Catalyzing Innovation: NIH National Center for Advancing Translational Sciences

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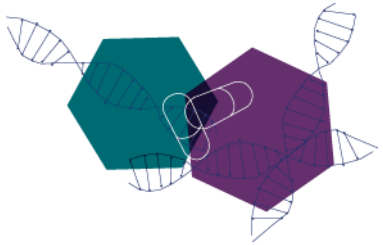
NIH National Center for Advancing Translational Sciences



Creation of the National Center for Advancing Translational Sciences (NCATS)

- Established on December 23, 2011
- Part of Consolidated Appropriations Act 2012 (PL 112-74)

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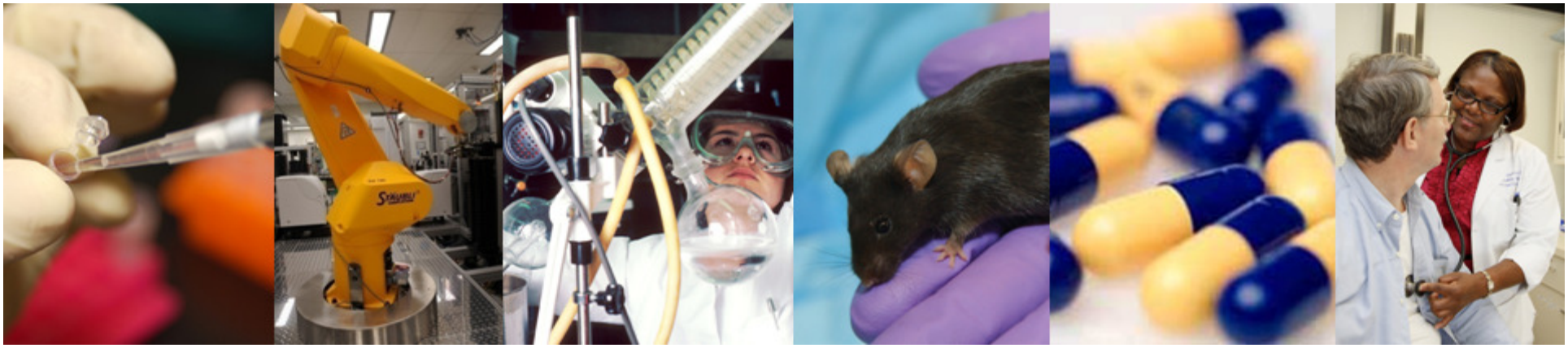
NCATS Mission



To catalyze the generation of innovative methods and technologies that will enhance the development, testing, and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions.

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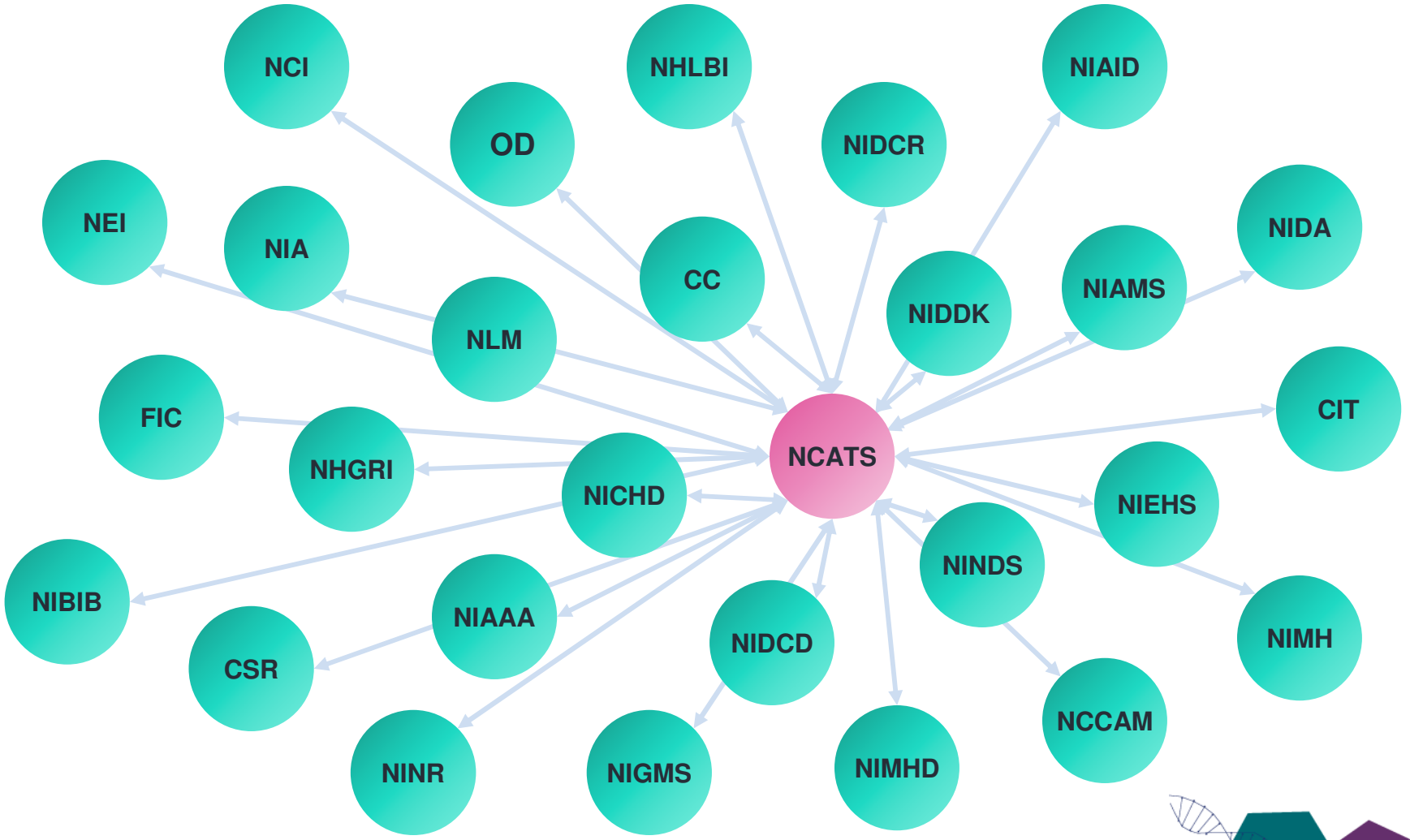
Catalyzing Collaborations Within NIH



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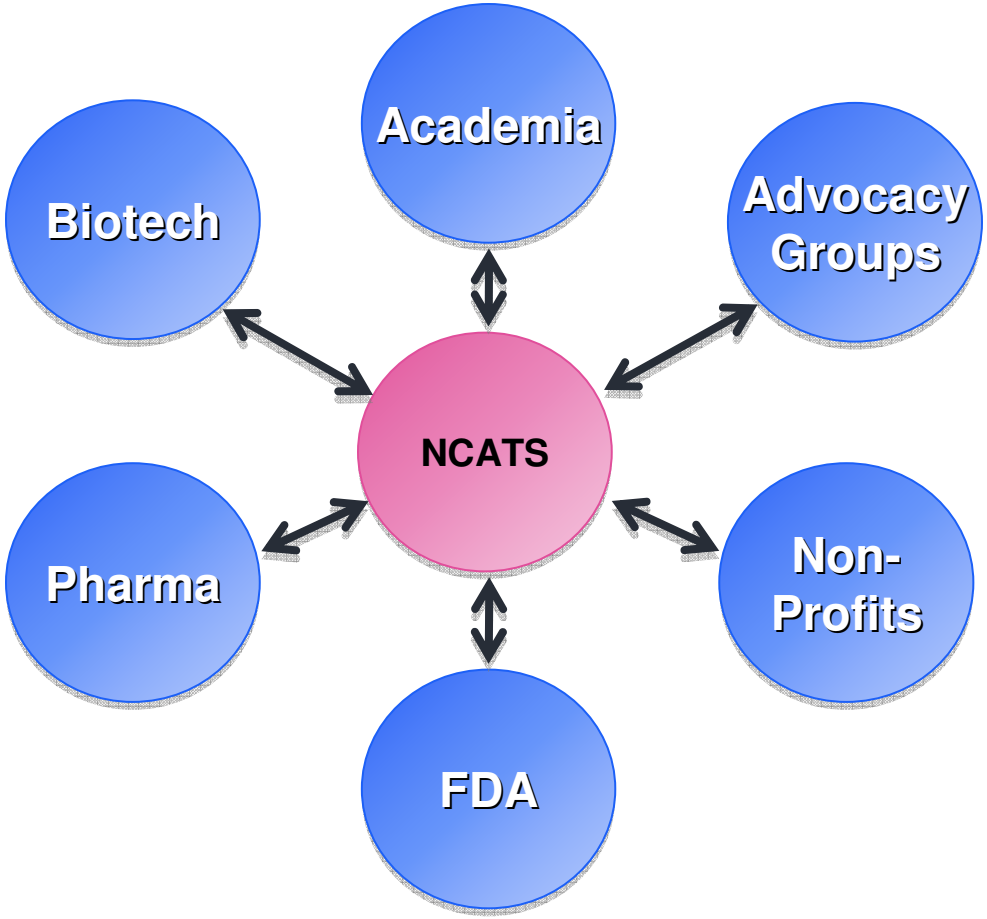
Catalyzing Collaborations Outside NIH



- Complements — does not compete with — the work of others
- Revolutionizes the process of translation by promoting innovative research
- Galvanizes and supports new partnerships
- Supports and augments regulatory science and its application
- Expands the precompetitive space

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NCATS Organization

COUNCIL/ CAN BOARD

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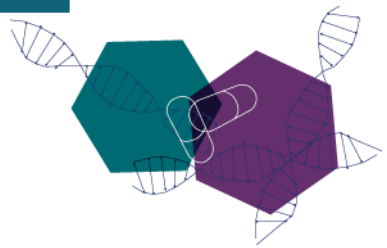
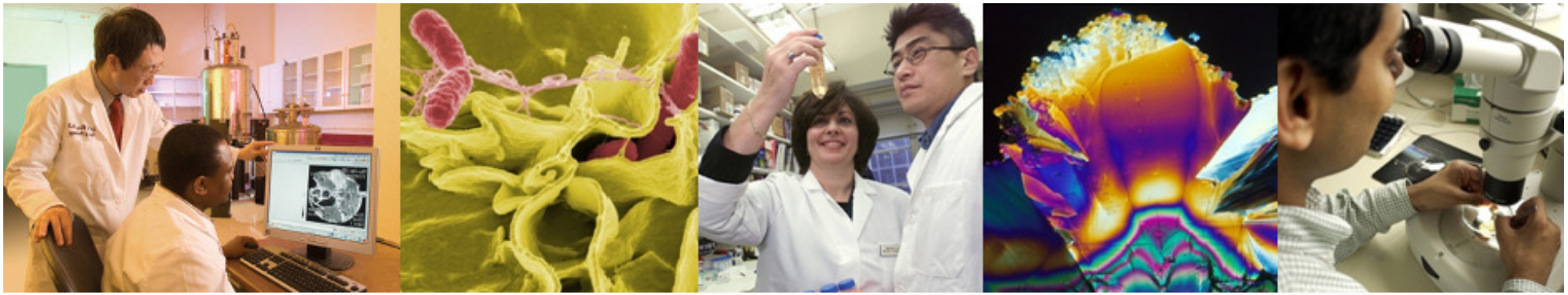


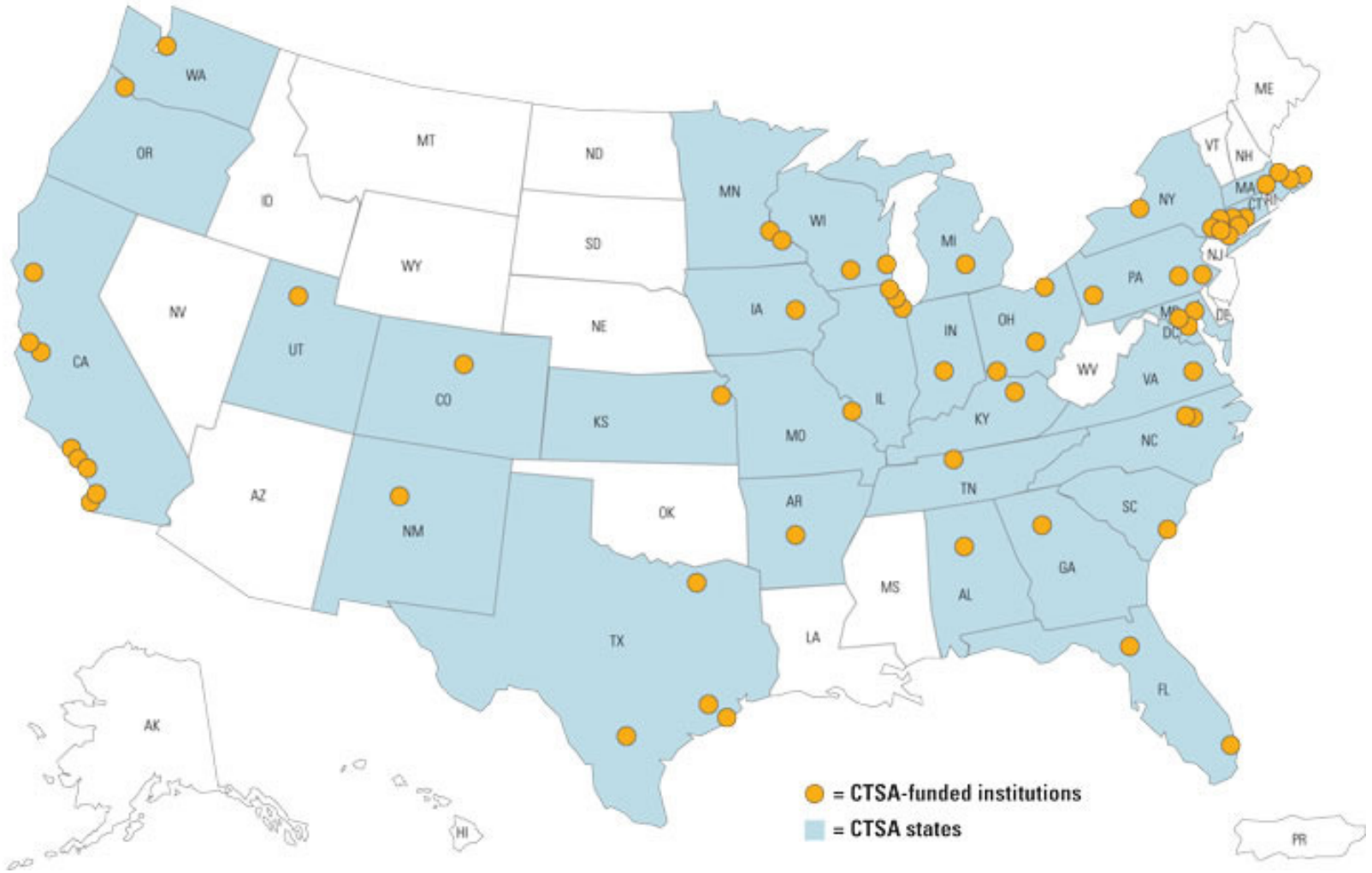
Clinical and Translational Science Awards are led by NCATS Division of Clinical Innovation

CTSAs:

- Support a national consortium of medical research institutions
- Work together to improve the way clinical and translational research is conducted nationwide
- Accelerate the research translation process
- Provide robust training for clinical and translation researchers

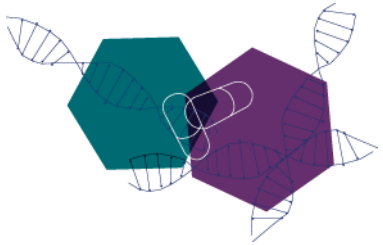


Clinical and Translational Science Awards (CTSA) Program Sites



CTSA Vision

- Strengthen the entire spectrum of NIH supported translational research
- Build upon and support institutional strengths
- Provide research resources and services that improve the quality, validity, generalizability, and efficiency of clinical and translational research
- Train the workforce for translational research
- Provide the foundation for translational research at academic institutions, particularly NIH supported research
- Promote innovation in the methods and processes to support high quality and efficient translational research at lower cost that are generalizable across disease and specialty domains



CTSA Public-Private Partnerships Key Function Committee

Nate Hafer, University of Massachusetts
Scott Steele, University of Rochester, Co-chairs

CTSA Intellectual Property Portal (CTSA-IP)

- Intellectual Property information exchange
- Aim to link publicly available licensing opportunities from CTSA Institutions in an easily searchable format and facilitate partnerships
- 32 CTSAs and the NIH now contribute technologies
- Linkage with several technology management systems
- Collaboration with iBridge to establish CTSA-IP community

Recent CTSA-OTT Survey

Purpose: Explore how CTSAs interface with their respective technology transfer offices (TTO) to identify and support the development and commercialization of medical innovations to improve public health.

Next Steps: Created a writing team to summarize data for publication. Evaluate programs and initiatives to potentially pilot across CTSA Consortium.

CTSA Public-Private Partnerships Key Function Committee

Webinar series

- Highlight examples of PPPs that facilitate research translation
- Hosted 19 presentations since July 2011
- Examples have come from CTSAs, industry, NIH and FDA programs, foundations
- Covered many key PPP models and initiatives
- All recorded and available on ctsacentral.org

Regulatory Science Workgroup

•Joint initiative between PPP KFC and Regulatory Knowledge KFC
•Participants include CTSAs, FDA, CERSIs, NCATS
•Exploring needs and opportunities for CTSA's to participate in collaborative Regulatory Science research and training programs aligned with FDA and NIH goals

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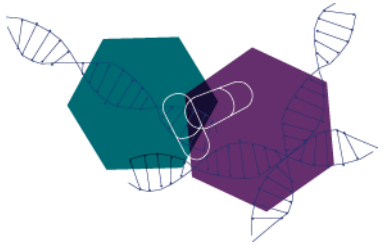
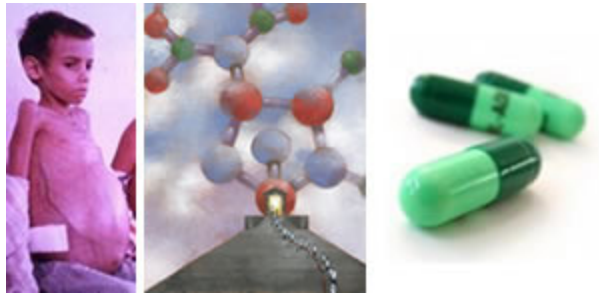
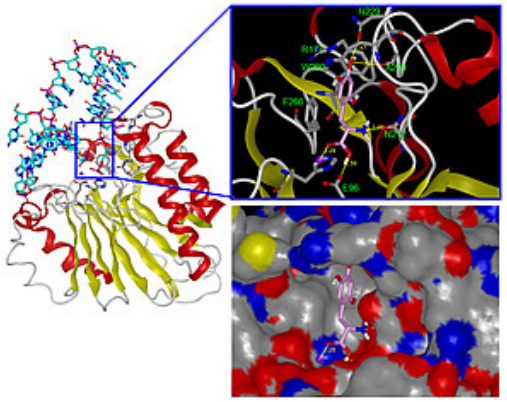


Division of Pre-Clinical Innovation (DPI)

- Therapeutics for Rare and Neglected Diseases (TRND)
- Toxicology in the 21st Century (Tox21)
- Bridging Interventional Development Gaps (BrIDGs)
- Molecular Libraries Probe Production Center
- Assay Development





DPI currently has 300+ collaborations with investigators across the U.S. and around the world.

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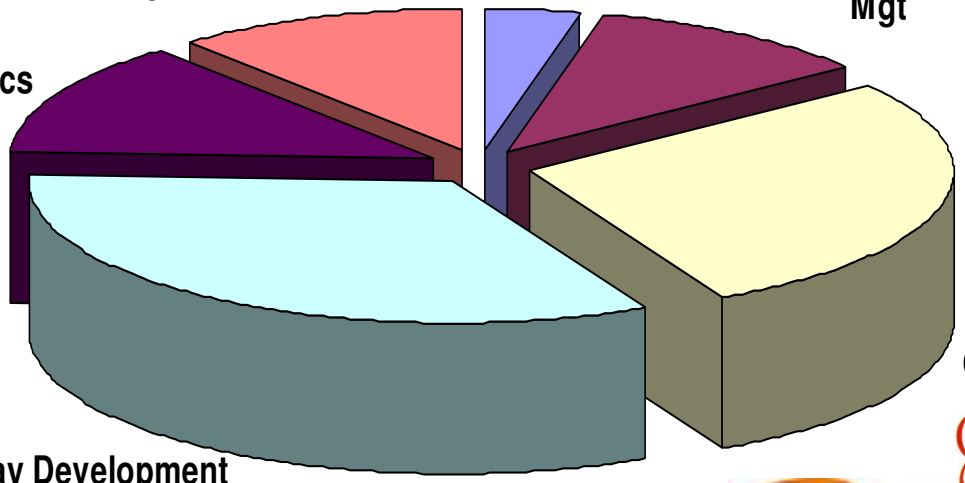
NCATS' DPI Staff

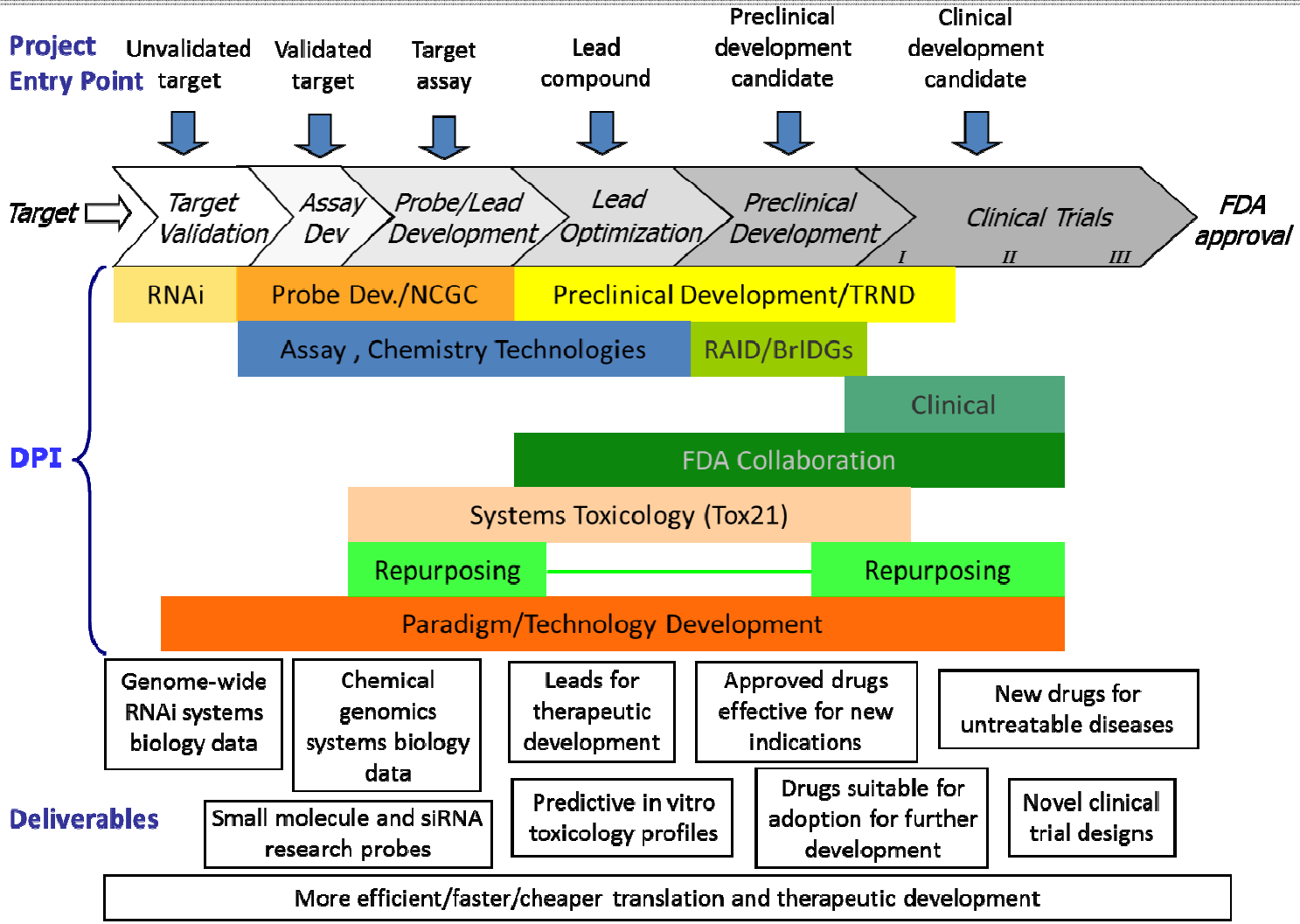


Amphora
Pfizer
Lilly
HGS
NORTHROP GRUMMAN
DEFINING THE FUTURE
CELERA
an Applera Corporation Business
LARGE SCALE BIOLOGY
AMGEN
Wyeth
ArQule
Lexicon pharmaceuticals
SANOFI
Johnson & Johnson
MERCK
gsk GlaxoSmithKline
Caliper LifeSciences
Infinity PHARMACEUTICALS
Pharmacopeia
BD BD Biosciences
AstraZeneca

DPI is Different in Science and Operation

- DPI is administratively intramural
  - No independent PIs, **no tenure** system
  - All projects are **collaborations,** 90% of which are with extramural investigators/foundations/companies
  - Projects are selected via **solicitation/review**
- Science is intermediary between mechanistic research and commercialization
  - **"Adaptor" function**
  - Each project has **tangible deliverable** and technology/paradigm development components
- It is **disease agnostic,** works across disease spectrum
  - **Common mechanisms** and principles to make translation better/faster/cheaper for all
- Focuses on **new technologies, enabling tools,** dissemination

NCATS DPI: A Collaborative Pipeline



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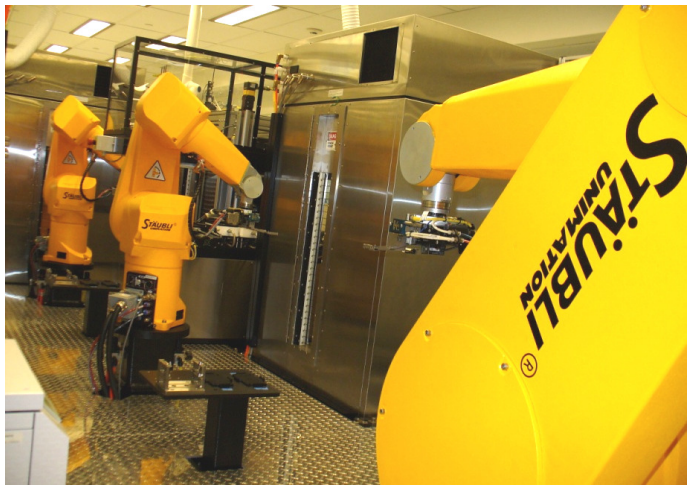
NIH Chemical Genomics Center

- **Founded 2004, part of MLP**
- **85 scientists**
- **> 200 collaborations with investigators worldwide**
- **Assay development, HTS, chemical informatics, medicinal chemistry: "target to lead"**
- **Focus is unprecedented targets, rare/neglected diseases**
- **Mission**
  - Chemical probes/leads
  - New technologies/paradigms to improve efficiency and success rates of target-to-lead stage of drug development
  - Chemical genomics: general principles of small molecule – target interactions



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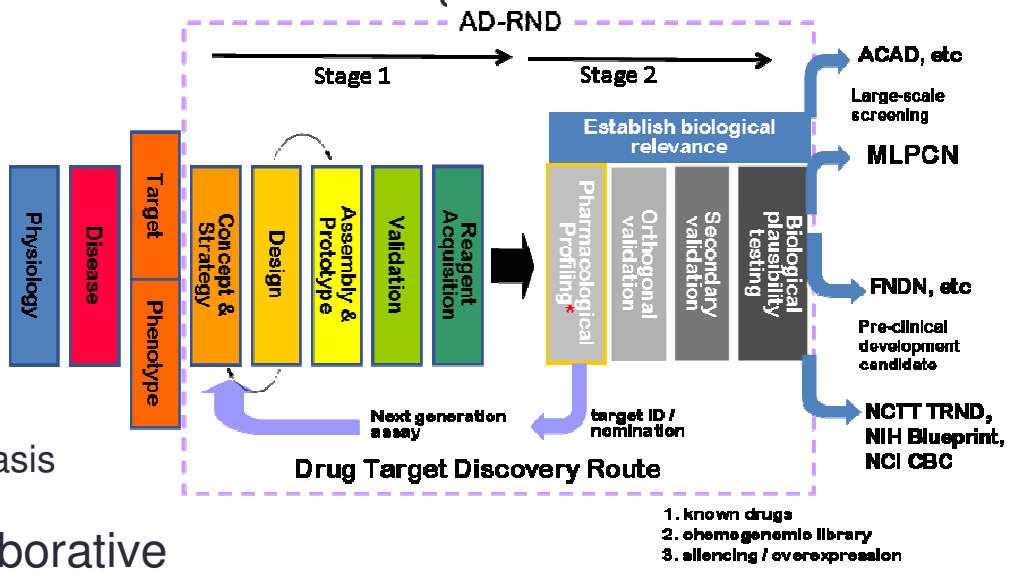
Assay Development and High Throughput Screening Technologies (ADST)

The ADST Laboratory focuses on the development of a more efficient gateway to the drug discovery paradigm through evaluation, development, and refinement of assay strategies and technologies in collaboration with key experts and stakeholders.

Create/guide the primary and follow-up assay portfolio needed in the pursuit of therapeutics discovery and development for rare and neglected diseases.



➢ Current pilot projects:

- Peripheral and Optic neuropathies
  - —Charcot-Marie-Tooth Disease (CMT)
  - — Retinitis pigmentosa & Glaucoma
- Erythroblastopenia
  - —Diamond–Blackfan Anemia (DBA)
- Parasitic infections
  - —Lymphatic filariasis & Onchocerciasis
  - —Malaria

➢ Funding Mechanisms: Highly Collaborative

- Foundations' gifts
- CRADAs, RCAs
- In-kind research support

Goal: *To formalize this resource through a program/solicitation for* ***assay development for rare and neglected diseases (AD-RND).***

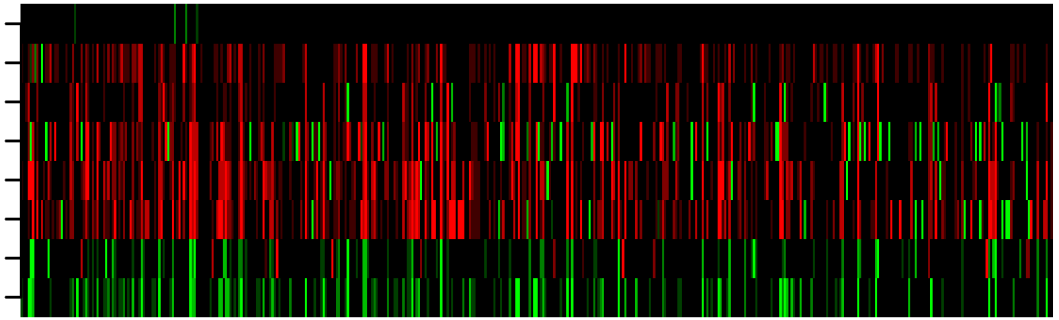
Chemistry Technology Development

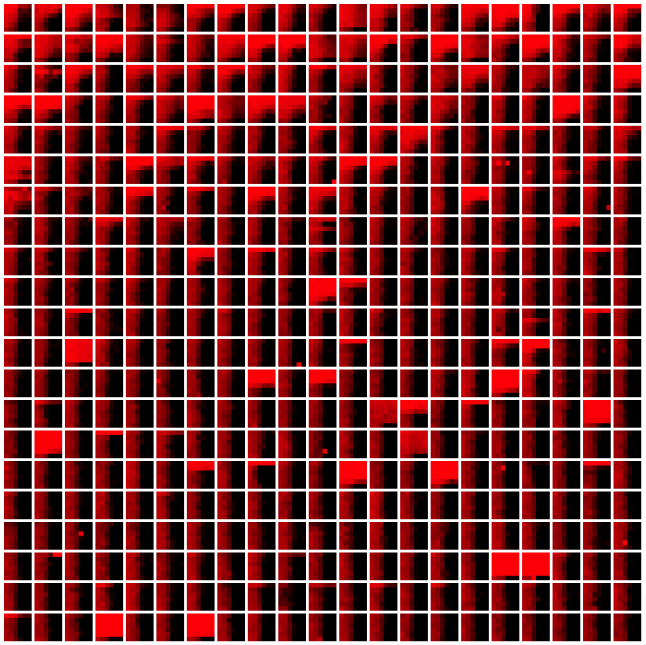
Mission: *To expand and support translational initiatives through the application of new research ideas at the interface of chemistry and biology.*

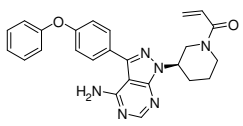
❖ ***Matrix Screening:*** *To establish a dose matrix 1536-well format screening platform for the discovery of novel drug combinations.*

Funding Mechanism: *NCI Major Opportunities Program. Current Projects are mostly NCI oncology-related projects, however, future projects/collaborations may be possible through Request for Proposals, but that is yet to be determined.*

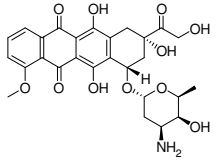
Matrix Drug Screening for Combination Therapies in Cancer Program: Phenotypic and Combination Screening for the Discovery of novel Drug-Drug Pairs



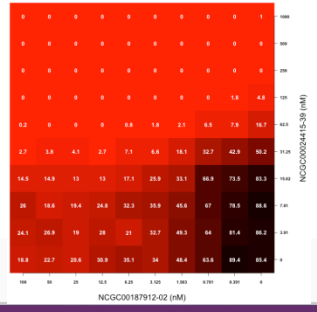




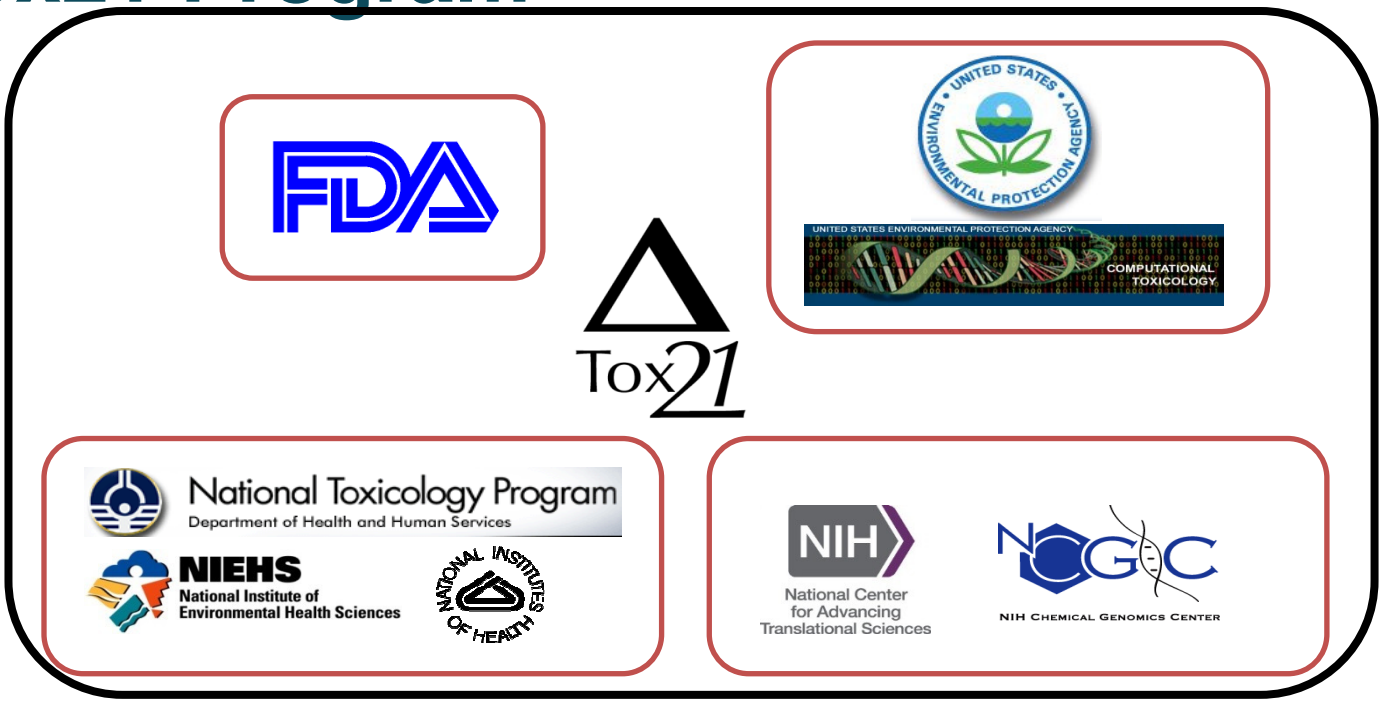
Ibrutinib
NCGC00187912



Doxorubicin
NCGC00024415



Toxicology Technology Development: The Tox21 Program



- Project Initiation through the Tox21 Assay and Pathways Working Group: Receives, reviews, and approves nominations for proposed assays from the scientific community

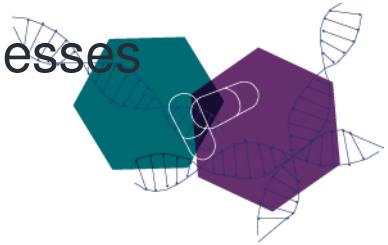
Goals of Program:

1. *Identify mechanisms of compound-induced biological activates*
2. *Prioritize chemicals for more extensive toxicological evaluation*
3. *Develop predictive models for biological response in humans*

- Once an assay is approved, NCATS/NCGC optimizes, validates, and screens a specially designed library of environmentally relevant compounds; roughly 11,000 compounds are screened by quantitative-High Throughput Screening for each approved assay.

Bridging Interventional Development Gaps (BrIDGs) Program

- Model: Contract access collaboration between DPI and extramural labs (Formerly NIH-RAID Program)
- Projects
  - Enter with clinical candidate identified
  - Any disease eligible
  - Gap analysis followed by data generation using DPI contracts to generate data necessary for IND filing
  - Exit at or before IND
  - Milestone driven
  - Therapeutic modalities: any (small molecules, peptides, oligonucleotides, gene therapy, antibodies, recombinant proteins)
- Eligible Applicants
  - Academic (US and Ex-US), Non-Profit, SBIR eligible businesses



BrIDGs Highlights

- 180 applications submitted since 2005
  - 34 approved
- 19 completed projects (two in FY12)
  - 12/12 submitted INDs approved
  - 5 projects in Phase 1, three in Phase II
  - 5 agents licensed during or after BrIDGs involvement

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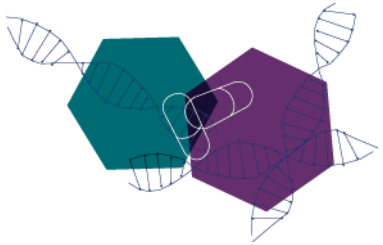

BrIDGs Portfolio

Applicant	Organization Name	Org Type	Agent	Disease	Funding
Au, Jessie	Optimum Therapeutics	Biotech	Small Molecule	Pancreatic Cancer	Common Fund
Bankiewicz, Krystof	University of California San Francisco	Academic	Gene Vector	Aromatic L-amino acid decarboxylase	CF/NINDS
Bloch, Kenneth	Massachusetts General Hospital	Academic	Small Molecule	FOP & Anemia of Inflammation	CF/NIAMS/NIDDK
Darling, Thomas	Edunn Biotechnology	Biotech	Oligonucleotide	Alzheimer's disease	CF/NIA
De Leon, Diva	Children's Hospital of Philadelphia	Academic	Peptide	Hyperinsulinism	Common Fund
Donn, Karl	Parion Sciences, inc.	Biotech	Small Molecule	Chronic dry eye	Common Fund
Dowling, Peter	University of Medicine and Dentistry of New Jersey	Academic	Peptide	Multiple sclerosis	Common Fund
Evans, Christopher	Beth Israel Deaconess Medical Center	Academic*	Gene Vector	Osteoarthritis	Common Fund
Kunos, George	NIH/NIAAA	Intramural*	Small molecule	Metabolic syndrome	Common Fund
Mannstadt, Michael	Massachusetts General Hospital	Academic*	Peptide	Hypoparathyroidism	Common Fund
Mellon, Synthia	University of California San Francisco	Academic	Small Molecule	Niemann-Pick C	CF/NINDS
Miller, Kenneth	Kemmx Corporation	Biotech	Small molecule	Rheumatoid arthritis	CF/NIAMS
Rogawski, Michael	University of California, Davis	Academic*	Small molecule	Epilepsy	CF/NINDS
Sutula, Thomas	University of Wisconsin Madison	Academic*	Small Molecule	Epilepsy	Common Fund
Turner, Scott	Kinemed, Inc.	Biotech	Peptide	Atherosclerosis	Common Fund

* indicates that the investigator is partnered with a company

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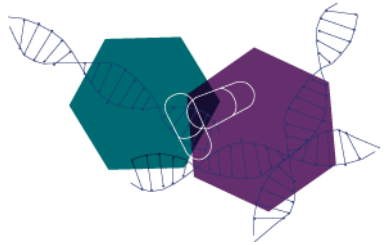

Therapeutics for Rare and Neglected Diseases (TRND) Program

- Model: Comprehensive drug development collaboration between DPI and extramural labs with disease-area / target expertise
- Projects
  - May enter at various stages of preclinical development
  - Disease must meet FDA orphan or WHO neglected tropical disease criteria
  - Taken to stage needed to attract external organization to adopt to complete clinical development/registration, max 2a
  - Milestone driven
  - Therapeutic modalities: small molecules, proteins
  - Serve to develop new generally applicable platform technologies and paradigms
- Eligible Applicants
  - Academic, Nonprofit, Government Lab, Biotech / Pharma
  - Ex-U.S. applicants accepted

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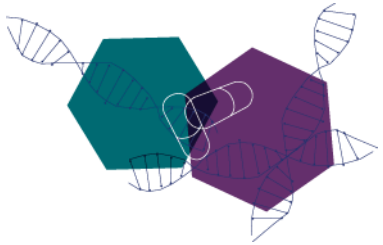
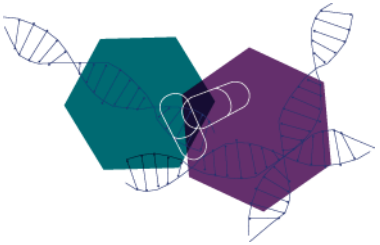


TRND Highlights

- **14 projects through pilot phase & 2 public solicitations since 2009**
  - Mix of small molecules and biologics
  - Two innovative platform technologies
- **3 investigational drugs taken into humans**
  - CLL: IND filed with US FDA 7/12/11, approved 8/5/11
    - Phase I trial commenced 9/11
  - SCD: IND filed 10/14/11, approved 11/10/11
    - Phase I trial commenced 12/11
  - HIBM: Complete response filed 7/27/12, approved 8/24/12
    - Phase 1 trial in patients commenced 9/13/12
- **Initiated first natural history study**
  - HIBM: NIH Clinical Center, 1st patient enrolled September 2011
- **Every project is a unique Public-Private partnership**
  - Many include foundation and patient advocacy input

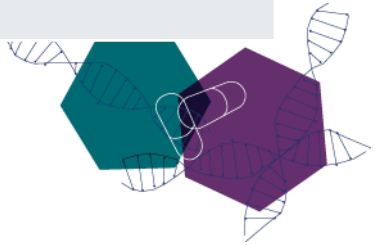


TRND Portfolio

Collaborator	Organization Name(s)	Partner Type(s)	Agent	Therapeutic Area / Disease
TRND Pilot Project	**NPC-SOAR, Washington Univ., Einstein College of Medicine, NICHD, NHGRI**	**Disease Foundation, Academic, DIR**	**Repurposed Approved Drug**	**Niemann-Pick C**
TRND Pilot Project	New Zealand Pharmaceuticals, NHGRI	Biotech, DIR	Intermediate Replacement	Hereditary Inclusion Body Myopathy
TRND Pilot Project	**Aes-Rx, NHLBI**	**Biotech, DIR**	**NME**	**Sickle Cell Disease**
TRND Pilot Project	Leukemia & Lymphoma Society, Kansas Univ. Cancer Center	Disease Foundation, Academic	Repurposed Approved Drug	Chronic Lymphocytic Leukemia
Reeves, Erica	**ReveraGen BioPharma**	**Small Business**	**NME**	**Duchenne Muscular Dystrophy**
Campbell, David	Afraxis, Inc.	Small Business	NME	Fragile X Syndrome
Garvey, Edward	**Viamet Pharmaceuticals, Inc.**	**Small Business**	**NME**	**Cryptococcal Meningitis**
Liu, Paul	NHGRI	DIR	Repurposed Approved Drug	Core Binding Factor Leukemia
Kimberlin, David	**University of Alabama**	**Academic**	**Nucleotide Analog Pro-drug**	**Neonatal Herpes Simplex**
Trapnell, Bruce	Cincinnati Children's Hospital	Academic	Biologic	Autoimmune Pulmonary Alveolar Proteinosis
Bloch, Kenneth	**Massachusetts General Hospital**	**Academic**	**NME**	**Fibrodysplasia Ossificans Progressiva**
Liu, Julie	CoNCERT Pharmaceuticals	Small Business	NME	Schistosomiasis
Davis, Robert	**Lumos Pharma**	**Small Business**	**NME**	**Creatine Transporter Defect**
Sazani, Peter	AVI BioPharma, Inc.	Small Business	Oligo (PMO)	Duchenne Muscular Dystrophy

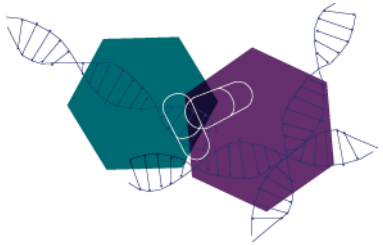
Comparison of BrIDGs and TRND

BrIDGs	TRND
Contract Resource	Team-based Collaboration
PI must have identified lead agent	PI may start with lead optimized
No clinical trial support provided	Some clinical trial support provided
IP retained by owner	TRND may generate IP
Universal disease scope	Rare and neglected diseases only
Investigator prepares IND	Regulatory affairs assistance provided



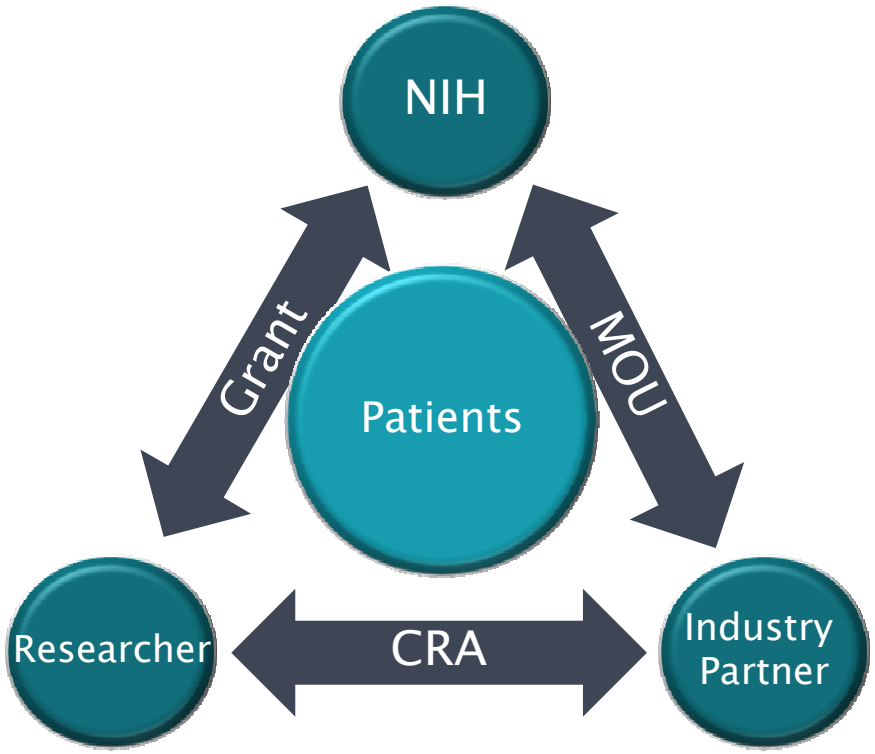
Characteristics of New NCATS Initiatives

- Address significant bottlenecks in the process of translation
- Highly collaborative across NIH, other government agencies, and with the private sector
- Quick to respond to needs of biomedical researchers



Discovering New Therapeutic Uses for Existing Molecules (Therapeutics Discovery)

NIH - Industry Pilot Program: Launched May 2012



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Therapeutics Discovery Pilot: Drug Rescue and Repurposing

- Collaborative pilot program matching researchers with compounds in an effort to find new uses for patients
- Creation of template agreements to streamline negotiations between researchers and pharmaceutical companies
- 58 compounds from eight companies:
  - Abbott
  - AstraZeneca
  - Bristol-Myers Squibb Company
  - Eli Lilly and Company
  - GlaxoSmithKline
  - Janssen Pharmaceutical Research & Development, L.L.C.
  - Pfizer Inc.
  - Sanofi

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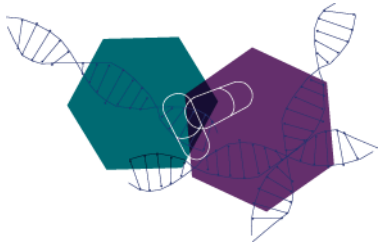
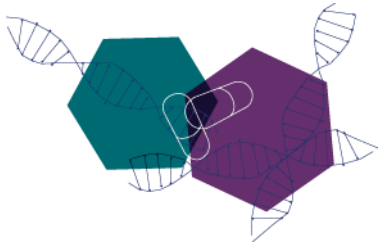


Therapeutics Discovery Pilot: Timeline

- **June 2012**: Funding announcement issued
- **August 2012**: X02 pre-applications received
- **December 2012**: Full applications due
- **May 2013**: Applications to council
- **May/June 2013**: Awards to be issued
- Program will be evaluated for success:
  - Does the use of template agreements speed negotiation time?
  - Does the pilot advance disease understanding?
  - Does the pilot result in promising new therapeutics?



Tissue Chip for Drug Screening: Microsystems Initiative

- Aims to develop tissue chips that mimic human physiology to screen for safe, effective drugs using best ideas in engineering, biology, toxicology
- NIH Investment (NCATS + Common Fund) = $70M/5 years
- DARPA Investment = $75M/5 years
- FDA Investment = Regulatory and toxicology expertise
- NCATS and DARPA independently manage and fund separate, but highly coordinated programs

FY12 Appropriated and Reimbursable Funds = $13.9M

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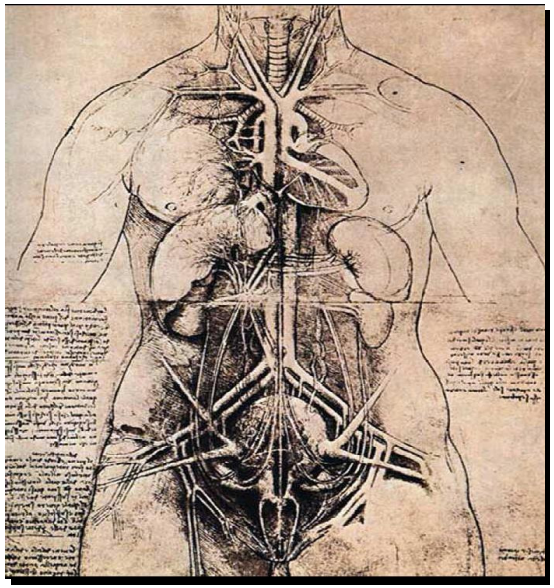
Tissue Chip Program

GOAL: Develop an *in vitro* platform that uses human tissues that will be predictive of efficacy, pharmacokinetics, safety and toxicity of promising therapies in humans and suitable for regulatory science use.



- All ten human physiological systems will be functionally represented by human tissue constructs:
- Circulatory
- Endocrine
- Gastrointestinal
- Immune
- Integumentary
- Physiologically relevant, genetically diverse and pathologically meaningful.
- Modular, reconfigurable platform for easy integration.
- Tissue viability for at least 4 weeks.
- Community-wide access.

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SBIR/STTR Topics of interest to NCATS

- Innovative platforms for identification and prioritization of targets for therapeutic intervention
- Technologies to determine alternative uses for existing therapeutic interventions
- Tools and technologies to allow assaying of activities of compounds on currently “non-druggable” targets
- Co-crystallization high-throughput screening techniques
- Small molecule and biologics analytical characterization
- Tools and technologies that increase the predictivity or efficiency of medicinal chemistry, biologic, or other intervention optimization
- Accelerate bioengineering approaches to the development and clinical application of biomedical materials, devices, therapeutics, and/or diagnostics
- Tools and technologies that increase the efficiency of human subjects research
- Educational tools for clinical and translational research

Learn More About NCATS

ncats.nih.gov

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