

# Disruptive Innovation at the National Institutes of Health

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December 1, 2011



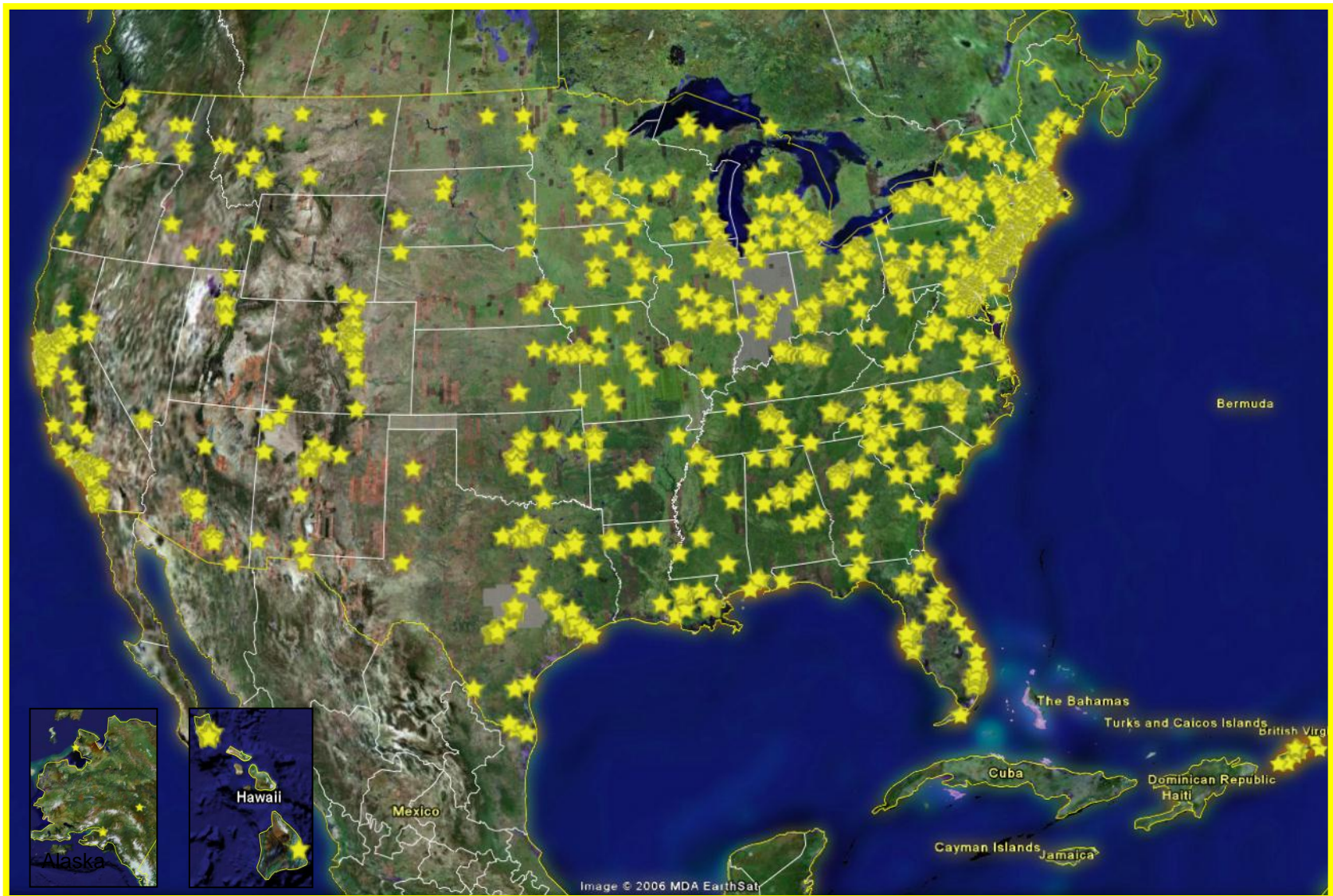
# NIH Mission

... 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 the burdens of illness and disability.



President Franklin D. Roosevelt at NIH dedication; October 31, 1940

# NIH Funds Scientists Across U.S.



# ...and around the globe ...

## INTERNATIONAL BIOMEDICAL RESEARCH ORGANIZATION SUPPORT (PROOF OF CONCEPT)

SITES TO SHOW: M MULTI-FUNDED NIH DIRECT AWARDS / COLLABORATIONS

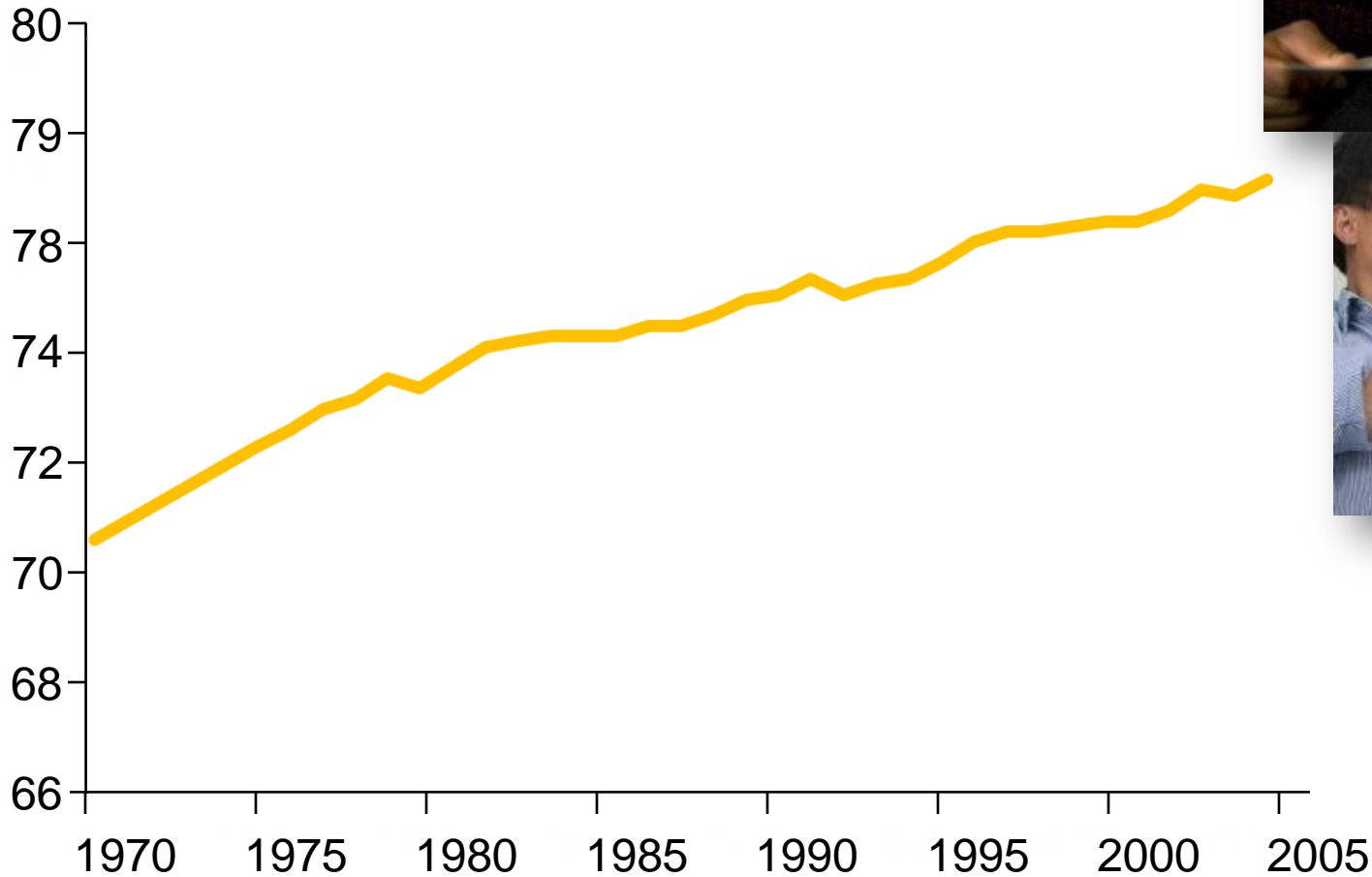
PASTEUR SITES  CIHR/GHRI SITES  WELLCOME SITES  
 EDCTP  NIH DIRECT AWARDS  NIH COLLABORATIONS

ALL COUNTRIES



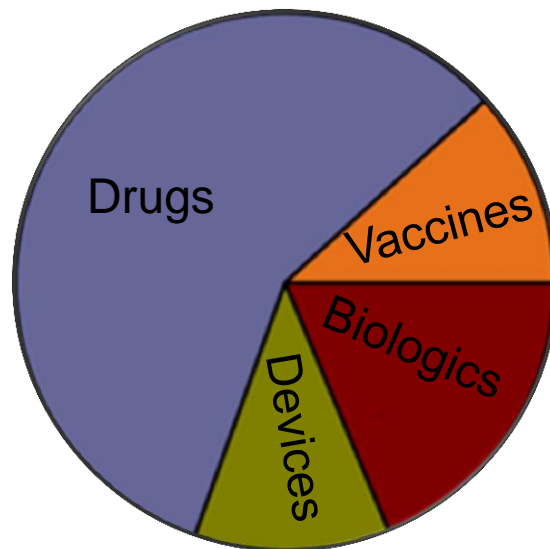
# The Benefits of Biomedical and Public Health Advances

## U.S. Life Expectancy



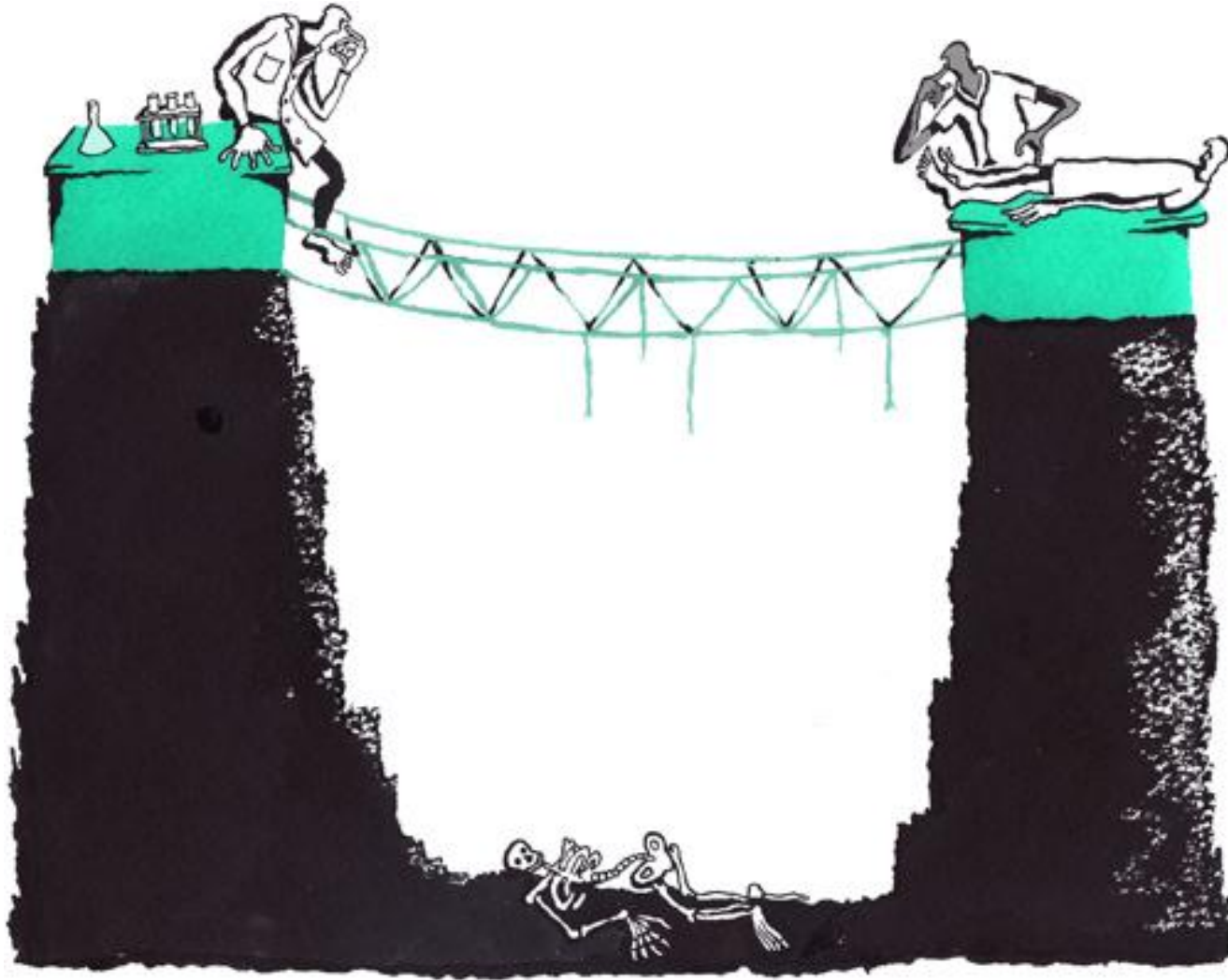
# Therapeutics Development at NIH

- A 2010 trans-NIH inventory of activities relevant to therapeutics development found:
  - Substantial investments in therapeutics development research
  - Approximately 65% for preclinical research; 35% clinical research
  - 550 activities reported of varying sizes and areas of emphasis

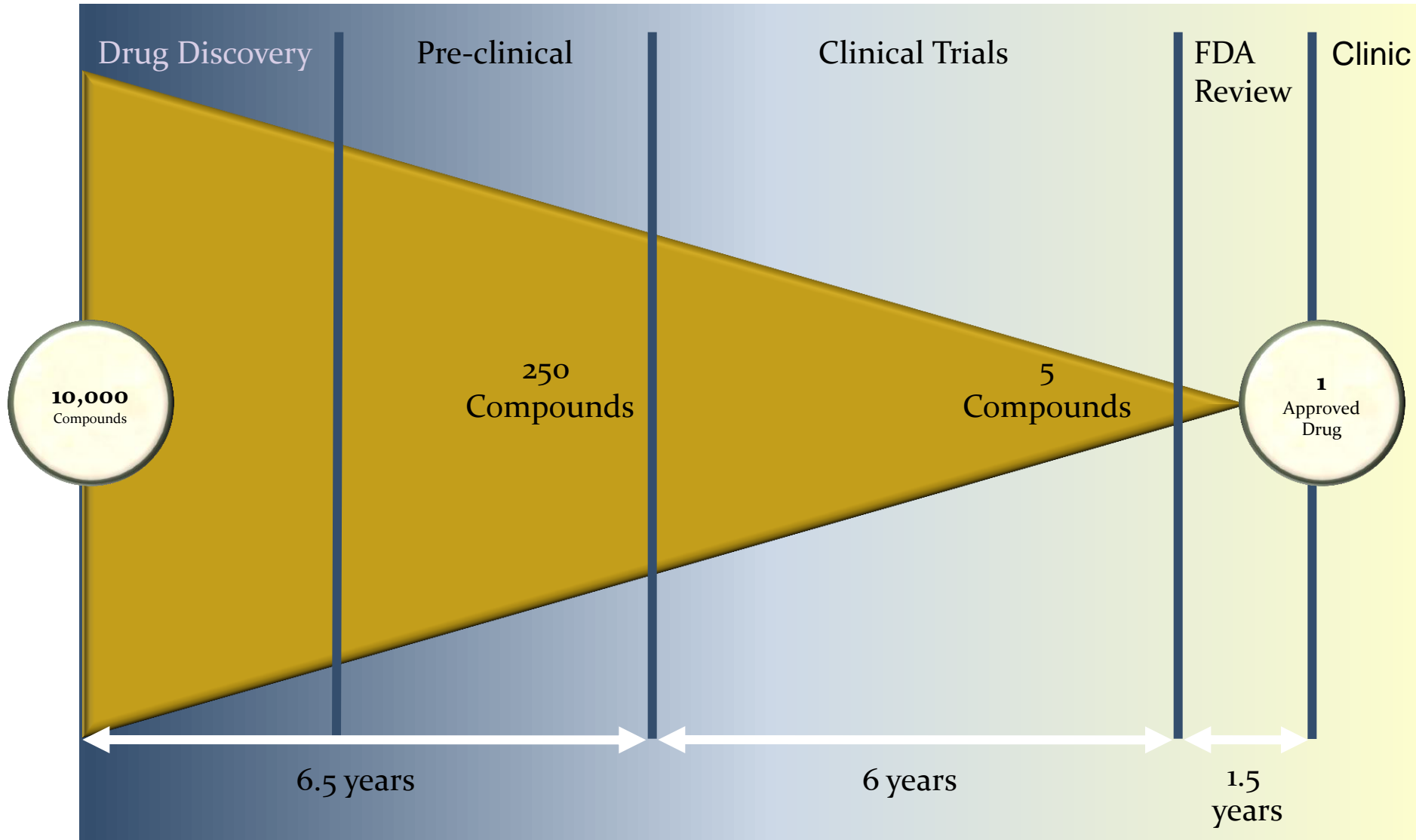


Distribution of Investment

# Valley of Death

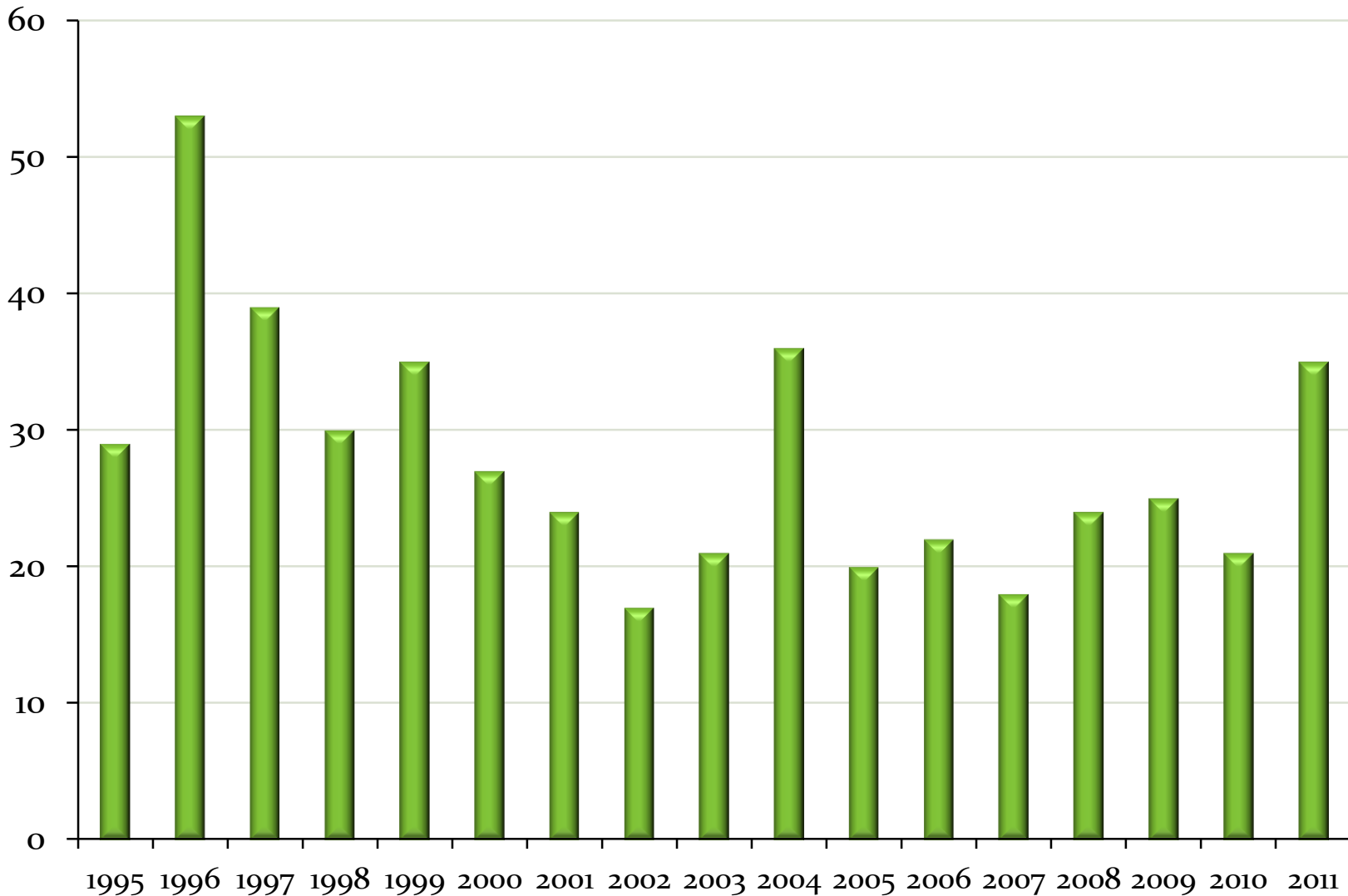


# The Problem: Development of New Therapeutics is Slow, Expensive, and Failure-Prone





# New Medicines in Your Medicine Cabinet: New Molecular Entities Entering Marketplace



Source: FDA

# Pursuing Opportunities for Disruptive Translational Innovation

POLICY

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.

Science  
Translational  
Medicine



Online issue 6 July 2011

“My administration is announcing a new center that will help companies reduce the time and cost of developing lifesaving drugs.”

*President Obama  
Signing of America Invents Act  
Thomas Jefferson High School  
September 16, 2011*



# NCATS:

## Pursuing Opportunities for Disruptive Innovation

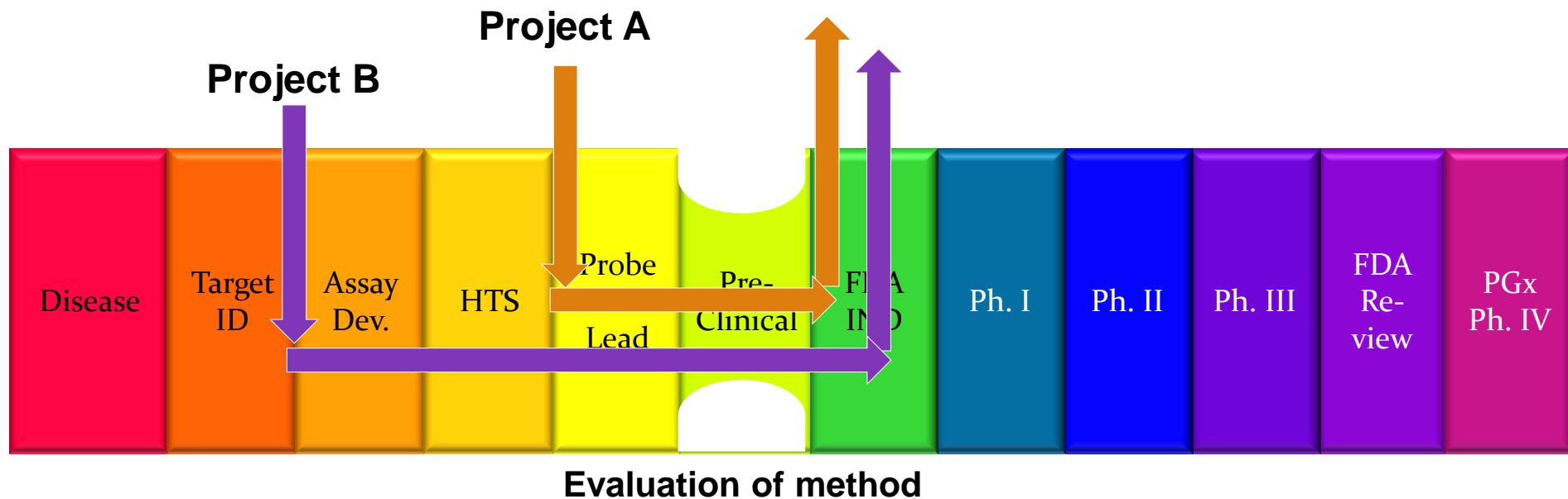
### Mission:

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



# Advancing the Science of Translation

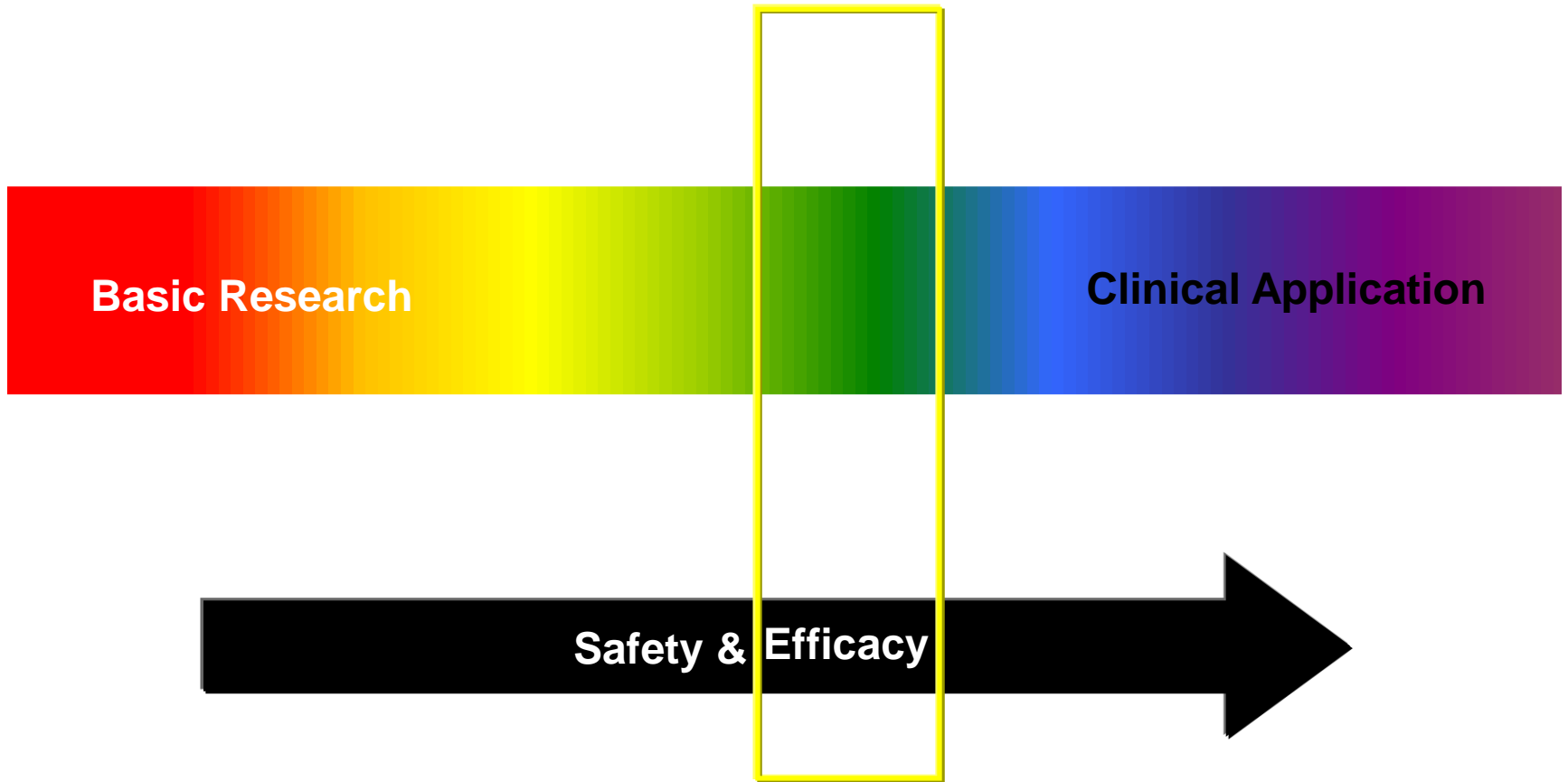
- Study the steps in the diagnostics & therapeutics development pipelines and identify bottlenecks amenable to re-engineering
- Experiment with innovative methods to streamline the process
- Evaluate novel methods with compelling therapeutic projects



# Examples of Translational Challenges

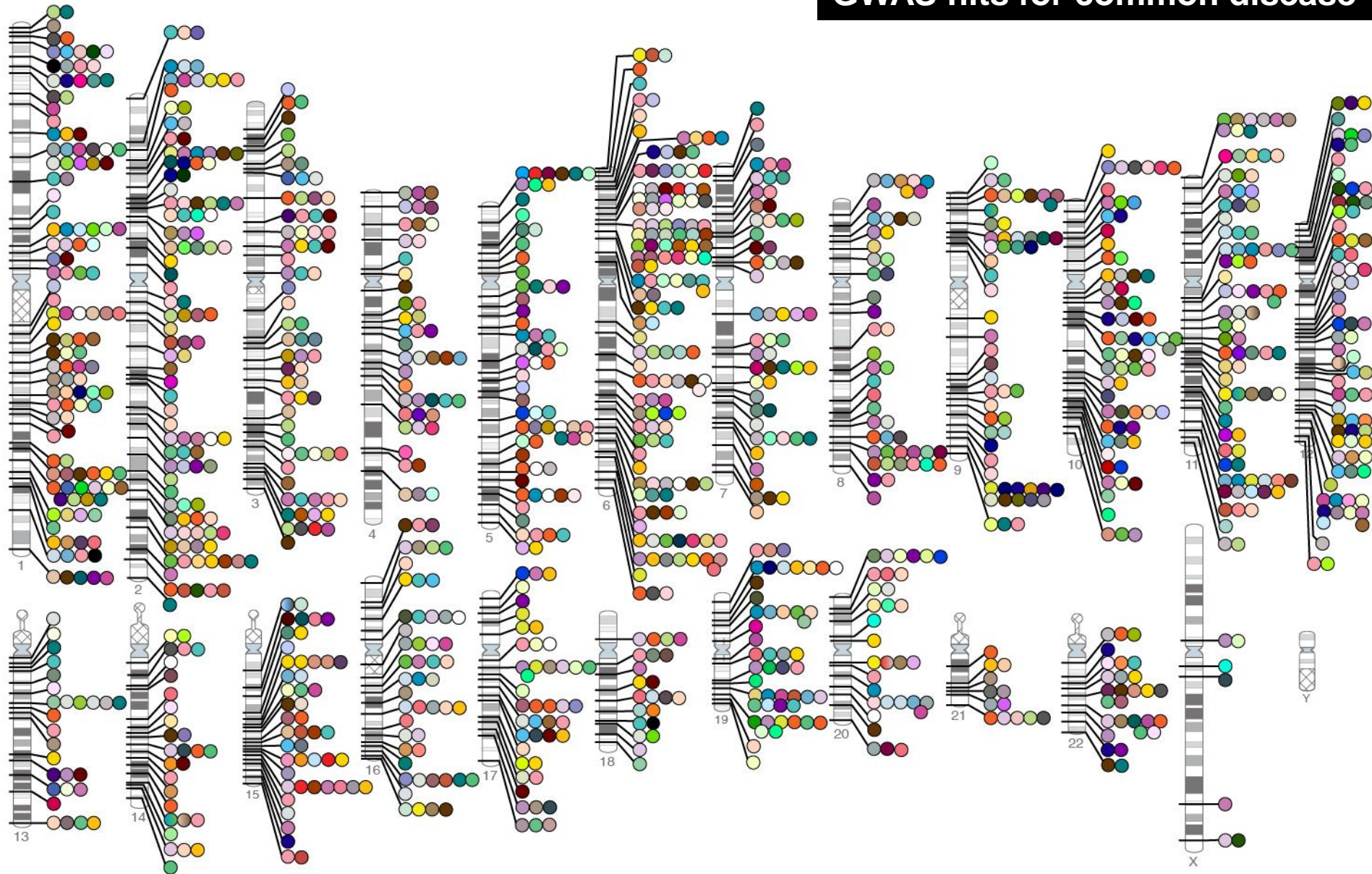
- Therapeutic target validation
- Chemistry
- Virtual drug design
- Preclinical toxicology
- Biomarkers
- Efficacy testing
- Phase zero clinical trials
- Rescuing and repurposing
- Clinical trial design
- Post-marketing research

# Target Validation



Need new methods, approaches, tools, and technologies  
to undertake validation in a  
more efficient and predictable fashion

# GWAS hits for common disease





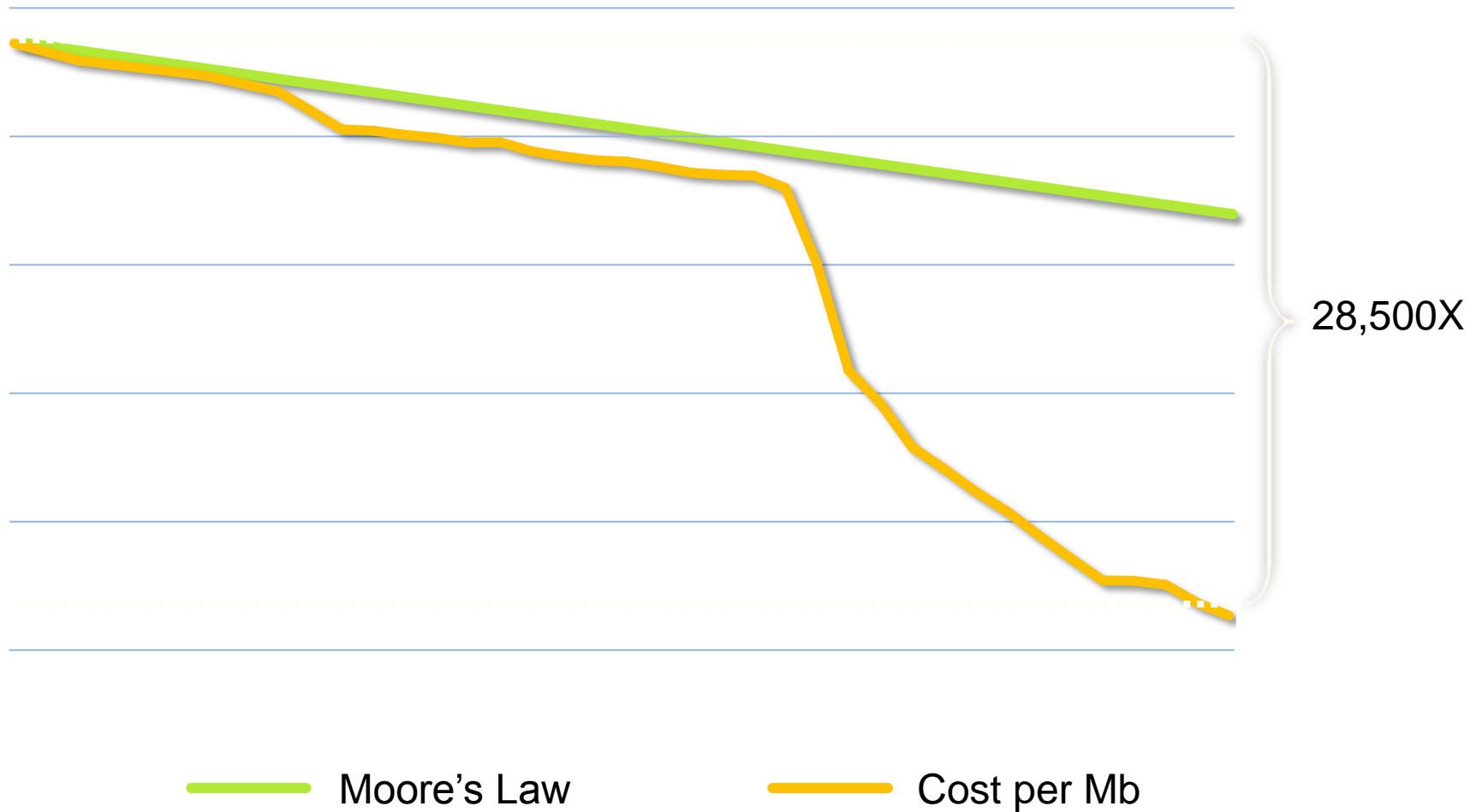
# “Positive controls” demonstrate power of GWAS to identify drug targets

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Disease	Total GWAS hits	GWAS hits associated with marketed drugs
Type 2 diabetes	44	6
Hyperlipidemia	39	2
Multiple sclerosis	36	5
Psoriasis	24	4

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# Sequencing Costs Drop Faster than Moore's Law



# Working Together: Target Validation NIH-Industry Workshop

Goal: to undertake target validation in a more systematic way

- Understand the landscape, including success and failures
- Develop new methods, approaches, tools, and technologies
- Capitalize on the wealth of new discoveries and resources

**Next Steps:** Standing Up a Target Validation Consortium

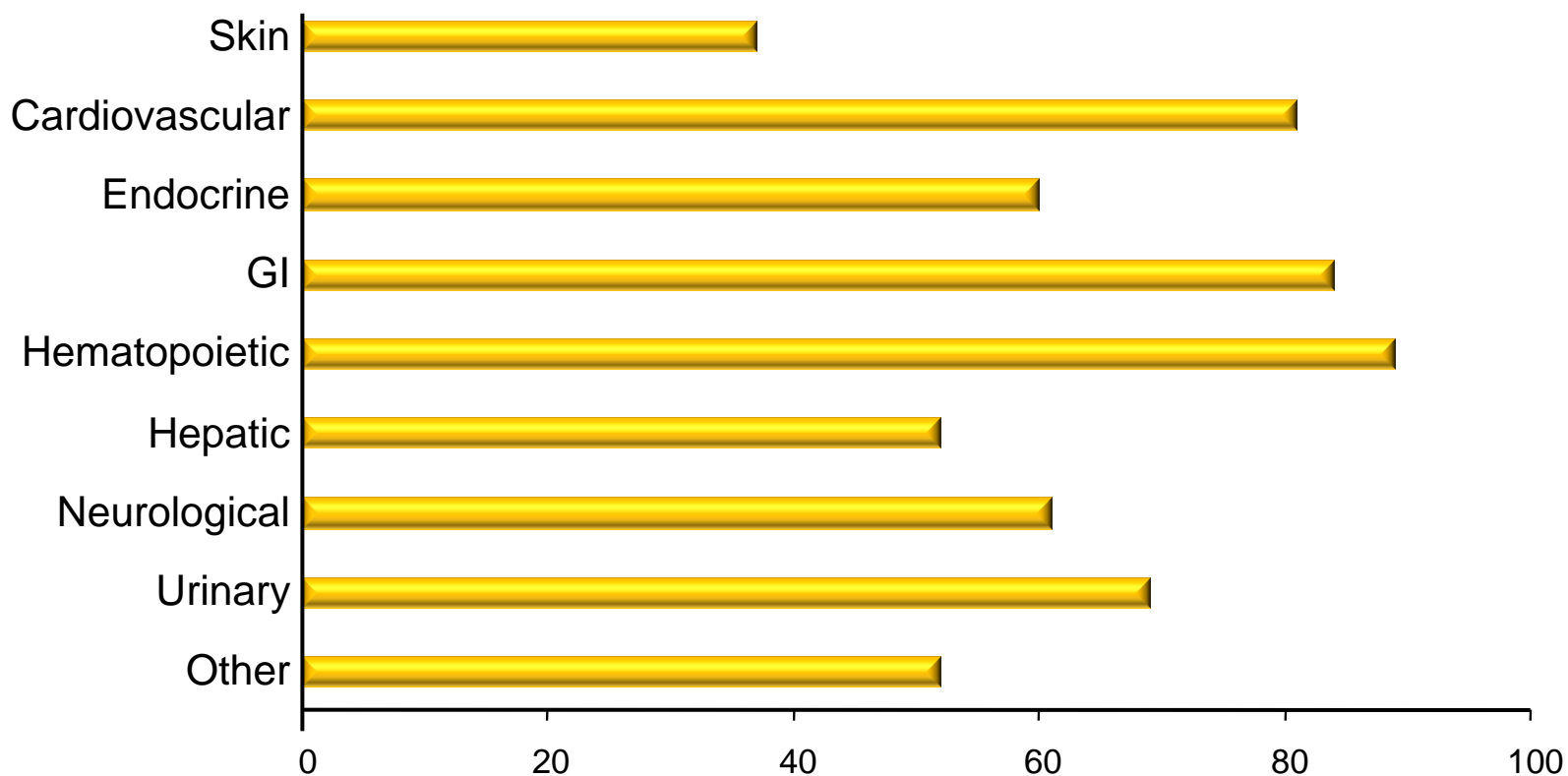
How is this different?

- Exceptional scientific opportunities
- Offers real change in the drug discovery paradigm
- Governance with high level involvement

# Pre-Clinical Toxicity Testing

**Constriction point: low concordance between animal and human toxicity**

Preclinical (21%) + Clinical (12%) Tox = 33% of all failures (Kola and Landis, *Nature Reviews Drug Discovery* 3, 711-716, 2004)

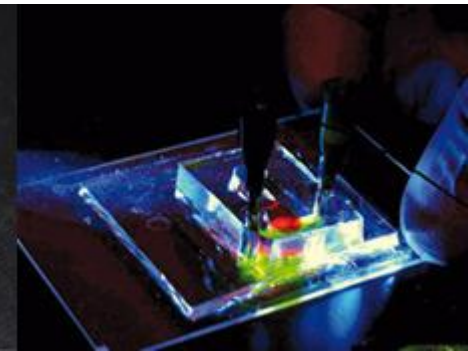
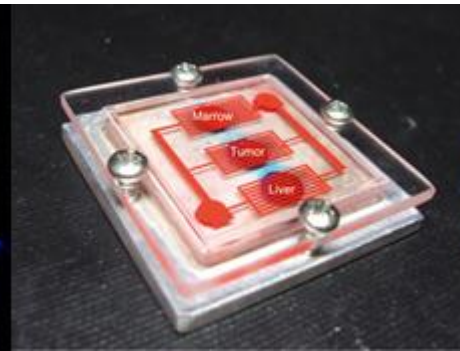
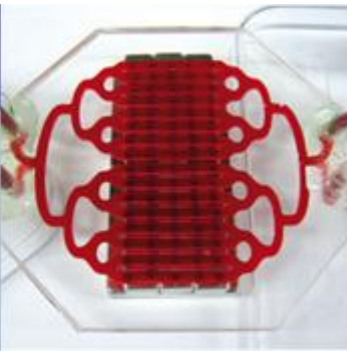
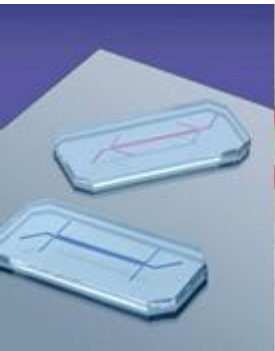


**% of compounds judged safe in animals that are non-toxic in humans**

# Better Ways to Predict Drug Safety

## New NIH-DARPA-FDA Collaboration

- Part of President's "Lab to Market" initiatives
- Goal: Develop chip to screen for safe, effective drugs
  - Liver, heart, lung, other cell types
  - Designed for multiple different readouts
- NIH, DARPA to commit ~\$70 million each over 5 years
- FDA to offer guidance
- RFA published in mid-November; applications due January 26th
  - Seeking best ideas in engineering, biology, toxicology



# Rescuing 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 aims and research, so far the main effort has been to put scattered existing programs under the same roof. But this month, NIH Director Francis Collins unveiled a new strategy: an 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.

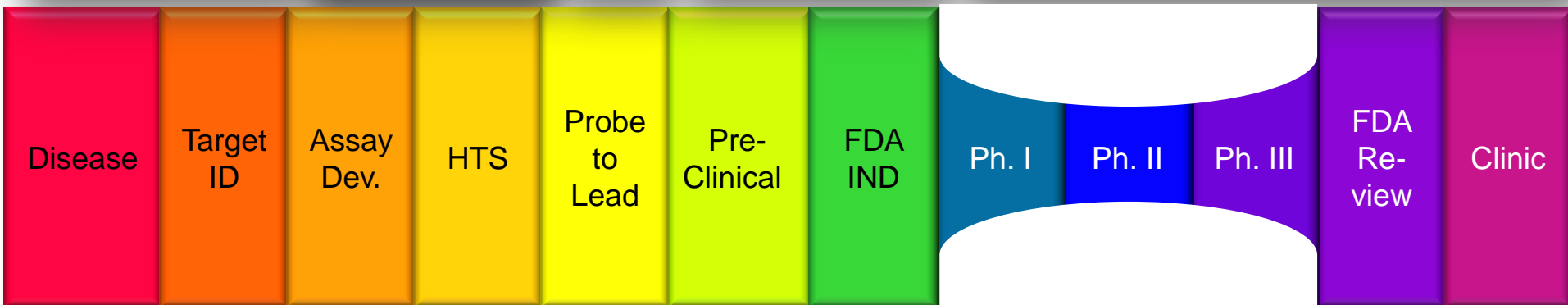
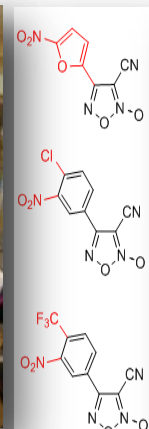
for repurposed drugs. And NIH says that says: the drug rescue and repurposing project will be led by a team at NCATS as "an integral

# Rescue and Repurposing



## New NIH-pharma Collaboration

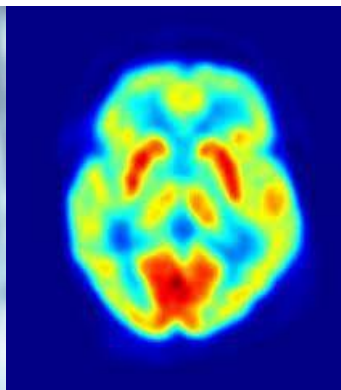
- Match compounds from pharma's "virtual medicine cabinet" with innovative ideas for new indications from NIH extramural scientists
- NIH provides: funding, RFA, review
- Pharma provides: compounds and pertinent data
- Terms are being worked out
- NIH-Industry working group – more partners following successful pilot?





# Changing Human Subjects Research Landscape

- Human subjects regulations have not kept pace with changes in the human research enterprise:
  - Growth in research volume
  - Increase in multi-site studies
  - Increase in health services and social science research
  - New technologies: e.g., genomics, imaging, informatics
  - Increased role of private sector
  - Increased sharing of specimens and data



# Revamping Human Subjects Protections: Enhancing Protections & Reducing Burden

- Advance Notice of Proposed Rulemaking (ANPRM) on Revisions to the Common Rule
- Issued by the Office of the Secretary in coordination with Office of Science and Technology Policy
- Interagency working group: representatives from NIH, FDA, HHS, OHRP, VA, OMB, OSTP

# Regulatory Reform: Two Overarching Goals

1. Enhance protection of research subjects
2. Improve the efficiency of the review process by reducing:
  - Unnecessary paperwork
  - Multiple reviews of studies
  - IRB reviews of very low-risk research
  - IRB reviews of information risks

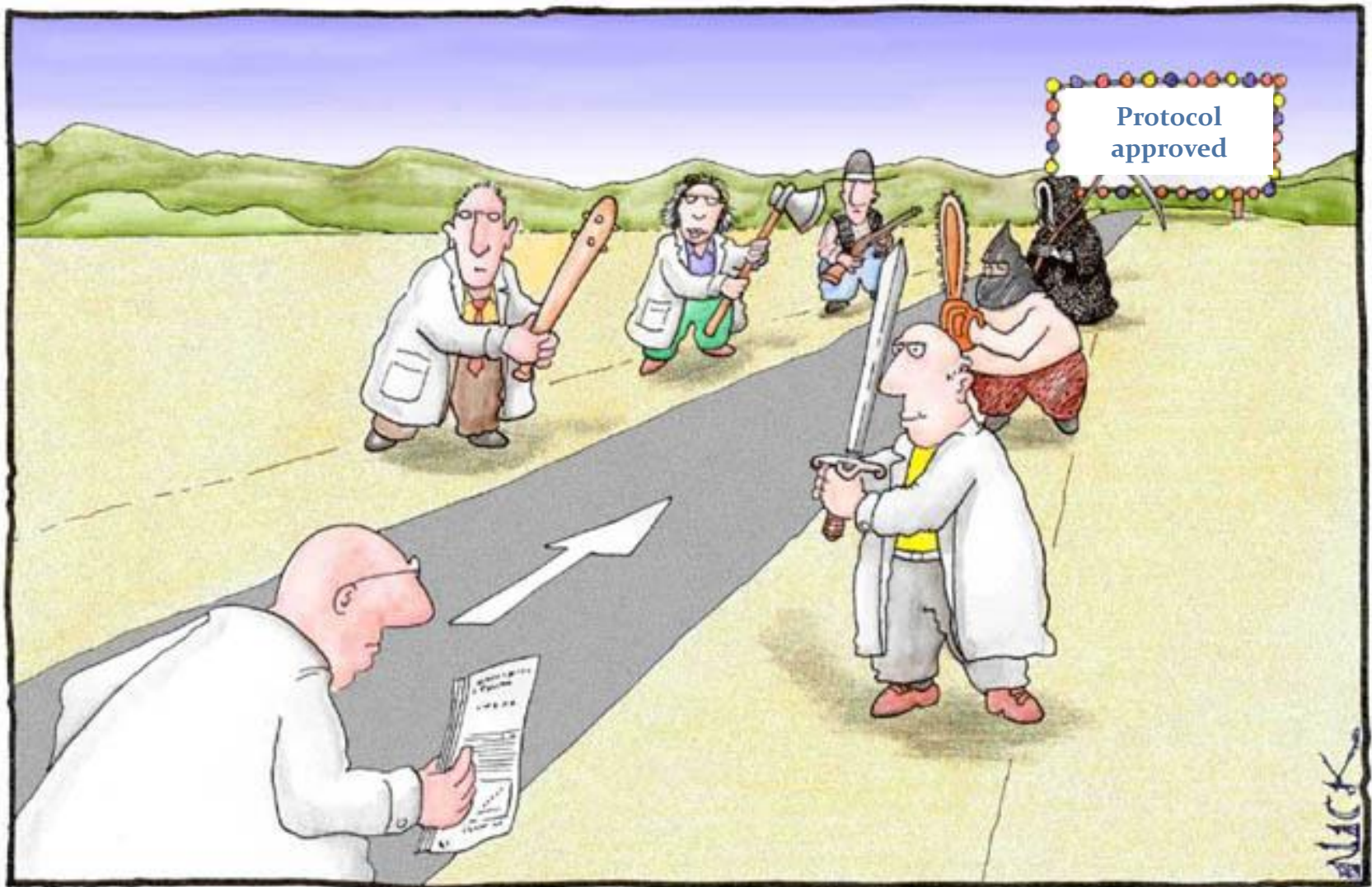
# Seven Proposed Regulatory Reforms

1. Refine existing risk-based framework
2. Utilize single IRB review of record for domestic multi-site studies
3. Improve consent forms and consent process
4. Establish mandatory data security and information protection standards for studies involving identifiable or potentially identifiable data
5. Establish systematic approach to collection and analysis of data on unanticipated problems and adverse events
6. Extend federal regulatory protections to all research conducted at U.S. institutions receiving federal funding
7. Establish single source of guidance on federal regulations

# Next steps for revision of Common Rule

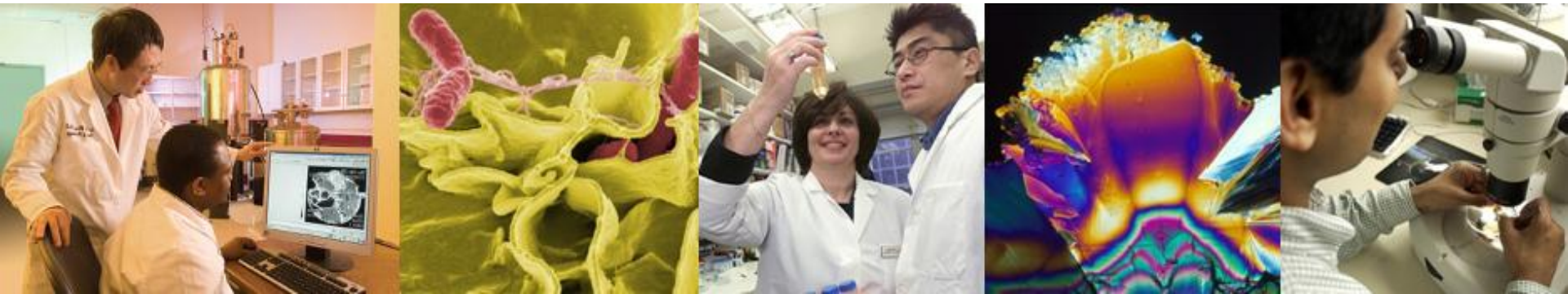
- Read and analyze public comments
- Publish draft revision – in the form of a notice of proposed rule making (NPRM) – early 2012
- Gather public comments on the NPRM
- Finalize regulation
- Assess impact on research participants and research progress

# IRB Review: There has GOT to be a better way!

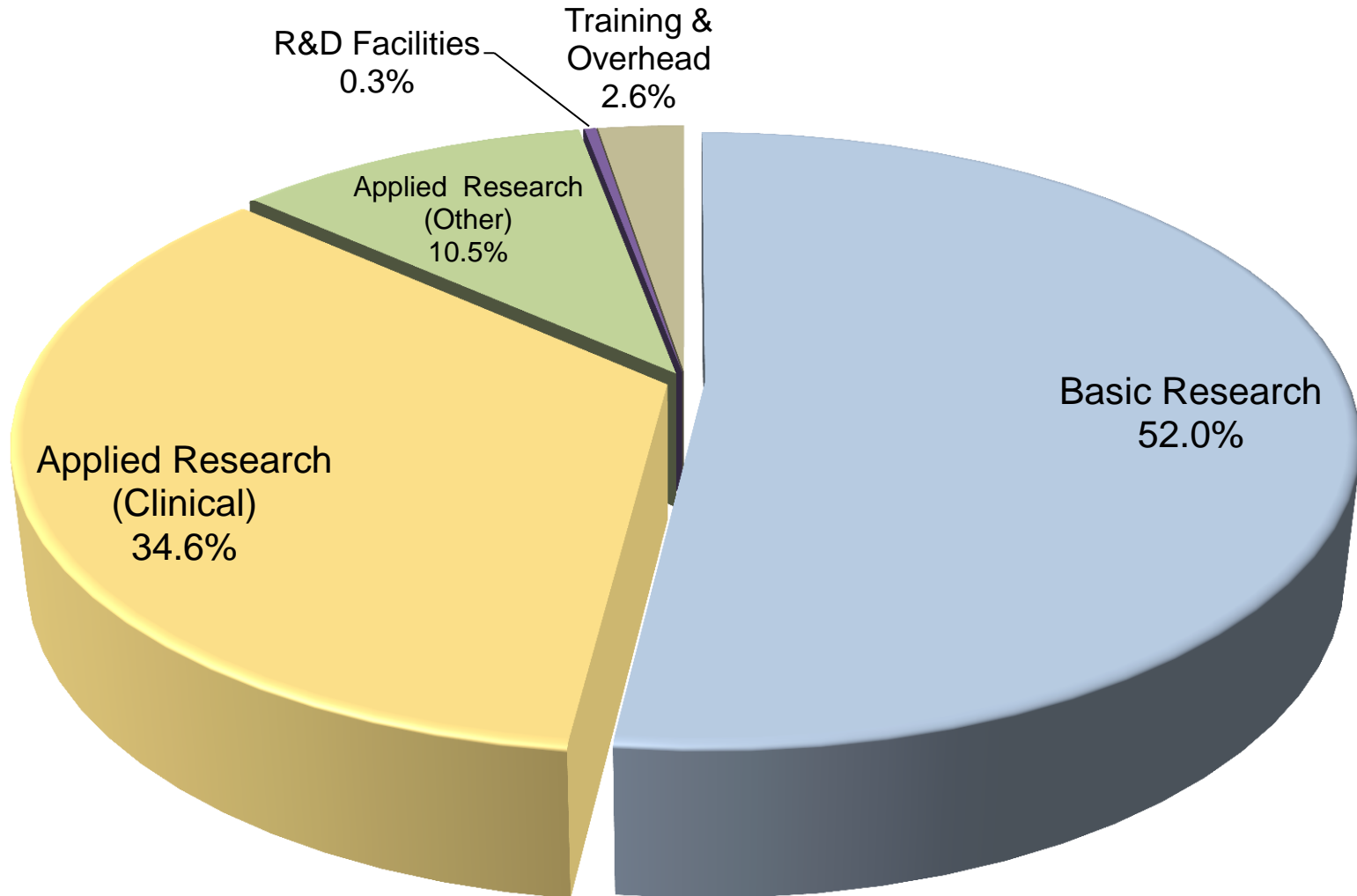


# NCATS will:

- Facilitate – not duplicate – the translational research activities supported and conducted by the ICs
- Complement – not compete with – the private sector
- Reinforce – not reduce – NIH's commitment to basic science research



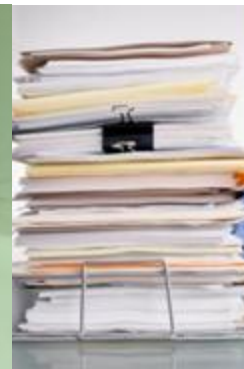
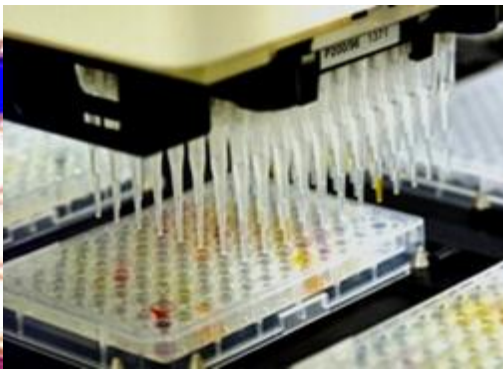
# FY 2010 Percent Distribution of Basic and Clinical Research





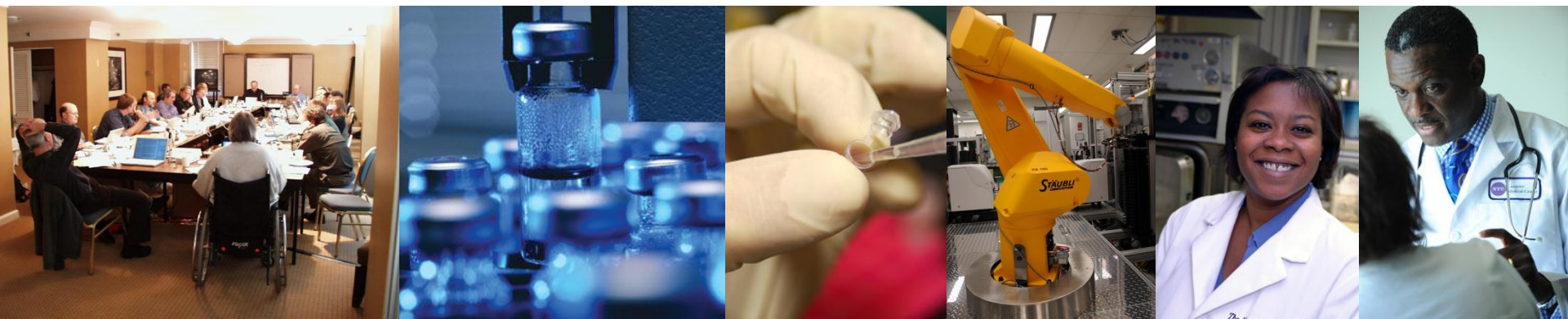
# NCATS Research Programs

- Components of Molecular Libraries Program
- Therapeutics for Rare and Neglected Diseases
- Office of Rare Diseases Research
- Rapid Access to Interventional Development
- Clinical and Translational Science Awards
- FDA-NIH Regulatory Science
- Cures Acceleration Network



# Cures Acceleration Network (CAN)

- Established by the Affordable Care Act
- Included in the Senate Report for FY12 at \$20M
- CAN will advance the development of “high need cures” and reduce barriers between research discovery and clinical trials
- Funding flexibilities:
  - Large Grant Awards: Up to \$15M per award per fiscal year
  - Partnership Awards: \$1 for every \$3 from NIH
  - Flexible Research Awards: DARPA-like authority



# The ACD-NCATS Working Group

*Provide high-level advice on the best ways that NCATS can speed the entire effort of getting effective medicines to patients.*

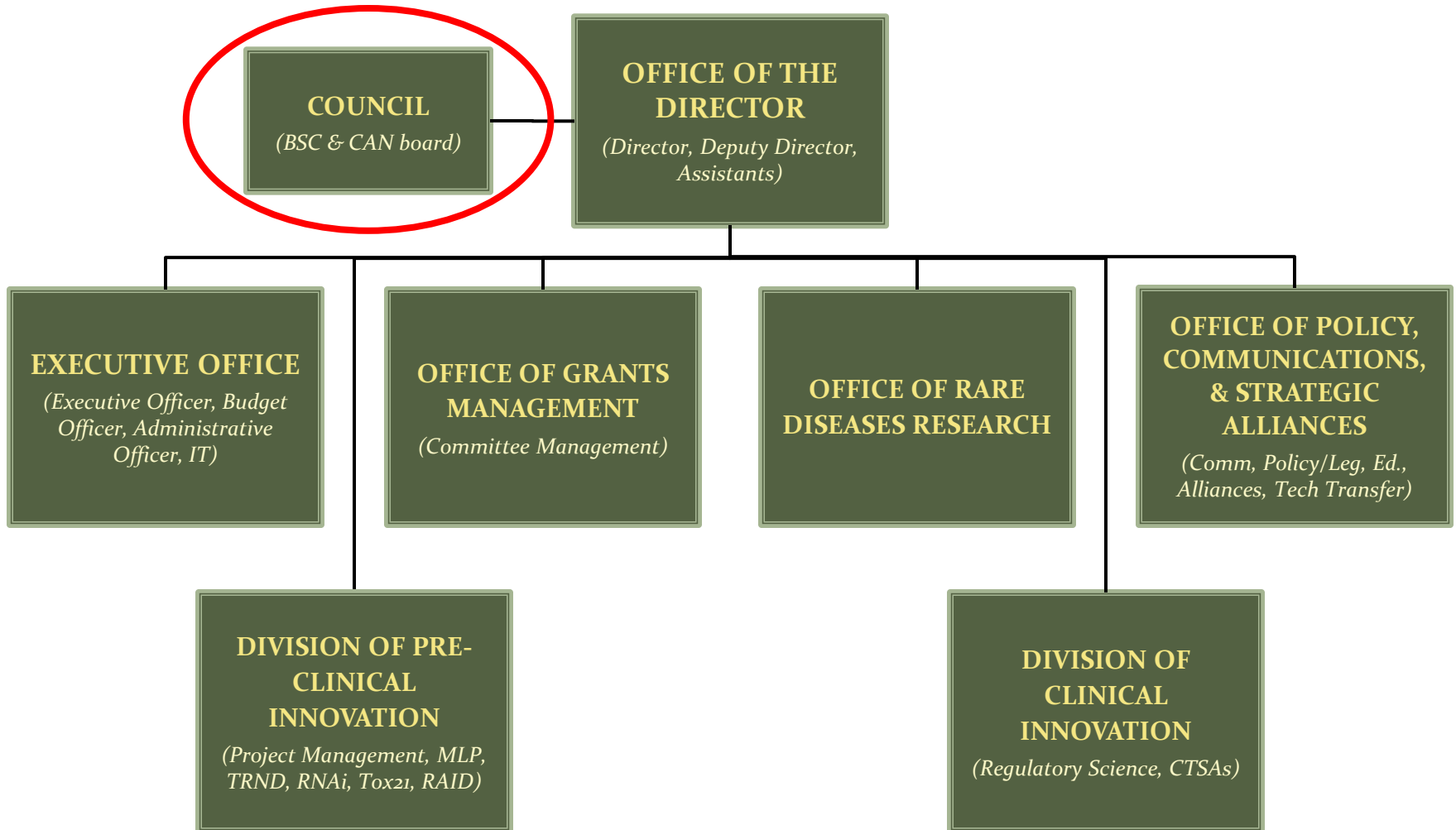
- **Maria C. Freire, Ph.D. (Chair)**  
Albert and Mary Lasker Foundation
- **Julian Adams, PhD**  
Infinity Pharmaceuticals, Inc.
- **Lee E. Babiss, PhD**  
Global Laboratory Services PPD, Inc.
- **Brook Byers, MBA**  
Kleiner Perkins Caufield & Byers
- **William W. Chin, MD**  
Harvard Medical School
- **Susan Desmond-Hellmann, MD**  
UCSF
- **David Ginsburg, MD**  
University of Michigan
- **Victoria Hale, PhD**  
Medicines360
- **Helen H. Hobbs, MD**  
University of Texas at Southwestern
- **Robert S. Langer, ScD**  
Massachusetts Institute of Technology
- **Stelios Papadopoulos, PhD**  
Exelixis
- **Mary K. Pendergast, JD**  
Pendergast Consulting
- **Moncef Slaoui, PhD**  
GlaxoSmithKline
- **Marc Tessier-Lavigne, PhD**  
Genentech, Inc.
- **David L. Valle, MD**  
Johns Hopkins

# ACD-NCATS Report Findings

## NCATS Can:

- Catalyze translation by promoting innovative research
- Galvanize and support new partnerships
- Support and augment the discipline of regulatory science and its application
- Expand the precompetitive space
- Harness the power of the CTSA Program
- Transformation through training
- Streamline administrative processes

# NCATS Organization



# CAN Board (and NCATS Council and BSC)

## Voting members

Venture Capitalist	4 Individuals
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Disease Advocate	8 Individuals
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Basic research

Medicine

Biopharmaceuticals

Discovery and delivery of medical products

Bioinformatics and gene therapy

Medical instrumentation

Regulatory review

Not specified	5 Individuals
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## Non-Voting members

National Institutes of Health

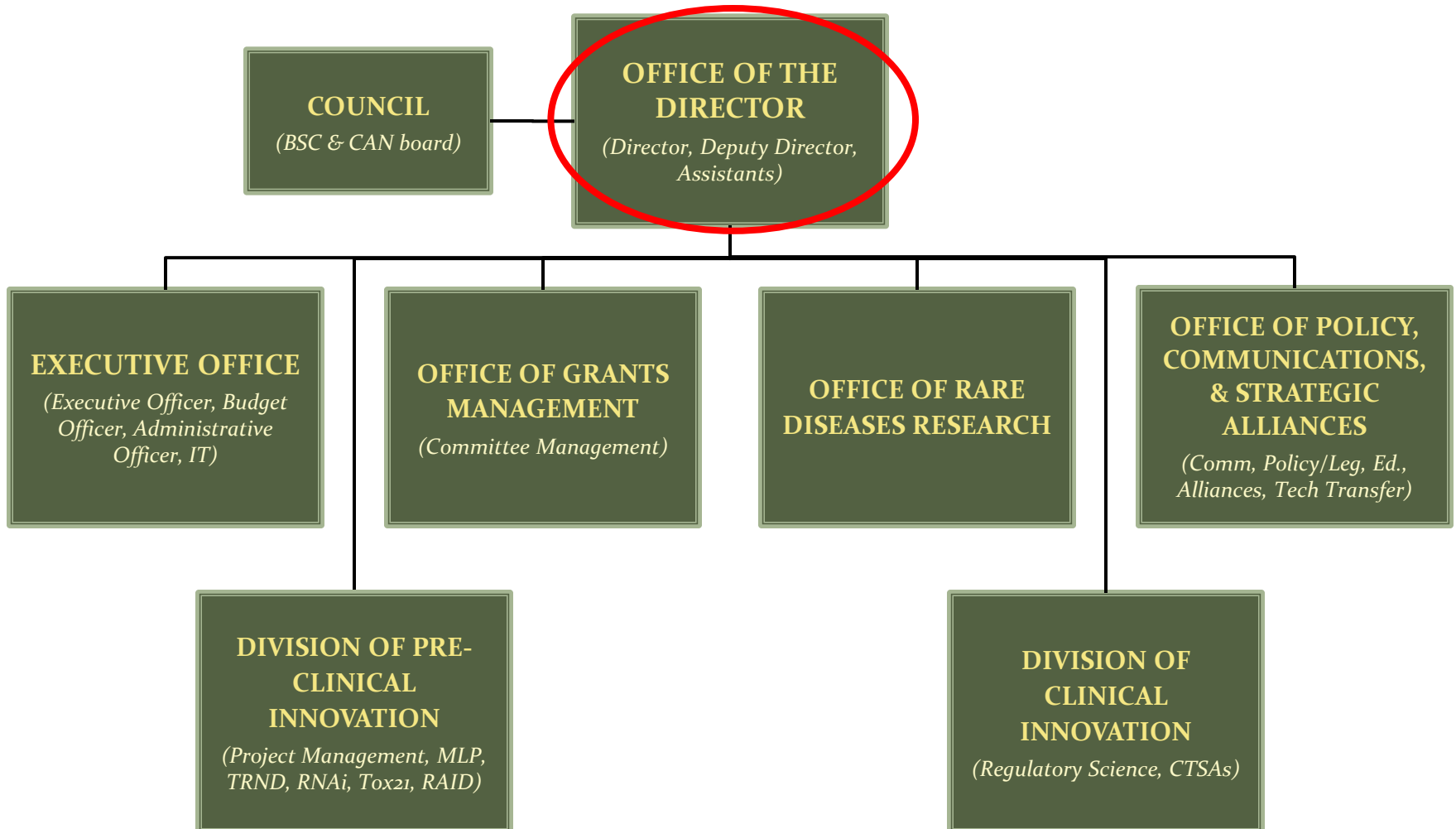
Food and Drug Administration

Office of the Assistant Secretary of Defense for Health Affairs

National Science Foundation

Veteran's Health Administration

# NCATS Organization



# NCATS Director: Search Committee

Co-chairs: Eric Green and Tom Insel

Members:

- NIH: Anthony Fauci and Story Landis
- Margaret Anderson, FasterCures
- Amy Comstock-Rick, Parkinson's Action Network
- Geoff Duyk, TPG Biotech
- Freda Lewis-Hall, Pfizer
- Brad Margus, Envoy Therapeutics
- Steven Marc Paul, Weill Cornell Medical College
- Marc Tessier-Lavigne, Rockefeller University
- Janet Woodcock, FDA



# NCATS Director

He or she must...

- Have expertise that transcends a single discipline
- Have experience in academia and the private sector
- Be able to convene diverse partners
- Be willing to engage in “disruptive innovation”



# **The Innovation Imperative ...**

**I have a great respect for incremental improvement, and I've done that sort of thing in my life, but I've always been attracted to the more revolutionary changes. I don't know why. Because they're harder. They're much more stressful emotionally. And you usually go through a period where everybody tells you that you've completely failed.**

**Steve Jobs**

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### PRESIDENT'S NEW DIRECTIVE FUELS TECHNOLOGY TRANSFER IDEAS

POSTED ON OCTOBER 28TH, 2011 BY DR. MARK ROHRBAUGH

Today, as part of his "Startup America" initiative, [President Obama announced his plan](#) to accelerate tech transfer and commercialization of Federal research in support of high-growth businesses. As the director of the NIH Office of Technology Transfer, I couldn't be more excited. NIH manages the largest biomedical patent and licensing portfolio among public sector institutions so we have every interest in seeing these technologies get to the private sector for commercialization so patients can benefit as soon as possible.

Most folks probably aren't aware that the NIH intramural research program has played a major role in new product development; we have contributed to 14% of all public sector institution inventions that have led to FDA approved drugs. In addition, there are more than 50 products undergoing clinical trials based on technologies licensed from the NIH. The President's directives clearly outline actions that Federal agencies can take to set clear goals, streamline processes, and develop new partnerships. The goal is to increase the successful outcomes of tech transfer and commercialization activities significantly over the next five years.

An area that I think can bring the fastest gains is streamlining processes; it just has to be made a lot easier. Last month, [we announced](#) a new effort to make it easier for startup companies to get license agreements for new technologies developed by NIH and FDA. This will help start-up companies attract the investment needed to develop promising medical products and get them into the hands of doctors and patients.

Another exciting change at NIH is a new centralized web-based materials transfer agreements system, called the [Transfer Agreement Dashboard](#) or TAD, which helps make the thousands of tangible research materials easily transferrable to promote research. TAD is intuitive, less time consuming, and nearly paperless . . . welcome to the 21st Century! Finally, we've embraced several new technologies to foster collaboration, including Pipeline-2-Partnerships, a new web platform that makes it easier to form partnerships with companies that are developing NIH technologies.

### TWEETS FROM @NIHFORHEALTH

- ◊ [Radio: Intestinal stem cells respond to food by supersizing the gut](#)  
<http://t.co/54ozPVtW>  
16 hours ago
- ◊ [News: Mouse study explains bacterium's unique role in periodontitis](#)  
<http://t.co/Wk6hpFw>  
21 hours ago
- ◊ [News: NIH nurse practitioner chosen for Excellence in Nursing Award](#)  
<http://t.co/AG8E3ETe>  
21 hours ago
- ◊ [News: Neurons grown from skin cells may hold clues to autism](#)  
<http://t.co/1LRGcgUB>  
1 day ago
- ◊ [News: Training peers improves social outcomes for some kids with ASD](#)  
<http://t.co/cYHziUE5>  
1 day ago



# NIH...

## Turning Discovery Into Health

