

Opportunities for Research and NIH

The promise of fundamental advances in diagnosis, prevention, and treatment of disease has never been greater.

Francis S. Collins

The mission of the National Institutes of Health (NIH) is science in pursuit of fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to extend healthy life and to reduce the burdens of illness and disability. The power of the molecular approach to health and disease has steadily gained momentum over the past several decades and is now poised to catalyze a revolution in medicine. The foundation of success in biomedical research has always been, and no doubt will continue to be, the creative insights of individual investigators. But increasingly those investigators are working in teams, accelerated by interdisciplinary approaches and empowered by open access to tools, databases, and technologies, so a careful balance is needed between investigator-initiated projects and large-scale community resource programs. For both individual and large-scale efforts, it is appropriate to identify areas of particular promise. Here are five such areas that are ripe for major advances that could reap substantial downstream benefits.

High-Throughput Technologies

In the past, most biomedical basic science projects required investigators to limit their scope to a single aspect of cell biology or physiology. The revolution now sweeping the field is the ability to be comprehensive—for example, to define all of the genes of the human or a model organism, all of the human proteins and their structures, all of the



diverse information about the genetic underpinnings of 20 major tumor types. This information will likely force a complete revision of diagnostic categories in cancer and will usher in an era where abnormal pathways in specific tumors will be matched with the known targets of existing therapeutics. Another example is the opportunity to understand how interactions between ourselves and the microbes that live on us and in us (the “microbiome”) can influence health and disease (2).

Translational Medicine

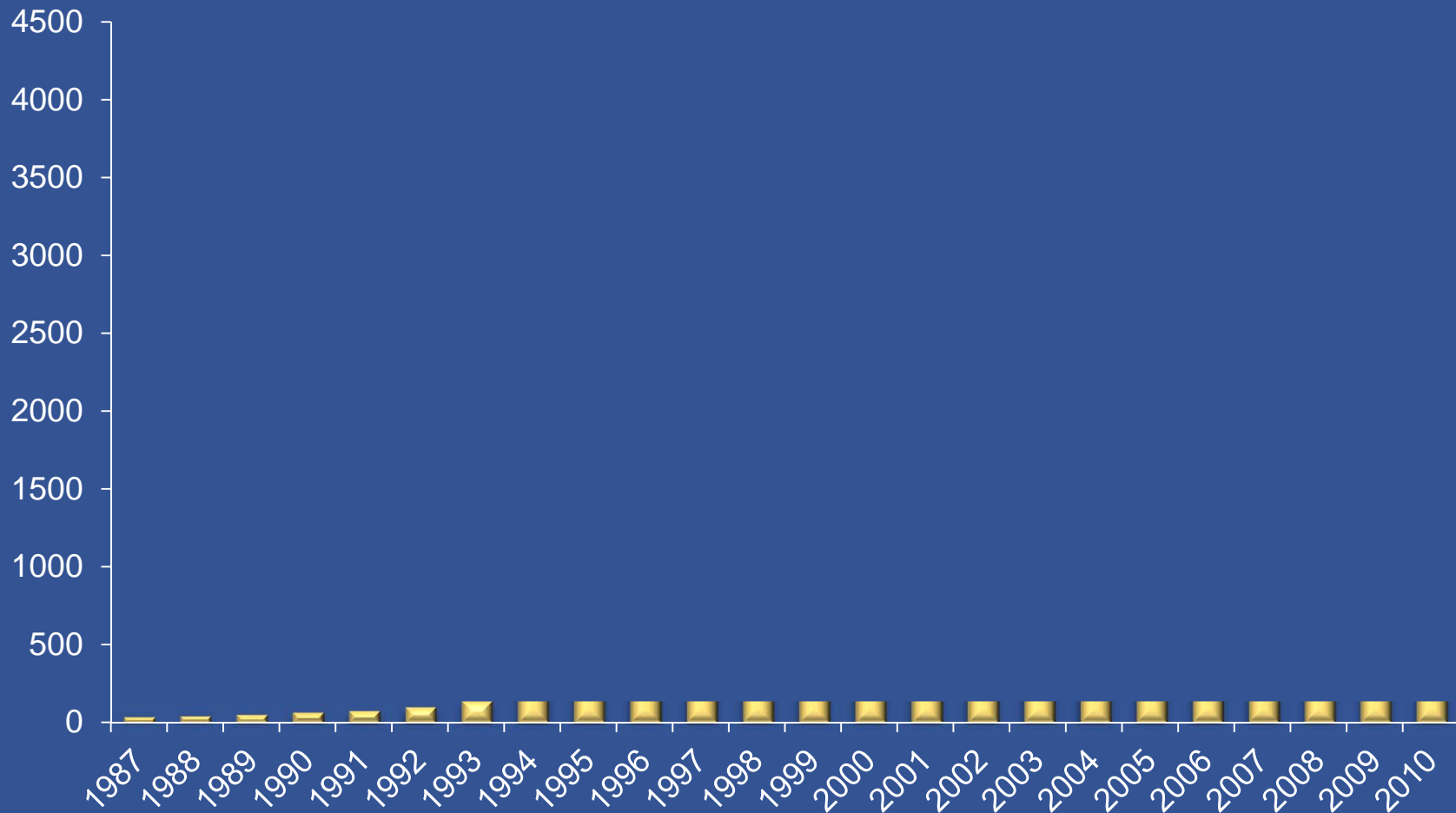
Critics have complained in the past that NIH is too slow to translate basic discoveries into new diagnostic and treatment advances in the

bring them to clinical trials and U.S. Food and Drug Administration (FDA) approval.

As one example, the NIH Therapeutics for Rare and Neglected Diseases (TRND) (3) program will allow certain promising compounds to be taken through the preclinical phase by NIH, in an open environment where the world’s experts on the disease can be involved. Furthermore, as information about common diseases increases, many are being resolved into distinct molecular subsets, and so the TRND model will be even more widely applicable.

The first human protocol (for spinal cord injury) involving human embryonic stem cells (hESCs) was approved by the FDA in 2009, and the opening up of federal support for hESC research will bring many

Disorders with Known Molecular Basis



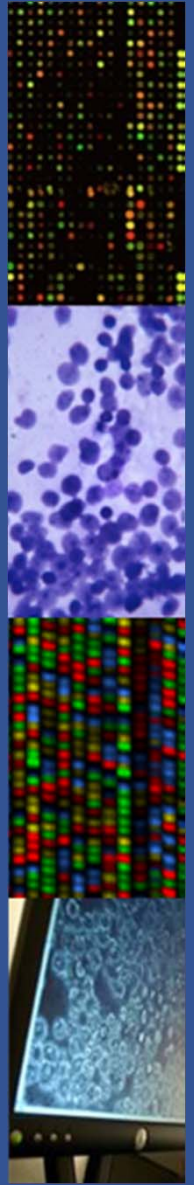
Source: *Online Mendelian Inheritance in Man*

GWAS hits for common disease



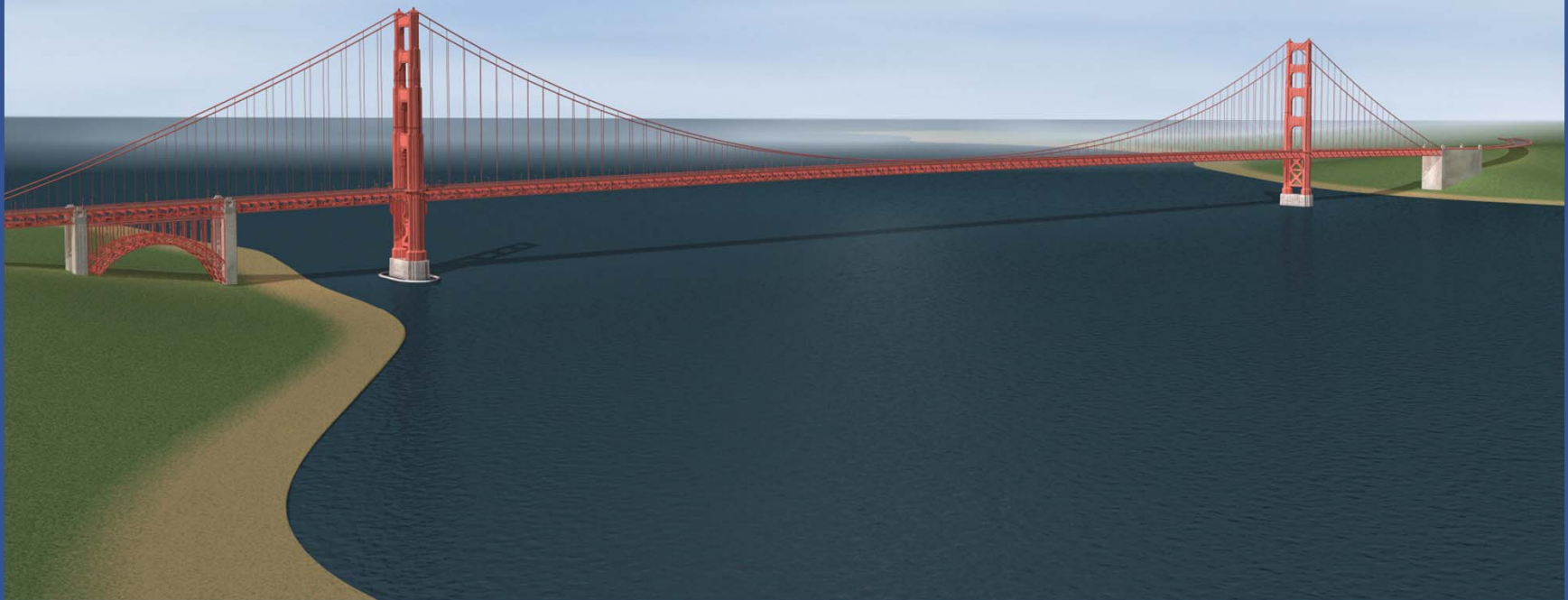
The Cancer Genome Atlas (TCGA)

- A comprehensive, collaborative effort led by NIH
 - To map genomic changes in major types, subtypes of cancer ...
 - To help chart a new course in cancer research
- Pilot project
 - Established scientific infrastructure; demonstrated “proof of concept”
 - Focused on 3 types of cancer: glioblastoma multiforme; ovarian; lung
- Current goal: to identify recurrent genomic and epigenomic drivers for at least 20 cancers over next 3 years



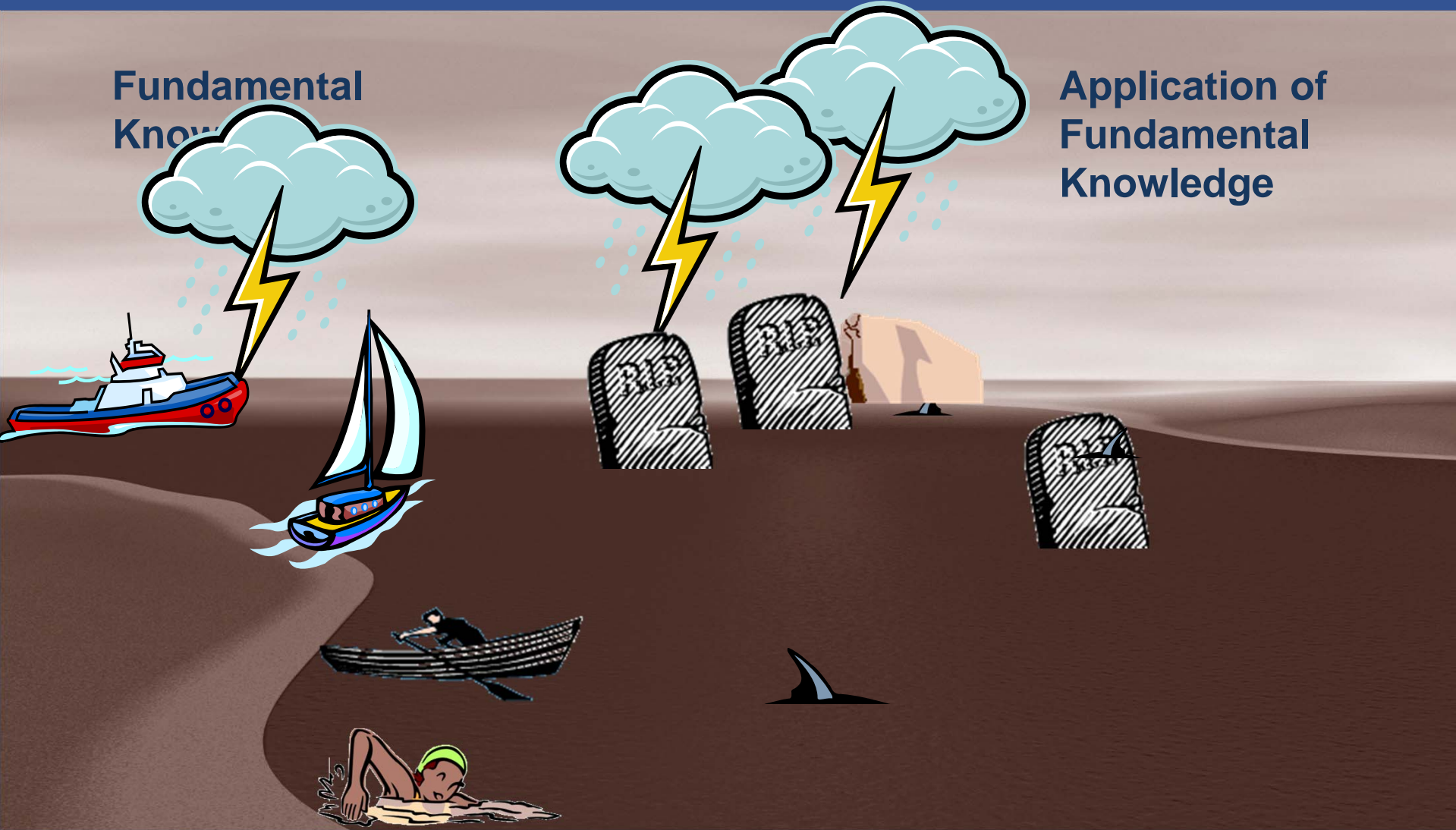
**Fundamental
Knowledge**

**Application of
Fundamental
Knowledge**



Fundamental
Know

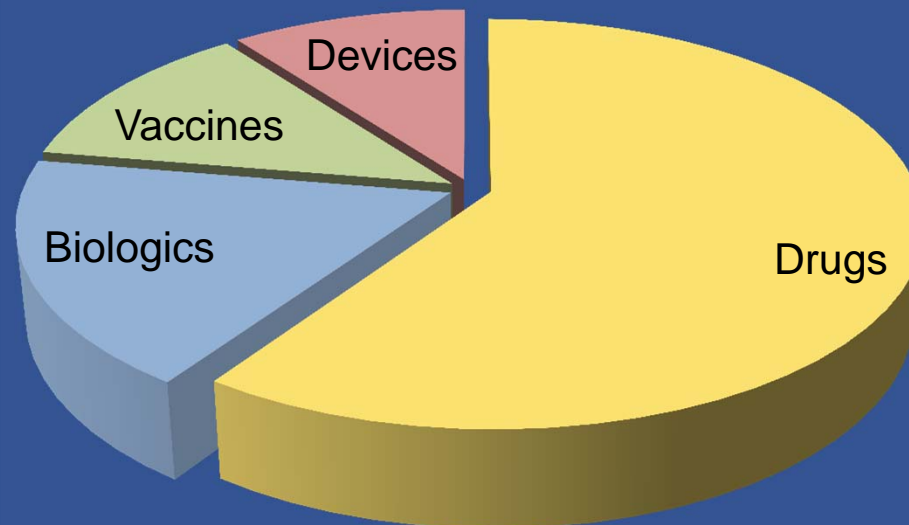
Application of
Fundamental
Knowledge



Therapeutics Development at NIH

A 2010 trans-NIH inventory of activities relevant to therapeutics development found:

- Substantial investments in therapeutics development research
- Approximately 65% preclinical research; 35% clinical research
- 550 activities reported of varying sizes and areas of emphasis



Distribution of Investment

Scientific Management Review Board (SMRB) Recommendations to NIH



- May 2010
 - NIH Director asks SMRB to determine how NIH could better support translational and therapeutic sciences
- December 2010
 - SMRB recommends (12 to 1) that a new translational medicine and therapeutics center be created
 - SMRB also recommends NIH undertake a more extensive and detailed analysis through a transparent process to evaluate the new center's impact

SMRB Members

- Norman Augustine (Chairman)
Lockheed Martin
- Jeremy Berg, NIGMS
- Josephine Briggs, NCCAM
- William Brody, Salk Institute for
Biological Studies
- Gail Cassell, Eli Lilly and Company
- Francis Collins, NIH (ex officio)
- Anthony Fauci, NIAID
- Dan Goldin, Intellisys Corporation
- Eric Green, NHGRI
- Richard Hodes, NIA
- Stephen Katz, NIAMS
- Thomas Kelly, Sloan-Kettering
Institute
- Deborah Powell, University of
Minnesota Medical School



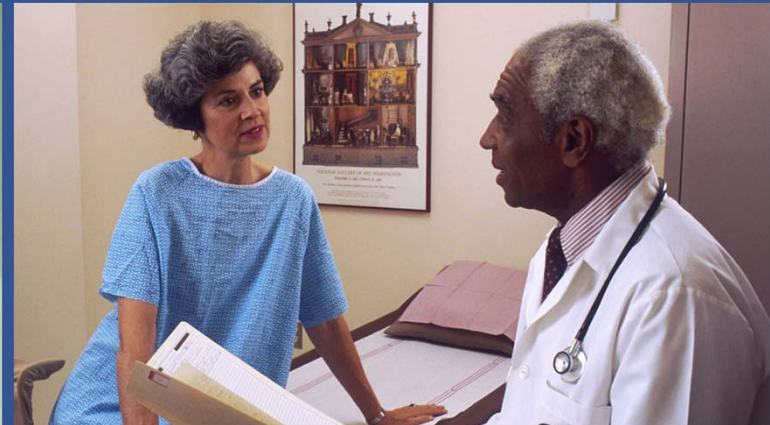
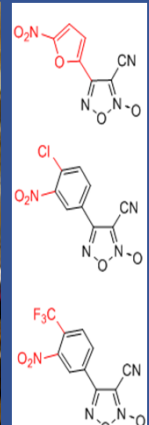
- Griffin Rodgers, NIDDK
- William Roper, University of North
Carolina
- Arthur Rubenstein, University of
Pennsylvania School of Medicine
- Susan Shurin, NHLBI
- Solomon Snyder, Johns Hopkins
University
- Huda Zoghbi, Baylor College of
Medicine
- Harold Varmus, NCI

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

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.

Updated 6.3.11





Disease

Target ID

Assay Dev.

HTS

Probe to Lead

Pre-Clinical

FDA IND

Ph. I

Ph. II

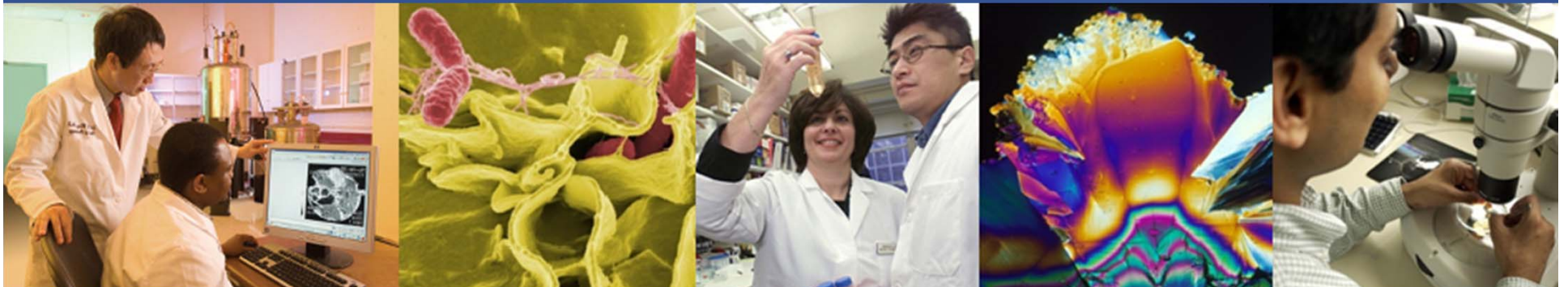
Ph. III

FDA Re-view

Clinic

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



kp3

Updated (?)

Kim Pelis, 6/14/2011

New Paradigms: Rescuing and Repurposing

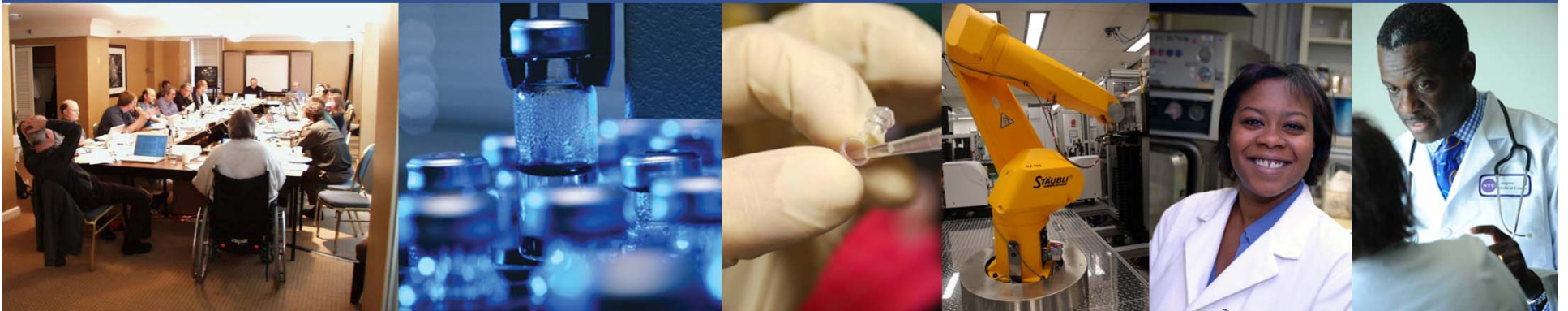
A graphic featuring a vertical column of five blue capsules on the left side. Below this, a horizontal band of light green background contains three diagonal columns of pills: a column of light green capsules, a column of blue tablets, and a column of pink capsules. The pills are arranged in a descending staircase pattern from left to right.

NIH – INDUSTRY ROUNDTABLE
April 21-22, 2011

Exploring New Uses for Abandoned and Approved Therapeutics

Cures Acceleration Network (CAN)

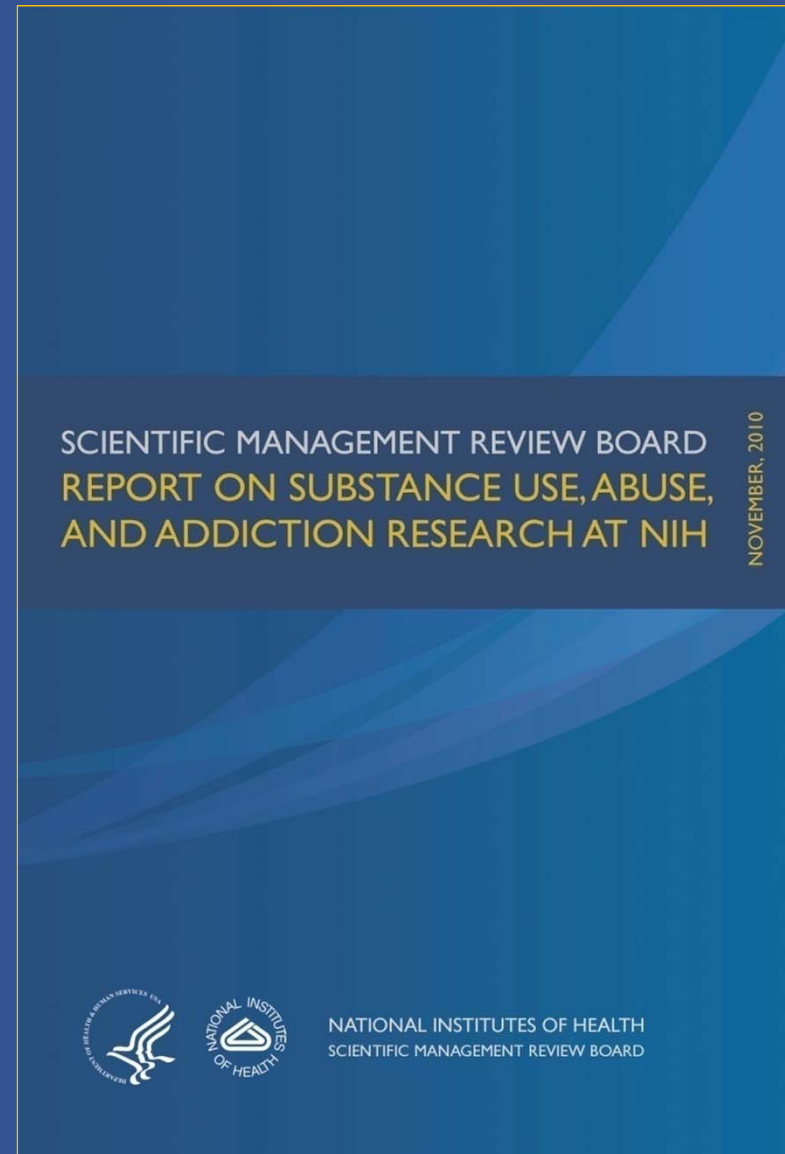
- Authorized in Affordable Care Act, awaits appropriation
- CAN will:
 - Advance development of “high need cures”
 - Reduce barriers to translation in areas the private sector is unlikely to pursue actively
- Funding mechanisms:
 - Grant Awards – with or without partnership:
 - Up to \$15 million per award per fiscal year
 - Flexible Research Awards:
 - DARPA-like authority
 - Not to exceed 20% of total appropriated funds /fiscal year



SMRB Recommendations

**Recommendation made,
November 16, 2010:**

- Create a new Institute focusing on substance use, abuse, and addiction (“SUAA”) research and related public health initiatives
- Integrate relevant research portfolios from NIDA, NIAAA, other ICs



Substance Use, Abuse, and Addiction Action Timeline

- January to March 2011: SUAA Task Force conducted internal discussions with NIH scientific staff in the ICs that could potentially be affected by the proposed changes
- April 2011: based on those discussions, Task Force developed **draft guiding principles**

Task Force Considerations and Guiding Principles

- **Science:** the nature of the science being conducted is the primary factor driving recommendations
- **Populations with Co-Morbid Addictive Behaviors:** addictive behavior frequently co-exists with other medical disorders, including mental disorders, e.g., post-traumatic stress, borderline personality, and schizophrenia
 - When the pathophysiology of the underlying disorder is distinct from the addictive behavior, the primary disorder requires separate consideration
- **Special Expertise:** the expertise of staff needed to manage and foster a research area is critical in recommending placement of programs

Substance Use, Abuse, and Addiction Action Timeline

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- April 2011: based on those discussions, Task Force developed draft guiding principles
- June 2011 to Fall 2012: Task Force, NIDA/NIAAA Intramural, IC Leadership
 - Complete portfolio analysis of all relevant grants, cooperative agreements, contracts, and intramural research projects; develop final portfolio integration plan
 - Develop Scientific Strategic Plan including input from stakeholders

Substance Use, Abuse, and Addiction Action Timeline

- Tobacco Research at NCI
 - The Task Force is currently analyzing the NCI portfolio and has determined that portions of the nicotine and tobacco portfolios related to addiction and control could be candidates for inclusion in the proposed Institute. However, this portfolio is complex and more time needs to be taken to determine what would make the most sense to be included in the proposed Institute.

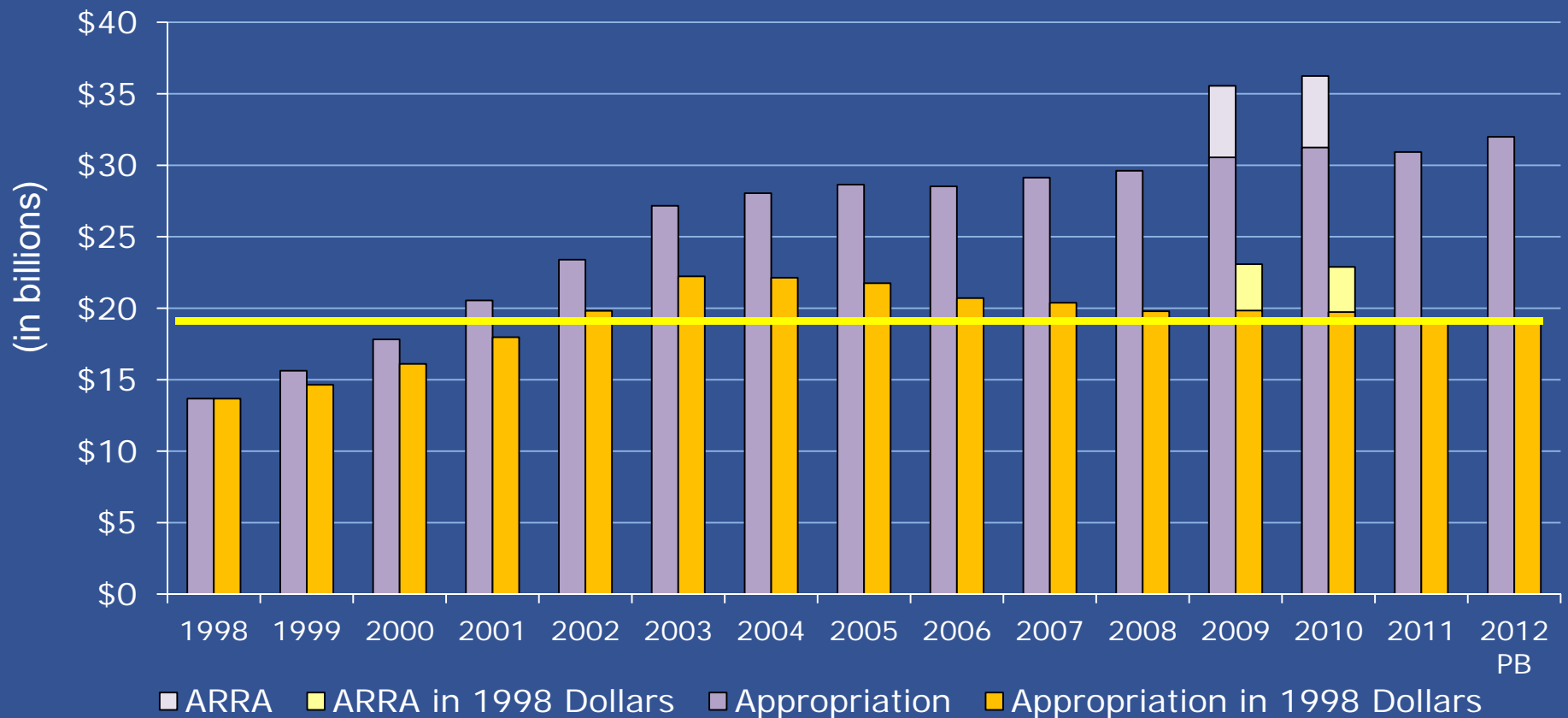
Substance Use, Abuse, and Addiction Action Timeline

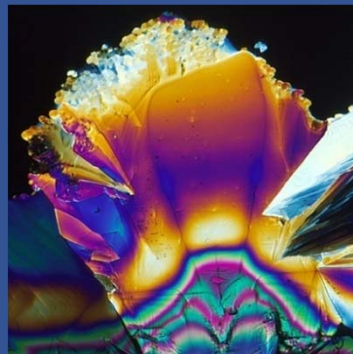
- Fall 2012:
 - Release of Portfolio Integration Plan and public comment period
 - Release of Scientific Strategic Plan and public comment period
- December 2012: Final Recommendations to NIH Director
- January/February 2013: Include in President's FY 2014 Budget
 - Start implementing parts of Scientific Strategic Plan not involved in reorganization
- October 2013 (FY 2014): National Institute of Substance Use and Addiction Disorders

Challenges to Biomedical Research

Appropriation History vs. Actual Purchasing Power

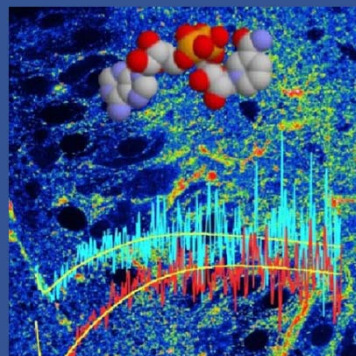
FY 1998 appropriation – FY 2012 Presidential Budget (\$ in billions)





NIH

*Turning discovery
into health*





NCATS: **Functions**

Improve the processes of diagnostics and therapeutics development, testing, and implementation by:

- Experimenting with innovative approaches in an open-access model
- Choosing therapeutic projects to evaluate these innovative approaches
- Promoting interactions to advance the field of regulatory science

Catalyze the development and implementation of new diagnostics and therapeutics by:

- Encouraging collaborations across all sectors
- Providing resources to enable diagnostics and therapeutic development and implementation
- Enhancing training in relevant disciplines

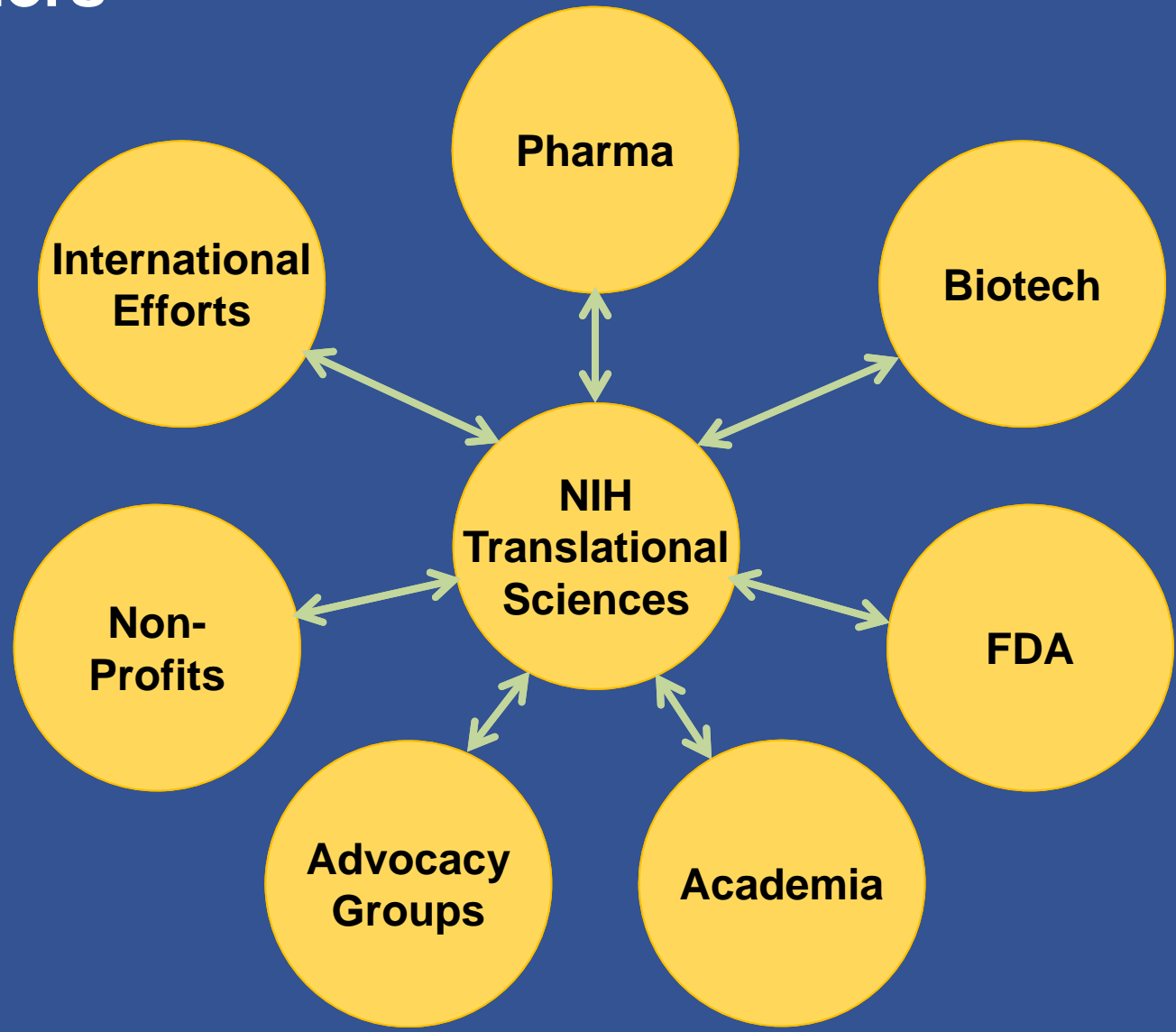
NIH-FDA Collaborations



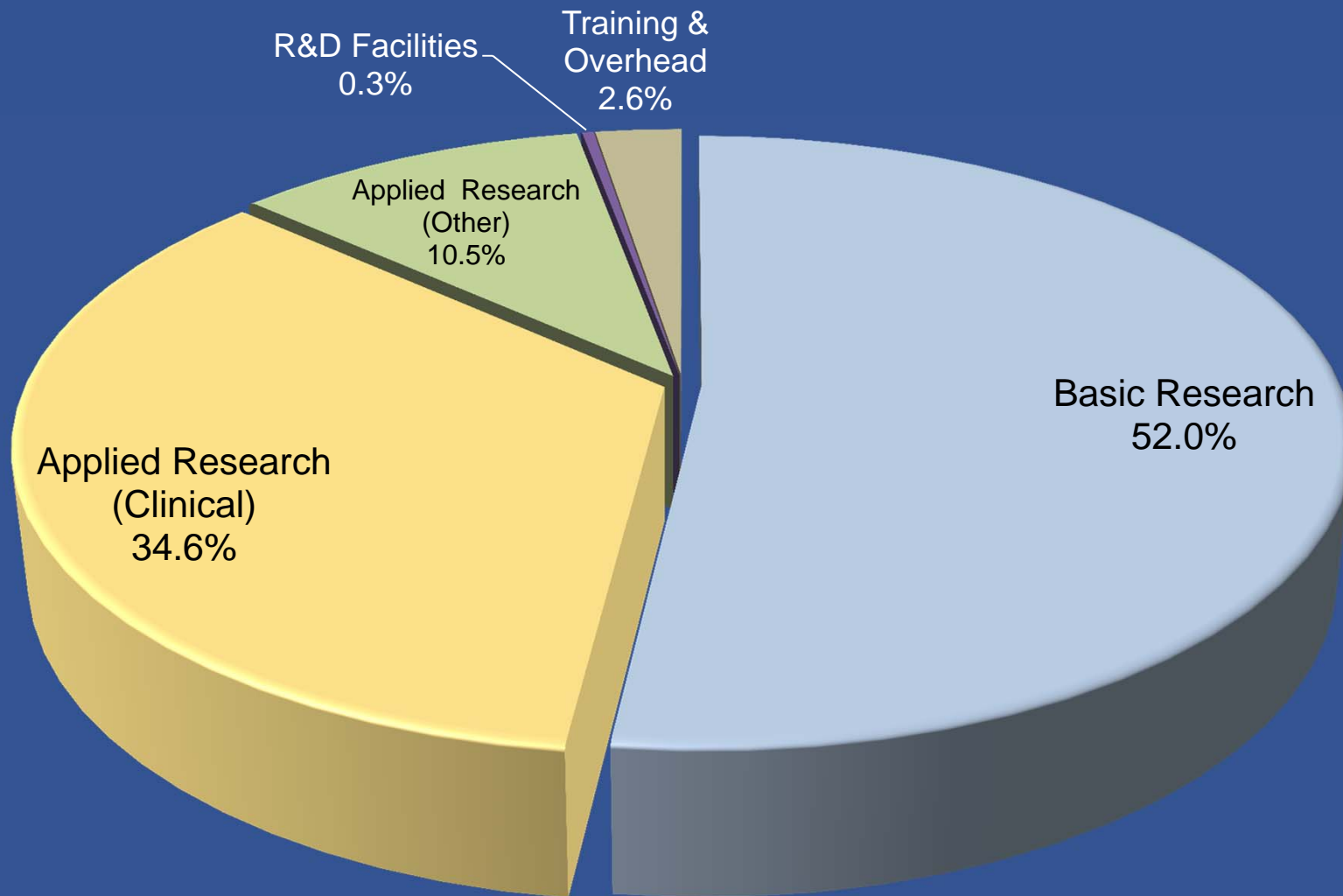
- NIH-FDA Regulatory Science Initiative: cooperative research grant awards to advance translational and regulatory science
- NIH-FDA Joint Leadership Council (est. 2010)
 - Goal: advance translational sciences by ensuring that:
 - Regulatory considerations are integral to biomedical research planning
 - The latest science informs the regulatory review process
 - Six working groups currently re
 - To better define regulatory
 - of co-developed diagnostic
 - To develop risk-based app
 - diagnostics



Catalyzing Collaborations With External Partners



FY 2010 Percent Distribution of Basic and Clinical Research



A Definitive List of Approved Drugs

- NIH Chemical Genomics Center (NCGC): national resource for translating genomic information into biological insights and new therapeutics
- NCGC Pharmaceutical Collection
 - Definitive list of all small-molecule drugs approved for human or veterinary use (U.S. and worldwide)
 - All data publically available
- Purpose: facilitate *undruggable* drug repurposing – e.g. for rare diseases



The image is a composite of two parts. On the left is the cover of a book titled 'PERSPECTIVE PHARMACOLOGY The NCGC Pharmaceutical Collection: A Comprehensive List of Approved Drugs from the NIH Chemical Genomics Center'. The authors listed are Ruili Huang, Noel Southam, and Ajit Jadhav, with Dac-Trung Nguyen as the editor. On the right is a screenshot of a web-based software interface for drug data. The interface shows a search for 'Zidovudine' and displays its chemical structure, CAS number (10352-17-2), and a list of various identifiers and synonyms. A table at the bottom lists 'Accessions' for '5-hydroxytryptamine receptor 1B' with their corresponding IDs.

Tell us what you think...

The image shows a screenshot of the National Institutes of Health (NIH) website. At the top, it displays the U.S. Department of Health & Human Services logo and the NIH logo with the tagline "Turning Discovery into Health". The URL "www.nih.gov" is prominently displayed in a yellow box. A navigation menu includes links for Health Information, Grants & Funding, News & Events, Research & Training, Institutes at NIH, and About NIH. The main content area features a "NIH RESEARCH Matters" section with a DNA helix image and a "More" button. To the right, there is an "IN THE NEWS" section with three news items: "Cancer Rates Continue to Decline", "YouTube Video: Dr. Collins speaks about his role as NIH Director", and "Weight-Control Information Network". Below this is the "THE NIH DIRECTOR" section, which includes a photo of the director and a list of links such as "Biographical Sketch" and "Photo Gallery". A "Feedback NIH" callout box is overlaid on the bottom right of the page, containing the text: "Provide input on important issues that affect NIH, the biomedical research community, and human health in general". The footer of the website includes social media icons forBookmark & Share, E-mail Updates, RSS Feeds, Get Widgets, Multimedia, NIH Radio, Twitter, Facebook, and YouTube.

U.S. Department of Health & Human Services

National Institutes of Health
Turning Discovery into Health

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NIH RESEARCH Matters

Stay informed with this weekly update of NIH research highlights.

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1 2 3 4 5

IN THE NEWS

Cancer Rates Continue to Decline: Report finds changes in brain tumor diagnoses and survival
March 31, 2011

YouTube Video: Dr. Collins speaks about his role as NIH Director
February 12, 2011

Weight-Control Information Network: Information on nutrition, exercise & fighting obesity
April 7, 2011

For the Press | Newsletters & Feeds

NIH at a Glance | Funding for Research | Labs at NIH | Training at NIH

NIH is the nation's medical research agency—supporting scientific studies that turn discovery into health.

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