Congressional Briefing
Russell Senate Building
Washington, D.C.
July 25, 2012
Today’s Agenda

• Introduction: Michael Milken, Milken Institute
• Francis Collins, National Institutes of Health
• Harold Varmus, National Cancer Institute
• Stephen Spielberg, U.S. Food and Drug Administration
• William Nelson, Johns Hopkins Medicine
• Ross DeVol, Milken Institute
• Margaret Anderson, FasterCures
• General discussion and Q&A
(1) Francis Collins and Margaret Anderson chat before the briefing. (2) Bill Nelson greets attendees. (3) Mike Milken introduces the speakers and frames the day’s discussion, highlighting that as much as half of all global economic growth over the past two centuries can be traced to advances in health.
Photos from the Briefing

(4) The speakers: pictured from left to right, foreground to background: Ross DeVol, Harold Varmus, Francis Collins (speaking at the lectern), Bill Nelson, Steven Spielberg, and Margaret Anderson. (5) Harold Varmus discusses the vital work of the National Cancer Institute. (6) Congressional and Administration staff members fill the Kennedy Caucus room.
(7) Francis Collins discusses several “Grand Challenges” the NIH is working to address. (8) Bill Nelson answers a question from the audience; (pictured foreground to background: Steven Spielberg, Nelson, Francis Collins, Margaret Anderson. (9) Spielberg speaks with attendees after the briefing.
Growth of World Population and the History of Technology

Population (millions)

-9000 -6000 -4000 -3000 -2000 0 1000 2000

Agricultural Revolution
Pottery
Invention of Plow
1st Irrigation
1st Cities
Metallurgy
Writing
Mathematics
Genome Project
Man Lands on Moon
High-Speed Computers
Invention of Airplane
Industrial Revolution
2nd Agricultural Revolution
Peak of Rome
Peak of Greece
Internet
PCs
Nuclear Energy
DNA Discovered
Penicillin
Automobile
Telephone
Germ Theory
Railroads
Watt Engine

Source: Robert Fogel/University of Chicago
Over the past two centuries, by far the most prosperous 200 years in human history, as much as 1/2 of all economic growth can be traced to advances in health.
One of every five American babies born in 1900 did not live to celebrate a 5th birthday.
Presidents who lost a young child

John Adams
Thomas Jefferson
James Monroe
John Q. Adams
William Harrison
John Tyler
Zachary Taylor
Franklin Pierce
Abraham Lincoln
Rutherford Hayes
James Garfield
Chester Arthur
Wm. McKinley
Dwight Eisenhower
John Kennedy
George H.W. Bush
Worldwide Life Expectancy Growth

- 1820: 26 Years
- 1900: 31 Years
- 1950: 49 Years
- 2010: 67 Years

Source: United Nations Development Program
Deaths related to heart disease and stroke dropped by 40 percent between 1997 and 2006.

Source: Diabetes Care (http://www.cdc.gov/media/releases/2012/p0522_heart_disease.html)
Economic Value of Eliminating Deaths

- Heart Disease: $60.5T
- Cancer: $58.1T
- Stroke: $9.5T
- AIDS: $9.3T

U.S. Balance Sheet 2012: $76T

Source: Estimates base on 1999 studies by Kevin Murphy and Robert Topel/University of Chicago
FDR dedicates the NIH campus - 1940
The March
September 1998
National Institutes of Health Budget
$US billions

Source: National Institutes of Health

$180 billion
• Kick-start renewed commitment to bioscience

• Improve the health of America’s people and economy
Three Solutions to Healthcare Challenges

- Prevention
- Care
- Cures
Obesity Prevalence Among U.S. Adults 1991

Sources: Trust for America's Health and the Robert Wood Johnson Foundation
Obesity Prevalence Among U.S. Adults 2010

Sources: Trust for America's Health and the Robert Wood Johnson Foundation
Obesity Rates: U.S. vs. World

<table>
<thead>
<tr>
<th>Country</th>
<th>MEN</th>
<th>WOMEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S.</td>
<td>36.5%</td>
<td>41.8%</td>
</tr>
<tr>
<td>Mexico</td>
<td>24.0%</td>
<td>34.3%</td>
</tr>
<tr>
<td>U.K.</td>
<td>21.6%</td>
<td>24.2%</td>
</tr>
<tr>
<td>Germany</td>
<td>20.9%</td>
<td>20.4%</td>
</tr>
<tr>
<td>France</td>
<td>7.8%</td>
<td>6.6%</td>
</tr>
<tr>
<td>China</td>
<td>1.6%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Japan</td>
<td>1.8%</td>
<td>1.5%</td>
</tr>
</tbody>
</table>

Source: World Health Organization / Estimated obesity rates for people aged 15 years and older / 2005
World University Ranking
Life Sciences and Medicine

1. Harvard University
2. University of Cambridge
3. University of Oxford
4. Stanford University
5. Berkeley
6. University of Tokyo
7. Johns Hopkins University
8. MIT
9. Yale University
10. UCLA
11. Imperial College London
12. UC San Diego
13. National University/Singapore
14. University of Melbourne
15. University College London
16. University of Toronto
17. University of Edinburgh
18. Kyoto University
19. University of Sydney
20. University of British Columbia

Source: QS World University Rankings
Foreign students account for 113% of student body growth.
Chinese students account for 39% of foreign-enrollment.
“Korea’s government provides seven times more funding for pharmaceutical industry-performed research as a share of GDP than does the United States, while Singapore and Taiwan provide five and three times as much, respectively.”

- Leadership in Decline report
Assessing The U.S. International Competitiveness in Biomedical Research
May 2012
Outlook for Biomedical Research Spending (2012)

Source: OECD - Government Budget Appropriations or Outlays for Research and Development (2012)
China has the world's largest next-generation sequencing capacity.
Advancing Technology

- Cost
- Speed
- Storage
- Access
What does technology make possible?

1990

13 years and $3 billion to sequence the human genome

2012

2 hours and $1,000 to sequence a human genome

Source: John Reed, PhD, Sanford Burnham Institute
## Consumer Spending

<table>
<thead>
<tr>
<th>Category</th>
<th>U.S.</th>
<th>Asia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Housing</td>
<td>32.7%</td>
<td>10%</td>
</tr>
<tr>
<td>Transportation</td>
<td>18.0%</td>
<td>15%</td>
</tr>
<tr>
<td>Food</td>
<td>12.8%</td>
<td>23%</td>
</tr>
<tr>
<td>Insurance/pensions</td>
<td>11.2%</td>
<td></td>
</tr>
<tr>
<td>Healthcare</td>
<td>5.7%</td>
<td>5.7%</td>
</tr>
<tr>
<td>Entertainment</td>
<td>5.1%</td>
<td></td>
</tr>
<tr>
<td>Apparel and services</td>
<td>4.1%</td>
<td></td>
</tr>
<tr>
<td>Supplemental education</td>
<td>2.0%</td>
<td>15%</td>
</tr>
</tbody>
</table>

Source: U.S. Bureau of Labor Statistics/CLSA Mr & Mrs Asia
Major Spending Initiatives in the U.S.

- National Heart Institute: $3.0B
- National Cancer Institute budget: $4.9B
- Consumer spending on potato chips: $5.3B
- 2012 U.S. political campaigns (est.): $9.8B

Sources: Center for Responsive Politics / Borrell Associates
The NIH Impact

• 90% of Ph.D. scientists rely on NIH to support their research training.

• NIH accounts for 80% of all funding for non-profit medical research.

• 74% of pharma and biotech companies have licensed patents from NIH-funded academic research.

• 17% of FDA-approved drugs cite NIH patents as their source.

• NIH grants issued in FY2000 generated 30,477 invention disclosures, 17,341 patent applications and 6,901 patents (to date!).

Source: John Reed, PhD, Sanford Burnham Institute
In 2011, NIH research funding led to ...

- 432,094 new jobs
- $62 billion in new economic activity in the US
- 500 patent applications worldwide
- 389 patents issued
- Support of 300,000 scientists and researchers at 2,500+ universities and research institutions, and 50,000 competitive grants

Source: Dr. Everett Ehrlich, United for Medical Research (NIH’s Role in Sustaining the U.S. Economy)
Medical Research ROI

• The Federal government invested $3.8 billion in the Human Genome Project from 1990 to 2003.

• This investment generated an economic output of $796 billion and created 310,000 jobs, representing a 141:1 return on investment.

Source: Batelle (5/11/11 report)
Recent strides in understanding antibodies — the first weapons the human immune system deploys to fight an infection — make researchers optimistic that they are “on the cusp of a period of major discovery leading to [an AIDS] vaccine.”

Source: Washington Post
First political cartoon in America
Ben Franklin, 1754: “Join or Die”
We need to join in public/private collaboration.
A CELEBRATION OF SCIENCE

Renewing Our Commitment to the Future
Washington, DC • September 7-9, 2012
NIH’s Impact on U.S. Health and Medicine

U.S. Life Expectancy

**NIH Accomplishments**

- **Cardiovascular disease:** Death rates for heart disease and stroke have fallen by ~70% over the last 50 years
- **Infant mortality:** 40% reduction over the past two decades
- **Cancer:** Death rates falling ~1% per year, saving ~$500 billion annually
- **Diabetes:** Between 1997–2006, deaths among people with diabetes from all causes fell 23%; from heart disease, 40%
- **HIV:** Treatments enable people diagnosed in their 20s to live past 70

Life expectancy has risen from 48 to 79; these gains are worth ~$3.2 trillion annually
Cost of Sequencing a Human Genome
2001–2011
Success Story: Noah and Alexis Beery
Success Story: Noah and Alexis Beery
Disorders with Known Molecular Basis

Source: Online *Mendelian Inheritance in Man*, Morbid Anatomy of the Human Genome

250 with therapy
Drug Development Pipeline

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

Total pipeline time: approximately 14 years.
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

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


Before

After

Amyloid beta peptides
The Effects of Inflationary Growth on Purchasing Power: NIH Appropriation vs. Appropriation in 1998 Dollars
FY 2013 President's Budget Request
Grant Success Rates
FY 1978-2013
NIH...
Turning Discovery Into Health™
WHY SUSTAINED INVESTMENTS IN RESEARCH BENEFIT THE USA AND THE WORLD

Harold Varmus
Director, NCI

July 25, 2012
1971: Nixon signs the National Cancer Act
SMOKING AND HEALTH
REPORT OF THE ADVISORY COMMITTEE TO THE SURGEON GENERAL OF THE PUBLIC HEALTH SERVICE
U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service

1964: SURGEON-GENERAL’S REPORT

CHEMOTHERAPY FOR CHILDHOOD LEUKEMIA
OVER THE NEXT FEW DECADES, INVESTMENTS IN BASIC RESEARCH--CANCER VIRUSES, CELL BIOLOGY, GENETICS--PRODUCED AT LEAST THREE MAJOR ADVANCES....
(1) CANCER GENES

Many cell genes and proteins produce cancers when damaged... they are targets for diagnosis and therapy....

CANCERS ARE A COMPLEX SET OF DISEASES CAUSED BY GENETIC CHANGE
Vaccines against hepatitis B and papilloma viruses protect millions against hepatoma, cervical cancer, etc.
(3) Progress against AIDS, which depended on understanding retroviruses, the most closely studied cancer viruses.
40+ YEARS AFTER THE NATIONAL CANCER ACT, THE OPPORTUNITIES ARE VAST, BUT....

IRONICALLY AND SADLY, BUDGETS ARE SHRINKING....

MANY REASONS TO BE OPTIMISTIC ABOUT DELIVERY ON SCIENTIFIC PROMISES....
CANCER DEATH RATES HAVE BEEN FALLING OVERALL (BUT NOT FOR ALL CANCERS) SINCE AROUND 1990
NEW KNOWLEDGE IS ACCRUING SWIFTLY

The New York Times

Genetic Aberrations Seen as Path to Stop Colon Cancer

By GINA KOLATA
Published: July 18, 2012

THE CANCER GENOME ATLAS PUBLISHES ITS LATEST REPORT---ON COLO-RECTAL CANCER
NEW CANCER DRUGS TARGETED AGAINST DAMAGED PROTEINS CONTROL DISEASE

GLEEVEC BLOCKS AN ONCOGENIC ENZYME AND KILLS CANCER CELLS (1998)
APPROVED BY FDA IN 2001 TO TREAT AN ADULT LEUKEMIA (CML);
ACTIVE ORALLY, FEW SIDE-EFFECTS

EFFECTIVE IN SEVERAL HUMAN CANCERS

RESTORES NORMAL LIFE EXPECTANCY IN CML PATIENTS
Accurate diagnosis based on genetic characteristics

Choice of therapy based on knowledge of targets

Prediction of outcome based on complex information specific to each patient

A Life-Death Predictor
Adds to a Cancer’s Strain
By GINA KOLATA
Published: July 18, 2012
Testing for mutations in lung cancer allows cost-efficient use of new and effective targeted therapies.
WITH TALENT AND IDEAS, TIME (DECADES), AND RESOURCES, THIS STRUGGLE CAN BE WON!
Cancer Research and Cancer Care from the “Frontline” of Cancer Medicine

William G. Nelson, M.D., Ph.D.
Director, Sidney Kimmel Comprehensive Cancer Center (SKCCC)
NIH/NCI-Funds to SKCCC Promote Team Science

Hematological Malignancies

Cancer Immunology
Viral Oncology
Cancer Prevention and Control
Chemical Therapeutics

Breast Cancer
GI Cancer
Prostate Cancer
Upper Aerodigestive Cancer
Brain Cancer

2006-2011
263 researchers
2032 collaborations
643 intra-Programmatic
1389 inter-Programmatic
NIH/NCI-Funds to SKCCC Promote Team Science

Hematological Malignancies

Cancer Immunology

Viral Oncology

Cancer Prevention and Control

Chemical Therapeutics

Brain Cancer

Upper Aerodigestive Cancer

Cancer Molecular and Functional Imaging

Breast Cancer

GI Cancer

2006-2011
263 researchers
2032 collaborations
643 intra-Programmatic
1389 inter-Programmatic
Opportunity: Allogenic bone marrow transplantation (alloBMT) has proven benefit in the treatment of hematological malignancies and inherited bone marrow disorders.

Challenge: HLA-matched bone marrow donors are under-represented among African-American and other minority populations.

Solution: Innovative strategy for establishing immune tolerance in bone marrow allografts reduces graft-versus-host disease (GVHD) and making alloBMT more accessible to minority patients.

Heterogeneous Responses to Anti-PD-1*

0/14 responses
pretreatment biopsies from subjects (n = 30) with melanoma treated with an anti-PD-1 antibody

11/16 responses


cytoplasmic or absent B7-H1 expression (14 cases)
membranous B7-H1 expression (16 cases)

0/14 responses

11/16 responses
Biomarker Discoveries

- germline DNA variants
- somatic DNA mutations, translocations, etc.
- somatic DNA somatic methylation changes
- RNA expression changes, splice variants
- protein expression changes

Biomarker Assay Platforms

- DNA Beaming, PARE, MSP, nanoMSP, MOB, COMPARE, GEMINI

Translational Development of Molecular Biomarkers at SKCCC and Elsewhere: What are the Challenges?

Regulatory/Systems Considerations

- CLIA, biospecimen collection/archiving, HIPAA, health record information technology

Integration into Clinical Practice

<table>
<thead>
<tr>
<th>Test</th>
<th>Marker</th>
<th>Specimen</th>
<th>Company</th>
<th>Disease</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PCA3</strong></td>
<td>RNA</td>
<td>urine</td>
<td>Dianon</td>
<td>prostate cancer</td>
<td>predicts prostate biopsy outcome</td>
</tr>
<tr>
<td><strong>MGMT</strong></td>
<td>DNA methylation</td>
<td>tissue</td>
<td>MDxHealth</td>
<td>glioblastoma</td>
<td>predicts response to temozolomide</td>
</tr>
<tr>
<td><strong>GSTP1</strong></td>
<td>DNA methylation</td>
<td>urine/tissue</td>
<td>LabCorp/MDxHealth</td>
<td>prostate cancer</td>
<td>predicts prostate biopsy outcome</td>
</tr>
<tr>
<td><strong>AMACR</strong></td>
<td>protein</td>
<td>tissue</td>
<td>many</td>
<td>prostate cancer</td>
<td>diagnosis aid</td>
</tr>
</tbody>
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Congressional Staff Hill Briefing
Washington, D.C.
July 25, 2012

Ross DeVol
Chief Research Officer
Milken Institute
# Size of biomedical industry

**2009**

<table>
<thead>
<tr>
<th>Industry</th>
<th>Employment</th>
<th>Wages, US$B</th>
<th>Output, US$B</th>
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</thead>
<tbody>
<tr>
<td>Biopharmaceuticals</td>
<td>283,700</td>
<td>$29.0</td>
<td>$82.4</td>
</tr>
<tr>
<td>Medical devices and equipment</td>
<td>409,200</td>
<td>$26.5</td>
<td>$59.4</td>
</tr>
<tr>
<td>Research, testing and medical labs</td>
<td>526,300</td>
<td>$40.3</td>
<td>$64.5</td>
</tr>
<tr>
<td>Total Biomedical</td>
<td>1,219,200</td>
<td>$95.9</td>
<td>$213.2</td>
</tr>
</tbody>
</table>

Sources: Bureau of Labor Statistics, Moody’s Analytics, Milken Institute.
Four largest European countries comprised more than half of all NCEs produced during 1970s.


<table>
<thead>
<tr>
<th>Country</th>
<th>NCEs</th>
<th>% Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S.</td>
<td>157</td>
<td>31</td>
</tr>
<tr>
<td>France</td>
<td>98</td>
<td>19</td>
</tr>
<tr>
<td>Germany</td>
<td>96</td>
<td>20</td>
</tr>
<tr>
<td>Japan</td>
<td>75</td>
<td>15</td>
</tr>
<tr>
<td>Switzerland</td>
<td>53</td>
<td>10</td>
</tr>
<tr>
<td>U.K.</td>
<td>29</td>
<td>6</td>
</tr>
<tr>
<td><strong>Total NCEs</strong></td>
<td><strong>508</strong></td>
<td></td>
</tr>
</tbody>
</table>
...but in the previous decade, the U.S. Share jumped to 57 percent

_NCEs = New chemical entities by headquarter country of inventing firm_

<table>
<thead>
<tr>
<th>Country</th>
<th>NCEs</th>
<th>% total</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S.</td>
<td>111</td>
<td>57</td>
</tr>
<tr>
<td>France</td>
<td>11</td>
<td>6</td>
</tr>
<tr>
<td>Germany</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>Japan</td>
<td>18</td>
<td>9</td>
</tr>
<tr>
<td>Switzerland</td>
<td>26</td>
<td>13</td>
</tr>
<tr>
<td>U.K.</td>
<td>16</td>
<td>8</td>
</tr>
<tr>
<td><strong>Total NCEs</strong></td>
<td><strong>194</strong></td>
<td><strong>-</strong></td>
</tr>
</tbody>
</table>

U.S. share of foreign students declining

Global destinations for international students
at the post secondary level

Sources: OECD; Atlas of Student Mobility, Institute of International Education.
Singapore: Innovation as a national priority
Recommendations on how U.S can retain and bolster its biomedical innovation leadership

- Increase R&D tax incentives and make them permanent
- Cut corporate tax rates to match the OECD average
- Extend support for emerging biomedical research fields
- Provide adequate resources for the FDA and the NIH to expedite regulatory reviews and clinical trials
- Leverage existing strengths in medical devices
- Build human capital for biomedical innovation
- Promote and expand role of universities by adopting best practices in tech transfer and commercialization
Margaret Anderson
Executive Director

FasterCures
THE CENTER FOR ACCELERATING MEDICAL SOLUTIONS
IT TAKES TOO LONG.

1 OF EVERY 10,000

SCIENTIFIC DISCOVERIES

MAKE IT TO MARKET.

80-90%

OF DRUG DEVELOPMENT PROJECTS FAIL BEFORE THEY GET TESTED IN HUMANS.

15 YEARS

THAT'S HOW LONG IT TAKES TO TURN A SCIENTIFIC DISCOVERY INTO A NEW MEDICAL SOLUTION THAT COULD IMPROVE AND SAVE LIVES.

15 YEARS

$1 BILLION

1 IN 3

AMERICANS

NO TIME TO WASTE

LIVES WITH A DEADLY OR DEBILITATING DISEASE FOR WHICH THERE ARE NO CURES, AND FEW MEANINGFUL TREATMENT OPTIONS.

Every...

68 SECONDS

SOMEONE DEVELOPS ALZHEIMER'S DISEASE.

24 SECONDS

SOMEONE IS DIAGNOSED WITH CANCER.

18 SECONDS

SOMEONE IS DIAGNOSED WITH DIABETES.

And, the List Goes On...

IT COSTS TOO MUCH.

$100 BILLION

PER YEAR SPENT ON R&D.

ONLY 5¢

OF EVERY U.S. HEALTH DOLLAR GOES TO MEDICAL RESEARCH.

>$1 BILLION

TO BRING ONE NEW THERAPY FROM LAB TO MARKET.

IT'S ABOUT SAVING LIVES.

WE ALL KNOW SOMEONE

WHO COULD USE A

Faster Cure.

TO SAVE LIVES, WE NEED TO

SAVE TIME.

timeequalslives.org
Q&A slides
NIH funding increasingly goes to older researchers.

In 1980, nearly 10% of all NIH grants went to “young researchers” - between age 31 and 33.

In 2006, young researchers accounted for 1%.

In 2007, more grants were given to 70-year-old researchers than those under age 30.

Source: The Wall Street Journal 2/20/10
Job “Opportunities” in the Sciences

- Since 2000, U.S. drug firms have slashed 300,000 jobs.
- 14% of biology and life-science PhDs land a coveted academic position within five years.
- Unemployment among chemists is 4.6% - the highest in 40 years.
- 38 percent of new PhD chemists were employed in 2011.
- $10 billion in federal stimulus funds to the NIH in 2009 “created or retained” 50,000 science jobs - many of which are now at risk.

Source: Dr. Everett Ehrlich, United for Medical Research (NIH’s Role in Sustaining the U.S. Economy)
The NIH Grant-Funding Process

• Only 25% percent of NIH grantees are “young investigators,” down from 29% in 1990.

• The average age of a first-time NIH-funded researcher has jumped from 39 years to 43 years since 1990.

• Only 18% of first-time applicants receive awards (2007).

Source: Dr. Everett Ehrlich, United for Medical Research (NIH’s Role in Sustaining the U.S. Economy)
• The Chinese Academy of Sciences approved the applications of 477 senior foreign scientists and 179 young fellows to come to China for research collaboration (2010 and 2011).

• China’s goal is to raise the proportion of research input to above 2.5% of GDP by 2020.

Source: China Daily 6/10/11

• The number of peer-reviewed papers published by Chinese researchers rose 64-fold over the past 30 years.

• China is second to the US in terms of academic papers published, and will take first place by 2020.

Source: The Telegraph 1/25/10