Research Administration of Clinical and Translational Sciences Awards (CTSAs)

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Abstract

The administration of large collaborative, multi-institutional, multi-faceted projects is complex. The CTSA grant recipient institutions must be flexible to an ever-changing structure that increases exponentially in scope. For top-tier research to take place, the researchers must be supported with top-tier research administration. The three CTSAs represented here are demonstrating that when we collaborate, everyone WINs.

Introduction

The CTSA's are funded by multi-million dollar support from the National Center for Advancing Translational Sciences (NCATS).

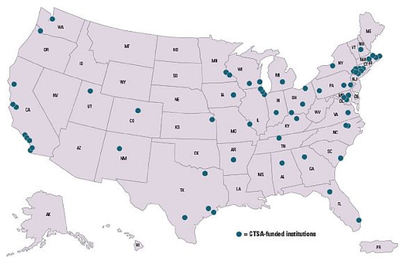
WU (ICTS): The mission of the Washington University Institute of Clinical and Translational Sciences (WU ICTS) is to speed the translation of research findings into their application to improve prevention, diagnosis, and treatment. The ICTS is a catalyst for intra- and inter-institutional cooperation and collaboration at Washington University (WU) its partnering health care system BJC HealthCare, and our academic partners Saint Louis University (SLU), the St. Louis College of Pharmacy (STLCOP), and the University of Missouri-Columbia (MU). These and other partnerships with academic, health care, and community organizations support the ICTS mission and the overarching goals of the national CTSA consortium.

IU (CTSI): The Indiana Clinical and Translational Sciences Institute (CTSI) is a statewide collaboration of Indiana University, Purdue University and the University of Notre Dame, as well as public and private partnerships, which facilitates the translation of scientific discoveries in the lab into clinical trials and new patient treatments in Indiana and beyond. Our overall goal is to transform the participating institutions to create an environment that facilitates the conduct of clinical and translational science research.

NWU (NUCATS): The Northwestern University Clinical and Translational Sciences (NUCATS) Institute launched in 2007 and received a $30 million Clinical and Translational Science Award (CTSA) grant from the National Institutes of Health (NIH) in 2008. In August 2015, the NIH renewed NUCATS CTSA grant for $27.2 million over four years. It is positioned as the homebase for clinical and translational science at Northwestern University and its clinical affiliates. NUCATS functions as an integrated hub supporting and accelerating clinical and translational science across Northwestern University (including six schools), our three nationally-renowned clinical partners, our Chicago community and stakeholders, and the broad consortium of CTSA-funded institutions. Our vision is to transform NUCATS into a national model of highly integrated academic nexus that continually increases the quality, safety, efficiency and speed of innovative clinical and translational research.

CTSA Nationwide

To reduce the length of time between scientific discoveries becoming health benefits, the National Center for Advancing Translational Sciences created an innovative national network of more than 50 medical research centers that work together to improve the translational research process. Currently, it is estimated that it takes an average of 17 years for only 14% of new scientific discoveries to enter day-to-day clinical practice.[1] The CTSA Program was created to enhance the efficiency of the translational research enterprise. The CTSA hubs locally and regionally catalyze innovation in training and research resources.[2]



References

1 Westfall JM, Mold J, Fagnan L. Practice-Based Research—"Blue Highways" on the NIH Roadmap. *JAMA*. 2007;297(4):403-406. doi:10.1001/jama.297.4.403

2 Clinical and Translational Science Awards Program Factsheet: https://ncats.nih.gov/files/CTSA-factsheet.pdf

3 Smart IRB: https://smartirb.org/

4 ACTA: https://www.ara4us.org/

CTSA Programs

CTSA services are available for every phase of clinical and translational research projects. The cores and programs under the CTSA offer support for investigators at each phase of the clinical and translational research process:

Idea: transforming an initial idea into a testable hypothesis
Protocol: developing a protocol, budget and IRB submission
Implementation: supporting implementation of the research project, including data services, patient facilities and advanced imaging
Analysis: assisting with data analysis and interpretation of results
Dissemination: providing expertise about identification and resolution of barriers to implementation of evidence-based practice in community settings
Translation: assisting with translating research discoveries into commercial application and evidence-based practice

Examples of CTSA Program Support at WU, IU, and NWU

Infrastructure	Project Development	Clinical and Translational Research	Translational Workforce Development
• Governance/Administration • Regulatory Support • Evaluation and Continuous Improvement • Quality and Efficiency	• Informatics • Pilot Funding/Project Development Teams • Research Design and Biostatistics • Research Ethics • Community Engagement	• Recruitment of Research Participants • Clinical Interactions • Multi-Site Study Support • Genetics and Genomics • Implementation Science & Entrepreneurship	• Institutional Career Awards (KL2) • NRSA Training Grant (TL1) • Masters and Certificate Programs • Summer internships • Staff

Impact on Research Administration

National Initiatives

SMART IRB

The CTSA program encourages collaboration across CTSA institutions nationwide. These collaborations can often lead to regulatory and administrative burdens which may result in a delay of study activation. To assist in easing the potential burdens of obtaining multiple IRB approvals for multisite studies, NCATS supported a single institutional (IRB) platform for Multisite clinical studies through the CTSA program: the NCATS Streamlined, Multisite, Accelerated Resources for Trials (SMART) IRB Platform. SMART IRB is a platform designed to ease common challenges and burdens associated with initiating multisite research and provide a roadmap for institutions to implement the NIH Single IRB Review policy. Through a flexible master IRB reliance agreement, standard operating procedures, and complementary tools and resources, SMART IRB supports and encourages collaboration and harmonization across the nation while ensuring a high level of protection for research participants. To date, SMART IRB has 152 participating institutions, including all 64 CTSA hubs. [3]

ACTA Accelerated Clinical Trial Agreement

The goal of the CTSA sponsored initiative is to increase the speed of study initiation of multi-site clinical trials by providing a pre-agreed upon template. The position of the ACTA is straightforward and incorporates needs of both the Industry Sponsor and the Institution. More than 50 organizations representing over 225 sites have agreed that the terms of the ACTA would be acceptable. Outreach has begun to initiate pilots, and 5 pilot studies are currently active. [4]

Multi-Institutional Funding

The CTSA's multi-institutional partnerships not only require the use of standard subcontracts, but other mechanisms to transfer funds to the appropriate institution. The CTSA's along with being award recipients of NCATS, also act as awarding agencies, operating multiple pilot funding competitions. When internal pilot funds are awarded from one institution to another, it can create challenges. Sometimes the awarded institution is asked to use their own match funds for the award, other times collaboration between the institutional central offices is necessary. In other cases, the award recipients may be community partners who need guidance on the rules and regulations of the funding.

Account/Subaccount Structure

For one CTSA award, multiple accounts and subaccounts are used in order to connect the funding to the applicable program. The CTSA's operate multiple programs that act in the same way as a Division, but are generally not set up formally in that way. This requires account and subaccount naming convention and mapping, not only so the research administrators can easily recall the accounts and their corresponding programs, but also to enable internal financial reporting over the life of the grant.

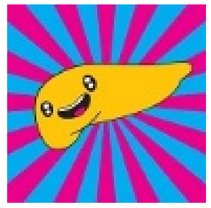
Success Stories

WU ICTS Pilot Funding Program & Regulatory Support Center

Wolfram Syndrome (WS) is a rare, autosomal recessive disorder characterized by juvenile diabetes, optic nerve atrophy, deafness, and neurodegeneration. WS is often fatal by mid-adulthood due to multi-organ health complications. Dr. Fumihiko Urano received ICTS support to understand the molecular ER dysfunction mechanisms in WS, develop biomarkers to monitor progression and to identify patient-based therapeutics to identify actionable targets. In 2011, Dr. Urano received a **2-year ICTS pilot award** to establish a yearly clinic for phenotypic characterization of children with WS and to collect/bank iPSCs from patients and family members to uncover biomarkers. Study results confirmed that WS has a pronounced impact on early brain development, accompanied with impairments in gait and balance and Identified Calpain-2, a Ca+2 dependent protease implicated in ER –stress mediated and amyloid- mediated neuronal and beta cell death. The **ICTS Regulatory Core** then assisted in preparation of Orphan Drug Designation request for dantrolene sodium to the FDA. Dr. Urano received an **ICTS STAR Award** for "Dose Escalation Studies for Dantrolene in Mouse and iPSC Models of WS" and an **ICTS JIT award** to prepare regulatory documents for "Phase 1b Clinical Trial for Dantrolene in Patients with Wolfram Syndrome (IND 133439)". A Phase 1b Safety and Tolerability Trial in pediatric and adult WS patients was initiated and the FDA approved dantrolene sodium in WS treatment. To date, 3 patients have been enrolled in the Dantrolene Clinical Trial.

Indiana CTSI Community Health Engagement Program

Blood Sugar, Your Pancreas and Unicorns: Engaging Patients to Prevent and Treat Diabetes



The **Patient Engagement Core** was instrumental in the development of the diabetes management plan of Dr. Tamera Hannon's study, "Advancing Diabetes Management in Adolescents Using Health Information Technology." The diabetes management plan was developed in collaboration with youth-parent pairs who gave input into what would help promote adherence to treatment while easing family conflict that so often occurs in these families. The collaboration produced the booklet, "Why are you testing me for diabetes? A book about blood sugar, your pancreas & unicorns." According to Dr. Hannon, "The voice of the patient is key to developing a cost-effective, real world, pragmatic lifestyle modification interventions that can be routinely integrated at a population level in communities and health care systems and readily accessed and utilized by those youth at highest risk for diabetes and their families."[3]

NUCATS, TL1 Pre-Doctoral Training Program & Center for Education and Career Development (CECD)

Peanut Allergy Turned off by Tricking Immune System

As part of the **TL1 Pre-Doctoral Training Program,** Charles Smarr, PhD Candidate, worked with mentor Stephen Miller, PhD, in his research on turning off life-threatening allergic response to peanuts by tricking the immune system into thinking the nut proteins aren't a threat to the body, according to a new preclinical study from Northwestern Medicine. The peanut tolerance was achieved by attaching peanut proteins onto blood cells and reintroducing them to the body – an approach that ultimately may be able to target more than one food allergy at a time.

Using a mouse model that mimics a life-threatening peanut allergy, researchers attached peanut proteins onto white blood cells called leukocytes and infused those back into the mice. After two treatments, the mice were fed a peanut extract. They did not have the life-threatening allergic reaction because their immune system now recognized the protein as safe.

Miller also has used the same approach in autoimmune diseases. His previous published research has shown the same technique to stop the progression of multiple sclerosis and type 1 diabetes, both autoimmune diseases, in animal models. This approach is currently being tested in multiple sclerosis patients in a phase I/IIa clinical trial.

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