Extraordinary Opportunities for Biomedical Research

Francis S. Collins, M.D., Ph.D.
Director, National Institutes of Health
Council of Councils
February 1, 2012
“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 reduce the burdens of illness and disability.”
NIH Extramural & Intramural Funding
FY 2012 Enacted: $30.9 Billion

Spending at NIH
$5.2 B
17%

Spending Outside NIH
$25.7 B
83%

- $3.4 B Intramural Research
- $1.5 B Research Management & Support
- $0.3 B Buildings and Facilities, Other

- Supports over 325,000 Scientists & Research Personnel
- Supports over 3,000 Institutions
FY 2011 Percent Distribution of Basic and Clinical Research

- Basic Research: 52.0%
- Applied Research (Clinical): 34.6%
- Applied Research (Other): 10.5%
- Training & Overhead: 2.6%
- R&D Facilities: 0.3%
Grant Success Rates
FY 1978-2013

[Graph showing the grant success rates from FY 1978 to FY 2013 with a significant decline in recent years.]
“But the bravest are surely those who have the clearest vision of what is before them, glory and danger alike, and yet notwithstanding go out to meet it.”

– Thucydides
Extraordinary Opportunities

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

NIH-supported Nobel Prize Winners: 135
Sequencing Costs Drop Faster than Moore’s Law

Cost per Megabase of DNA Sequence

- **28,500X**

- **Moore’s Law**
- **Cost per Mb**
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Exciting Technologies
Human iPS Cells

Induced Pluripotent Stem Cell Lines Derived from Human Somatic Cells

Junying Yu,1,2* Maxim A. Vodyanik,2 Kim Smuga-Otto,1,2 Jessica Antosiewicz-Bourget,1,2 Jennifer L. Frane,1 Shulan Tian,3 Jeff Nie,3 Gudrun A. Jonsdottir,3 Victor Ruotti,3 Ron Stewart,3 Igor I. Slukvin,2,4 James A. Thomson1,2,5*


Induction of Pluripotent Stem Cells from Adult Human Fibroblasts by Defined Factors

Kazutoshi Takahashi,1 Koji Tanabe,1 Mari Ohnuki,1 Megumi Narita,1,2 Tomoko Ichisaka,1,2 Kiyoshi Tomoda,3 and Shinya Yamanaka1,2,3,4,5*
Model disease *in vitro* to screen potential drugs.


- > 45 diseases to date
  - Neurological
  - Hematological
  - Metabolic
  - Cardiovascular
  - Primary Immunodeficiency
  - Other
iPS Models of Disease: Long QT

Patient-Specific Induced Pluripotent Stem-Cell Models for Long-QT Syndrome

Alessandra Moretti, Ph.D., Milena Bellin, Ph.D., Andrea Welling, Ph.D., Christian Billy Jung, M.Sc., Jason T. Lam, Ph.D., Lorenz Bott-Flügel, M.D., Tatjana Dorn, Ph.D., Alexander Goedel, M.D., Christian Höhnke, M.D., Franz Hofmann, M.D., Melchior Seyfarth, M.D., Daniel Sinnecker, M.D., Albert Schöning, M.D., and Karl-Ludwig Laugwitz, M.D.

Modelling the long QT syndrome with induced pluripotent stem cells

Ilanit Itzhaki, Leonid Maizels, Irit Huber, Limor Zwi-Dantsis, Oren Caspi, Aaron Winterstern, Oren Feldman, Amira Gepstein, Gil Arbel, Haim Hammerman, Monther Boulos & Lior Gepstein

Nature | Vol 471 | 10 March 2011
Human iPS Cells, 5 Years Later: Promise for Research and Therapy

Model disease in vitro to screen potential drugs

Facilitate personalized cell therapy

Nature, Jan 19, 2012 vol 481
NIH Center for Regenerative Medicine (NIH-CRM)

- Vast unmet need; therapies exist for ~200 of ~4000 conditions with defined molecular causes
- Tap into NIH Intramural’s proven ability to assemble interdisciplinary teams, build community resources
- Desire to capitalize on NIH Clinical Center’s strengths
  - Well-defined patient cohorts, many with life-threatening, rare, or neglected diseases
  - GMP facility for cellular therapies
  - Expertise in gene therapy/stem cell transplantation
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- Accelerating Discovery Through Technology
- **Advancing Translational Sciences**
- Encouraging New Investigators and New Ideas
Advancing Translational Sciences

- Drug Discovery: 10,000 Compounds (6.5 years)
- Pre-clinical: 250 Compounds
- Clinical Trials: 5 Compounds (6 years)
- FDA Review: 1 Approved Drug (1.5 years)

Total: 3 years
PCSK9 Inhibitors: The Next Statins?

- Certain mutations result in reduced PCSK9 protein, lower levels of LDL, and decreased risk of heart disease
- Possible new target for managing cholesterol
- Multiple PCSK9 inhibitors now in early phase clinical trials
Toxicity is the Most Common Reason for Drug Development Failure

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

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
- First Requests for Proposals (due January 26, 2012)
  - Seeking best ideas in engineering, biology, toxicology
Exploring New Uses for Abandoned and Approved Therapeutics

NIH – INDUSTRY ROUNDTABLE
April 21–22, 2011

Rescuing, Repurposing, Repositioning

NIH’s Secondhand Shop for Tried-and-Tested Drugs

Although the U.S. National Institutes of Health (NIH) has made waves with a proposed new center aimed at translational research, so far the main innovation has been to put scattered existing programs under the same roof. But this month NIH Director Francis Collins unveiled something fresh: an effort to persuade drug companies to open up their troves of abandoned drugs to academics, who would look for new uses.

University in St. Louis, university researchers have access to a database of 500 Pfizer drugs and failed candidates that they test in animal models. But NIH officials think there’s merit in a more systematic effort. One reason is efficiency. NIH Associate Director for Science Policy Amy Patterson explained to the NIH board this month. Although only 1 in 10,000 potential therapeutic compounds will become a drug, the majority fail in late trials because of lack of efficacy, not safety. That means toxicity often isn’t a barrier, Patterson said. She cited an estimated success rate of 30% for repurposed drugs. And NIH says that...

As for logistics, the agency has made a small start. In April, NIH’s intramural Chemical Genomics Center unveiled a public database listing all 8000 or so approved drugs along with structural data (Science Translational Medicine, 27 April, http://scim.ag/chem-genome). Researchers can apply to have the center test their cell or molecular assays against the drugs to look for “hits,” or possible biological activity.

For unapproved drugs, Patterson says, NIH envisions a system of databases that would allow researchers to “window-shop” by viewing public data. If they see a compound that interests them, they might access a company’s proprietary data through service companies.

NIH hopes to complete the model master agreement within 6 to 8 months, Patterson says. The drug rescue and repurposing project will be led by a team at NCATS as “an integral
National Center for Advancing Translational Sciences (NCATS)

Mission:
To advance the discipline of translational science and catalyze the development, testing, and implementation of novel diagnostics and therapeutics across a wide range of human diseases and conditions.

http://ncats.nih.gov/
NCATS:

- Complements – does not compete with – the private sector
- Facilitates – does not duplicate – the translational research activities supported and conducted by the NIH Institutes and Centers
- Reinforces – does not reduce – NIH’s commitment to basic science research
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Opportunities for Tomorrow

NIH Investing in New, Transformative Ideas

- NIH-Lasker Clinical Research Scholars
- Transformative R01
- NIH Director’s Pioneer Award
- New Innovator Award
- **NIH Director’s Early Independence Awards**
John Calarco
Harvard University

James S. Fraser
UC San Francisco

Jeffrey M. Kidd
Stanford University

Harris H. Wang
Harvard Medical School
ACD Working Group on the Future Biomedical Research Workforce

- Shirley Tilghman, Ph.D., co-chair
  Princeton University
- Sally Rockey, Ph.D., co-chair
  NIH
- Sandra Degen, Ph.D.
  University of Cincinnati
- Laura Forese, M.D.
  Weill Cornell Medical Center
- Donna Ginther, Ph.D.
  University of Kansas
- Arthur Gutierrez-Hartmann, M.D.
  University of Colorado Denver
- Freeman Hrabowski, Ph.D.
  Univ of Maryland, Baltimore County
- James Jackson, Ph.D.
  University of Michigan, Ann Arbor
- Leemor Joshua-Tor, Ph.D.
  Cold Spring Harbor Laboratory
- Richard Lifton, M.D., Ph.D.
  Yale School of Medicine
- Garry Neil, M.D.
  Johnson & Johnson
- Naomi Rosenberg, Ph.D.
  Tufts University
- Bruce A. Weinberg, Ph.D.
  The Ohio State University
- Keith Yamamoto, Ph.D.
  Univ of California, San Francisco
Opportunities for Tomorrow
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
NIH’s Plan for Action:

Weaving a Richer Tapestry in Biomedical Science

Lawrence H. Tabak* and Francis S. Collins*

As much as the U.S. scientific community may wish to view itself as a single garment of many diverse and colorful threads, a sobering consideration of actual data reminds us that our nation’s biomedical research workforce remains nowhere near as rich as it could be. An analysis performed by a team of researchers primarily supported by the National Institutes of Health (NIH) and published in this issue of *Science*, reveals that from 2000 to 2006, black (I) grant applicants were significantly less likely to receive NIH research funding than were white applicants. The gap in success rates amounted to 10 percentage points, even after controlling for factors, country of origin, training, employer characteristics, previous research awards, and publication record (2). Their analysis also showed a gap of 4.2 percentage points for Asians; however, the differences between Asian and white
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
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- M. Roy Wilson, M.D., M.S.
  Charles R. Drew University
- Keith Yamamoto, Ph.D.
  University of California, San Francisco
- Clyde Yancy, M.D.
  Northwestern University
“If we’re going to create jobs now and in the future, we're going to have to out-build and out-educate and out-innovate every other country on Earth.”

President Obama
Signing of America Invents Act
Thomas Jefferson High School
September 16, 2011
NIH...
Turning Discovery Into Health