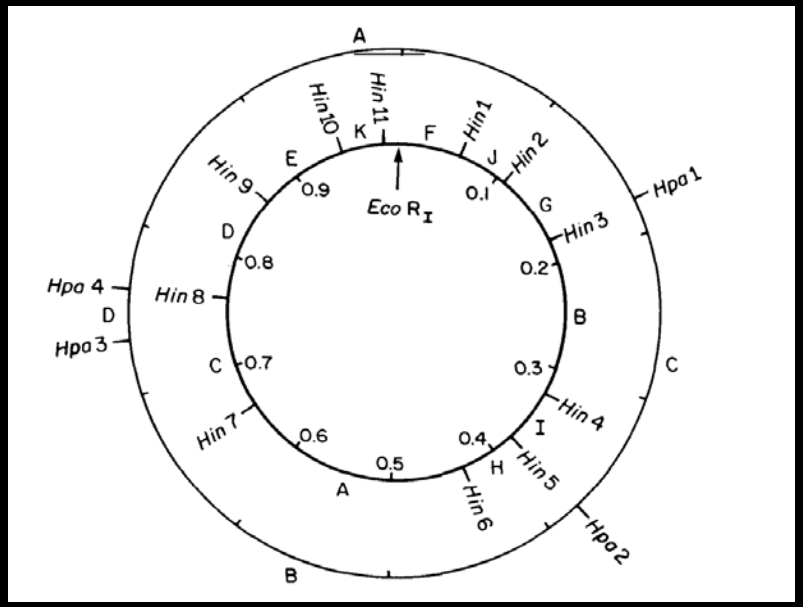
The Best of Times: The Worst of Times

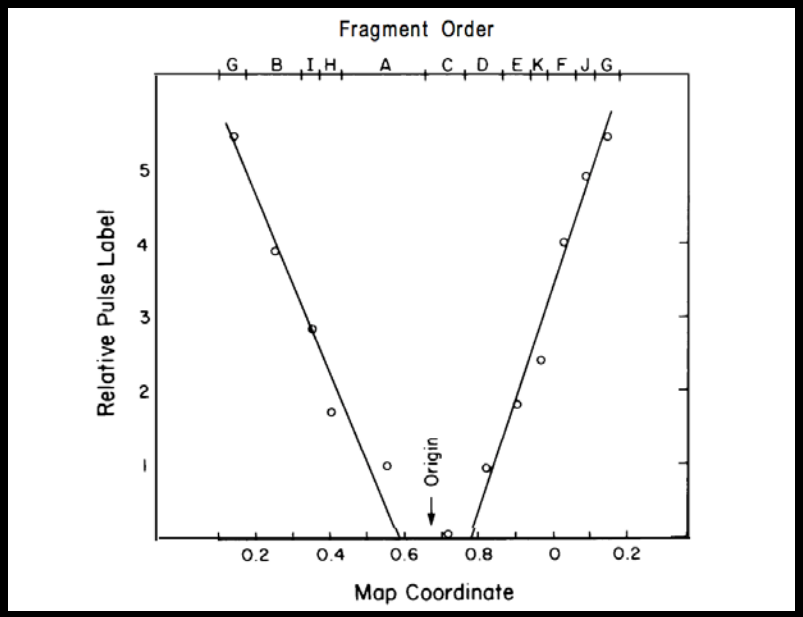
A Life in Biomedical Science

The Daniel Nathans Lecture in Molecular Genetics

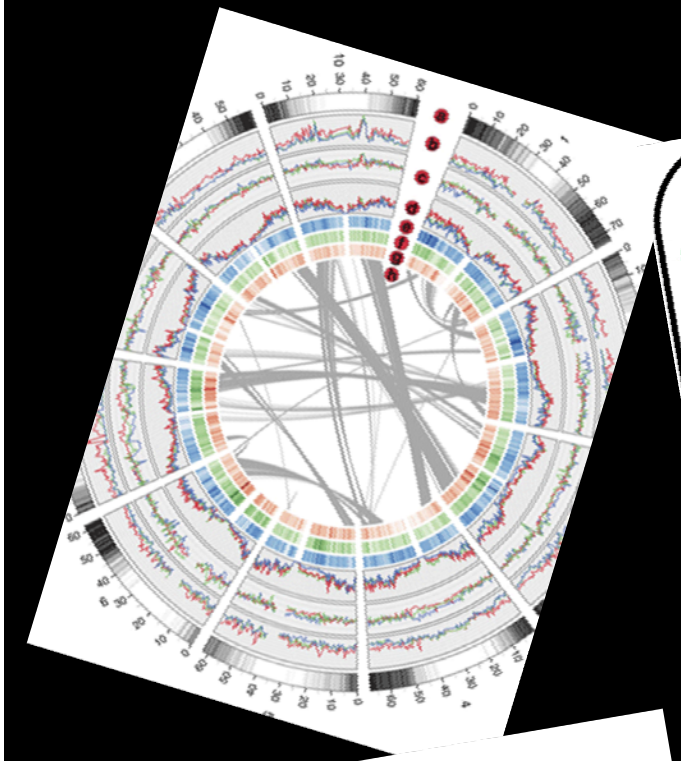
April 7, 2016

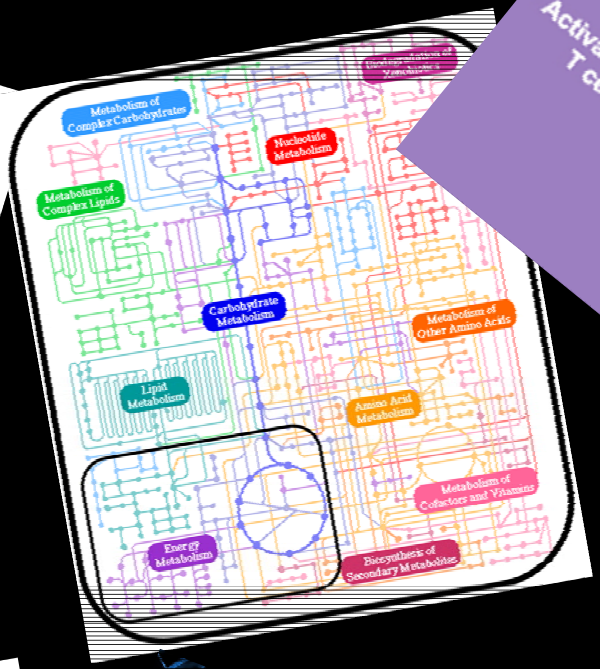
Daniel Nathans

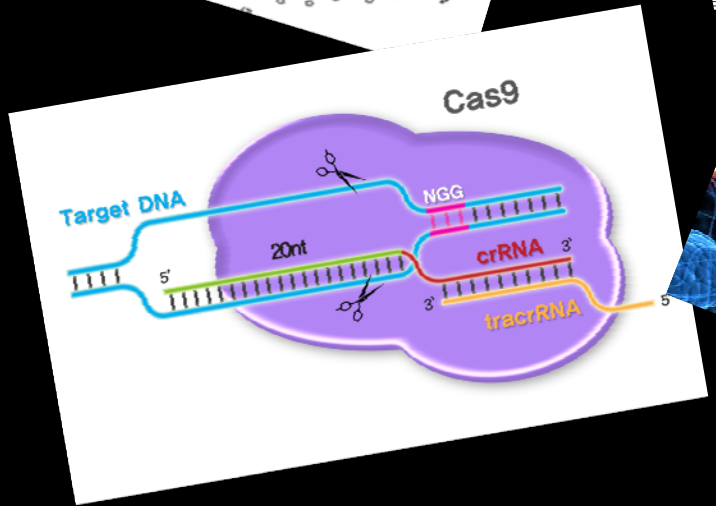


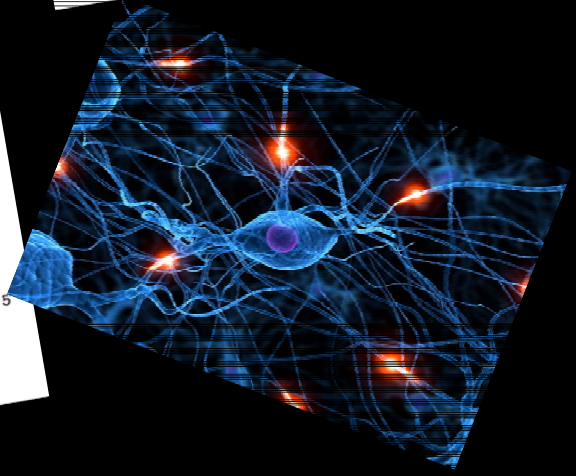


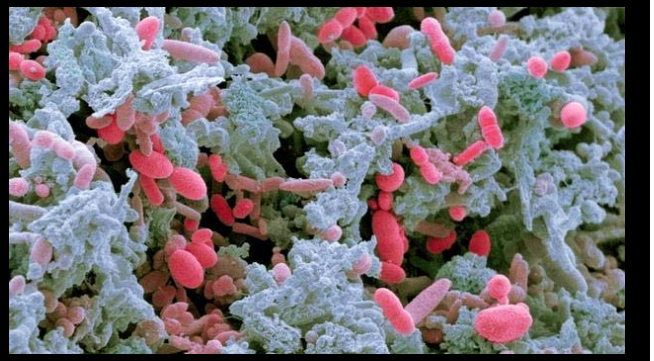
The Best of Times - 2016



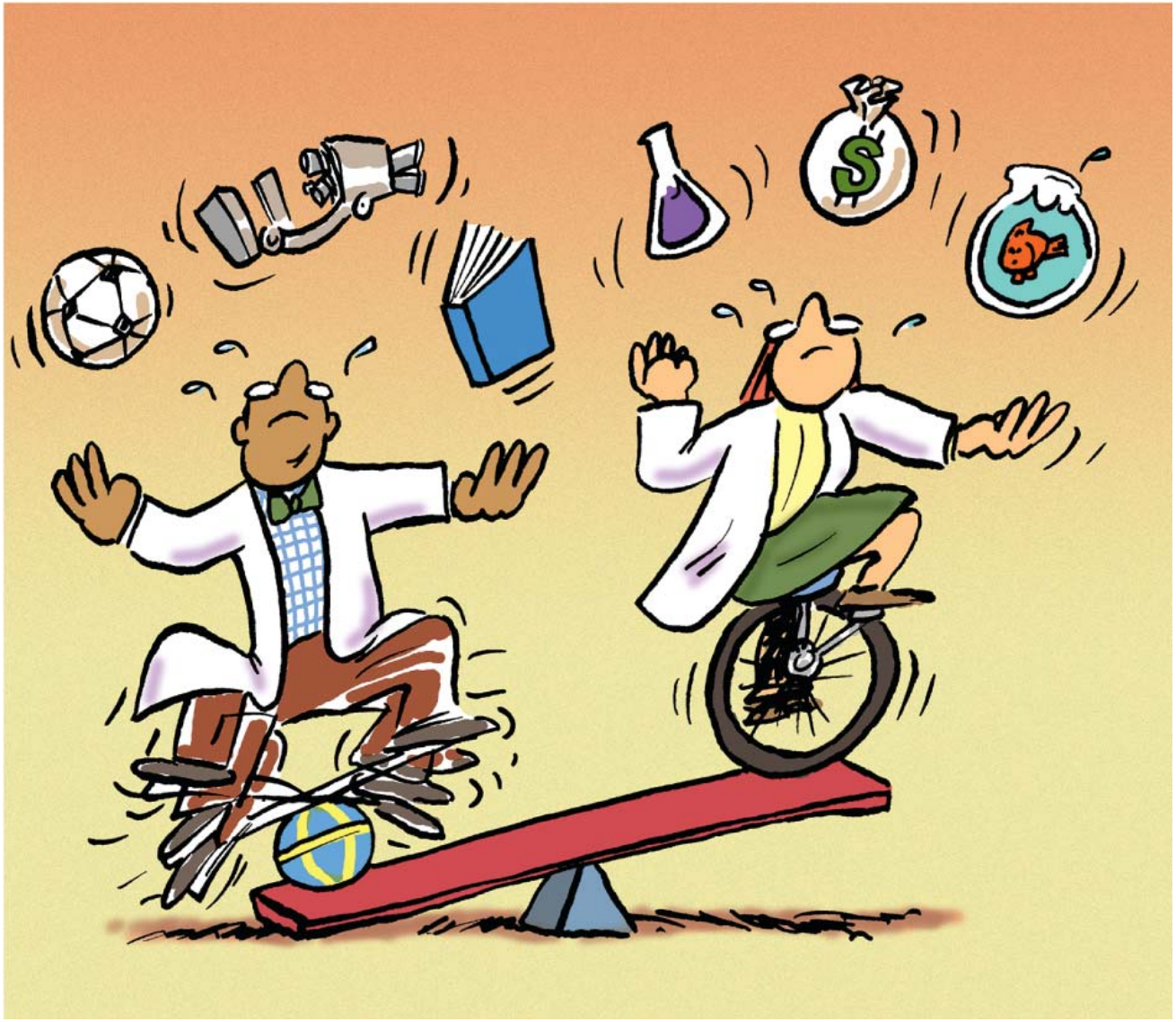








So why is it feeling like the worst of times……?

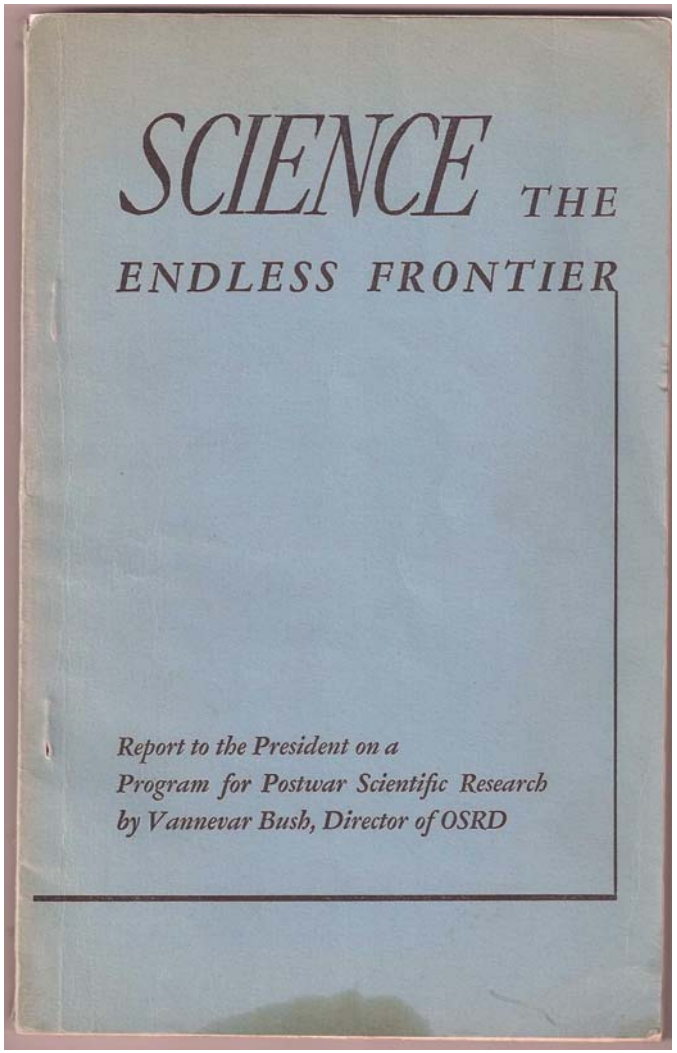


American Association for the Advancement of Science
Science 2013;342:36-38

Science
AAAS

The Best of Times did not happen by chance

Vannevar Bush

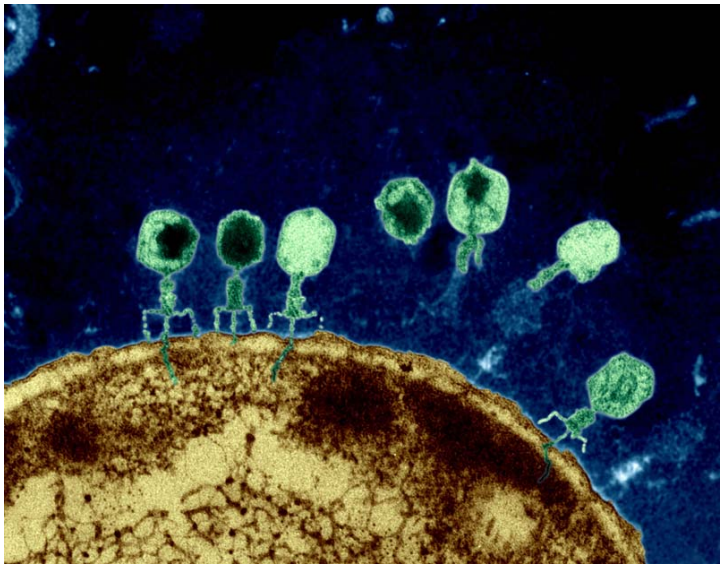


1945

The Bush Vision for The Endless Frontier

- The federal government should support *basic* research and provide incentives to the private sector to fund applied research and development - a research ecosystem

1960's and 1970's



1976

1982

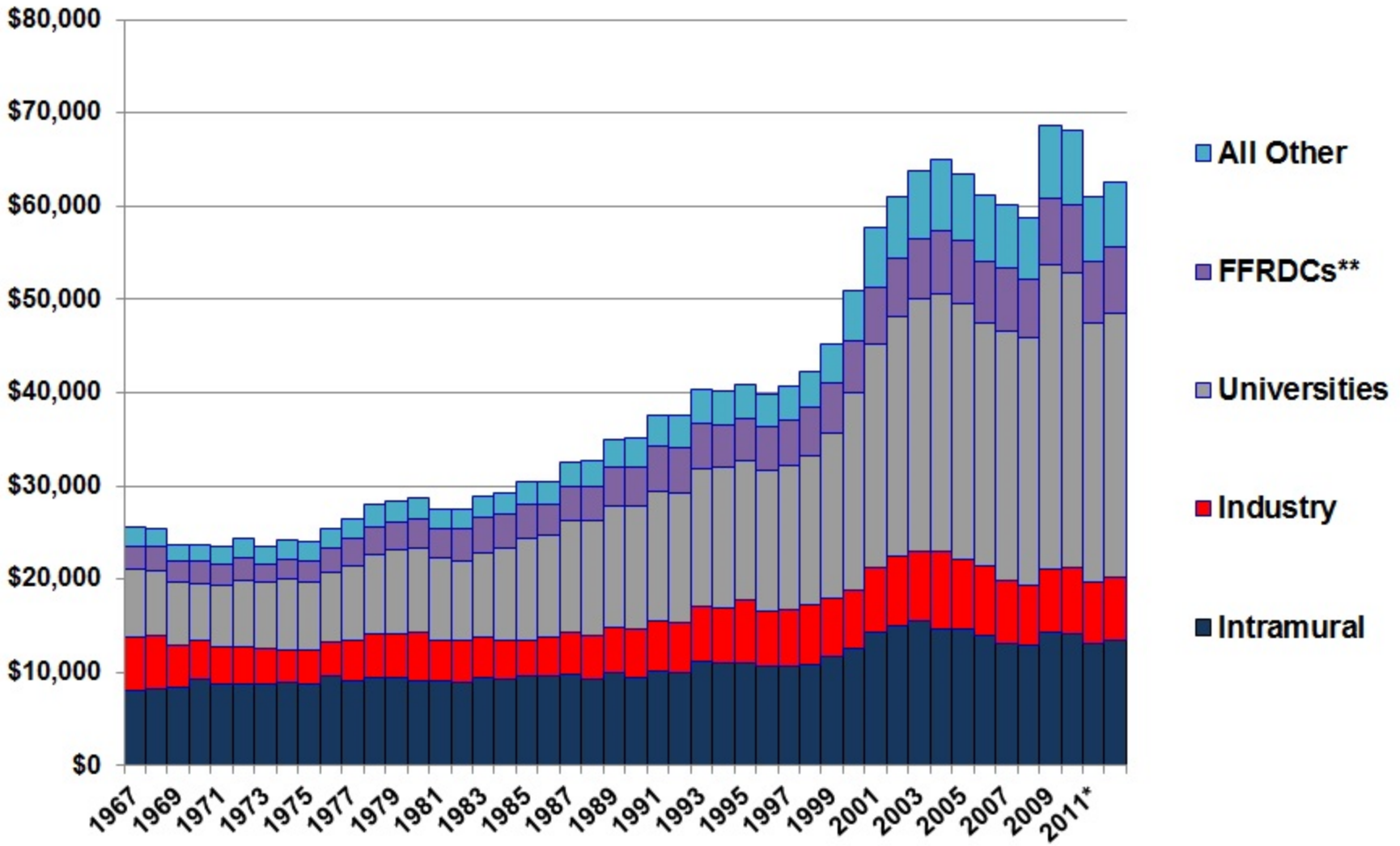
The Bush Vision for The Endless Frontier

- The federal support should be directed toward research universities, academic medical centers and research institutes, not federal labs

- The conduct of research should be tied to the education of future scientists – graduate students - but "only that proportion of the youthful talent ***appropriate to the needs of science"***

Federal Research Funding By Performer, 1967-2012

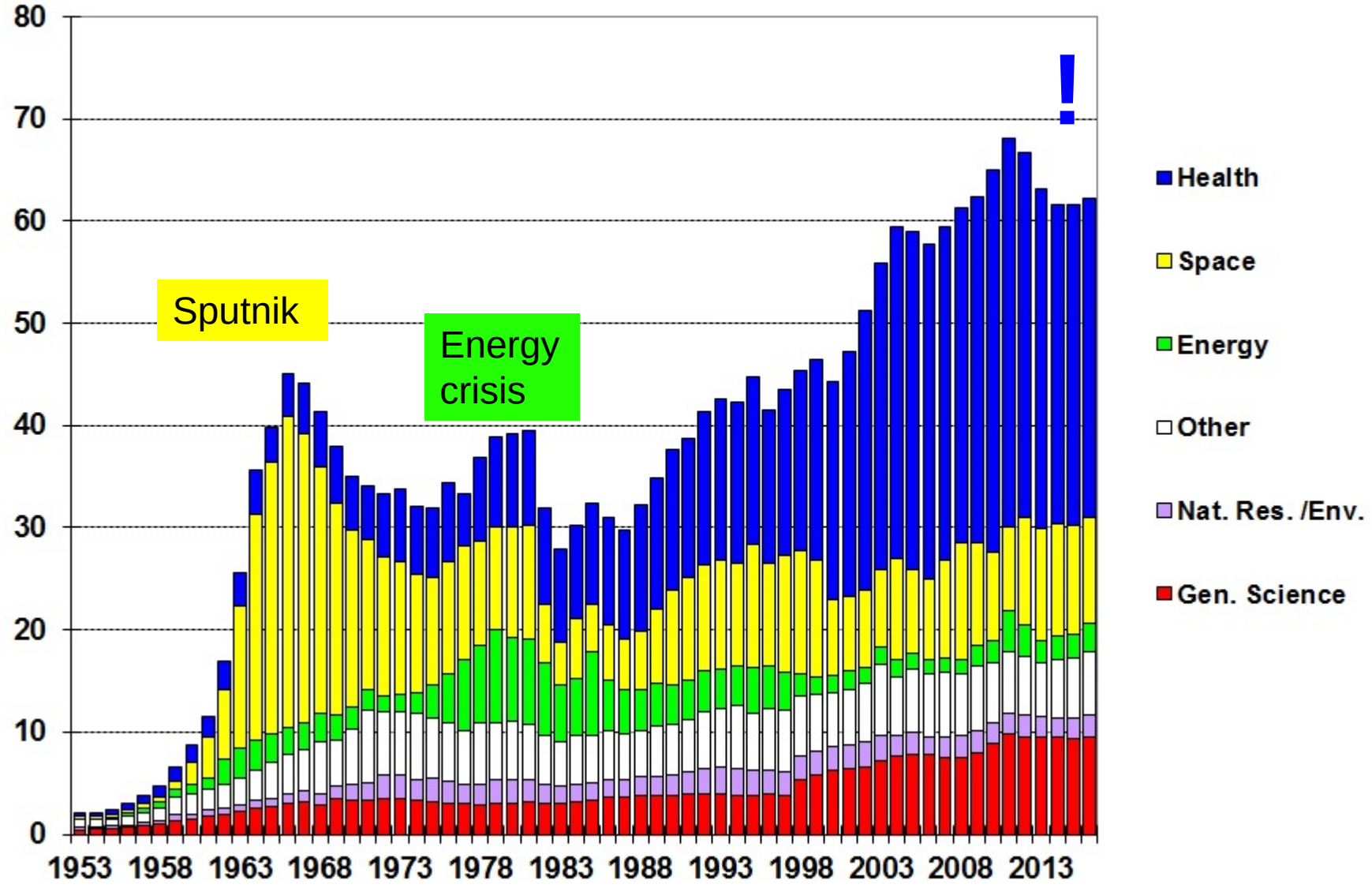
Obligations in millions of constant FY 2014 dollars



Source: NSF, National Center for Science and Engineering Statistics, *Federal Funds for R&D* series, based on national survey data.
*FY 2011 and FY 2012 data are preliminary.

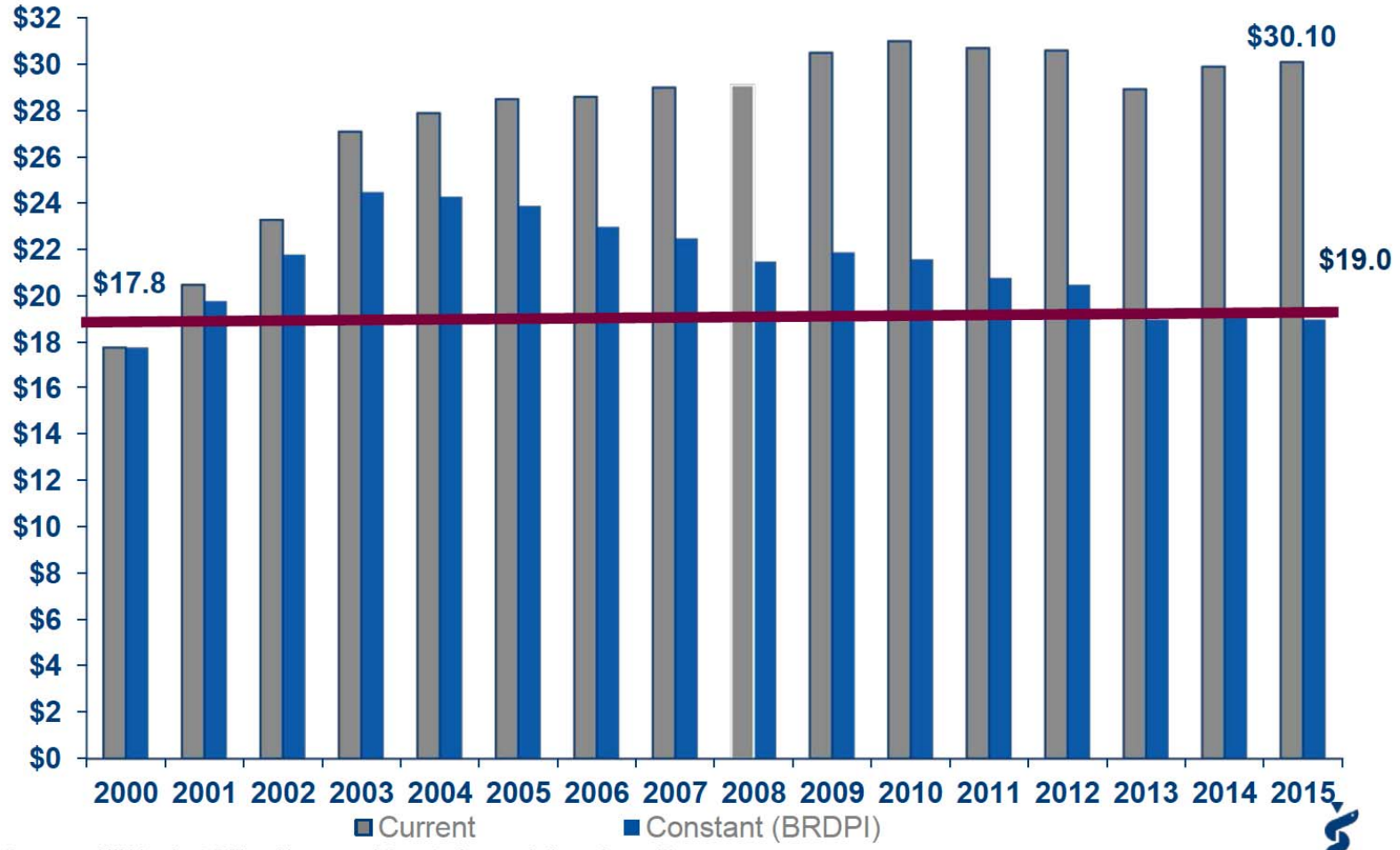
Trends in Nondefense R&D by Function

outlays for the conduct of R&D, billions of constant FY 2015 dollars



Source: AAAS, based on OMB Historical Tables in *Budget of the United States Government FY 2016*. Some Energy programs shifted to General Science beginning in FY 1998.

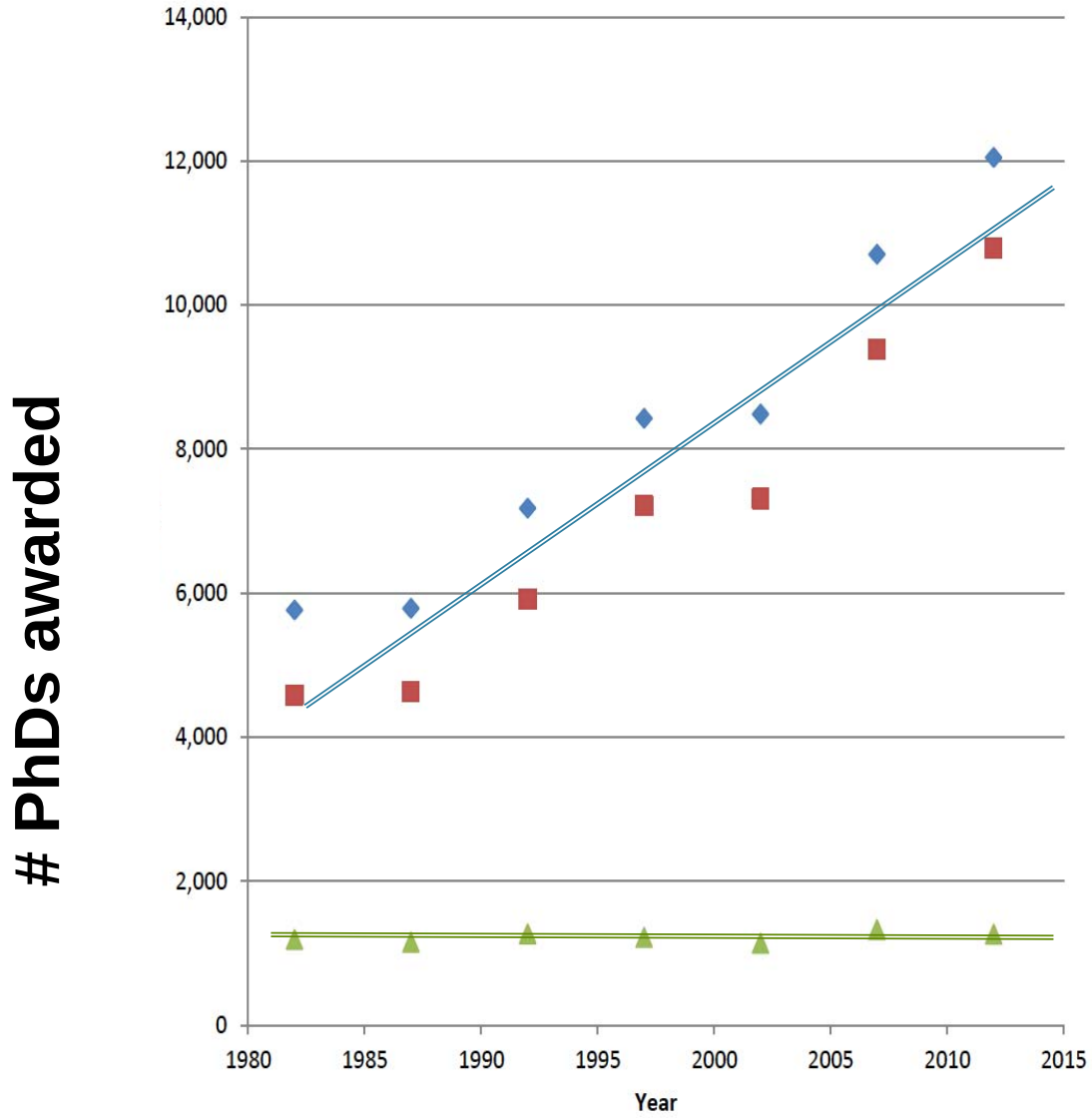
No Net Increase in NIH funding in last 15 years



Sources: NIH Budget Office; House and Senate Appropriations Committees

AAMC

Lack of correlation between funding and production of new Ph.D. scientists



Total Life Sciences

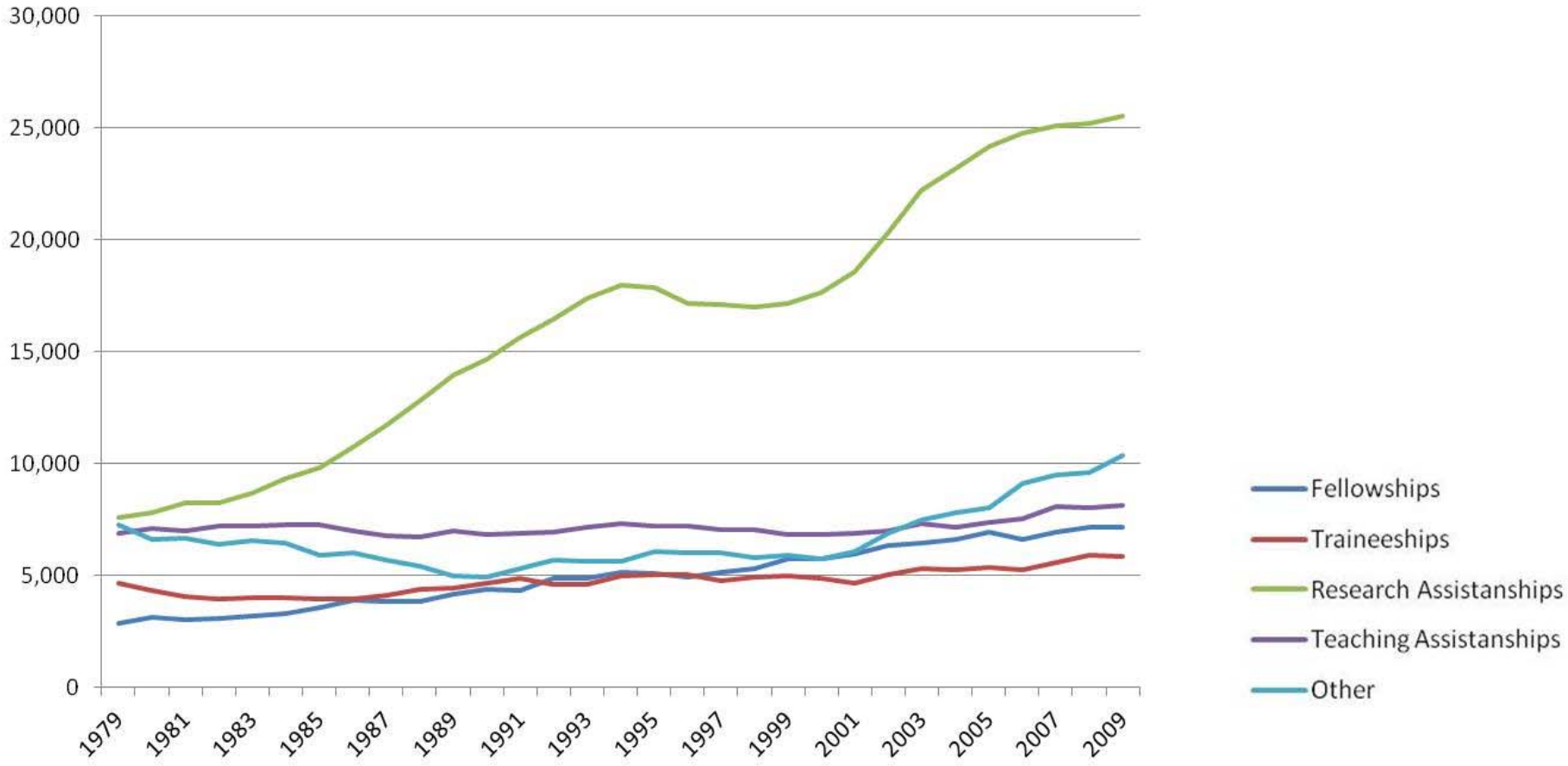
Biomedical Sciences

Agriculture & natural sciences

Source Charles Liarakos, NSF via Michael S. Teitelbaum

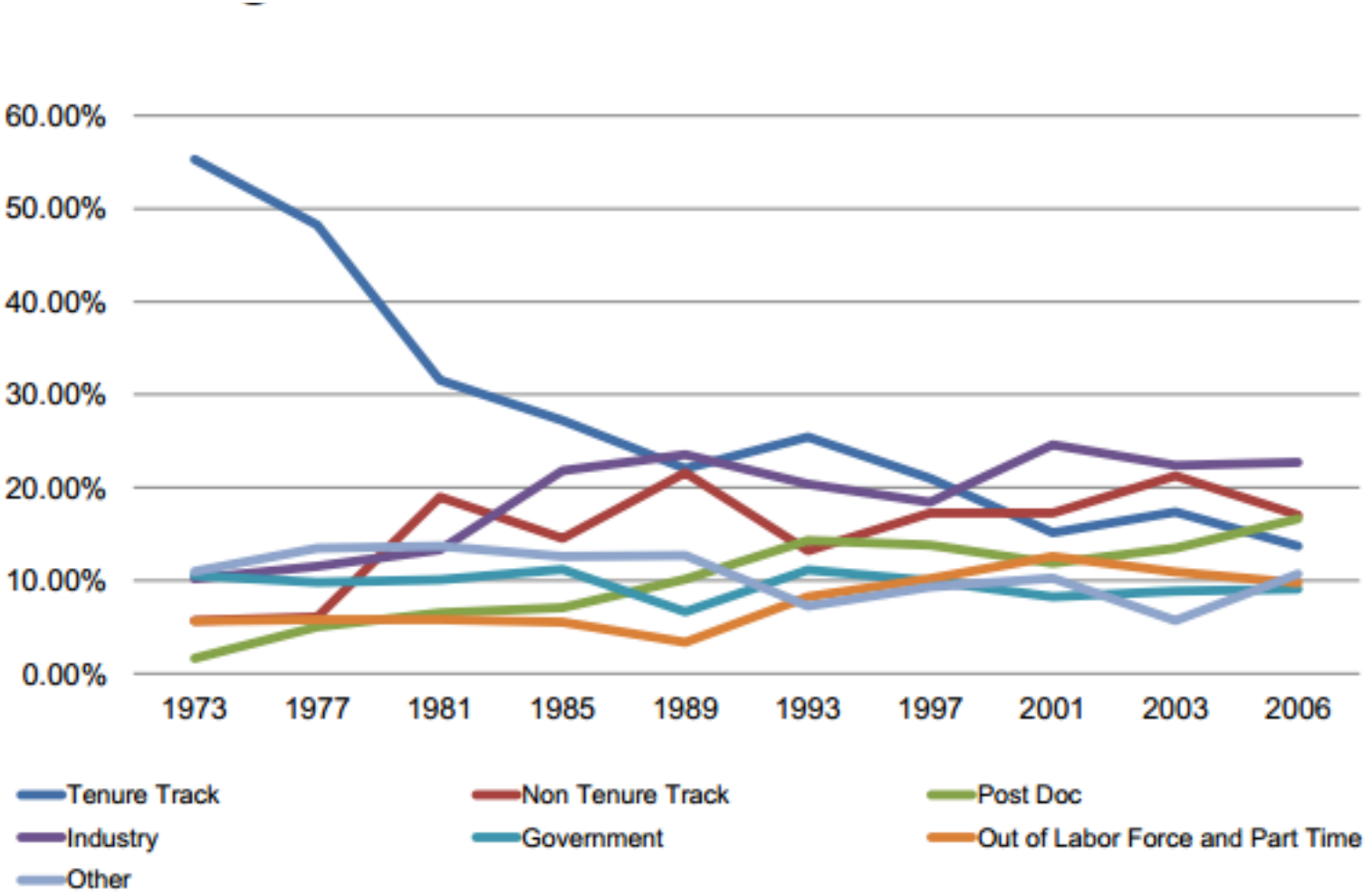
The Bush Vision for The Endless Frontier

- Graduate students should be supported with individual fellowships that are awarded to the "best and brightest" of their generation



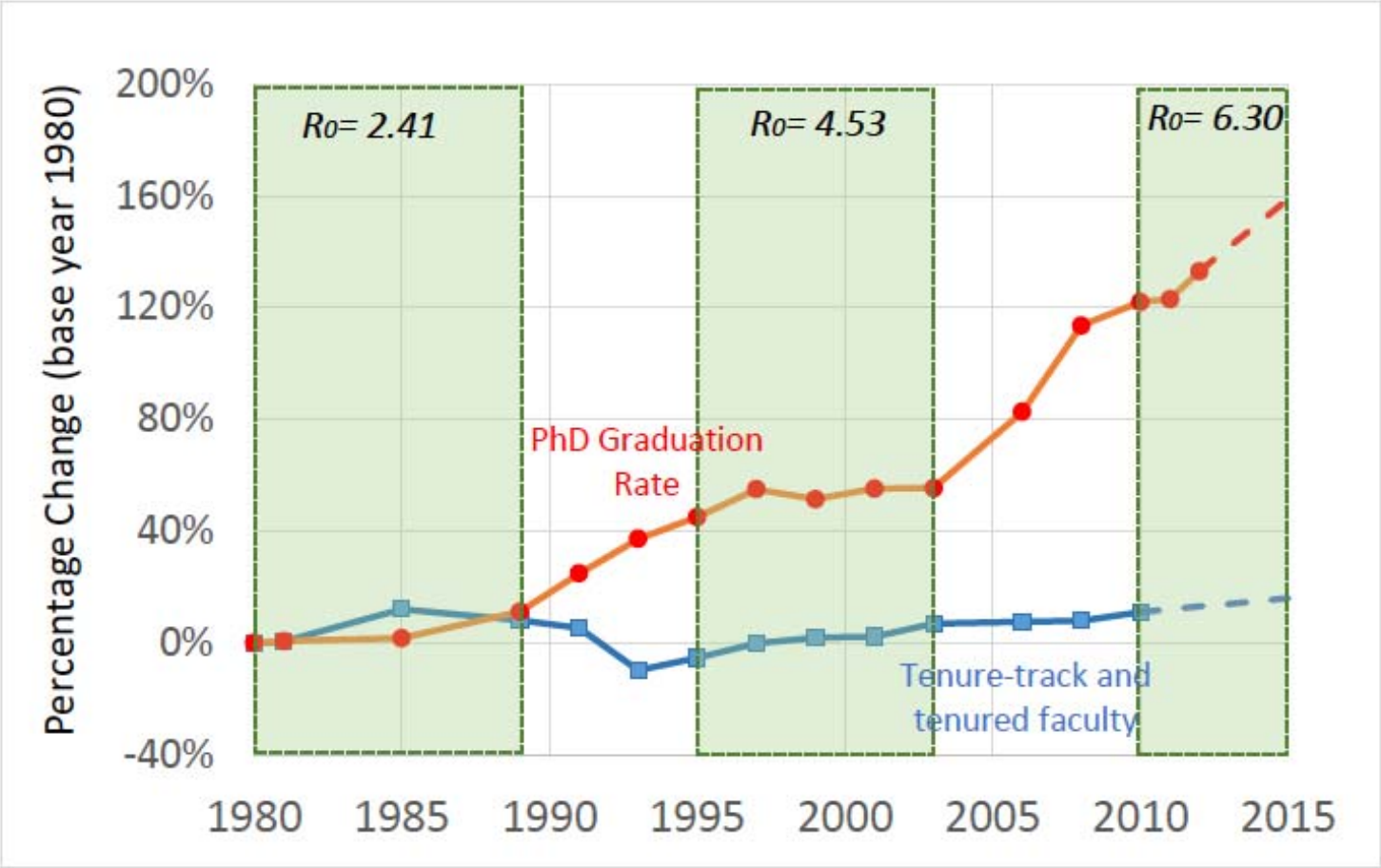
Graduate students transformed from being "trainees" to "workers"

U.S. Trained Biomedical PhD employment
5-6 years post-Ph.D.



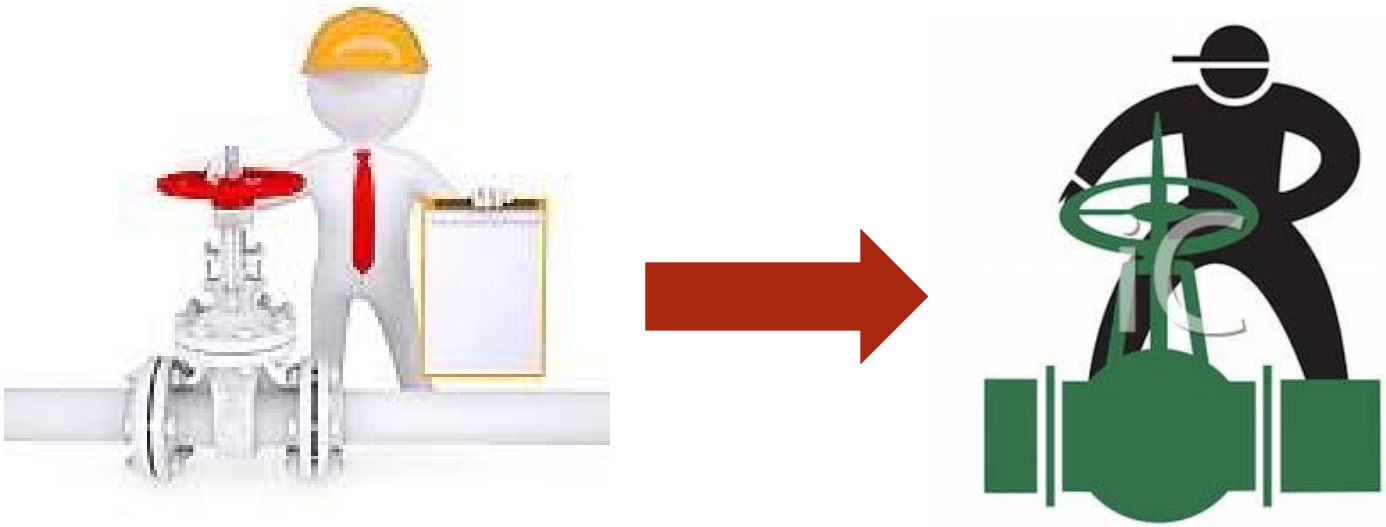
Source: Survey of Doctorate Recipients

Lack of correlation between PhD production and the number of faculty positions

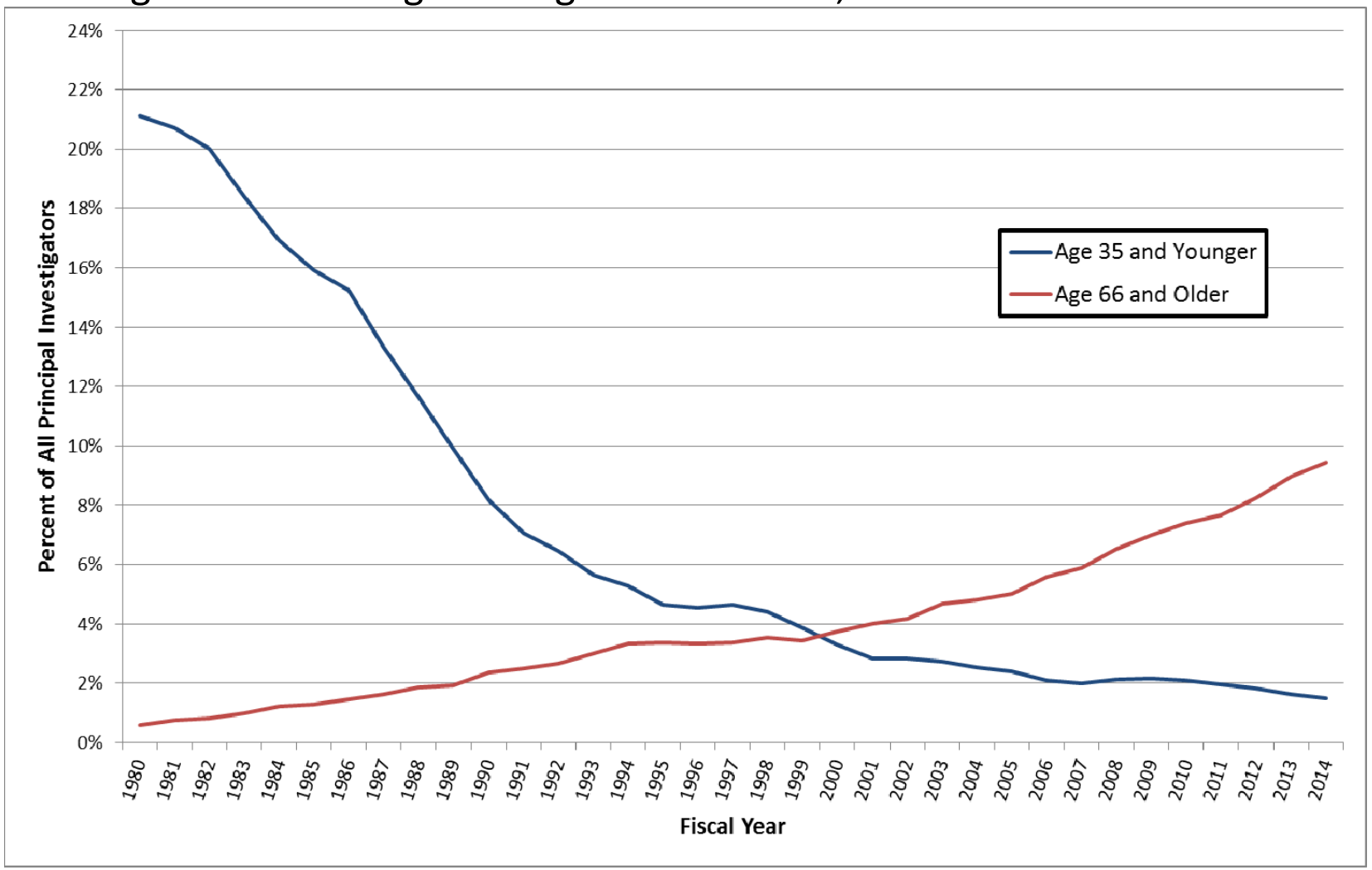


Ghaffarzadegan et al 2014 Systems Research and Behavioral Science Syst. Res (2014)

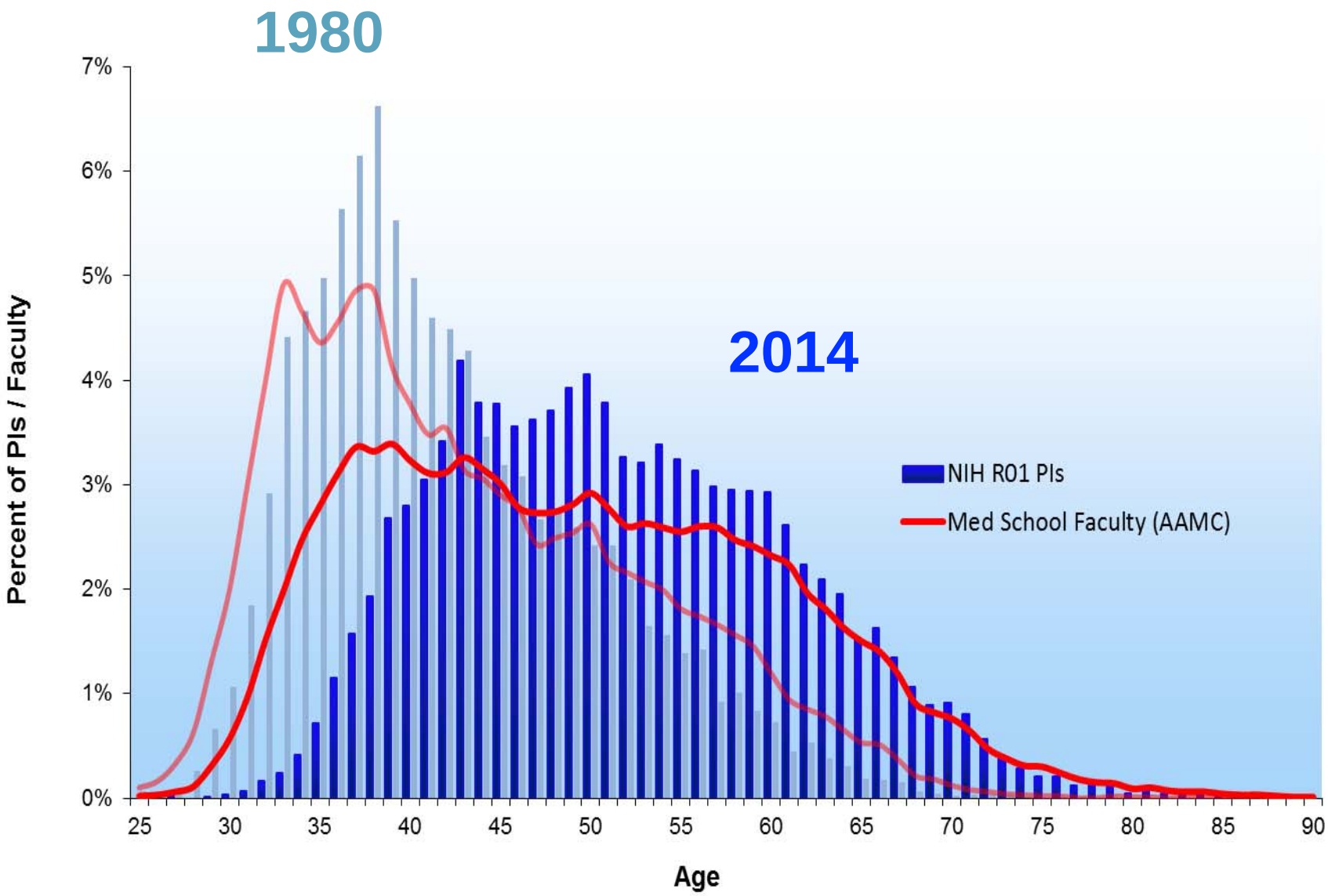
A Bulging Pipeline



Percentage of NIH R01 Equivalent Principal Investigators of All Degrees: Age 35 and Younger vs. Age 66 and Older, Fiscal Year 1980 - 2014



The average age of an investigator receiving his or her first NIH R01 grant is approaching 42 years of age!


1980
2014
7%
6%
5%
4%
3%
2%
1%
0%
Percent of PIs / Faculty
25
30
35
40
45
50
55
60
65
70
75
80
85
90
Age
NIH R01 PIs
Med School Faculty (AAMC)

Bush's vision – a need for renewal

- Basic research must be unfettered, curiosity-driven; requires long horizons; "the supreme importance of affording the prepared mind complete freedom for the exercise of initiative"

The mismatch between supply and demand of PhDs has created a hypercompetitive environment that is not conducive to producing the best science

As competition for research grants has become fierce – with success rates dipping close to single digits, researchers and grant reviewers have become risk-averse, threatening the quality of discovery

Because of competition scientists are spending greater percentages of their time rewriting grants and papers, and not enough time thinking about their experiments

Will this career path continue to attract the best and brightest?

PERSPECTIVE

Rescuing US biomedical research from its systemic flaws

Bruce Alberts[a], Marc W. Kirschner[b], Shirley Tilghman[c,1], and Harold Varmus[d]

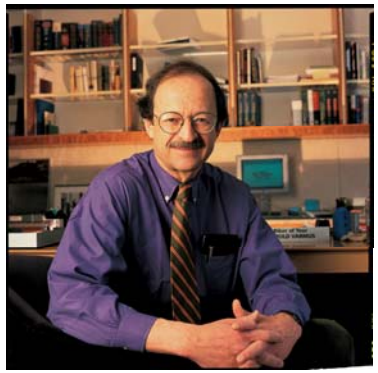
[a]Department of Biophysics and Biochemistry, University of California, San Francisco, CA 94158; [b]Department of Systems Biology, Harvard Medical School, Boston, MA 02115; [c]Department of Molecular Biology, Princeton University, Princeton, NJ 08540; and [d]National Cancer Institute, Bethesda, MD 20892

Edited by Inder M. Verma, The Salk Institute for Biological Studies, La Jolla, CA, and approved March 18, 2014 (received for review March 7, 2014)

The long-held but erroneous assumption of never-ending rapid growth in biomedical science has created an unsustainable hypercompetitive system that is discouraging even the most outstanding prospective students from entering our profession—and making it difficult for seasoned investigators to produce their best work. This is a recipe for long-term decline, and the problems cannot be solved with simplistic approaches. Instead, it is time to confront the dangers at hand and rethink some fundamental features of the US biomedical research ecosystem.

Bruce Alberts

Marc Kirschner



Harold Varmus

PERSPECTIVE

A generation at risk: Young investigators and the future of the biomedical workforce

Ronald J. Daniels[1]

President, Johns Hopkins University, Baltimore, MD 21287

PERSPECTIVE

Toward a sustainable biomedical research enterprise: Finding consensus and implementing recommendations

Christopher L. Pickett[a,1], **Benjamin W. Corb**[a], **C. Robert Matthews**[b], **Wesley I. Sundquist**[c], **and Jeremy M. Berg**[d]

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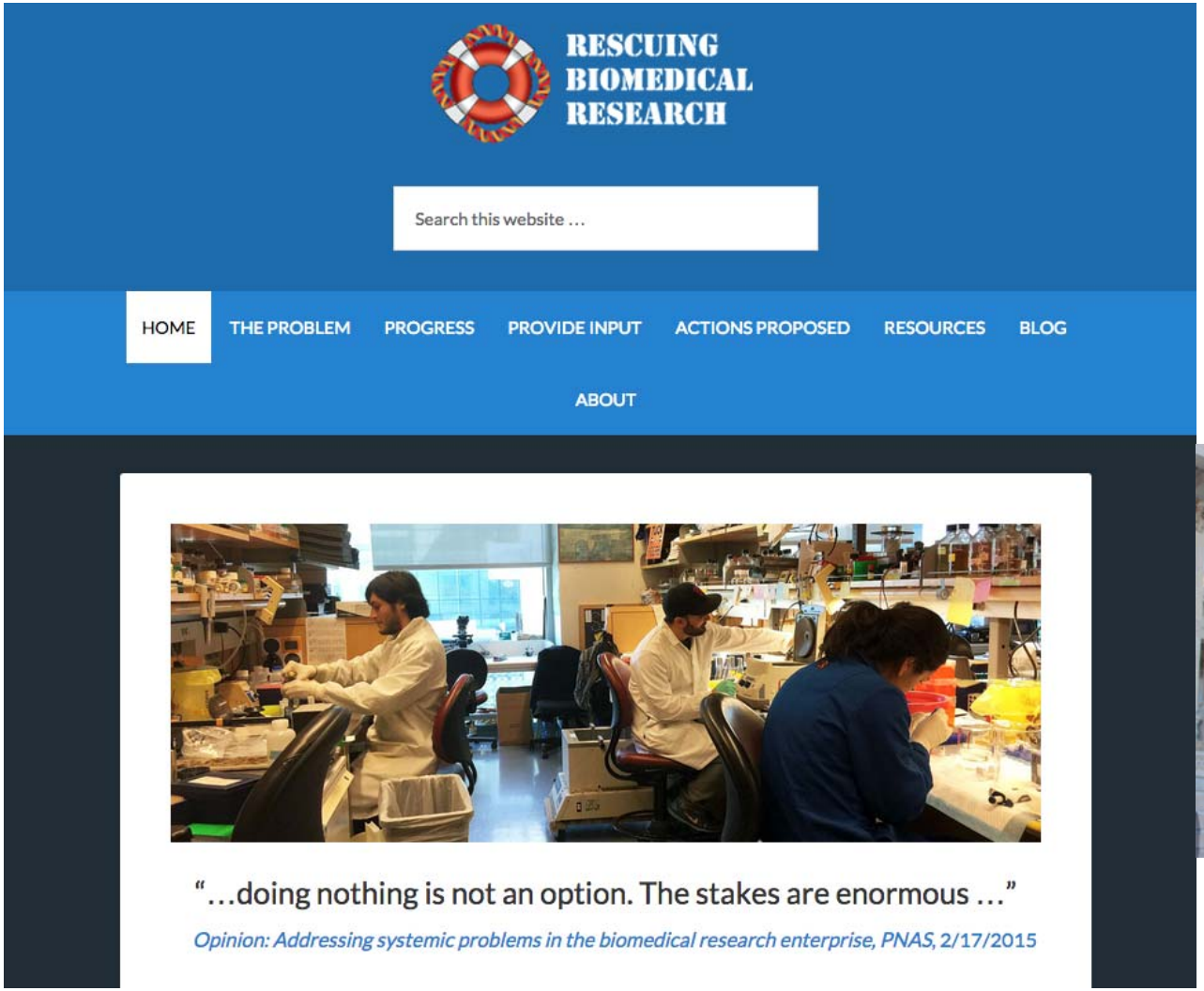
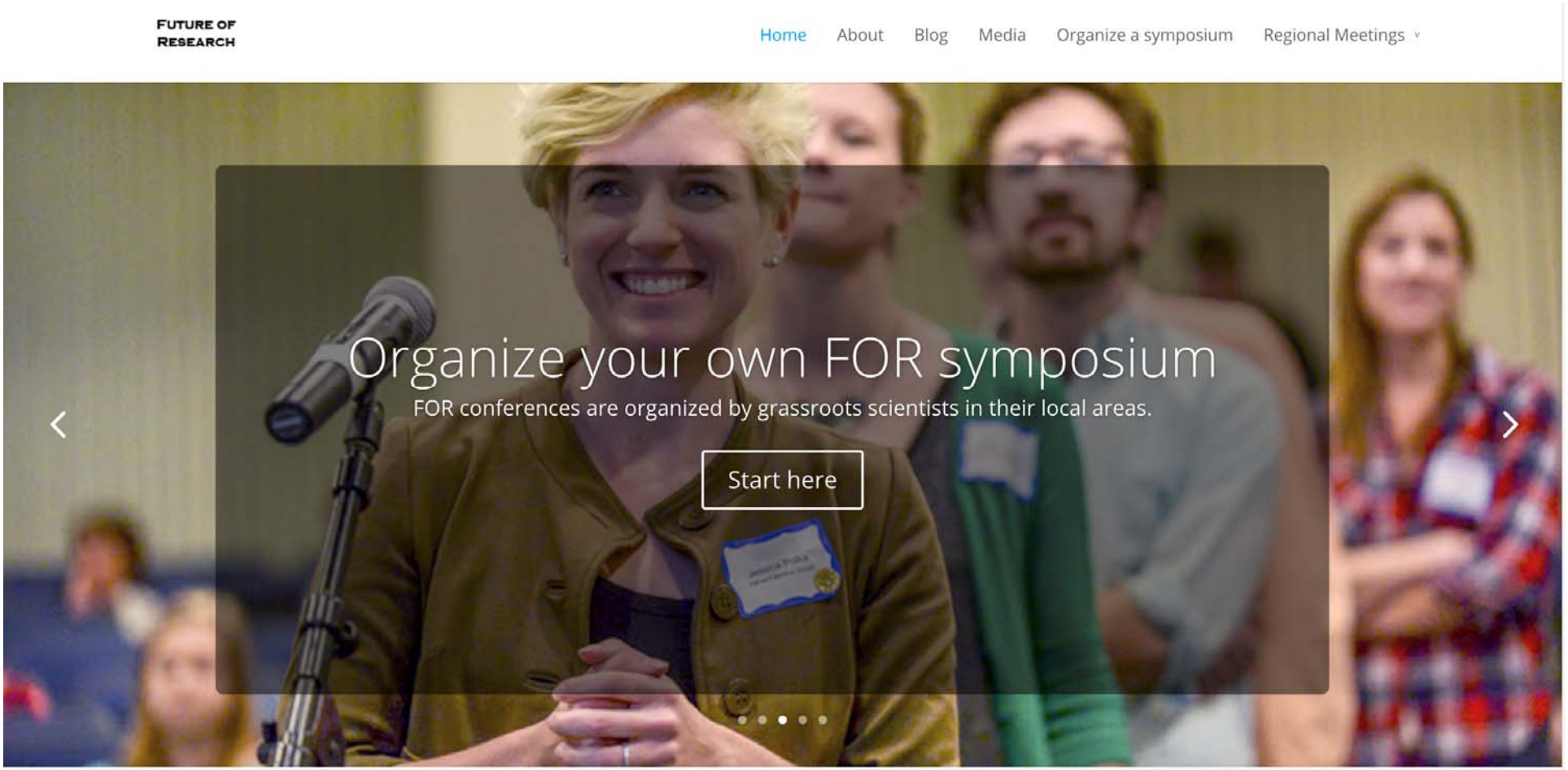


Christopher Pickett, Ph.D.
Executive Director

www.rescuebiomedicalresearch.org

"To catalyze changes that address systemic flaws in the biomedical research enterprise and promote more effective, creative and valuable scientific policies and culture."



“We are a group of postdocs in the Boston area invested in improving the Scientific endeavor. Specific areas of interest include:

- metrics and incentives in science
- Funding
- Training
- The structure of the workforce”

What to do? Progress on solutions!

- Transparency – each graduate program should be required to provide accurate career outcomes for prospective graduate students – NIGMS

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- **Diversification in training – educating graduate students for the diversity of jobs that will be available for them – BEST grants – "Broadening Experiences in Scientific Training" – 17 sites**

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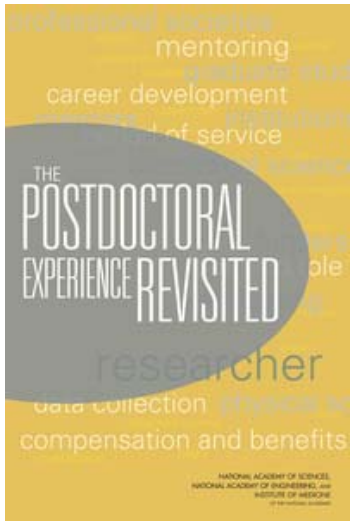
- Reserve the postdoc for those who wish to go on to research careers – not a default step as it tends to be now
- Strengthen and expand Master's programs directed to labor market demands
- **Significantly increase the use of training grants as the preferred mechanism for graduate support**

What to do? Progress on solutions!

- Pay for postdoctoral fellows should reflect their education and experience - Stanford



Greg Petsko

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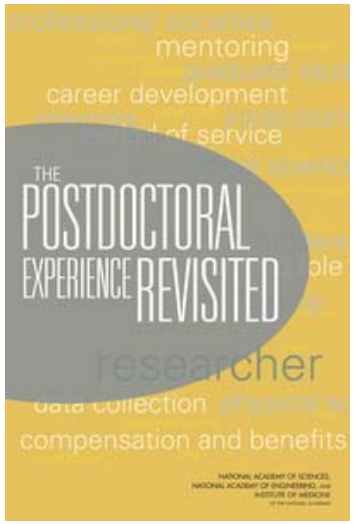

- Decrease the ratio of trainees/permanent staff in labs

- Increase use of core facilities overseen by experienced PhDs – Janelia Farms, Broad Institute, Cancer Research UK Cambridge Institute

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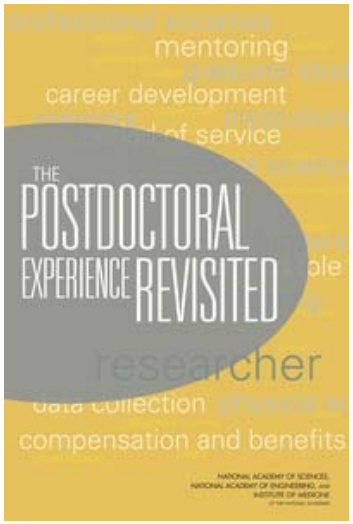

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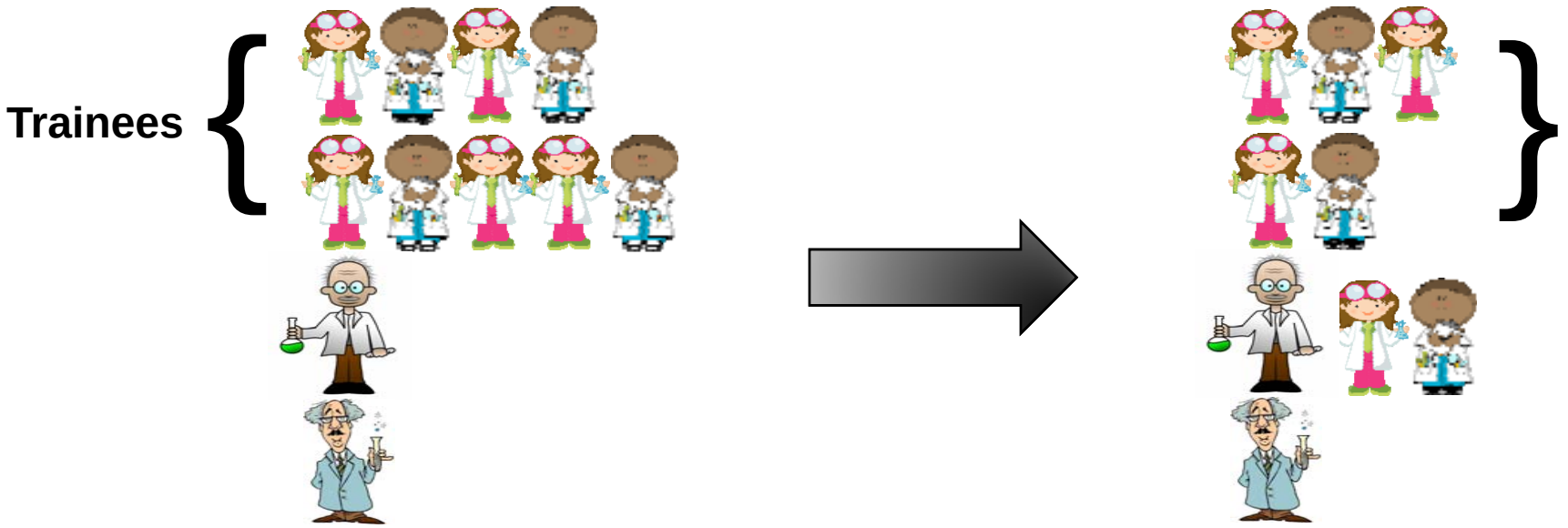
- **Dramatically** increase the number of grants that encourage early independence for postdoctoral fellows and changes in research direction – Burroughs Welcome; K99/ROO Pathway to Independence Awards; Early Independence Awards; New Innovator Awards; European Research Council (ERC) Starting Grants

What to do?

The Structure of the Laboratory

Changing the Malthusian Laboratory



The Best of Times - 2016