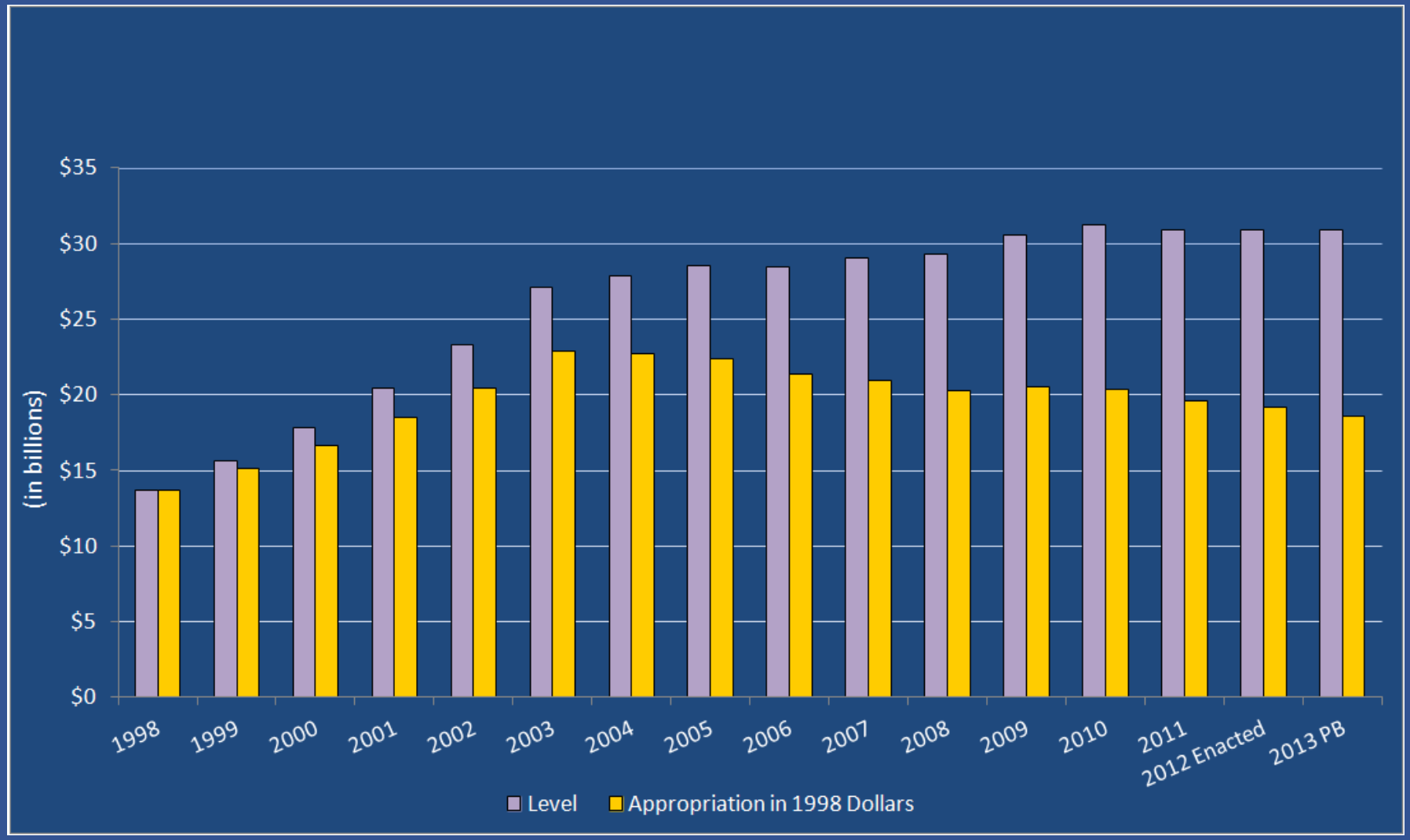
NIH Update

Francis S. Collins, M.D., Ph.D.
Director, National Institutes of Health

Council of Councils
September 5, 2012

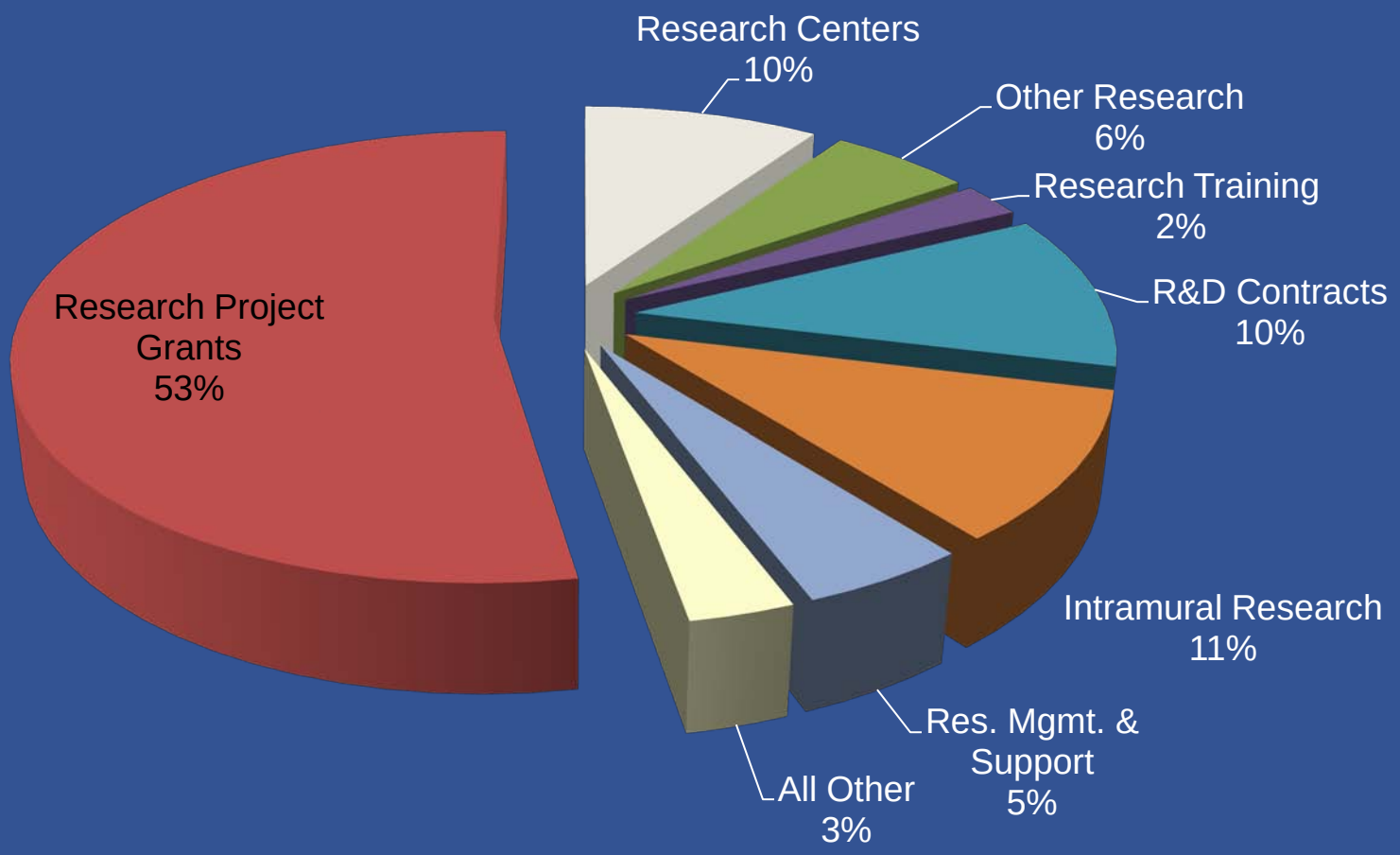
NIH Appropriation vs. Appropriation in 1998 Dollars
FY 2013 President's Budget Request



FY 2013 President's Budget Request

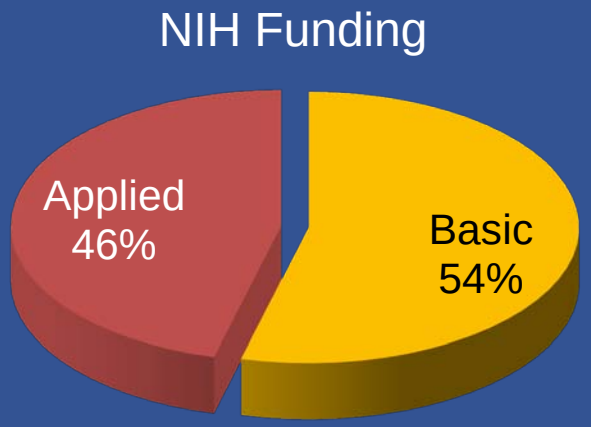
NIH Total Program Level

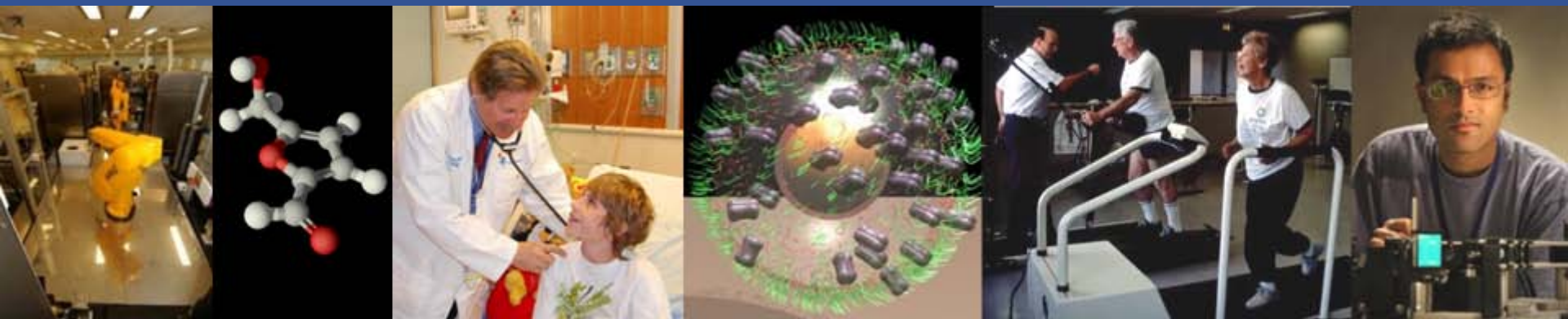
$30,860 Million



Extraordinary Scientific Opportunities — FY 2013

- Investing in Basic Research
- Accelerating Discovery Through Technology
- Advancing Translational Sciences
- New Investigators, New Ideas





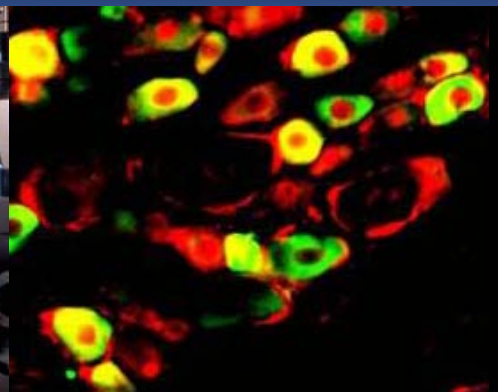
Investing in Basic Research

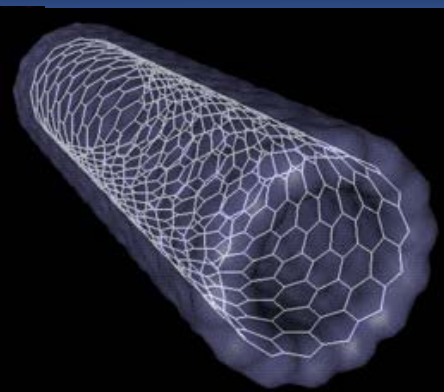
"… the hope of major advances lies in sustaining broad and free-ranging inquiry into all aspects of the phenomena of life, limited only by the criteria of excellence, the scientific importance, and the seriousness and competence of the investigator."

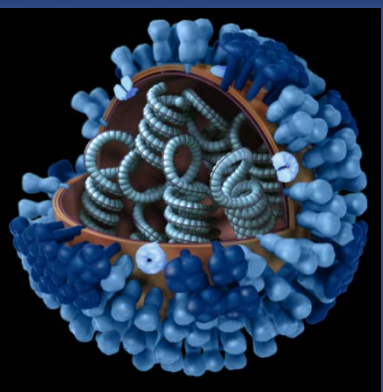
– James A. Shannon, M.D.

8th Director of NIH

135 NIH grantees/trainees have become Nobel Laureates

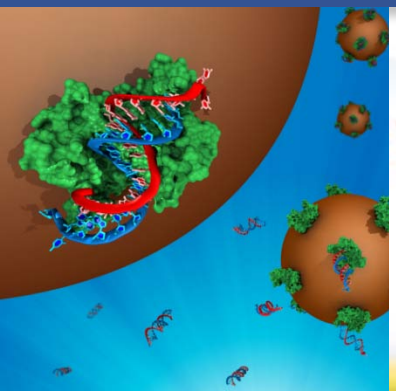


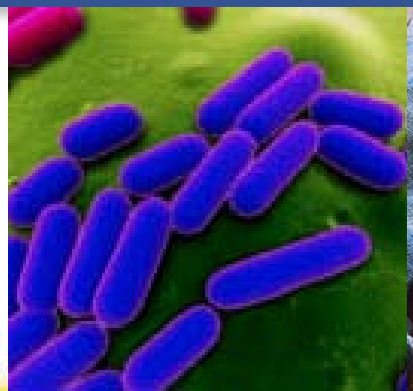




Investing in Basic Research

- Lots of connections with the Common Fund
- Unlocking the potential of microRNAs (miRNAs)
- Exploring the microbiome
- Single cell biology






Francis S. Collins is director of the U.S. National Institutes of Health, Bethesda, MD. E-mail: collinsf@mail.nih.gov

NIH Basics

"WHEN EVERYBODY GETS TO ONE SIDE OF THE BOAT, IT USUALLY TIPS OVER." THAT SAYING MAY have originated on Wall Street, but it also stands as a warning to those charting the future of U.S. biomedical research. If the United States focuses too much of its investment on one part of the research continuum, the entire enterprise may sink.

Perhaps with this in mind, some have questioned whether, in its quest to draw attention to translational research, the U.S. National Institutes of Health (NIH) may be underemphasizing basic research. The NIH will most assuredly continue its strong tradition of supporting basic research, which it defines as systematic study directed toward fuller knowledge or understanding of the fundamental aspects of phenomena and of observable facts without specific applications in mind. Since 2003, the proportion of NIH funds spent on basic research, defined in this way, has ranged from 53 to 57%, standing at 54% for fiscal year (FY) 2012.

A scan of *Science*'s top breakthroughs of 2011 shows that NIH-funded research and/or research resources enabled four of the six advances related to life sciences: three basic (cell senescence, human microbiome, archaic human DNA) and one clinical with deep roots in basic research (HIV treatment as prevention). Basic research also accounts for most of the 135 Nobel Prizes won by NIH-supported scientists, including the 2011 awards to Bruce Beutler and Jules Hoffmann for their discoveries about innate immunity, and the late Ralph Steinman for adaptive immunity. Likewise, current NIH grantee Arthur Horwich and past grantee F. Ulrich Hartl captured 2011 Lasker awards for landmark explorations of the cell's protein-folding machinery. Their work, which provided insights on protein misfolding in neurodegenerative disease, is among countless examples of basic research, including that with model organisms,* giving rise to medical advances.

But what is NIH doing to fuel the next generation of breakthroughs? The agency is supporting basic research in all of *Science*'s biomedical "Areas to Watch" in 2012: elucidating metabolic pathways in stem cells; whole-genome sequencing for epidemiology; and developing new models of developmental brain disorders. NIH's institutes and centers also survey the basic research horizon for exciting opportunities in their realms. Examples include efforts to understand the roles of microRNAs and competing endogenous RNA in gene regulation; detailed analyses of *Drosophila* and *Caenorhabditis elegans* biology supported by modENCODE (the identification of all functional elements of selected model organism genomes); and a trans-NIH effort to map the brain's wiring in high resolution. The NIH Common Fund† has built a portfolio designed to tackle some of biology's most fundamental questions, including new efforts in extracellular RNA communication and single-cell analysis. The Common Fund's High-Risk/High-Reward program has grown from $7.3 million in 2004 to $191.8 million in 2011, and further increasing the number of Pioneer and New Innovator awards will be a top NIH priority in FY2014. These awards are open to exceptionally creative scientists in any area of biomedical research, and if past trends continue, basic research will dominate.

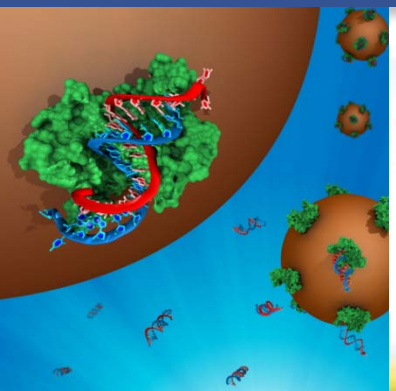
In this time of severe budget constraints,‡ Americans need to know that today's basic research is the engine that powers tomorrow's therapeutic discoveries. They need to know that basic research is the type of science that the private sector, which requires rapid returns on investment, cannot afford to fund. They need to know that, because it is impossible to predict whence the next treatment may emerge, the nation must support a broad portfolio of basic research. And they need to hear it from all aboard the biomedical research ship, whether they are port, starboard, or somewhere in between.

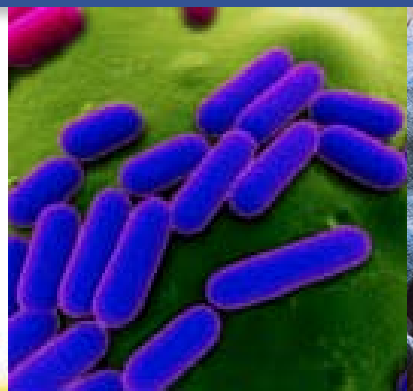
– Francis S. Collins

10.1126/science.1227820

Accelerating Discovery Through Technology

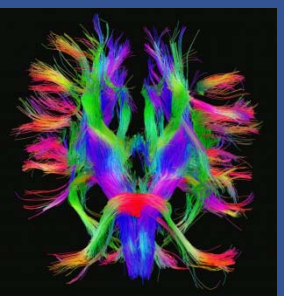
- iPS cells
- Nanotechnology
- Imaging
- DNA/RNA sequencing

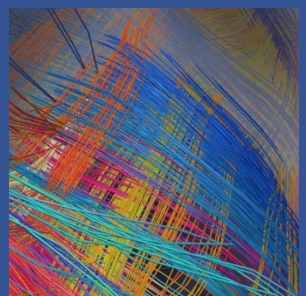





The Human Connectome Project (HCP)

- Launched under NIH Blueprint for Neuroscience Research, the HCP:
  - Supports projects to map brain's connections
  - Speeds development of related tools and technologies
- HCP-supported advance: Connectom diffusion magnetic resonance imaging scanner
  - Greatly improves scan speed, detail
  - Reveals grid structure: 2D sheets of parallel neuronal fibers that cross paths at right angles
    - Relevance for brain evolution; normal, pathological development





NIH Blueprint for Neuroscience Research

Cost of Sequencing a Human Genome
2001–2011

$100,000,000
$10,000,000
$1,000,000
$100,000
$10,000
$1,000

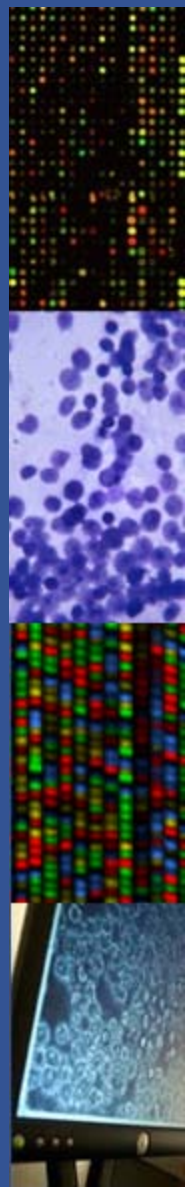
09/01 01/02 05/02 09/02 01/03 05/03 09/03 01/04 05/04 09/04 01/05 05/05 09/05 01/06 05/06 09/06 01/07 05/07 09/07 01/08 05/08 09/08 01/09 05/09 09/09 01/10 05/10 09/10 01/11 05/11 09/11

1000 Genomes in the Cloud

- 1000 Genomes Project (www.1000genomes.org)
  - Leverages recent improvements in next generation sequencing technology
  - Largest set of data on human genetic variation
- Data now freely available in Amazon's cloud
  - 200 terabytes of data
  - Researchers who would not otherwise have capacity or computing systems now have access

The Cancer Genome Atlas (TCGA) and the International Cancer Genomics Consortium

- Comprehensive, collaborative effort to map genomic changes in major types, subtypes of cancer
- NIH pilot (2006) expanded to 25 tumor types (2009)
  - Every case (tumor + germline) gets comprehensive characterization (SNP, exome, mi/RNAseq, methylation)
  - All data available pre-publication once quality controlled
  - 6,600+ cases now in pipeline
    - Seek to complete 11,000 by end of 2014
- International Cancer Genomics Consortium further expands program to many other tumor types
- Ultimate goal: improve our ability to diagnose, treat, and prevent cancer



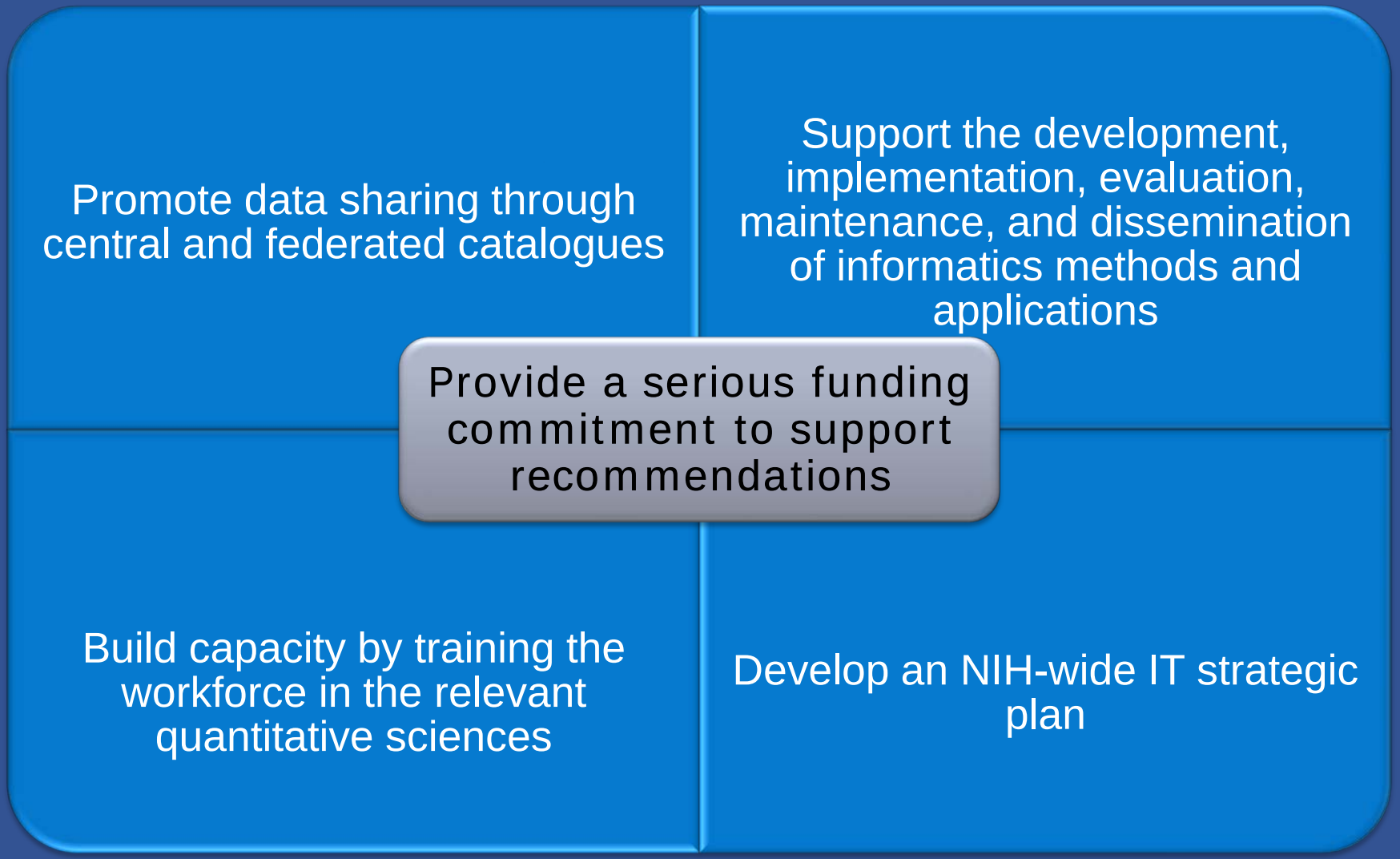
Big Data: What Is It, and What Do We Need to Do?

- Era of massive data sets
- Recent explosion of biomedical data
  - Genome sequence data
  - Public health databases
- Need for new and better ways to make the most of this data
  - Speed discovery and innovation
  - Ultimately lead to improvements in health, the economy

ACD Working Group on Data and Informatics

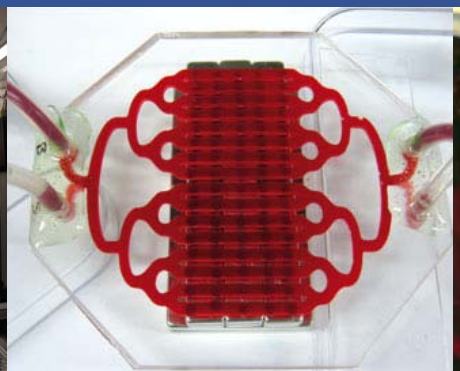
Name	Institution	Title
David DeMets, Co-Chair	University Wisconsin - Madison	Professor, Department of Biostatistics & Medical Informatics
Lawrence Tabak, Co-Chair	NIH	Principal Deputy Director
Russ Altman	Stanford University	Professor and Chair, Department of Bioengineering
David Botstein	Princeton University	Director, Lewis-Sigler Institute
Andrea Califano	Columbia University	Chief of Biomedical Informatics
David Ginsburg, ACD Member; Chair, NCBI Needs-Assessment Panel	University of Michigan	Professor, Department of Internal Medicine; HHMI
Patricia Hurn	The University of Texas System	Associate Vice Chancellor for Health Science Research
Dan Masys	University of Washington	Affiliate Professor, Department of Biomedical Informatics and Medical Education
Jill Mesirov, Ad Hoc Member, NCBI Needs-Assessment Panel	Broad Institute	Associate Director and Chief Informatics Officer
Shawn Murphy	Harvard University	Associate Director, Laboratory of Computer Science and Assistant Professor, Department of Neurology
Lucila Ohno-Machado	University of California, San Diego	Associate Dean for Informatics, Professor of Medicine, and Chief, Division of Biomedical Informatics

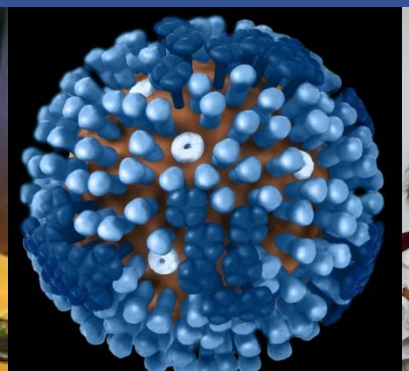
Overview of Recommendations



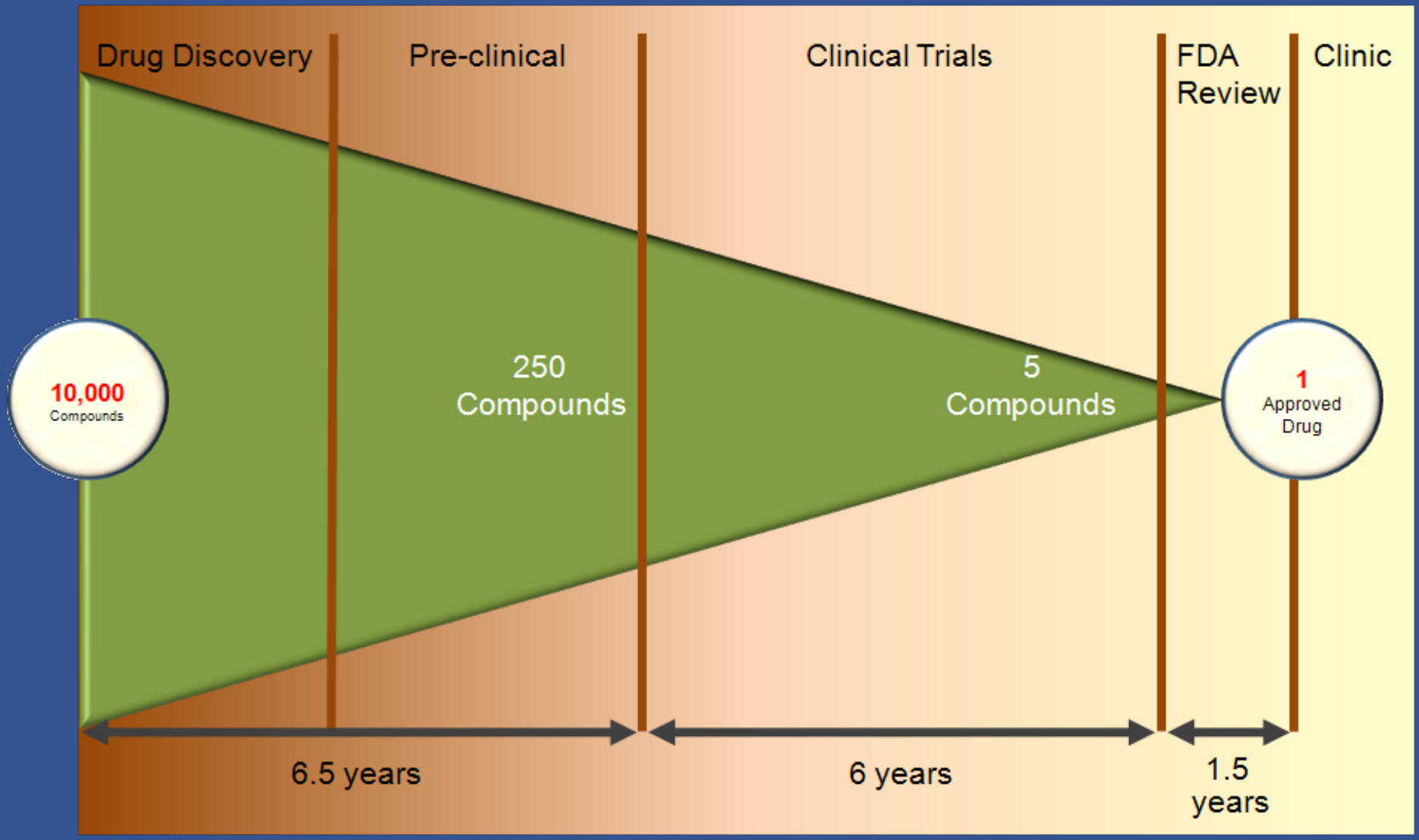
Advancing Translational Sciences

- Making the most of the deluge of discovery about the molecular causes of disease
- An AIDS-free generation
- New strategies to prevent and treat Alzheimer’s disease
- National Center for Advancing Translational Sciences (NCATS) established in FY 2012




Drug Development Pipeline



National Center for Advancing Translational Sciences

- Biochip for Drug Safety Screening to develop chip to screen for safe, effective drugs
  - NIH, DARPA contribute $70M over 5 years; FDA provides guidance
  - Awards announced July 24, 2012
- Rescuing and Repurposing
  - June, 2012: NIH partners with eight pharmaceutical companies
  - Program matches 58 pharma compounds already proven safe in humans with NIH-funded scientists' ideas for new uses
  - Features template legal agreements to:
    - Reduce time, cost, effort
    - Provide roadmap for handling intellectual property

Drug Rescue and Repurposing: Alzheimer's Disease and Bexarotene

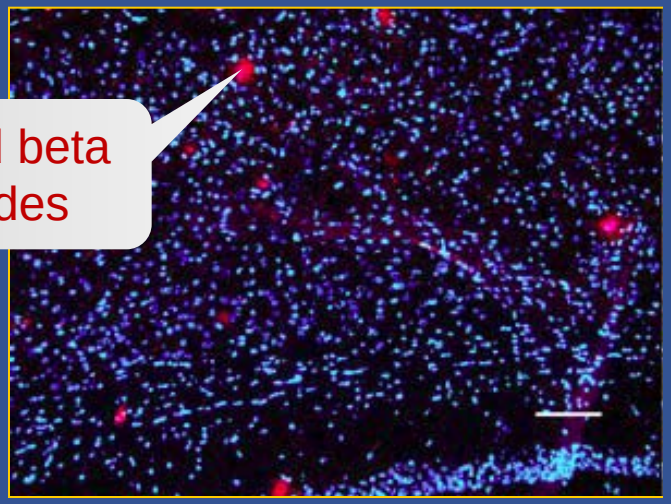
Sciencexpress Report

9 February 2012

ApoE-Directed Therapeutics Rapidly Clear β-Amyloid and Reverse Deficits in AD Mouse Models

Paige E. Cramer,[1] John R. Cirrito,[2] Daniel W. Wesson,[1,3] C. Y. Daniel Lee,[1] J. Colleen Karlo,[1] Adriana E. Zinn,[1] Brad T. Casali,[1] Jessica L. Restivo,[2] Whitney D. Goebel,[2] Michael J. James,[4] Kurt R. Brunden,[4] Donald A. Wilson,[3] Gary E. Landreth[1*]

Before



New Investigators, New Ideas

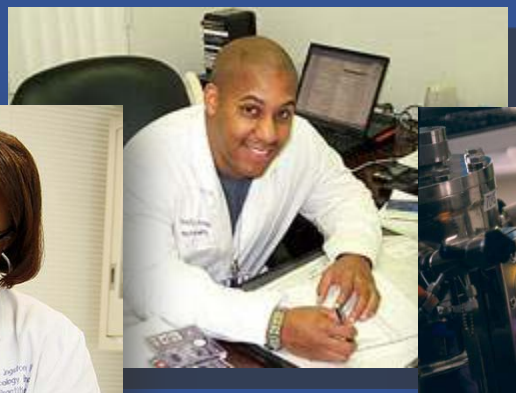
- NIH Director's Early Independence Awards
- NIH-Lasker Clinical Research Scholars
- New Innovator Award
- Transformative R01
- NIH Director's Pioneer Award

New investigators supported at success rates equal to those of established investigators for new RPGs

Greater Diversity in Research Workforce

African Americans, Hispanics, and Native Americans:

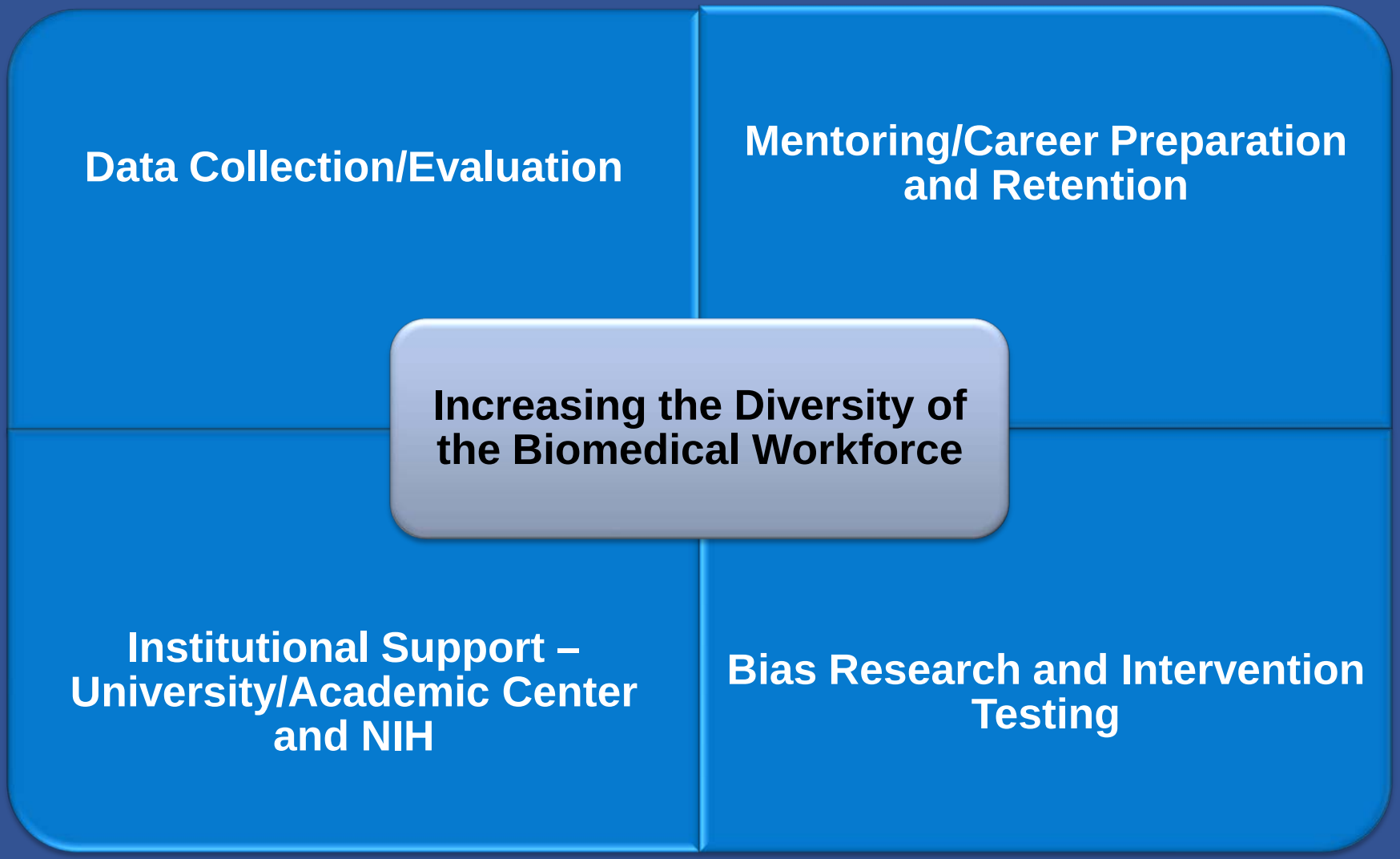
- Represent 31% of U.S. college age population but only account for 14% of undergraduates in life sciences
- And even fewer in later stages



ACD Working Group on Diversity in the Biomedical Research Workforce

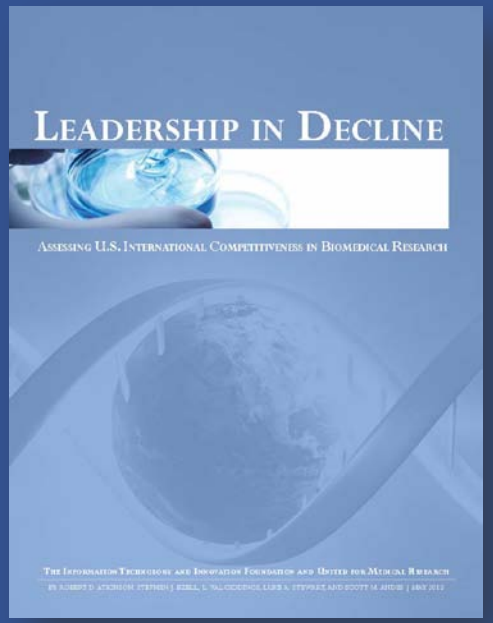
- Reed Tuckson, M.D., co-chair
  UnitedHealth Group
- John Ruffin, Ph.D., co-chair
  NIH
- Lawrence Tabak, D.D.S., Ph.D., co-chair
  NIH
- Ann Bonham, Ph.D.
  AAMC
- Jordan Cohen, M.D.
  AAMC
- José Florez, M.D., Ph.D.
  Harvard Medical School
- Gary Gibbons, M.D.
  Morehouse School of Medicine
- Renee Jenkins, M.D.
  Howard University
- Tuajuanda Jordan, Ph.D.
  Lewis and Clark College
- Wayne Riley, M.D., M.P.H., M.B.A.
  Meharry Medical College
- Samuel Silverstein, M.D.
  Columbia University Medical Center
- Dana Yasu Takagi, Ph.D.
  University of California, Santa Cruz
- Maria Teresa Velez, Ph.D.
  University of Arizona
- M. Roy Wilson, M.D., M.S.
  NIH
- Keith Yamamoto, Ph.D.
  University of California, San Francisco
- Clyde Yancy, M.D., M.Sc.
  Northwestern University

Summary: A Comprehensive Strategy



U.S. Economic Return and Global Competitiveness

- NIH funding is the foundation for U.S. competitiveness in biotech, drug development, and devices
- U.S. life sciences industry supports 7 million jobs, accounts for $69 billion annually in economic activity
- But, after adjusting for inflation, U.S. investment in NIH-supported research has declined every year since 2003
- Global competition has intensified:
  - UK and Germany are increasing investments in life sciences research, despite the European economic crunch
  - Singapore is investing nearly five times what the U.S. spends, as share of GDP
  - China will spend double the U.S. amount on life sciences research over the next five years



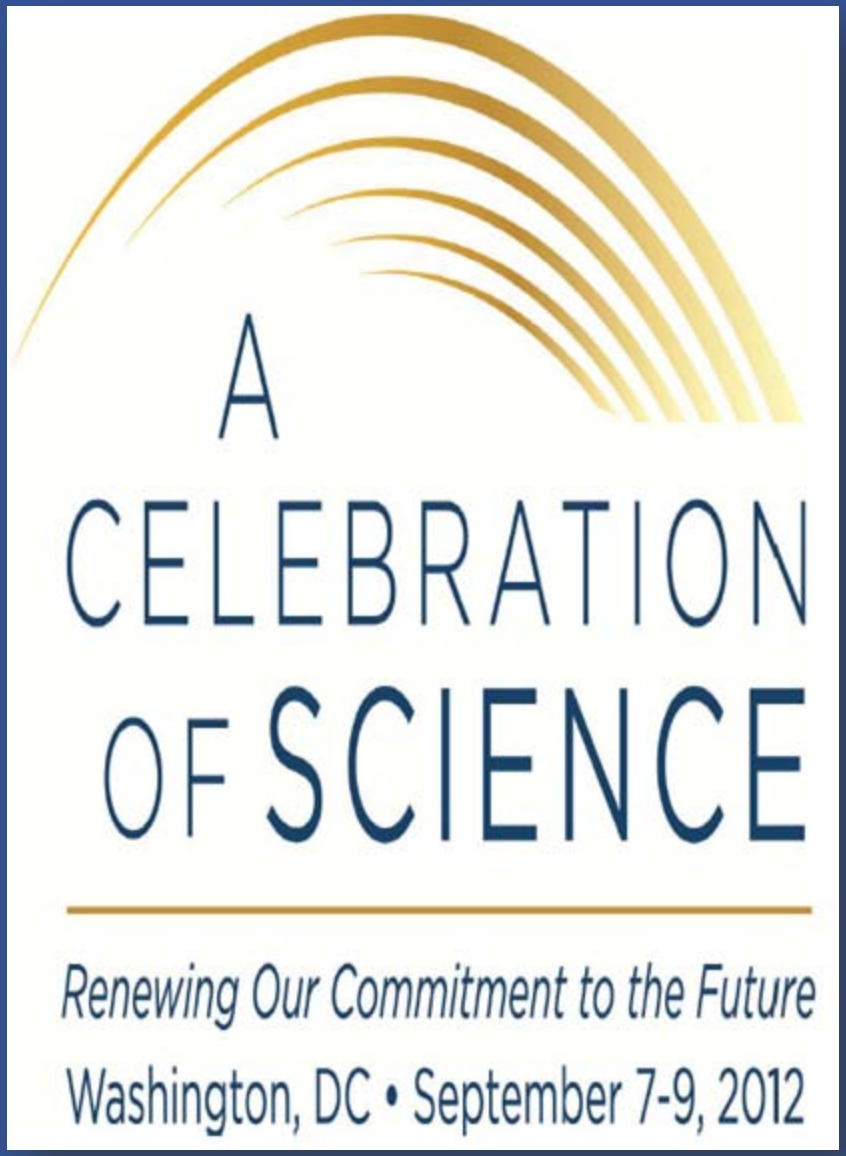
Impact
Our Health
Our Economy
Our Communities
Our Knowledge
News
Toolbox

Impact of NIH Research

NIH is the leading supporter of biomedical research in the world. This research has had a major positive impact on nearly all of our lives by improving human health, fueling the U.S. economy, and creating jobs in our communities.

Due in large measure to NIH research, a baby born in the United States today can expect to live to nearly age 79—about three decades longer than one born in 1900. Not only are we living longer, but our quality of life is improving. Over the last quarter century, the proportion of older people with chronic disabilities has dropped by nearly one-third.

NIH also drives job creation and economic growth. NIH research funding directly supports hundreds of thousands of American jobs and serves as a foundation for the medical innovation sector, which employs 1 million U.S. citizens.



- Kick-start renewed commitment to bioscience
- Improve the health of America's people and economy

http://celebrationofscience.org




NIH...

Turning Discovery Into Health®