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**June 2012 COGR Meeting Thursday Afternoon NCATS Presentation - Insel**

Author: Thomas Insel

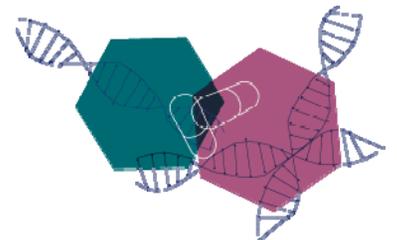
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# Catalyzing Innovation NIH National Center for Advancing Translational Sciences

Thomas R. Insel, M.D., Acting Director  
COGR Presentation  
June 7, 2012



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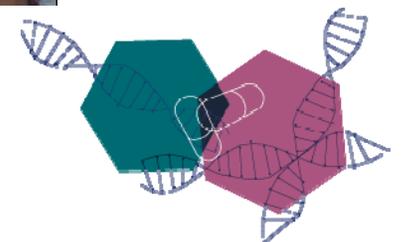


# Creation of the National Center for Advancing Translational Sciences (NCATS)

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



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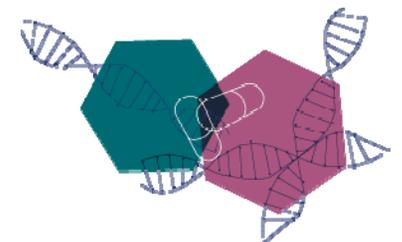
# Pursuing Opportunities for Disruptive Innovation



*“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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# The Need for NCATS

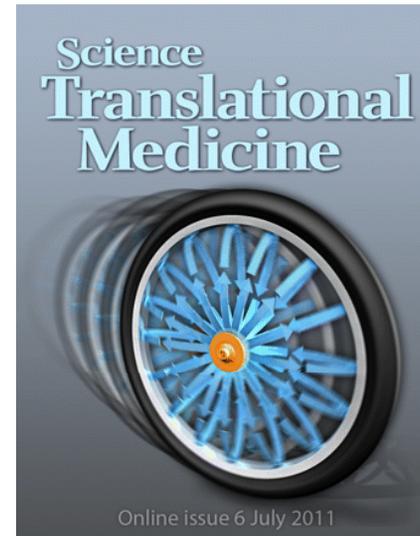
POLICY

[www.ScienceTranslationalMedicine.org](http://www.ScienceTranslationalMedicine.org) 6 July 2011 Vol 3 Issue 90 90

## Reengineering Translational Science: The Time Is Right

Francis S. Collins

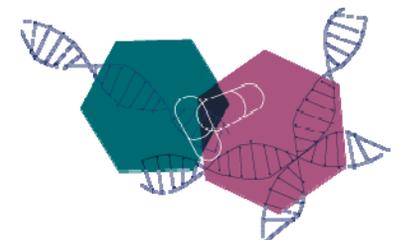
Despite dramatic advances in the molecular pathogenesis of disease, translation of basic biomedical research into safe and effective clinical applications remains a slow, expensive, and failure-prone endeavor. To pursue opportunities for disruptive translational innovation, the U.S. National Institutes of Health (NIH) intends to establish a new entity, the National Center for Advancing Translational Sciences (NCATS). The mission of NCATS is 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 diseases and conditions. The new center's activities will complement, and not compete with, translational research being carried out at NIH and elsewhere in the public and private sectors.



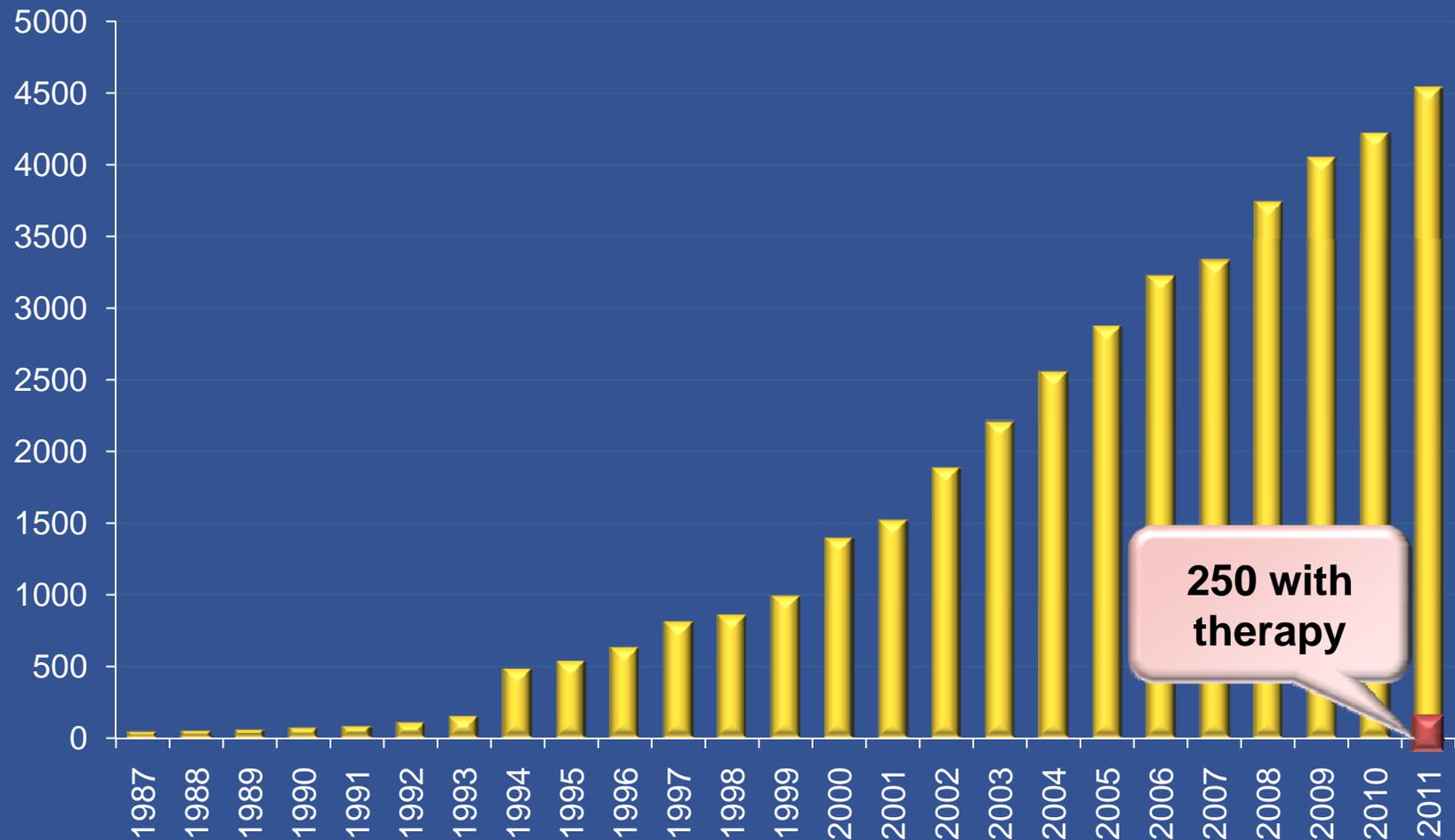
- Biomarkers – Precision Medicine
- More efficient treatment development (incl. rare diseases)
- More effective translation (T1 – T4)
- Training for translational science (T1 – T4)



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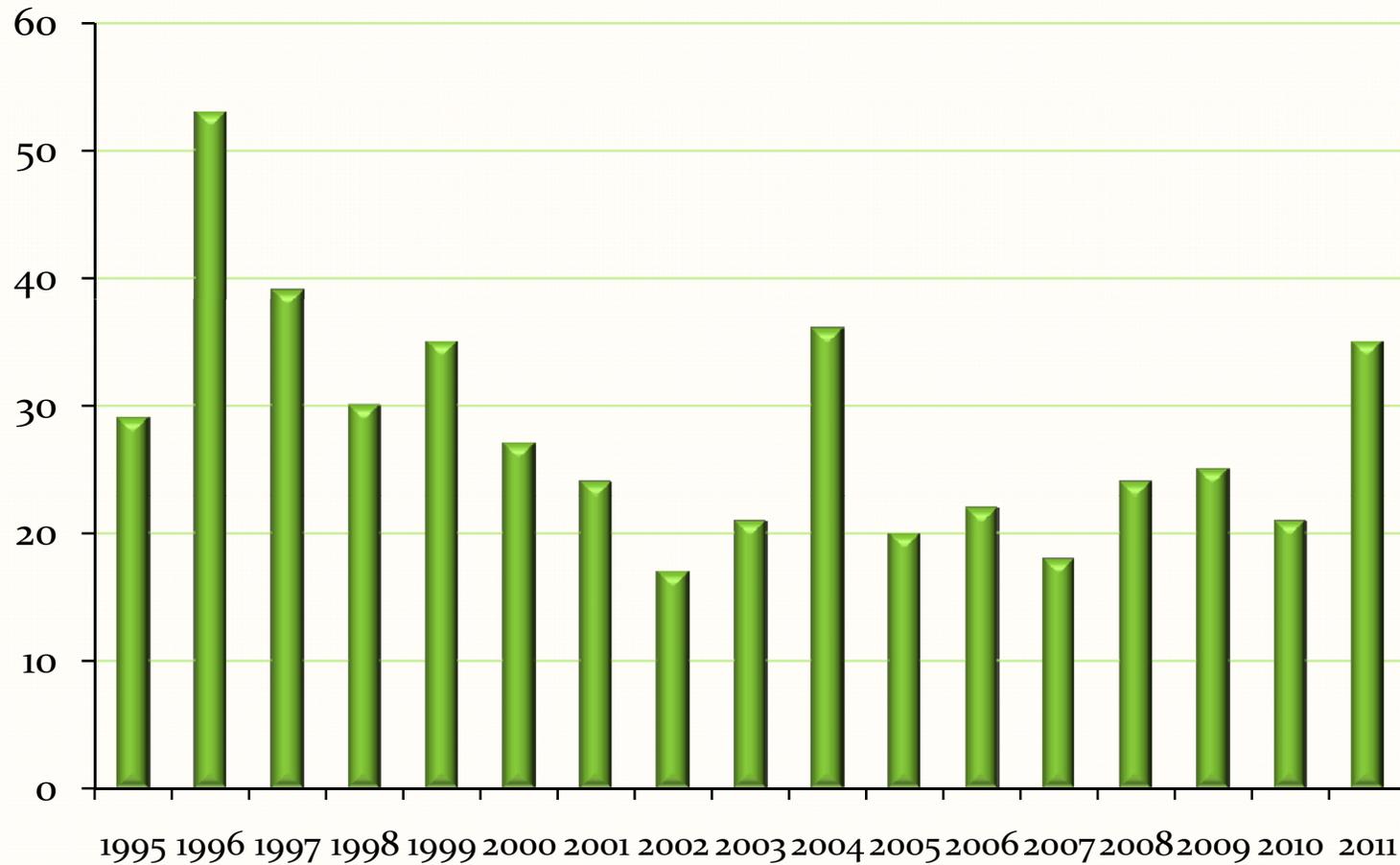
# Disorders with Known Molecular Basis



Source: Online *Mendelian Inheritance in Man*, *Morbid Anatomy of the Human Genome*

# NCATS: The Need

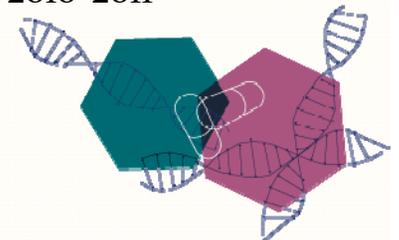
## New Molecular Entities Entering Marketplace



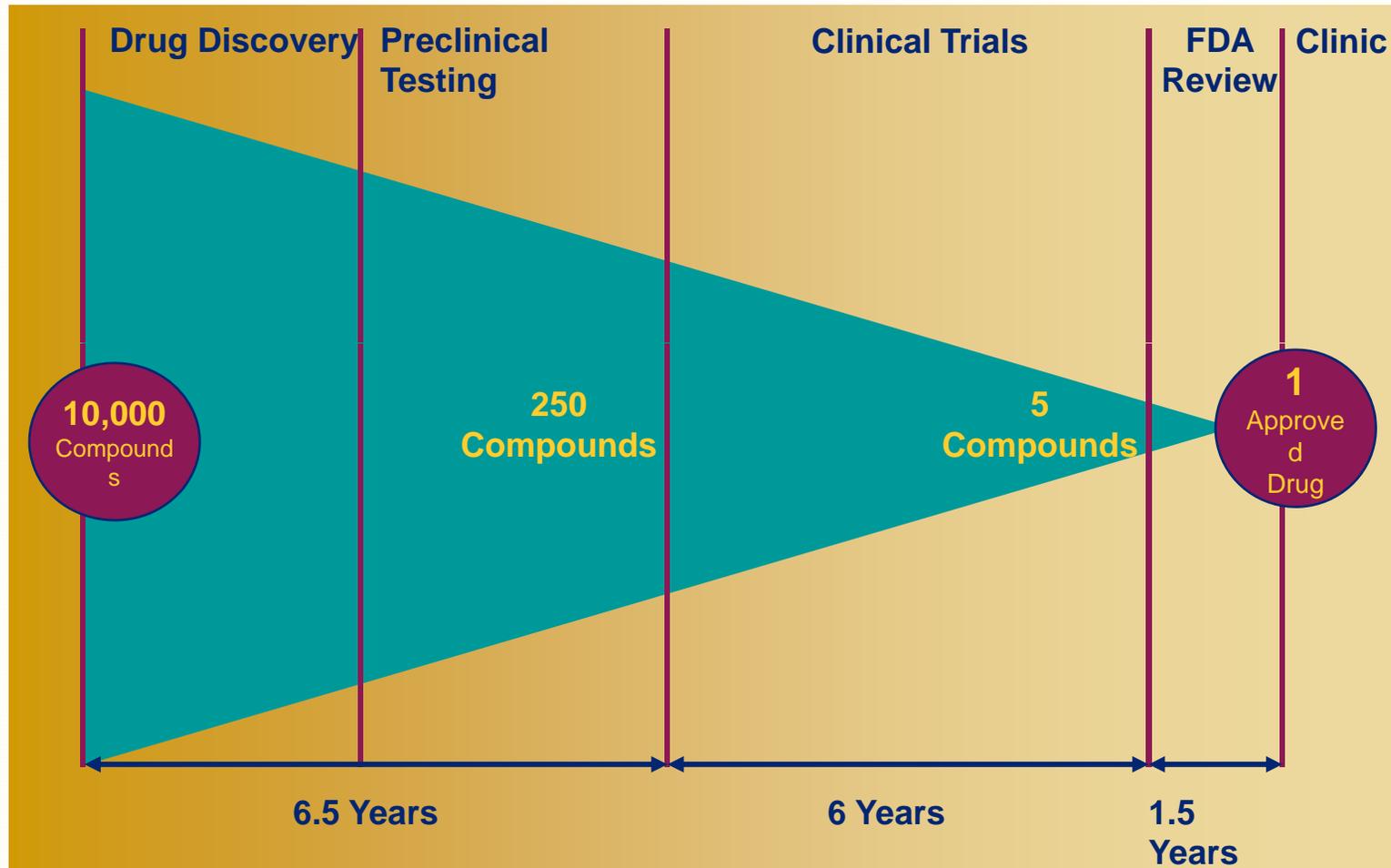
Source: FDA



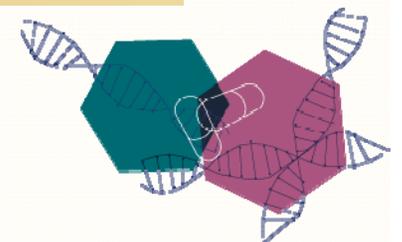
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# Development of New Therapeutics Is Slow, Expensive and Failure-Prone



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N Engl J Med 2011;364:535-41.

The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL ARTICLE

# The Role of Public-Sector Research in the Discovery of Drugs and Vaccines

Ashley J. Stevens, D.Phil., Jonathan J. Jensen, M.B.A., Katrine Wyller, M.B.E.,  
Patrick C. Kilgore, B.S., Sabarni Chatterjee, M.B.A., Ph.D.,  
and Mark L. Rohrbaugh, Ph.D., J.D.

## RESULTS

We found that during the past 40 years, 153 new FDA-approved drugs, vaccines, or new indications for existing drugs were discovered through research carried out in PSRIs.

PSRI-discovered drugs are expected to have a disproportionately large therapeutic effect.

# Challenges & Opportunities

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- Deluge of new discoveries of potential targets
- Unmet therapeutic needs for many conditions, especially rare and neglected diseases
- Need to view drug development pipeline as a scientific problem – ripe for experimentation and process engineering



# Programs and Initiatives

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## Clinical and Translational Science Activities

- Clinical and Translational Science Awards

## Rare Diseases Research and Therapeutics

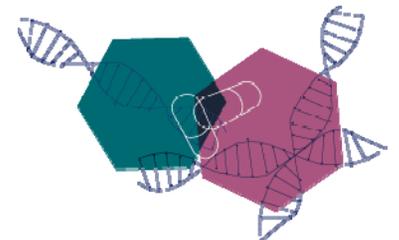
- Therapeutics for Rare and Neglected Diseases
- Office of Rare Diseases Research

## Re-engineering Translational Sciences

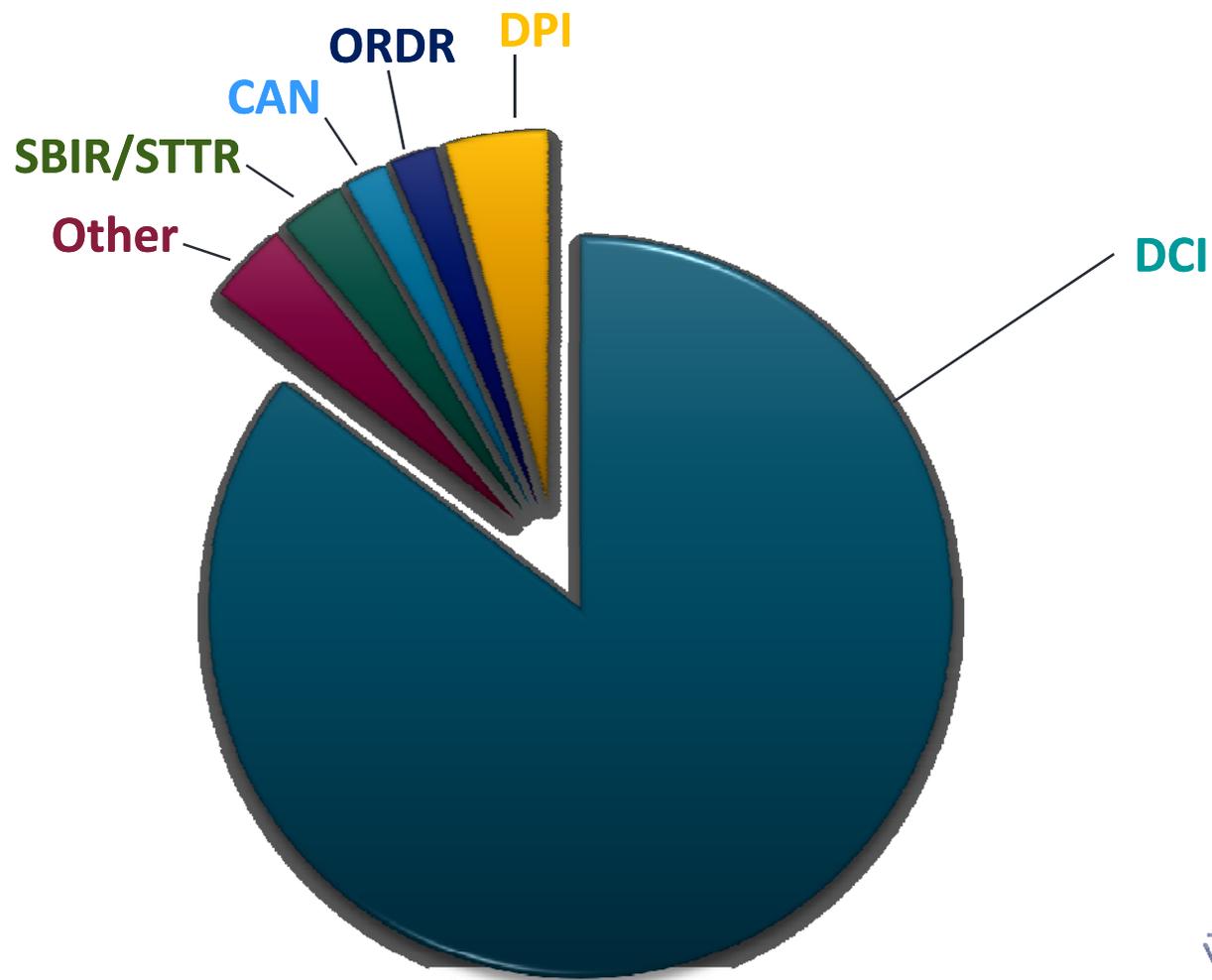
- Tox-21 and Tissue Chip Programs
- Repurposing
- New Therapeutic Uses for Existing Drugs



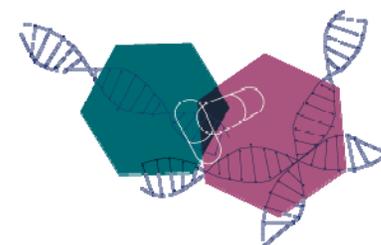
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# FY12 Research Budget (\$576M)



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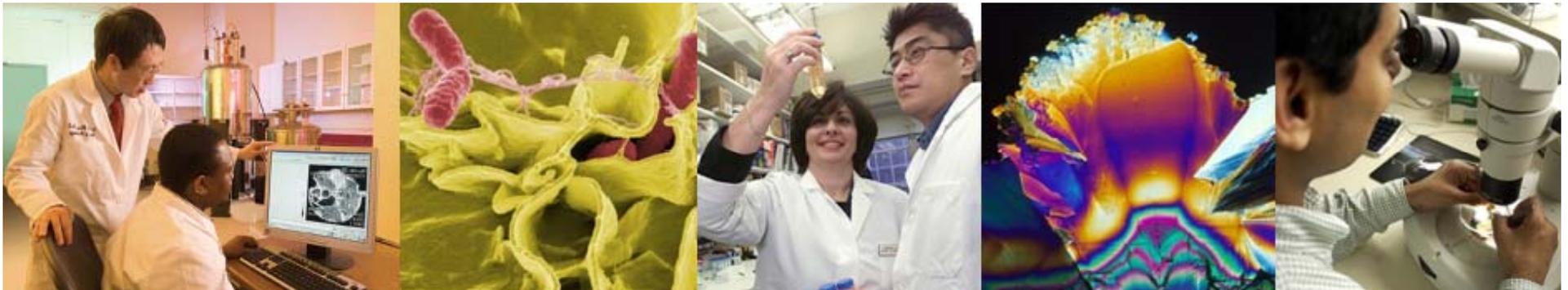


# Clinical and Translational Science Activities

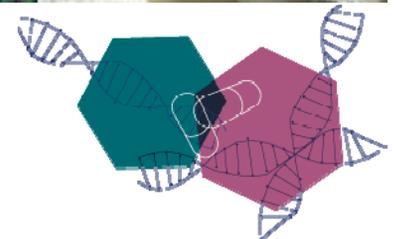
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## *Clinical and Translational Science Awards (CTSAs)*

- Support a national consortium of medical research institutions
- Work together to improve the way clinical and translational research is conducted nationwide
- Aim to accelerate the research translation process



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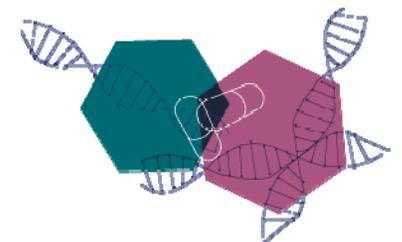


# CTSA: Accelerating Translation

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## Research Electronic Data Capture (REDCap)

- Easy-to-use, freely available tool for clinical study management and data capture
- Secure Web application that enables investigators to:
  - Create standardized surveys
  - Easily transfer data
  - Export data into a variety of statistical programs
- Makes it faster and easier to securely build and manage online surveys and databases
- Visit [redcap.org](http://redcap.org)



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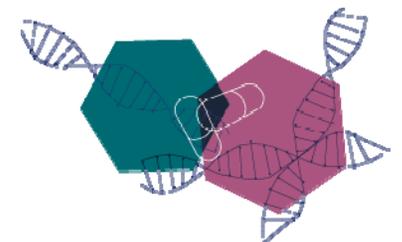
# CTSAs: Accelerating Translation

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## ResearchMatch:

### *Enabling New Opportunities for Research Participation (Researchmatch.org)*

- A free, secure, Web-based registry to improve clinical research
- Enables investigators and volunteers to find the right “match”
- Database of more than 20,000 registrants includes:
  - Rare diseases, common diseases, no disease
- Reduces recruitment costs
- Increases study enrollment
- Speeds research progress



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# Rare Diseases Research and Therapeutics

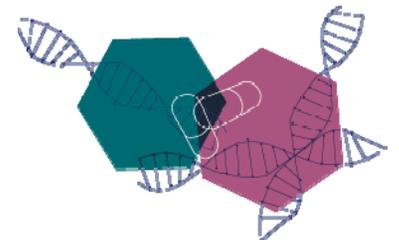
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## *Therapeutics for Rare and Neglected Diseases (TRND) Program*

- Designed to re-engineer the development of new drugs for rare and neglected diseases
- Specifically intended to stimulate research collaborations for drug discovery and development between NIH and:
  - Academic scientists
  - Nonprofit organizations
  - Pharmaceutical and biotechnology companies



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# Why the low success rate in R&D?

High Rate of Phase 2 Failures – Efficacy, Toxicity, Commercial

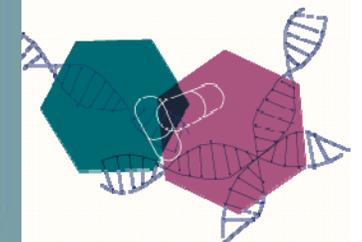
## Development Success Rates

NME Success Rates By Phase And Overall  
2006-2010 Industry



Success Rate = (number of successes) / ((number of terminations) + (number of successes))

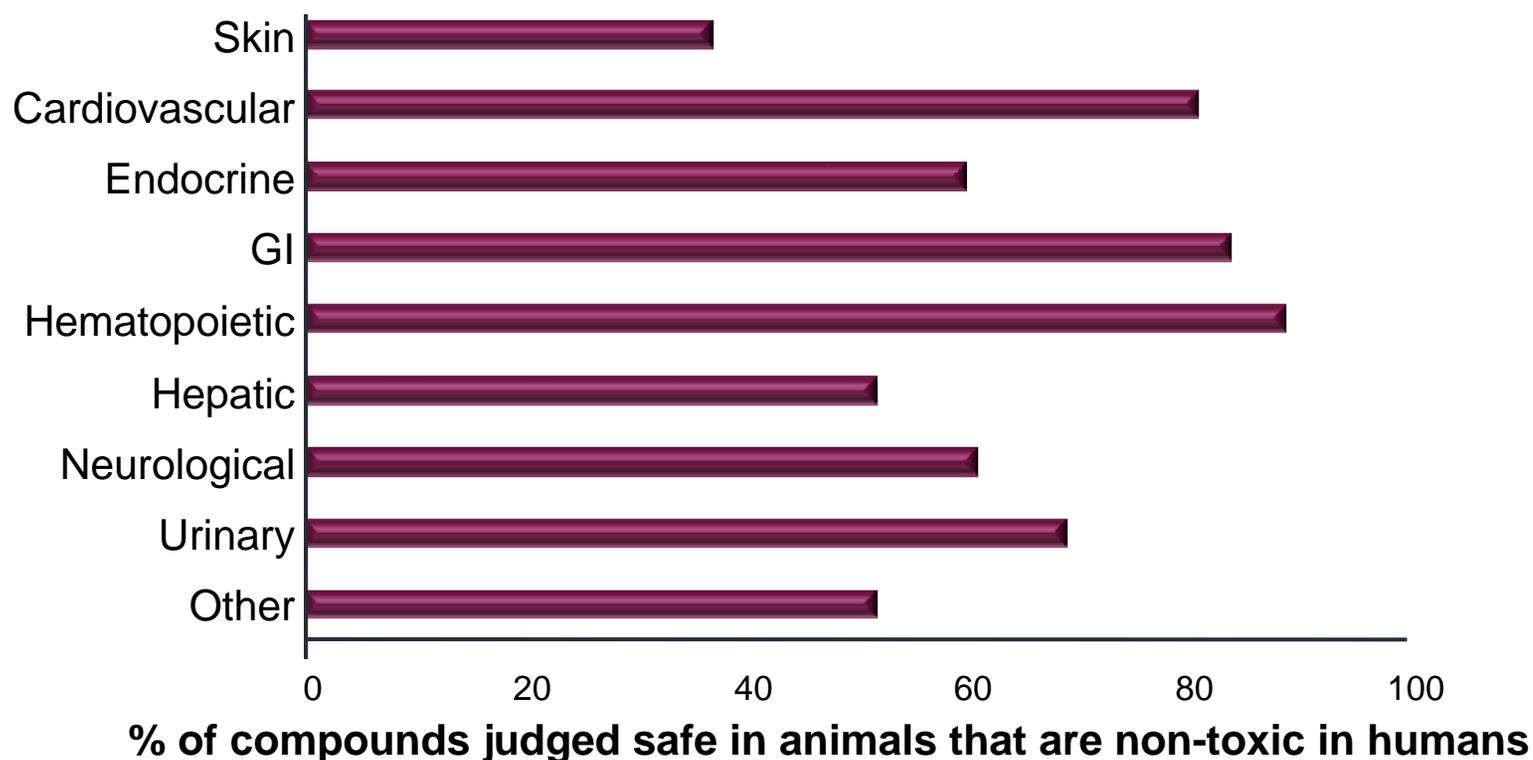
© KMR Group, Inc.



# Why the low success rate? Toxicity

Preclinical (21%) + Clinical (12%) Tox = 33% of all failures

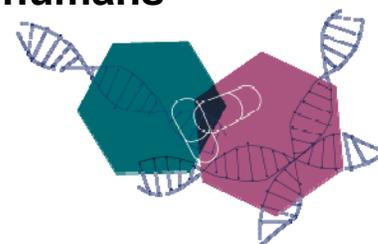
(Kola and Landis, Nature Reviews Drug Discovery 3, 711-716, 2004)



Source: Nature Reviews Drug Discovery 3, 227-236, 2004



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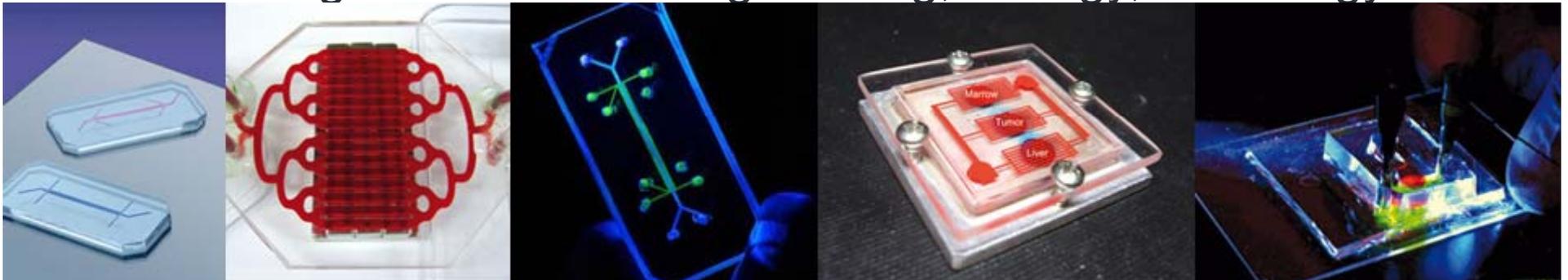
# Predictive toxicology

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## *Tissue Chip for Drug Screening*

Aims to develop a tissue chip that mimics human physiology to screen for safe, effective drugs

- Liver, heart, lung, other cell types
- Designed for multiple types of readouts
- NIH and Defense Advanced Research Projects Agency (DARPA) contribute \$70M over 5 years; FDA provides guidance
- Seeking best ideas in engineering, biology, toxicology



# Predictive toxicology

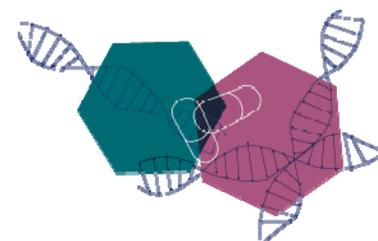
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## *Tox21: Toxicology in the 21<sup>st</sup> Century*

- A collaboration with:
  - NIH's National Institute of Environmental Health Sciences
  - U.S. Environmental Protection Agency
  - U.S. Food and Drug Administration
- Designed to screen a collection of 10,000 compounds composed of environmental chemicals and drugs approved for use
- Looks for compounds' potential to disrupt biological pathways that may be toxic



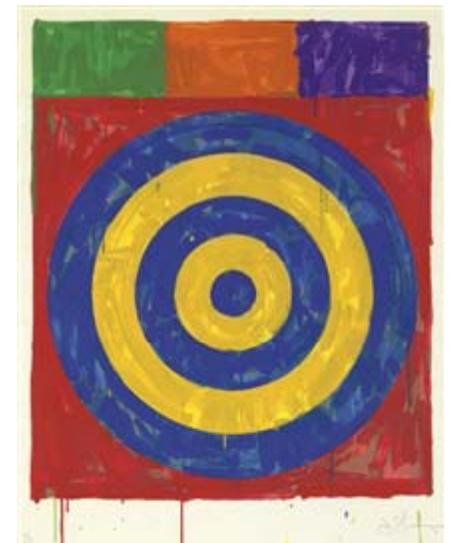
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# Improving Efficacy: Target Validation

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- Many, many potential drug targets
- Genotype to Phenotype (G2P); Phenotype to Genotype (P2G)
- Opportunity to work collaboratively across sectors in precompetitive way to speed drug development
- Early stage of development



# Drug Rescue and Repurposing



**NIH – INDUSTRY ROUNDTABLE**

April 21–22, 2011

**Exploring New Uses for Abandoned and Approved Therapeutics**



## NIH DRUG REPURPOSING

Drug	Initial Indication	Subsequent Indication
AZT	Antineoplastic	HIV/AIDS
Ceftriaxone	Bacterial infection	Amyotrophic lateral sclerosis
Hydroxyurea	Cancers	Sickle cell anemia
Metformin	Type 2 diabetes	Breast cancer
Pioglitazone	Type 2 diabetes	Hepatic steatosis
Raloxifene	Osteoporosis	Breast cancer
Tamoxifen	Breast cancer	Bipolar disorder

BIOMEDICINE

### NIH's Seco

Although the U.S. National Institutes of Health (NIH) has made it a top priority to propose new center aimed at drug repurposing research, so far the main effort has been to put scattered existing projects under the same roof. But this month, NIH Director Francis Collins unveiled a new initiative to effort to persuade drug companies to dig up their troves of abandoned drugs, who would look for



Double duty. NIH researchers have found new uses for several therapeutics.

for repurposed drugs. And NIH says that the drug rescue and repurposing project will be led by a team at NCATS as "an integral



# Drug Rescue and Repurposing

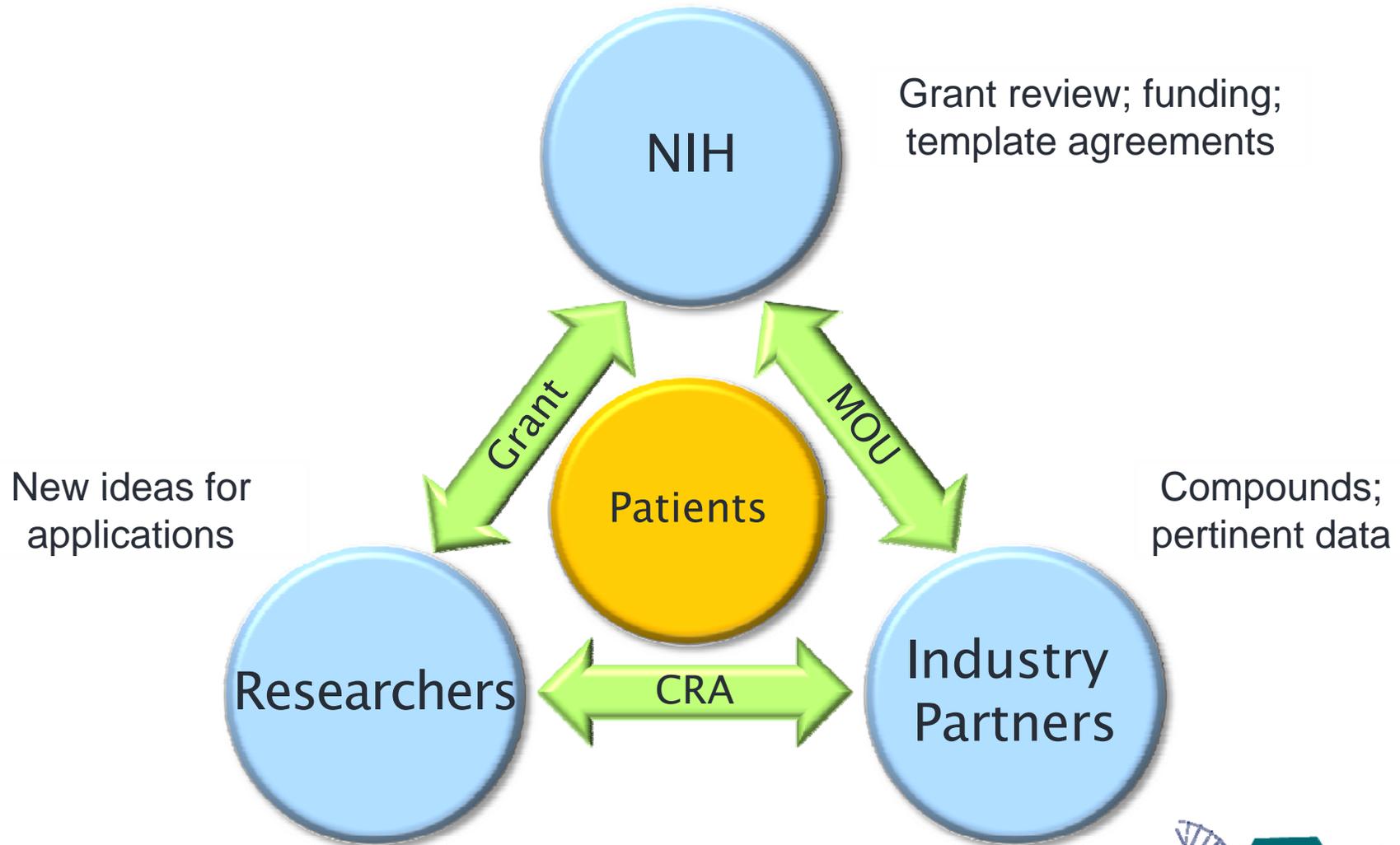
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- Match abandoned compounds from pharma with innovative ideas for new indications from NIH scientists
- NIH provides: RFA, review, funding
- Pharma provides: compounds and pertinent data
- Grantees provide: Great ideas and access to patients
- Program to launch this year, awards early in FY13
- Can this new model for collaboration deliver new medicines faster?

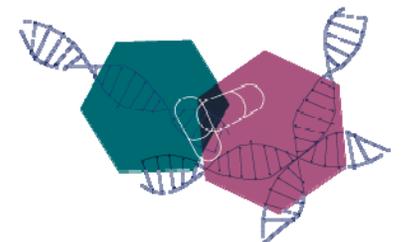


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# Drug Rescue and Repurposing



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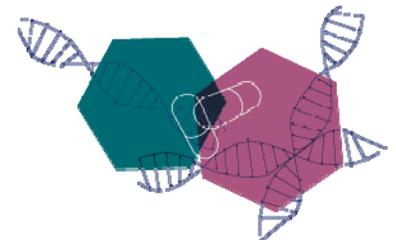
# Cures Acceleration Network

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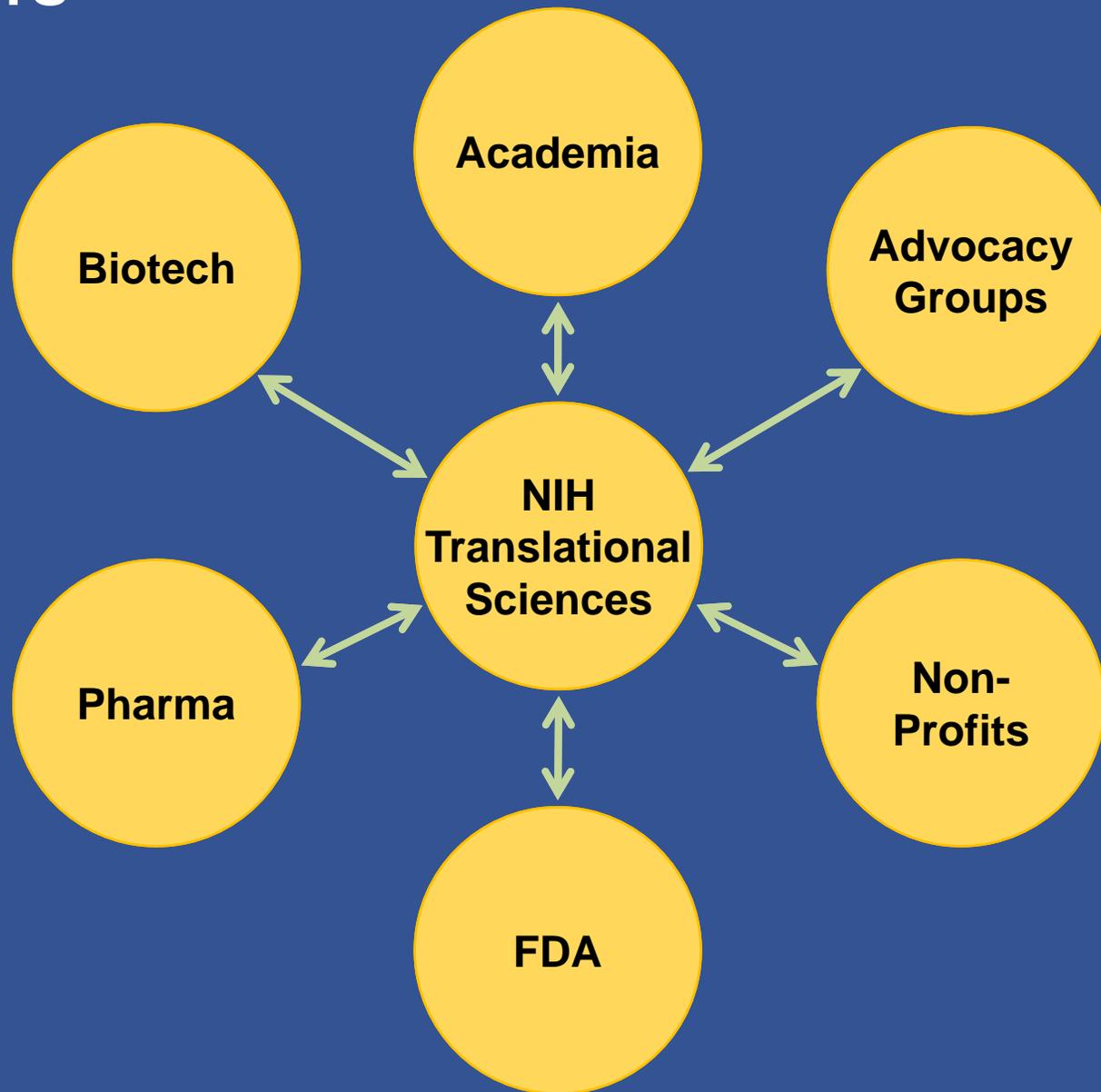
- Created to advance development of “high need cures”
- Reduces barriers to translation in areas the private sector is less likely to pursue
- Funded via:
  - Grant awards with or without partnership
  - Flexible Research Awards: DARPA-like authority
    - Not to exceed 20 percent of total appropriated funds per fiscal year
- FY 2012 budget: \$10 million



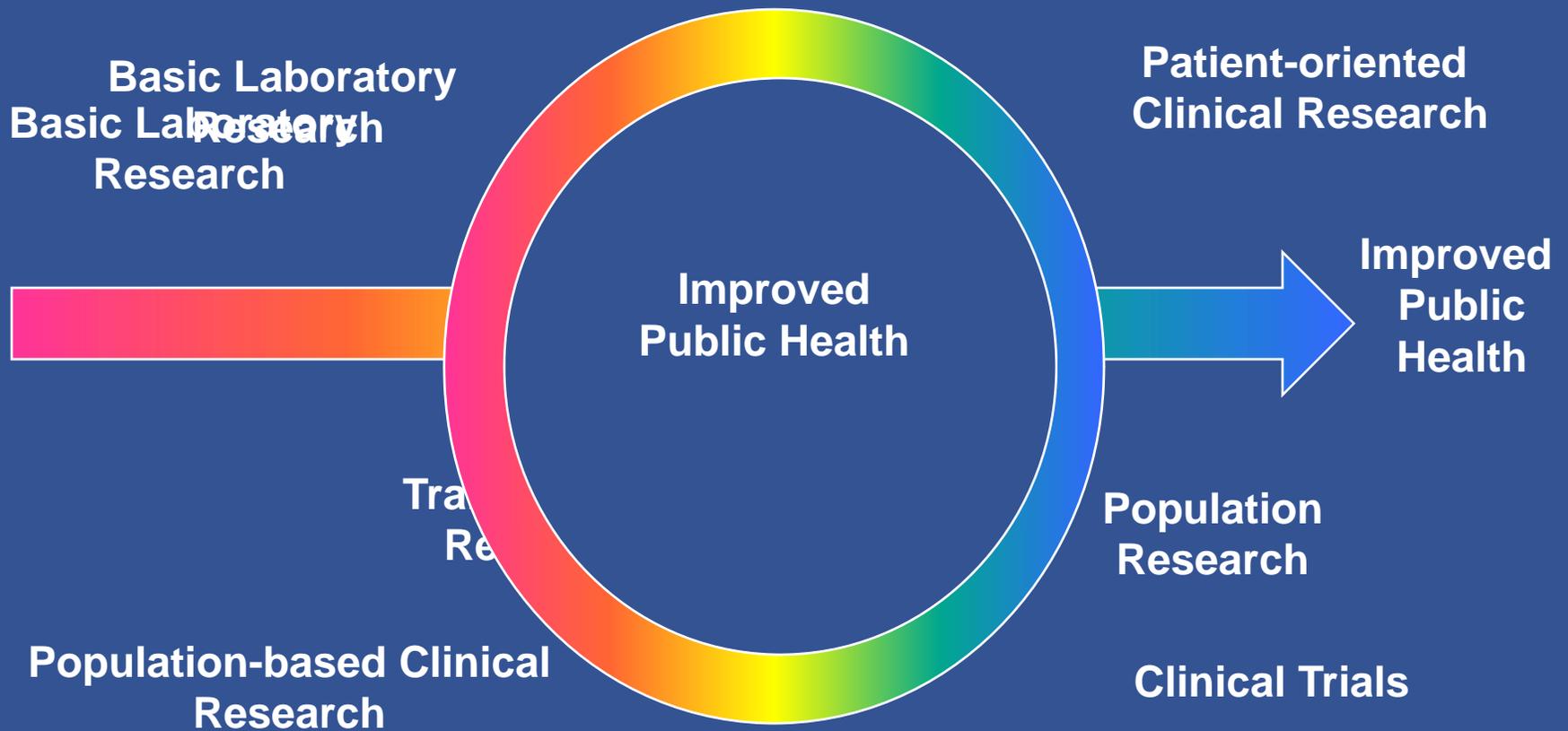
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# Catalyzing Collaborations With External Partners



# Standard Model The Way it Should Work



# Learn More About NCATS

[ncats.nih.gov](http://ncats.nih.gov)

- **Questions:** [info@ncats.nih.gov](mailto:info@ncats.nih.gov)
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