations produce an effective immunogen.

With this engineered SARS-CoV-2 spike protein, the NIAID collaborator, AbCellera, was able to use its proprietary high-throughput, machine-based process to search among millions of antibody-producing cells from a patient who recovered from COVID-19 infection. The result was a small selection of the most effective or potent antibodies, which may not have been identified with more conventional methods. Among these was the precursor of bamlanivimab.

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NIDDK - National Institute of Diabetes and Digestive Diseases

The NIDDK's Technology Advancement Office (TAO) has expanded its technology transfer service center functions in 2021 to include The National Institute of Dental and Craniofacial Research (NIDCR), The Fogarty International Center (FIC), Office of Research Services (ORS), and The NIH Office of the Director, Division of Program Coordination, Planning, and Strategic Initiatives (OD/DPCPSI).

Dr. Ken Jacobson, section chief in the Laboratory of Bioorganic Chemistry, at the NIDDK was named a fellow of the American Society for Pharmacology and Experimental Therapeutics. He is recognized for four decades of developing and advancing experimental therapeutics targeting G-protein coupled adenosine receptors.

The clinical success of Dr. Jacobson's novel therapeutics are now bearing fruit in clinical trials for a wide variety of indications, as reported in the Innovative Collaborations section of this report.

TAO contributed to the efforts of the NIDDK Office of Clinical Research Support and the NIDDK extramural U01 clinical networks and programs by developing a variety of policies, template language, and best practices for 3rd party collaboration agreements to study new therapies and devices.

One success in 2021 from the NIDDK U01 collaborative clinical networks:

U.S. FDA Approves LIVMARLI (maralixibat) as the First and Only Approved Medication for the Treatment of Cholestatic Pruritus in Patients with Alagille Syndrome One Year of Age and Older.

Mirum Pharmaceuticals, Inc., a leader in rare liver disease, today announced that the U.S. Food and Drug Administration (FDA) has approved LIVMARLI™ (maralixibat) oral solution for the treatment of cholestatic pruritus in patients with Alagille syndrome (ALGS) one year of age and older. LIVMARLI, a minimally absorbed ileal bile acid transporter (IBAT) inhibitor, is the first and only FDA-approved medication in this rare liver disease which affects 2,000 to 2,500 children in the United States. LIVMARLI is now available for prescribing. In conjunction with the approval, Mirum received a rare pediatric disease priority review voucher.

"*Children with Alagille syndrome suffer from cholestatic pruritus, which is serious, unremitting, and debilitating. Their sleep is disrupted, and they endure bleeding and scarring of the skin due to unrelenting scratching,*" said Binita M. Kamath, MBBChir, Pediatric Hepatologist, The Hospital for Sick Children (SickKids), Toronto, Ontario, Canada. "*There have been no approved treatments to date for cholestatic pruritus in Alagille syndrome, and many children ultimately require major surgical interventions such as liver transplantation for refractory pruritus. The approval of LIVMARLI signifies a meaningful shift in the treatment paradigm for Alagille syndrome and provides hope for the many families who have lived with persistent itch for far too long*."

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ALGS is a rare genetic disorder caused by abnormalities in bile ducts that can lead to progressive liver disease. Malformed or reduced bile ducts cause cholestasis, the accumulation of bile acids in the liver, which leads to inflammation and liver injury, and prevents the liver from working properly. Cholestasis in ALGS is associated with pruritus which is among the most common indications for liver transplant in ALGS.

The approval of LIVMARLI is based on the pivotal ICONIC study as well as five years of data from supportive studies conducted in collaboration with The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) at NIH and their extramural U01 collaboration programs resulting in a robust body of evidence in 86 patients with ALGS. Data from ICONIC demonstrated statistically significant reductions in pruritus, one of the most common and arduous symptoms associated with the disease, which was maintained through four years.

"*Today is a great day for the Alagille syndrome community with the approval of a much-needed new treatment option to address one of the most debilitating effects of this disease,*" said Chris Peetz, president and chief executive officer of Mirum. "*We are grateful to the patients, families, and healthcare professionals who advanced the research and participated in the LIVMARLI clinical studies. Today is also a landmark day for Mirum as we take steps forward in developing potentially life-changing medicines for rare liver disease.*"

Credit: Mirum Pharmaceuticals, Inc.

"*We have had the pleasure of being part of and closely following the clinical progress of LIVMARLI in many ways. Since the first study's initiation more than a decade ago, we have dreamed of today, seeing LIVMARLI receive FDA approval, marking an incredibly meaningful milestone for the ALGS community,*" said Roberta Smith, president, Alagille Syndrome Alliance and an ALGS mom. "*Until now, patients have had limited-to-no treatment options to address the severe and unrelenting itch that significantly impacts both patients and their families. Additionally, because pruritus associated with ALGS greatly impacts caregivers, having a strong support program like Mirum Access Plus to reduce the strain on families is so important. The ALGS community has been waiting for a long time for a treatment and we're so pleased that LIVMARLI is now available in the United States.*"

LIVMARLI will be accessible to patients with a prescription through Mirum Access Plus (MAP), the company's patient support services program and single-source specialty pharmacy. The MAP program has fully dedicated and experienced coordinators who will work with healthcare providers and families to provide insurance coverage and access support, as well as help with financial support options for LIVMARLI. A dedicated Navigator team will also provide health education and will connect families to resources and tools to support their disease.

Alagille syndrome (ALGS) is a rare genetic disorder in which bile ducts are abnormally narrow, malformed and reduced in number, which leads to bile accumulation in the liver and ultimately progressive liver disease. The estimated incidence of ALGS is one in every 30,000 people.1 In patients with ALGS, multiple organ systems may be affected by the mutation, including the liver, heart, kidneys and central nervous system. The accumulation of bile acids prevents the liver

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from working properly to eliminate waste from the bloodstream and, according to recent reports, 60% to 75% of patients with ALGS have a liver transplant before reaching adulthood.3 Signs and symptoms arising from liver damage in ALGS may include jaundice (yellowing of the skin), xanthomas (disfiguring cholesterol deposits under the skin), and pruritus (itch)2. The pruritus experienced by patients with ALGS is among the most severe in any chronic liver disease and is present in most affected children by the third year of life.

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 supports 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 503 agreements in FY2021 with 407 Material Transfer Agreements (261 of those are with Addgene), 1 Clinical Trial Agreement (extramural), 16 Confidential Disclosure Agreements, 53 Data Transfer Agreements, 3 Copyright/Publisher Agreements, and 23 Research Collaboration Agreements.

NIMH - National Institute of Mental Health

MedInvest Life Science Conference with Special Day on Neurology

MedInvest Conferences is a leading conference series in healthcare and life sciences and featured a neurological disease and mental health disorder focused conference in September 2021. The conference featured informative panel discussions, keynote talks, corporate presentations, and one-on-one meetings with the goal of facilitating startup biotechnology, medical, and health care technology companies forming partnerships with or obtain funding from angel investors, foundations, and venture funds.

NIMH and NINDS Technology Transfer Offices (TTOs) spoke about partnership opportunities and unique neuroscience resources at the NIH. These opportunities ranged from traditional technology transfer mechanisms such as CRADAs and collaborations to the other organizational programs such as the BRAIN Initiative, HEAL, and SBIR/STTR programs. The TTOs drew

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attention to scientific resources that businesses may not have access to, such as Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET) Cores, that are available as a collaborative opportunity with industry. The TTOs also highlighted repositories with precious resources such as the NeuroBioBank, a human post-mortem brain tissue repository with specimens that have neurological, neuropsychiatric, and neurodevelopmental diseases and disorders, and NINDS' Human Cell and Data Repository, a Resource for Stem Cells including iPSCs and fibroblasts. By leveraging the capabilities of NIH's intramural program, access to unique resources, facilities and materials, the TTOs promoted ways to work with the ICs to further advance their collective public health missions.

Study on Impact of Sleep Restriction on CNS Structural Integrity and Clearance of Toxins From the Brain

In collaboration with Walter Reed Army Institute of Research and Walter Reed National Military Medical Center, NIMH conducted a study to elucidate the role of chronic sleep deprivation and clearance of toxins from the brain. Epidemiological studies suggest that chronic sleep restriction has a significant negative impact on health and human performance. In this study, a variety of PET and fMRI endpoints will be used to determine whether and the extent to which sleep restriction in humans results in neuroinflammation and neurodegeneration, and whether sleep restriction impacts central nervous system structural integrity and clearance of toxins from the brain. In particular, PET imaging will be used to measure how inflammation, the deposition of tau protein, and synaptic density change in the brain according after sleep deprivation. These data will be correlated with behavioral (e.g., cognitive performance) electrophysiological (EEG), and polysomnographic data to help determine the physiological basis of behavioral deficits resulting from sleep loss, and the rate at which the physiological effects of sleep loss are reversed following recovery sleep. If successful, the results will reveal which brain processes underlie a putative causal relationship between chronic sleep restriction and long-term decrements in health, and point the way to development of novel interventions to sustain brain health and performance during continuous and sustained military operations.

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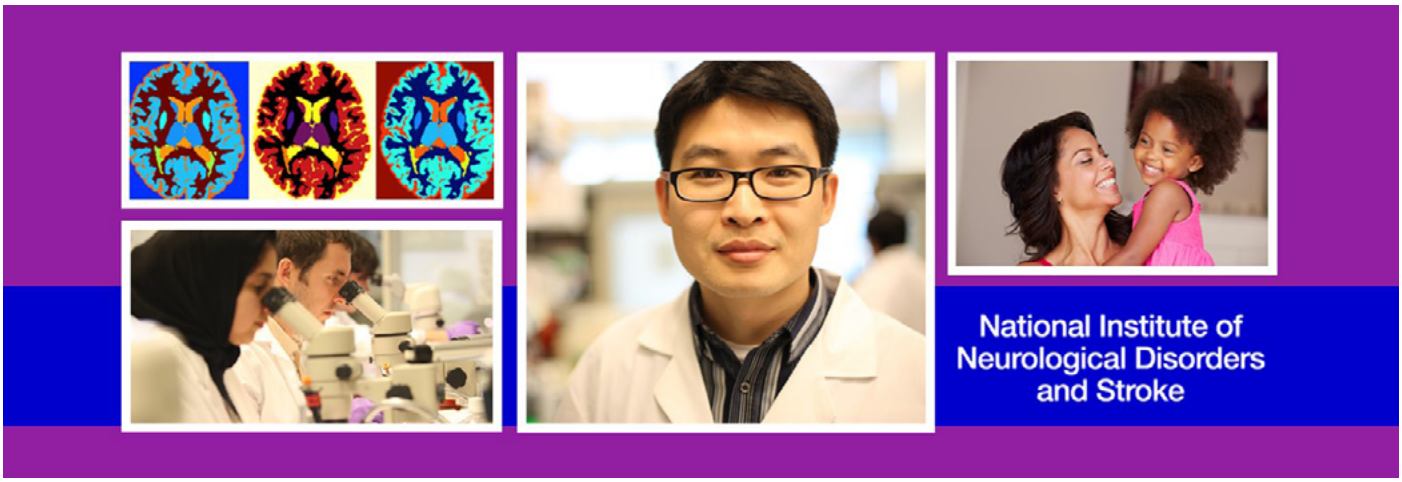
NINDS - National Institute of Neurological Disorders and Stroke

The mission of NINDS is to seek fundamental knowledge about the brain and nervous system and to use that knowledge to reduce the burden of neurological disease for all people.

To support this mission, NINDS:

- Supports and performs basic, translational, and clinical neuroscience research through grants-in-aid, contracts, scientific meetings, and through research in its own laboratories, and clinics.
- Funds and conducts research training and career development programs to increase basic, translational and clinical neuroscience expertise and ensure a vibrant, talented, and diverse work force.
- Promotes the timely dissemination of scientific discoveries and their implications for neurological health to the public, health professionals, researchers, and policy-makers.



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Dissemination of CEPT — A New Chemical Foundation for iPSC Research and Clinical Application

Human pluripotent stem cells are cells that, in theory, can grow forever and serve as an inexhaustible source for specialized cells, such as brain, kidney and heart cells. But stem cells are sensitive, and their potential uses in medicine are hampered by the stress of growing in a cell culture dish, which can damage their DNA and lead to cell death. Improving cell culture conditions specifically for human stem cells (e.g., media formulations, coating substrates) has been a daunting challenge for the field for more than 20 years.

The NCATS Stem Cell Translation Laboratory (SCTL) lead by Dr. Ilyas Singec addressed the cell viability problem by performing innovative high-throughput combinatorial screening of nearly 16,000 compounds in 1536-well format.They discovered that the combination of chroman 1, emricasan, polyamines, and trans-ISRIB (CEPT) dramatically improves cell survival of induced pluripotent stem cells (iPSCs) as well as differentiated cell types (e.g., neurons, cardiomyocytes, and hepatocytes). CEPT represents a unique polypharmacology strategy for comprehensive cytoprotection, providing a new rationale for efficient and safe utilization of iPSCs.The researchers showed, for example, that CEPT improved the biobanking of stem cells, called cryopreservation, which involves freezing the cells and typically is very stressful for them.The cocktail dramatically improved the process. Other potential uses for the cocktail are in tissue engineering and the biomanufacturing of various cell types for regenerative medicine and drug development.

OSA diligently worked with the inventors to obtain strong and appropriate intellectual property protection for the CEPT cocktail and is currently prosecuting several patent applications in several countries. To disseminate the technology as widely and as quickly as possible to all researchers in the stem cell field, OSA has devised a strategy of non-exclusive licensing for the CEPT cocktail. Under this strategy, OSA has negotiated and executed various non-exclusive licenses with different industry partners and stem cell reagent companies both in the US and abroad. The successful efforts of OSA are ensuring that stem cell researchers everywhere can use CEPT to culture and produce next-generation stem cell lines at high quality before moving them into the clinic.

Commenting on the significance of this novel invention, NCATS Acting Director Joni Rutter, Ph.D. said:

> *"By finding new ways to protect stem cells from damage, these results could eventually have wide-ranging implications for many different diseases, including cancer, Alzheimer's disease, and more."*

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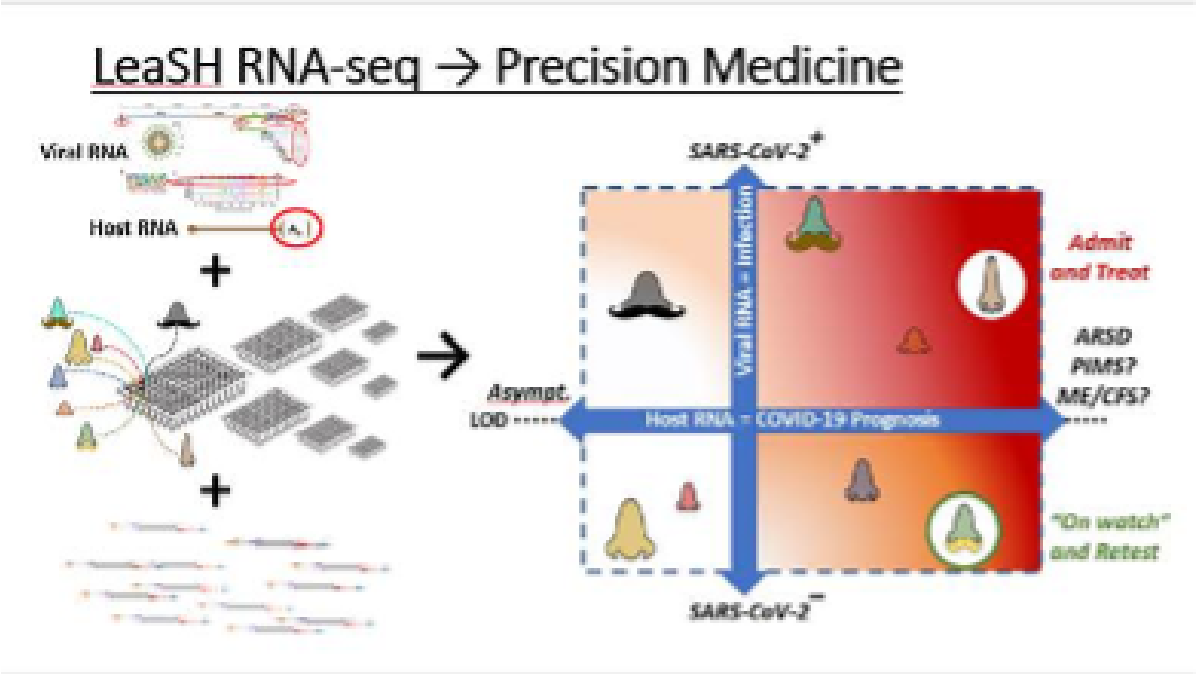
NCATS scientists have devised a small-molecule cocktail called CEPT that helps protect human pluripotent stem cells from potential DNA damage due to the stresses of being grown in a dish. Here, frozen human stem cells were thawed, placed on cell culture plates in the presence of different reagents, and analyzed 12 hours later. In the left and center panels, Caspase 3/7 (green), a marker for dead cells, indicates poor cell survival of stem cells treated with a control (DMSO) and Y-27632. In stark contrast, the right panel shows that virtually all cells survived in the presence of the CEPT cocktail.

COVID-19 Invention From NIEHS Enters PCT Stage Of Filing and Sparks Licensing Interest

To meet the global need to diagnose COVID-19 and understand the biological pathways at play in patient responses at the genetic level, scientists at NIEHS invented a massively paralleled multi-patient assay for pathogenic infection diagnosis and host physiology surveillance using nucleic acid sequencing called Leader Sequence Homology-enriched (LeaSH) RNA-Seq. NIEHS OTT followed up on last year's achievements by successfully submitting a PCT application for LeaSH RNA-Seq and attracted interest from companies to license and collaboratively develop the invention.

NIEHS OTT nominated this laboratory group for a 2021 Group Merit Award for "developing an innovative diagnostic method to assist in combating the COVID-19 pandemic." Winning this award grants public recognition of the NIEHS scientists' endeavors to meet immediate public health needs in an innovative fashion.



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2021 Technology Showcase Successful In Its Fifth Year

The 5th annual NCI/Frederick National Laboratory (FNL) Technology Showcase on September 1, 2021, proved to be another successful event. It attracted over 300 attendees representing biotech, investors/angels, economic development, academia, foundations/philanthropies and technology transfer. The event is organized under a co-sponsorship agreement by the NCI Technology Transfer Center, the Frederick National Laboratory, the City of Frederick Department of Economic Development, the County of Frederick Department of Economic Development, TEDCO and the Federal Laboratory Consortium. The program features included:

- Keynote addresses by Mark Stewart, Ph.D., VP of Science Policy for the Friends of Cancer Research, and James Cherry, Ph.D. on detail as NCI Scientific Program Director (SeroNet).
- Technology Opportunity Pitches from NCI and FNL inventors
- Panel Sessions:
  - Panel 1: “How collaborators can tap into laboratory resources at the Frederick National Laboratory”
  - Panel 2: “Foundations and philanthropies as strategic partners”
  - Panel 3: “How to work with the National Cancer Institute and the Frederick National Laboratory”
  - Panel 4: “Funding and resources for startups”
- A Lightning Pitch and Poster Session organized by the NCI Technology Transfer Ambassadors Program (TTAP)

The 2021 event was held virtually and featured 23 technologies presented by nine NCI and FNL inventors and 14 presenters from TTAP. For the first time, the panel sessions included a cancer survivor/patient advocate. The success story panel included the CEO of Precigen, an NCI CRADA partner. The full agenda can be viewed here.

TTC Staff on the Technology Showcase Planning Committee included Michele Newton, Michael Salgaller, Ph.D. and Laura Prestia, Ph.D. TTC’s Invention Development and Marketing Unit (IDMU) responded to multiple follow-up requests for more information.

Save the date for next year: September 7, 2022.

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NIDDK Partner BioIntervene Raises $30M to Move Nerve Pain Drug Into the Clinic

In the past seven years BioIntervene has been working to develop “ultra-selective” compounds to target an adenosine receptor associated with pain relief and developed in the laboratory of Dr. Ken Jacobson at NIDDK.

Now the San Diego-based biotech has $30 million and a chief scientific officer, Charles Cohen, to guide its lead compound, BIO-205, into human testing for neuropathic pain. The company announced the Series A financing round and CSO hire on Monday.

BioIntervene’s BIO-205 is an A3 adenosine receptor (A3AR) agonist, which means it homes in on and activates the A3 receptor on adenosine.

BioIntervene’s new CSO, Cohen, in a prepared statement, said BIO-205’s preclinical data demonstrated activity in models of neuropathic and inflammatory pain by itself and in combination with morphine and gabapentin, drugs used currently to manage such conditions. If the data are reproducible in humans, the drug could provide clinicians more options for pain management, he said.

“Our belief is that when there’s nerve damage, there is an ongoing inflammatory state, and that inflammatory state is mediated and can be quelled and suppressed by an adenosine agonist that hits the A3 receptor only,” Ed Hurwitz, BioIntervene’s chairman, told Xconomy. Hurwitz is a managing director at MPM Capital, the Boston-based healthcare investment firm that led BioIntervene’s financing round *“By agonizing with these molecules this particular receptor subtype, we’ve been able to get away from side effects that are seen when you agonize other adenosine receptors, and really have a pure analgesic effect,”* he said.

That’s what BioIntervene has seen in animal models, at least. The proceeds from the Series A will be used to move BIO-205 through human proof-of-concept studies in neuropathic pain, testing the company plans to start in the second half of this year.

Neuropathic pain, often called nerve pain, can occur when certain nerves and parts of the brain are damaged. Nerve pain may result from variety of causes, including physical injury, surgery, cancer drugs, and neurological diseases such as multiple sclerosis.

Current treatments include opioid painkillers such as morphine and gabapentin, an anti-seizure medication.

“The world needs drugs other than morphine and opioids because they’re generally not seen as very effective in neuropathic pain, and as a result of that, people overdose and ultimately become addicted, partly because the drugs aren’t very effective,” Hurwitz said. *“We saw a really compelling body of animal data that show that this pharmacology and these compounds have the potential to*

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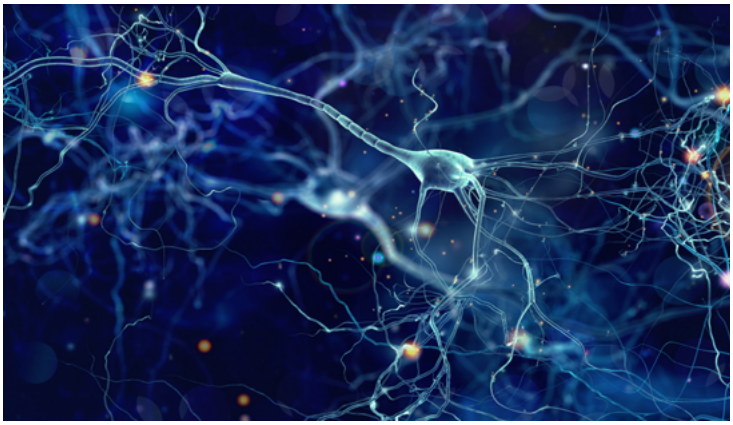
be more potent than morphine and more potent than gabapentin, but also much safer, so that was really the basis for us deciding to make the investment."

Founded in 2014, BioIntervene was formed to advance work by Daniela Salvemini at Saint Louis University, who discovered the roles of A3AR in neuropathic pain and neurodegenerative conditions, and Ken Jacobson at the National Institutes of Health. A collaboration between Salvemini and Jacobson led to the filing of a portfolio of patents that BioIntervene exclusively licensed.

Company co-founder Gary Bennett is an adjunct professor in the department of anesthesiology at UC San Diego.

Can-Fite BioPharma, an Israeli biotech with a US office in Waltham, MA, is also developing drugs that target A3AR; its experimental treatments, for inflammation and for liver disease, are in clinical testing. Can-Fite is advancing Piclidenoson a novel, first-in-class, A3 adenosine receptor agonist (A3AR) small molecule, orally bioavailable drug with a favorable therapeutic index demonstrated in Phase II clinical studies. and developed in the laboratory of Dr. Ken Jacobson at NIDDK.



Prior to Phase III Psoriasis Data Release Can Fite Reports that Piclidenoson Destroys Pathological Skin Cells in vitro.pre-clinical studies with skin cells, modeling psoriasis in humans, show that Piclidenoson, the Company's drug candidate for the treatment of psoriasis, destroys pathological skin cells. The Company's scientists reported that in a cell culture of human HaCaT cells, incubated with Piclidenoson, cell apoptosis was induced with an increase in the caspase protein, known to mediate apoptotic responses

The Company expects to announce topline results during 2022 from its randomized, double blind, active and placebo-controlled study currently being conducted in Europe, Israel, and Canada. The study's primary endpoint is the proportion of patients who achieve a PASI score response of ≥75% (PASI 75) vs. placebo at week 16. Secondary endpoints include non-inferiority to Otezla® in weeks 16 and 32. Patients enrolled in the study have been selected based on their over-expression of A3AR, Can-Fite's therapeutic target.

"The data shown in our lab experiments are important and support the mechanism of action of Piclidenoson and supply additional support for the drug effect. We are encouraged by the positive interim analysis data reported last year based on 200 patients' data and hope that it will be reproducible and that psoriasis patients will benefit from safety and long term relief from the symptoms of psoriasis," stated Can-Fite CEO Dr. Pnina Fishman.

According to iHealthcareAnalyst, the psoriasis therapeutic market is estimated to reach $11.3 billion by 2025. Piclidenoson has been out-licensed for the indication of psoriasis in major markets including Canada, Europe, and Asia with deal terms including potential upcoming milestone payments and double-digit royalties upon regulatory approval.

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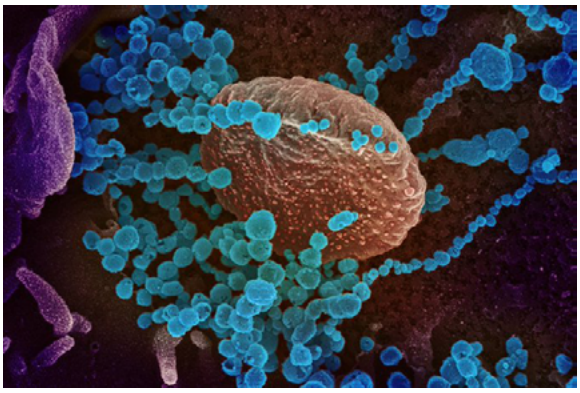
INNOVATIVE COLLABORATIONS

Antiviral Program for Pandemics (APP)

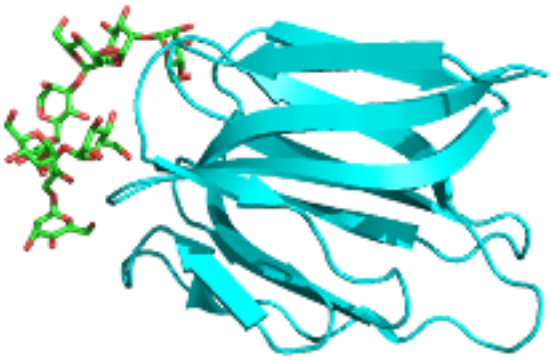


Launched in June 2021, the Antiviral Program for Pandemics (APP) is a 5-year, $3.2B Biden Administration scientific program aimed at accelerating development of antivirals for not only the COVID-19 pandemic, but future pandemics that the country may face. The program is based on in-kind support and funding via public-private partnerships (PPPs), Antiviral Drug Discovery (AViDD) Centers and APP partner agencies: NCATS, National Institute of Allergy and Infectious Diseases (NIAID), and Biomedical Advanced Research and Development Authority (BARDA). This highly collaborative arrangement leverages partners in academia, pharma, biotechnology, and foundations to respond to immediate and ongoing global crises such as the COVID-19 pandemic.

OSA has been supporting NCATS with the implementation of agreements to support screening & drug development collaboration activities. Since the launch in June, approximately 30 APP related agreements have been executed including CDAs, MOUs and one CRADA. In addition to agreement management, OSA is at the center of program coordination providing expertise in scope determination, intellectual property, and APP partner agency liaisons.

Multi Party C-RCA to Develop Griffithsin as a Covid Prophylaxis

Griffithsin (shown here in teal) is a lectin protein produced by Griffithsia algae that binds tightly to several viral glycoproteins and prevents viral entry into mammalian cells. Initially shown to be active against HIV in two successful Phase I trials, Griffithsin has now been shown to be active against all strains of coronaviruses at nanomolar concentrations. To test Griffithsin's effectiveness against COVID-19, a 4-way collaboration amongst NCATS, NCI and the Universities of Pittsburgh and Louisville was initiated.



The collaboration agreement, which had the goal of developing Griffithsin as a preventive for SARS-CoV-2, needed to move fast. A regular CRADA would have taken months, and 4-Party CRADA even longer. Using the C-RCA mechanism, the collaborative work could be initiated in a matter of days to weeks. Preliminary results have borne out the original hypothesis. Griffithsin was able to reduce viral replication in epithelial airway cell cultures and in mice challenge studies, survival of mice infected with SARS-CoV-2 improved greatly when treated with Griffithsin. Following these preclinical studies with this agent, Investigational New Drugs Phase I human trials are being planned. The ultimate goal of the collaboration and the follow-on commercial work would be to establish Q-Griffithsin (a modified

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form of Griffithsin with improved stability) as a broad-spectrum antiviral agent that can be used by front line workers, travelers or others that may need a preventive treatment for COVID-19, its variants, or other coronavirus diseases.

N3C Data Enclave – Continuous Improvement and Innovation

The NCATS 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. Companioned with the physical effort of standing up the actual enclave, a significant and sustained staff effort also ensued to support the security and operations of the Enclave. This included multiple discussions daily with regard to how the N3C Data Enclave would physically operate, how the Data Enclave would work with respect to the planned operations and governance with the CD2H, and how the Data Enclave would navigate existing federal regulations and NIH policies. Work on the N3C Data Enclave began in April of 2020. Governance teams met daily, often multiple times a day, to address a host of issues relating to governance, policy, and regulatory requirements for the operations of the Enclave. By September 2020, the Data Enclave was open for accepting requests to access the data, formal agreements for data transfer and data use were in place and being negotiated, the Data Access Committee and its operations team were holding their initial meeting for review and approval of data use requests.

The immediate and urgent need for COVID-19 clinical data has been recognized nation-wide and the N3C Community has actively contributed to the scientific governance within the Data Enclave and encouraged the research community to participate in its use. The N3C Data Enclave continues to grow both in terms of the data and sources coming into the enclave and the number of scientists who are using the data enclave to conduct groundbreaking research. This has entailed a number of new data transfer agreements to be developed from OSA, including one with the Centers for Medicare and Medicaid. To date, almost 100 institutions have deposited data in the Enclave and ~300 data use agreements have been executed by investigators who want to access the data.

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MOU with PCORI

NCATS and the Patient-Centered Outcomes Research Institute (PCORI) executed a Memorandum of Understanding (MOU) to detail the joint objectives between the two agencies and provide the framework for the collaboration (including the sharing of information) by NCATS and PCORI. Both NCATS and PCORI have a shared interest in generating evidence relating to the treatment of COVID-19 in the outpatient setting through clinical trials using the PCORnet® infrastructure (known as the "**ACTIV-6 Clinical Trial Initiative**").

ACTIV-6 funding has been provided by the Department of Health and Human Services Countermeasures Acceleration Group (CAG). As a related matter, ACTIV-1 was funded by Operation Warp Speed which was created by the Trump administration and active from May 15, 2020-February 24, 2021. ACTIV-6 was an important initiative and as such, NIH leadership had requested that the ACTIV-6 Clinical Trial Initiative be able to start with the first prioritized agents in April 2021 or sooner if possible. Waiting several months for NCATS to conduct a competitive solicitation would have resulted in a significant negative impact on the health of the United States population who needed,and continue to need, effective COVID-19 outpatient treatments that can be delivered through multiple types of health care delivery systems.

One goal of the ACTIV-6 Clinical Trial Initiative is to leverage electronic health records ("**EHRs**") as much as possible to collect study outcomes. PCORnet® is a large, distributed, representative national clinical data network that includes several large Clinical Research Networks spanning over 70 healthcare systems across the United States, a Coordinating Center, and the capacity to link to other complimentary data sources including health plan data. PCORnet® represents a diverse set of patients and institutions, ranging from academic medical centers to local community health clinics, which have developed a collaborative network governance structure and operational mechanisms that enable strong functioning relationships among the PCORnet® Coordinating Center and PCORnet® participating networks.

Further, PCORnet® enables research that uses millions of EHRs within its associated clinical sites to facilitate large-scale, multi-site research. The ability of PCORnet® to facilitate collection of data remotely as needed and utilize electronic health records as much as possible to collect data is critical to the ACTIV-6 Clinical Trial Initiative, allowing the trials to be conducted rapidly and efficiently.

NCATS and PCORI intend to collaborate and coordinate efforts that will help support the effectiveness of the ACTIV-6 Clinical Trial Initiative.

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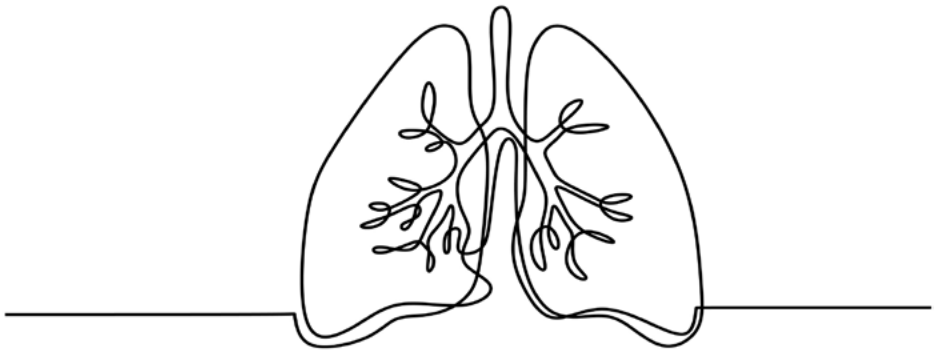
NIH Partnership Results in Key FDA Orphan Drug Designation for Rare Respiratory Disease Therapy

A partnership between the National Institutes of Health and Precigen Inc. led to a milestone regulatory designation that could significantly decrease treatment costs and improve quality of life for patients living with an incurable respiratory disease. In March 2021, the Food and Drug Administration (FDA) granted an Orphan Drug Designation for PRGN-2012, an investigational therapeutic vaccine being developed to treat recurrent respiratory papillomatosis (RRP). It is the first human regulatory designation for this investigational agent, being developed by the NCI in collaboration with the National Institute on Deafness and Other Communication Disorders (NIDCD) and Precigen.

The partnership brings together Precigen's PRGN-2012 vaccine and platform technologies and NIDCD's and NCI's expertise in research, design, and execution of preclinical and clinical studies to develop a treatment for RRP. RRP is a rare, difficult-to-treat, and sometimes fatal disease caused by human papillomavirus (HPV) infection. Approximately 1,500 new cases of RRP are diagnosed each year in the United States. The disease causes benign tumors (papillomas) to grow in the air passages leading from the nose and mouth to the lungs (respiratory tract), affecting a patient's ability to talk and breathe easily. In rare cases (1% - 3%), RRP can transform into invasive cancer (invasive squamous cell carcinoma). There is no cure for RRP, and the current standard-of-care is repeated surgeries to remove the papillomas. Unfortunately, papillomas often recur after surgical removal, which necessitates repeated surgeries that expose patients to clinical risks and emotional distress.

In October 2017, NCI executed a confidential disclosure agreement (CDA) with Intrexon Corporation (which subsequently became Precigen) to discuss a possible collaboration to study Precigen's investigational therapies. PRGN-2012 used Precigen's "gorilla adenovector technology," a proprietary gene therapy delivery technology that is part of the company's AdenoVerse™ platform. In February 2018, TTC executed a CRADA which allowed NCI to evaluate Precigen's proprietary vaccine platform for the treatment of cancer. In December 2020, the CRADA was amended to expand the scope of the research. Preclinical studies, conducted by researchers from NCI and NIDCD, showed robust immune responses to the vaccine in human patient samples and animal models. Orphan Drug Designation was based on these data; a clinical trial in patients with RRP began in March 2021 and is ongoing. Michael Pollack, Ph.D., TTC Unit Supervisor, manages this technology transfer effort.



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TTC Helps Overcome Data Sharing Challenges to Facilitate NCI Collaboration with Digital Health Coaching Company

Terri Armstrong, Ph.D., ANP-BC, FAAN, FAANP, Deputy Chief of the NCI CCR Neuro-Oncology Branch (NOB), wanted her research group to collaborate with Pack Health, a digital health coaching company. NOB's hypothesis was that with use of Pack Health's digital health coaching, patients would develop the skills to increase self-efficacy and reduce distress; this could foster positive coping skills related to their disease.

In this collaboration, NCI patients will enroll in NCI NOB's Natural History Protocol and would be subsequently informed of the option to participate in the collaborator's online digital health coaching program. NCI patients who opt in would generate data in the Pack Health platform. The Pack Health-generated data will be provided to NCI for the project, and NCI-generated data will be shared with Pack Health.

TTC's Michael Pollack, Ph.D., the Supervisory Technology Transfer Manager (TTM) supporting NOB, recognized that this presented an unusual situation – since NCI patient data would go directly into the Pack Health IT system. Pack Health would collect the Identifiable Private Information (IPI) of the NCI participants who signed up for coaching. To address this, Dr. Pollack reached out to the NCI Information System Security Office (ISSO) team for guidance. ISSO concluded that this case was not eligible for a Federal Information Security Management Act (FISMA) exemption. They requested that Pack Health complete a simplified "Authority to Operate" process to address information security issues. This process took about a month. Once authorization was obtained, TTC moved forward with the Clinical Trial Agreement. Some special terms were added to the Agreement to protect NCI participant IPI in Pack Health's possession and acknowledge that the NCI participant IPI would be retained after the Agreement termination subject to the confidentiality terms of the Agreement and with the participant's informed consent.

TTC Supports NCI Serological Sciences Network for COVID-19 (SeroNET)

Before the COVID-19 pandemic struck, the serology lab in the Frederick National Laboratory for Cancer Research (FNL) focused on HPV research and has since pivoted to support COVID-19 research standardization. With TTC Unit Supervisor, Jeff Thomas, Ph.D. providing technology transfer support, the FNL formed the NCI Serological Sciences Network (SeroNet), the nation's largest coordinated effort to study the immune response to COVID-19. SeroNet aims to combat the pandemic by improving the ability to test for infection, especially among diverse populations, and speed the development of treatments and vaccines. With many moving parts, this effort required a variety of technology transfer mechanisms. Dr. Thomas supported this effort through negotiation of data sharing agreements, a CDA, and development of new agreement templates for outside collaborators to work within the consortium.

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From MTA, to CDA, to CRADA: NCI Surgery Branch Partners with Nurix to Study Compound Relevant to Tumor Infiltrating Lymphocyte Research

It started in fall of 2019 with a meeting at a conference between NCI's Steven Rosenberg, M.D., Ph.D., NCI CCR Surgery Branch (SB), and the CEO of Nurix, a startup company. The two connected because Nurix has a proprietary compound they believed improves immunogenicity and anti-tumor activity of tumor infiltrating lymphocytes (TILs). Dr. Rosenberg's lab at the NCI SB develops TILs for cellular immunotherapy. A compound that improves anti-tumor activity could be very valuable to Dr. Rosenberg's research and improve cellular immunotherapies for cancer patients. This initial conversation in 2019 swiftly led to execution of a Material Transfer Agreement (MTA), providing Dr. Rosenberg's lab access to NX-0255 to study the compound. At that point, NCI knew very little about NX-0255's composition and mechanism of action. Throughout the next year, an NCI postdoc conducted preliminary studies and received some positive data. At that point, Dr. Rosenberg wanted to continue working on the project more seriously and publish the data NCI generated. To allow for deeper discussions to determine how to move forward, the parties swiftly signed a Confidential Disclosure Agreement (CDA) in December 2020.

Credit: IStock/ Viktoria Kurpas

As a startup company, Nurix was protective of any information on the composition of their proprietary compound and was worried about design-around and IP problems if the structure and preliminary data from the study became public.Those stances clashed with NCI scientists' research freedom. NCI could not proceed with publication without access to the structure information and properties of the compound. The concerns of both the company and the NCI Surgery Branch were important in negotiating next steps. NCI TTC overcame the issues by understanding both positions and being flexible in finding solutions. Ultimately, the parties signed a Materials-CRADA in June 2021. Even though negotiations were complicated, TTC was able to find a mutually agreeable way forward. Nurix will have the benefit of having pre-clinical studies of their compound conducted by the NCI Surgery Branch. NCI SB will continue its study to improve the efficacy of TILs. A future clinical CRADA is possible. TTC Technology Transfer Manager, Aida Cremesti, Ph.D., managed this complex tech transfer.

NIH NATIONAL CANCER INSTITUTE

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NCI TTC Supports National Institute on Aging's (NIA) Collaborative Effort with Michael J. Fox Foundation to Support Global Parkinson's Genetics Program

NIA's Laboratory of Neurogenetics is leading the Global Parkinson's Genetics Program (GP2) in collaboration with the Michael J. Fox Foundation (MJFF). GP2 is a five-year, multi-party program. Its aim is to further understand the genetic architecture of Parkinson's Disease (PD) through genotyping diverse patient groups and studying rare familial forms of PD. Aligning Science Across Parkinson's (ASAP) is funding GP2, under which NIA also received an award.

GP2 is committed to global collaboration and open data. The study will engage existing global consortia and cohorts to expand genetic analysis efforts with samples from >150,000 volunteers around the world – including those with PD, people at risk of PD, and control volunteers. The resulting data will aim to provide new biological understanding, greater genetic resolution, better disease risk profiles, and data-driven insights into the full spectrum of PD. GP2 will also provide training and resources to a broad, diverse base of scientists and clinicians around the globe.

NCI TTC is an integral part of GP2. TTC developed a GP2 MTA to bring in the over 150K human samples from patient volunteers that are expected to be analyzed under this program. To date, TTC executed 15 GP2 MTAs. TTC also regularly engages our collaborative partner, MJFF, the NIA GP2 team, and NIH Office of General Council to ensure program alignment and solve technology transfer issues. With TTC's assistance, NIA can apply its expertise in Genome-Wide Association Studies (GWAS); all information/data generated by NIH under these MTAs is shared with all members of GP2 through Accelerating Medicines Partnership – Parkinson's Disease ("AMP-PD") data portal. Nicole Darack Guyton, Ph.D., TTC Unit Supervisor, and Zarpheen Jinnah, TTC Technology Transfer Manager for NIA, support this ongoing TT effort.

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NCI-led Phase 2 Trial of Clinical-stage Immunotherapeutic Agents for the Treatment of HPV-associated Cancers Yields Promising Results

The NCI Center for Cancer Research's (CCR) Laboratory of Tumor Immunology and Biology (LTIB) and Genitourinary Malignancies Branch (GMB) are jointly leading a Phase 2 clinical trial of the triple combination of PDS0101, bintrafusp alfa, and NHS-IL 12 for the treatment of HPV-associated cancers, including anal, cervical, head and neck, vaginal and vulvar cancers. NCI presented the following positive results at the 2021 American Society of Clinical Oncology (ASCO):

> While current standard of care treatment has objective responses of 12-24%, 83% of patients who had failed prior chemotherapy and radiation therapy had an objective response to the combination therapy. Among patients who failed checkpoint inhibitor therapy in addition to chemotherapy and radiation, the current standard of care has objective responses of 5-12%. Notably, for this population, 63% of patients had objective responses to the combination therapy.

Under separate CRADAs, NCI is collaborating with PDS Biotech to develop PDS0101, and with EMD Serono to develop bintrafusp alfa and NHS-IL 12. PDS0101 generates potent killer T-cells *in vivo* and promotes a synergistic anti-tumor response with bintrafusp alfa and NHS-IL12. TTC Unit Supervisor, Michael Pollack, Ph.D. manages the technology transfer supporting this collaboration.

Biological Materials License (BML) Expands Access to NCI Cancer Cell Lines

Commercial researchers will now have expanded access to NCI-developed cancer cell lines already easily accessible to academic and non-profit laboratories. Crown Biosciences – a global drug discovery and development service company providing translational platforms to advance the fields of oncology, immuno-oncology, and immune-mediated inflammatory disease – will now be able to directly offer access to a large number of NCI cancer cell lines for services it provides to its commercial clients. Rather than having to negotiate separate Agreements with NCI for each request, an April 2021 BML streamlines the process by which Crown's commercial clients request use of these cell lines as part of the broad range of contract research services the company offers. As part of the licensing process, the parties negotiated mutually beneficial financial terms that balanced the value of cell lines with Crown's business model and intended uses. Importantly, this agreement provides another option for companies to access these NCI cancer cell lines for their commercial research; it does not impact access by researchers from academic or non-profit laboratories. Jaime Greene, M.S., TTC Senior Technology Transfer Manager, negotiated the license with Crown Biosciences. See Crown Biosciences press release, April 2021.

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NIAID Negotiated Clinical Trial Agreements to Expedite Clinical Development of Multiple COVID-19 Therapies

NIAID technology transfer professionals played a pivotal role to facilitate key clinical trials for COVID-19 therapeutic agents in response to the COVID-19 outbreak and within the expedited timeframes of Operation Warp Speed (OWS). The NIAID Technology Transfer and Intellectual Property Office (TTIPO) worked in close collaboration with NIAID's Division of Clinical Research (DCR), the Division of AIDS (DAIDS), and the Division of Microbiology and Infectious Diseases (DMID) to spearhead these efforts. In addition to enabling several clinical trials that led to an Emergency Use Authorization (EUA) for an mRNA vaccine (see Outcomes/Success Stories), NIAID and TTIPO have also enabled the clinical evaluation of medical countermeasures that can address many facets of COVID-19, from prevention to treatment of severely ill patients.

The trials conducted under NIH's Accelerating COVID-19 Therapeutic Interventions and Vaccines program (ACTIV), specifically the ACTIV-2 and -3 master protocols, have informed decision making by the Food and Drug Administration (FDA) regarding the EUA designation for therapeutic antibodies and small molecules. Given the evolving nature of COVID-19 and the pandemic, both ACTIV-2 and -3 continue to evaluate novel therapies that may provide critical treatment options to both ambulatory and hospitalized patients respectively. Early in the pandemic, data generated under ACTIV-2 provided support that led to an EUA for bamlanivimab as a treatment for patients with mild to moderate symptoms caused by a confirmed SARS-CoV-2 infection.

Hospitalized patients with severe COVID-19 are still in need of novel therapies. The ACTIV-5 Big Effect Trial (BET) aims to test promising and readily available agents (for which human data exist) in combination with the antiviral drug remdesivir, compared to placebo and remdesivir, in hospitalized COVID-19 patients. The trial will test Risankizumab, a monoclonal antibody developed by Boehringer Ingelheim and Abbvie, as well as the investigational monoclonal antibody lenzilumab, developed by Humanigen. This effort builds upon results obtained in 2020 under an Adaptive COVID-19 Treatment Trial (ACTT) sponsored by DMID and facilitated by TTIPO, which led to the EUA and FDA licensure of remdesivir alone.

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NIEHS Participates in Trans-NIH Collaborations

Studying how the environment affects human health produces insights into a variety of physiological and infectious diseases. Therefore, the research paths of NIEHS investigators often lead them into disease areas outside of their immediate area of expertise. To help the investigators continue to pursue the research along paths beyond their expertise, NIEHS OTT has actively sought the expertise of other IC's to instigate collaborations. For example, an RCA has been executed between NIEHS, NCATS and NCI to screen for inhibitors of the inositol kinases, which may yield a new drug class for treating diseases. These activities will increase trans-NIH collaborations to allow the sharing of expertise between IC's and supports the NIEHS vision to perform innovative research that improves public health by preventing disease and disability.

NIEHS Collaborates With Industry To Develop New Technologies

NIEHS and Genome Protection Inc. entered into a Collaborative Research and Development Agreement (CRADA) to develop a novel therapy for Idiopathic Pulmonary Fibrosis (IPF)/Interstitial Lung Disease (ILD).

Unilever and NIEHS joined forces through a Research Collaboration Agreement (RCA) to develop enhanced version(s) of the Skin Allergy Risk Assessment (SARA) model for different Skin Sensitization hazard and risk assessment regulatory use-cases.

First Street Foundation (First Street) and NIEHS entered into a RCA to evaluate climate-related hazards on human health. First Street is a 501(c)(3) organization with a mission to, "make climate risk accessible, easy to understand and actionable for individuals, governments, and industry." NIEHS and Sylics (Synaptologics B.V., The Netherlands) are partnering through a RCA to study sex differences in mice through automated home-cage monitoring. The mission of Sylics is, "to contribute to the development of new treatments of neurological and psychiatric diseases by serving its clients with high quality research solutions in neuroscience."

NIEHS and Natural Cycles have struck a partnership through a RCA to evaluate digital Fertility Awareness Based Methods (FABMs) in birth control effectiveness. The mission of Natural Cycles is, "to pioneer women's health with research and passion – by empowering every woman with the knowledge that she needs to take charge of her health."

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NCATS Federal Technology Transfer: Measuring Impact, Innovation & Efficiencies Workshop

Technology Transfer (TT) encompasses a wide range of activities aimed at dissemination of knowledge and discoveries to the benefit of the public. Strategic alliance and TT functions at the National Center for Advancing Translational Sciences (NCATS), as a federal laboratory, include activities aimed at enhancing collaboration, innovation, and acceleration to advance the science of translation, the process of turning observations into interventions to improve health. In the United States, new knowledge and discoveries can originate either at universities or institutes receiving federal grants or funds (i.e., federally funded) or at federal laboratories (i.e., federally owned). Although both types of innovative entities use similar TT mechanisms to disseminate knowledge and discoveries, the laws, regulations, polices, and guidelines governing each of them can differ, resulting in significant divergence in the way the entities operate, implement, and evaluate their TT.

This metrics workshop was timely, particularly considering the unprecedented challenges to both science and TT posed by COVID-19; the lessons from our collective experiences and responses can help TT in moving the science forward quickly and efficiently. To have a successful TT ecosystem, there is a need to “raise all boats” that are both diverse and inclusive and that work together; so much of science and technology revolves around relationships, and TT is at the forefront of these interactions. Evaluating these efforts is helpful for scientists to learn, improve, and monitor the impacts of TT to affect the overall health of the public.

The two-day virtual workshop organized and held by the Office of Strategic Alliances aimed to present diverse perspectives on (a) ways of evaluating the contribution and impact of Technology Transfer Office (TTO) activities, outputs, and outcomes (e.g., agency-specific, economic, and public health) to their institutional/agency mission and (b) models, tools, and examples of measuring structural and functional efficiencies and innovations of TTOs. The goals of the workshop were to enhance awareness and knowledge among stakeholders about different perspectives and tools to identify TTO activities and outputs, as well as outcomes that help an agency’s mission while capturing the entirety of the U.S. government’s TT objectives. Various stakeholders’ voices, practitioners’ perspectives, and policymakers’ visions were shared. A total of four sessions held over the course of the two-day workshop focused on unique but interrelated topics. A total of 26 leaders in various aspects of TT spoke during the workshop. There were more than 400 registered attendees.

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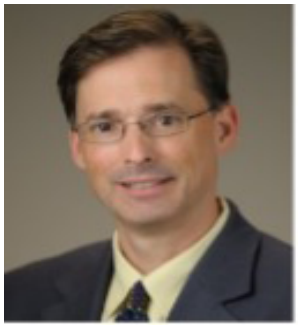
NCI Receives Federal Laboratory Consortium Mid-Atlantic Region Awards

The award winners were honored during the joint Mid-Atlantic and Northeast Regional Meeting, October 5-7, 2021. The FLC MAR selected “PRGN-2012, FDA Orphan Drug Designation for Recurrent Respiratory Papillomatosis” for the 2021 Excellence in Technology Transfer award. “The FLC MAR Excellence in Technology Transfer Award recognizes employees of FLC member laboratories in the region and non-laboratory staff who have accomplished outstanding work in the process of transferring federally developed technology. A panel of experts from industry, state and local government, academia, and the federal laboratory system judges the nominations.” Congratulations to the winning nominees:

Clint Allen, M.D.,
Principal Investigator in the section of Translational Tumor Immunology, NIDCD

Jeffrey Schlom, Ph.D.,
Chief
NCI CCR Laboratory of Tumor Immunology and Biology (LTIB)



James Gulley, M.D., Ph.D.
NCI CCR Genitourinary Malignancies Branch (GMB)

Christian Hinrichs, M.D.,
formerly with NCI CCR Genitourinary Malignancies Branch

Scott Norberg, D.O.,
NCI CCR Genitourinary Malignancies Branch

Michael Pollack, Ph.D.,
Supervisory Technology Transfer Manager, NCI TTC

Helen Sabzevari, Ph.D.,
President and CEO, Precigen

Douglas Brough, Ph.D.,
Senior Vice President and Head of Research, Precigen

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2021 NIH Clinical Center CEO Award

NCI TTC's Ken Rose, J.D. and Tedd Fenn, J.D. manage the technology transfer and patent activities for the NIH Clinical Center. When the COVID-19 pandemic broke in 2020 and as it continued in 2021, their "fast and competent action" [as stated by the Principal Investigator] coordinating, drafting, and negotiating complex agreements with universities and companies enabled the Clinical Center to partner with many institutions across the globe to help diagnose COVID-19 patients and predict clinical outcomes quickly and accurately. For this work, the Clinical Center recognized Mr. Rose and Mr. Fenn as part of a team for outstanding achievements with a 2021 NIH Clinical Center CEO Award.

NHGRI NIH Non-Inventor Cash Award

Claire Driscoll, NHGRI Technology Transfer Office Director, received a NIH Non-Inventor Cash Award (2021) from NHGRI for expert management of the patent portfolio and licensing of NHGRI-owned technology related to the drug lonafarnib as well as the negotiation of associated agreements for the clinical development of the drug over more than 15 years. Lonafarnib (trade name Zokinvy™; the drug is owned by Eiger Biopharmaceuticals, Inc.) became the first ever FDA-approved treatment for Hutchinson Gilford Progeria Syndrome (HGPS or Progeria), an ultra-rare genetic disease, in November 2020.

Eggerton Campbell, NHGRI Senior Licensing and Patenting Manager, received a NIH Non-Inventor Cash Award (2021) from NHGRI for assistance with the management of the patent portfolio and licensing of NHGRI-owned technology related to the drug lonafarnib. Lonafarnib (trade name Zokinvy™; the drug is owned by Eiger Biopharmaceuticals, Inc.) became the first ever FDA-approved treatment for Hutchinson Gilford Progeria Syndrome (HGPS or Progeria), an ultra-rare genetic disease, in November 2020.

The FLC MAR selected NCI TTC's Suna Gulay French, Ph.D. for the 2021 Rookie of the Year Award

"The Federal Laboratory Consortium (FLC) MAR Rookie of the Year Award recognizes the efforts of an FLC laboratory technology transfer professional (or technology transfer fellow) in the region who has demonstrated outstanding work in the field of technology transfer in a manner significantly over and above what was called for in the normal course of their work during the past year. The nominee must be new to technology transfer, with three years (or less) experience in a technology transfer position." The FLC MAR only selects one Rookie of the Year winner each year.

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2021 FLC National Award - CDC & NIAID Facilitate the Transfer of a CDC Trap for Control and Surveillance of Mosquitos, a Vital Public Health Tool

The Technology Transfer and Intellectual Property Office (TTIPO) at NIAID, in partnership with the CDC, oversaw licensing and patenting of a low-cost and pesticide-free trap to monitor and control mosquito populations.

Mosquitoes can spread deadly viruses — such as dengue, Zika, chikungunya, and yellow fever — that can cause significant outbreaks and disease. The World Health Organization reports that almost half of the world's population is at risk for dengue, and there are up to 390 million dengue infections annually. Aedes species mosquitoes can transmit viruses through bites to people. They are found throughout tropical and subtropical countries around the world, including U.S. territories and the southern United States.

Photo credit: CDC National Center for Emerging and Zoonotic Infectious Diseases (NCEZID) Puerto Rico Laboratory

CDC leveraged numerous technology transfer mechanisms in developing and commercializing the Autocidal Gravid Ovitrap (AGO) trap technology. Researchers collaborated with partners, conducted field studies and authored or co-authored 20 publications on this work. Inventors and staff promoted AGO traps via 38 scientific conferences and marketing. CDC's Technology Transfer Office handled first patent applications, agreements and licensing.

TTIPO initiated or facilitated 16 different agreements with interested parties, including a non-exclusive licensing agreement with AP&G signed in November 2016.

Partners at AP&G licensed, further developed and incorporated CDC's technology into a commercialized product under the company's Catchmaster® brand. AP&G entered the mosquito management industry with the CDC-developed non-toxic Ovi-CatchTM trap. AP&G sells the traps to pest management companies, consumers and property owners throughout the United States.

This effort furthers CDC's and NIAID's mission to protect Americans from health and safety threats, both foreign and domestic. AGO traps have proven successful in surveillance, mosquito control and disease reduction. Field trials in which AGO traps were installed in most homes in a community have shown that they reduce not only mosquito populations but also rates of infection. This important CDC invention and the technology transfer efforts that led to its commercialization continues to prevent mosquito-borne disease and improve lives for those in high-risk areas.

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2021 FLC National Award - HHS Agencies Unite to Fight COVID-19 by Rapidly Sharing SARS-CoV-2 Samples and Materials

Collaboration among three Department of Health and Human Services (HHS) agencies enabled rapid sharing of viral materials to accelerate the scientific and medical responses to the coronavirus disease 2019 (COVID-19) pandemic.

In early 2020, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified as a novel virus and tracked around the world. Rapid sharing of SARS-CoV-2 materials, especially SARS-CoV-2 virus strains, thus became essential to improve the general understanding of the virus and support the development of effective diagnostics, treatments, and vaccines.

Fortunately, the HHS agencies had previously developed a strategy for sharing viral and biological samples during the Zika virus epidemic in 2016. Since that time, NIAID, the Centers for Disease Control and Prevention (CDC), and HHS Office of Global Affairs developed a more efficient and collaborative approach for sharing critical viral materials.

Central to this effort, two mechanisms developed during the 2016 Zika outbreak were adapted to the COVID-19 pandemic. First, with critical input from technology transfer officers at NIAID, interagency partners developed a streamlined Materials Transfer Agreement for use in emergency situations. This Emergency Use Simple Letter Agreement (EUSLA) allows the materials to be used for any legitimate purpose required to rapidly prevent, detect, prepare for, and respond to the spread or transmission of SARS-CoV-2, including commercial development. Second, the team used a NIAID-supported biorepository to receive, grow, validate, and distribute viral materials. CDC reached out to its extensive global network of partner laboratories and sentinel surveillance sites to access SARS-CoV-2 samples in early February 2020. Similarly, NIAID was able to access samples from around the world by communicating through its grantee and contractor network.

The volume of transfers documented, and the diverse nature of the recipients attest to the success of this strategy:

- 29 organizations contributed materials to the biorepository
- 10,412 requests for materials fulfilled, all under EUSLA
- 7,541 agreements negotiated with 343 academic institutions, 744 companies, 55 federal and state agencies and 21 foreign governments
- Materials distributed to 50 states in the United States and Puerto Rico and 54 countries

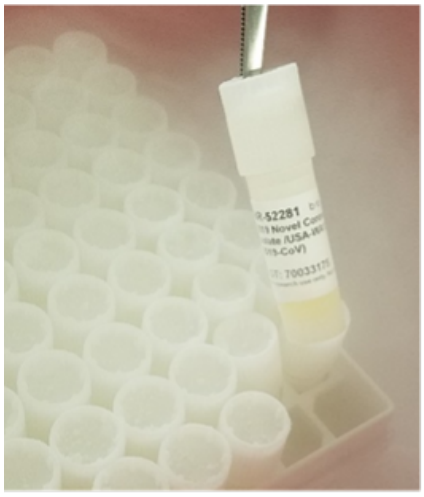

Figure 2. A SARS-CoV-2 isolate collected from a patient early in the pandemic. The vial is stored in NIAID supported repository and available upon request by qualified investigators.

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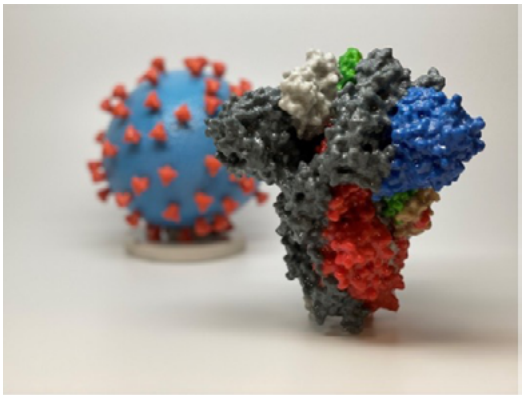
2021 FLC National Award for Excellence in Technology Transfer – NIAID Technology Transfer and rapid sharing of SARS-CoV-2 prefusion stabilized spike protein

Within hours of the public release of the viral genome sequence, scientists at the Vaccine Research Center (VRC) of the National Institute of Allergy and Infectious Diseases (NIAID) and their collaborators engineered a key protein from SARS-CoV-2, the virus that causes COVID-19, to enable its study as a vaccine candidate and for research applications. In the months that followed, NIAID, through its Technology Transfer and Intellectual Property Office (TTIPO), facilitated rapid distribution of the key protein to the global research community, enabling critical research and the global scientific response to the COVID-19 pandemic.



A 3-D printed model of a spike protein of SARS-CoV-2, the virus that causes COVID-19, in front of a 3D printed model of a SARS-CoV-2 virus particle. The spike protein (foreground) enables the virus to enter and infect human cells. Credit: NIAID

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 allow the virus membrane to fuse with the human cell membrane. The viral genes can then enter the host cell to be copied, producing more viruses.

Based on earlier work with SARS-CoV-1 and other coronaviruses, researchers at the VRC and collaborators were able to quickly engineer a version of SARS-CoV-2 with spike proteins stabilized in their prefusion conformation, which makes them more easily produced and a useful target for vaccine development relative to the native spike protein.

Despite similarities between the spike proteins of SARS-CoV-1 and SARS-CoV-2, three different antibodies for the SARS-CoV-1 spike protein did not bind to the SARS-CoV-2 spike protein in tests. This early finding suggested that potential vaccine and antibody-based treatments would need to be specific to SARS-CoV-2. It also demonstrated the importance of rapid sharing of SARS-CoV-2 prefusion stabilized spike proteins, and the plasmid molecules that encode them, with researchers working to develop treatments and vaccines.

As of October 8, 2020, NIAID had negotiated 83 Material Transfer Agreements (MTAs) with 70 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. Approximately 60% of the MTAs were signed within three days and more than 70% were completed within one week; nearly 80% were completed within two weeks.

To further expedite sharing for research use worldwide, NIAID leveraged its Biodefense and Emerging Infections Research Resources Repository (“BEI Resources”) to produce and distribute the spike materials. Since June 2020 BEI Resources has fulfilled 55 requests for SARS-CoV-2 spike plasmids. In September 2020 TTIPO also signed an agreement with National Institute for Biological Standards and Control (NIBSC), a large repository in the United Kingdom, to produce and distribute the materials.

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Additionally, 21 license agreements were executed with biotechnology and pharmaceutical companies for technologies related to SARS-CoV-2 prefusion stabilized spike proteins. Many of the licenses were signed within two weeks and the vast majority within one month. Most licensees planned to use the technology to support vaccine development.

2021 Licensing Executives Society (LES) Deal of Distinction - NIAID License to BioNTech Facilitated the Development of an mRNA Vaccine for SARS-CoV-2 (Comirnaty®)

The LES Deal of Distinction award recognizes major business transactions involving licensing, that exemplify best practices and creativity to achieve strategic product development objectives, with a significant impact on advancing innovation in the industry sectors that comprise LES which includes pharmaceutical and biomedical technology. This LES award specifically recognizes two deals that were negotiated by NIAID technology transfer officers with an array of partners in industry and academic institutions, or Industry University Government Interface (IUGI) sector. The result of this work was the development of one of the now widely recognized mRNA vaccines that provides a high level of protection against SARS-CoV-2 infection or the development of severe COVID-19.

In 2016, the National Institute of Allergy and Infectious Diseases (NIAID), the Scripps Research Institute, and Dartmouth College discovered that the spike proteins of a group of known coronaviruses can be engineered to maintain a shape that has many favorable properties for vaccine development. Once the SARS-CoV-2 genome sequence was released in January 2020, many members of the same collaborative team which now included employees of the University of Texas at Austin, worked to generate an engineered version of the SARS-CoV-2 spike protein and publish the results in less than 2 months.

Fauci receiving a COVID vaccine. Credit: NIAID

Shortly after the engineered SARS-CoV-2 spike protein was published, NIAID received a significant amount of interest from companies that wanted to obtain the right to incorporate the engineered SARS-CoV-2 spike into their vaccine platform technology, primarily to develop a commercial vaccine. At that point, it was not clear which potential vaccine candidate would be effective. Some of the potential licensees also planned to use novel but unproven platform technologies that had not been approved by the FDA or other regulatory agencies, such as mRNA. A multi-pronged development approach made the most sense, given the scope of the public health emergency posed by COVID-19. These circumstances made it clear that a non-exclusive license should be used to facilitate the development of many candidates, in case only one or few proved to be effective. Speed of development was also critical. This meant that an NIAID-Lead Inter-Institutional Agreement (IIA) to consolidate management of the patent rights with one party for patenting and licensing was also essential for rapid development. The federal licensing statutes and regulations require a formal review and approval

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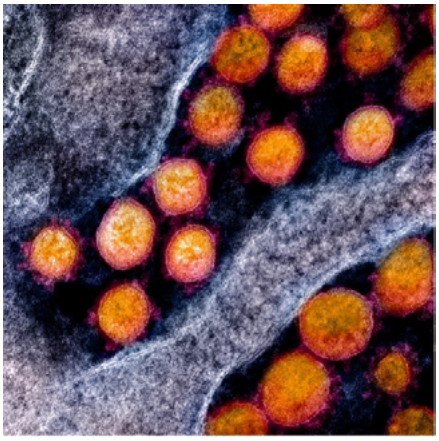
process before an exclusive license can be granted to any government owned intellectual property rights, so additional time was saved with a non-exclusive licensing strategy.

The 2020 license with BioNTech and subsequent partnership with Pfizer produced an mRNA-based vaccine that received a license to enter interstate commerce by the FDA and has been administered hundreds of millions of times across the world.

2021 FLC National Award - NIAID-Facilitated Clinical Trial Speeds Availability of Remdesivir for Treatment of COVID-19

A clinical trial of remdesivir for COVID-19 patients, sponsored by NIAID, wasn't just the first trial of its kind in the United States. In fact, findings from that trial led directly to two emergency use authorizations (EUAs) from the Food and Drug Administration (FDA) and ultimately to the FDA's first approval of a COVID-19 therapy without an emergency use qualifier.

The Technology Transfer and Intellectual Property Office (TTIPO) at NIAID worked with the NIAID Division of Microbiology and Infectious Diseases (DMID) to negotiate a Clinical Trial Agreement (CTA) with Gilead to obtain remdesivir and draft template agreements to expedite expanded testing within the United States and internationally. The creative technology transfer solutions and expeditiously negotiated agreements enabled initiation of the Adaptive COVID-19 Treatment Trial (ACTT) trial less than 2 months after identification of the virus responsible for the initial Wuhan outbreak.



Credit: NIAID

Remdesivir, an investigational antiviral drug developed by Gilead Sciences Inc., emerged as a promising early therapeutic candidate for COVID-19 based on preliminary studies involving other types of coronaviruses.

On February 21, 2020—before the World Health Organization had declared a pandemic—DMID and NIAID initiated the ACTT, a randomized, controlled clinical trial to evaluate the safety and efficacy of intravenous 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.

The FDA issued an EUA on May 1, 2020 for the emergency use of remdesivir to treat hospitalized patients with severe COVID-19, and on August 28 expanded the EUA by no longer limiting its use to patients with severe disease.

On October 22, 2020, the FDA approved remdesivir for the treatment of most COVID-19 patients that require hospitalization, the first therapy to receive a non-EUA approval for COVID-19 use.

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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

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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/

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