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TAG Treatment Action Group

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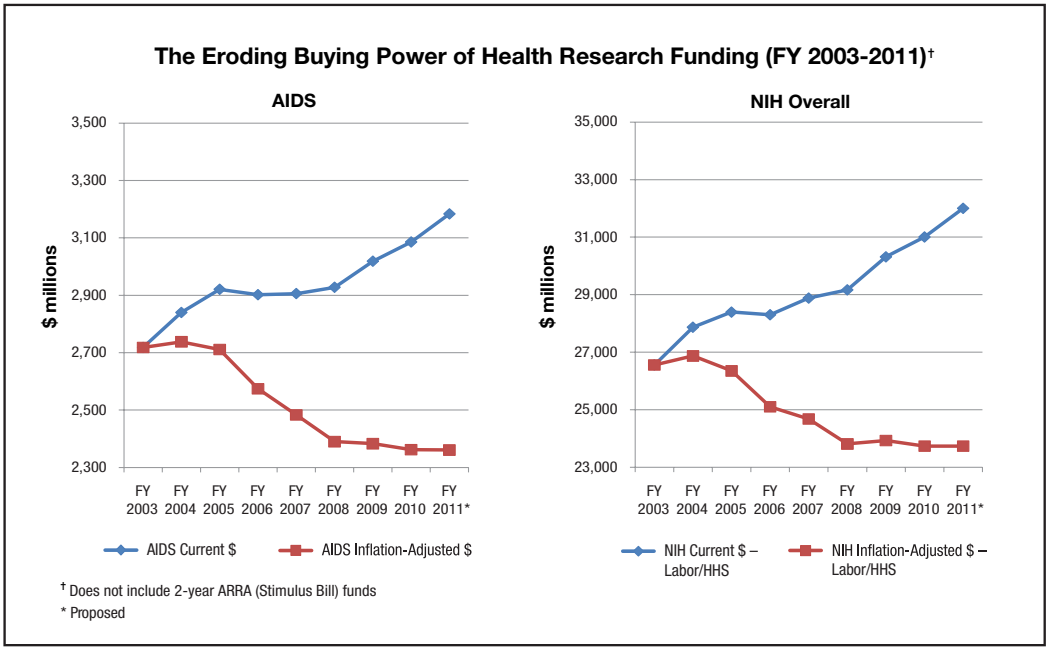
ISSUE BRIEF

A Sound Investment: The Multiplier Effect of AIDS Research

Investments in health research at the National Institutes of Health (NIH) have paid enormous dividends in the health and well-being of people in the U.S. and around the world. HIV and AIDS research supported by NIH has saved and improved the lives of millions and holds great promise for significantly reducing HIV infection rates and providing more effective treatments for those living with HIV/AIDS. Yet years of erratic funding levels for NIH have undermined our nation's leadership in health research and our scientists' ability to take advantage of the expanding opportunities to advance healthcare. The race to find better treatments and cures for cancer, heart disease, AIDS, and other diseases—and to control global epidemics such as AIDS, tuberculosis, and malaria—depends on robust long-term investment in health research at NIH.



Funding for AIDS and overall NIH health research, FY2003–FY2011 (proposed), in current and inflation-adjusted dollars. The red lines show funding in constant 2003 dollars, and demonstrate a progressive loss in purchasing power for AIDS and overall health research financing. These figures reflect base NIH resources and do not include two-year additional funding provided by the American Recovery and Reinvestment Act of 2009. (Source: Office of AIDS Research, National Institutes of Health)

Extraordinary Accomplishments in AIDS Research

The U.S. has been the global leader in research to prevent and treat HIV/AIDS and related serious health conditions. Over the past decades, the comprehensive AIDS research program at the NIH has led to scientific advances that have saved the lives of millions of people with HIV/AIDS and prevented millions more from becoming infected. The story of AIDS research is remarkable.[1, 2]

1982: Scientists name a new disease, acquired immune deficiency syndrome (AIDS), a year after its discovery.

1984: American and French scientists confirm that the human immunodeficiency virus (HIV) causes AIDS.

> "Medical miracles do not happen simply by accident. They result from painstaking and costly research—from years of lonely trial and error, much of which never bears fruit—and from a government willing to support that work. From life-saving vaccines, to pioneering cancer treatments, to the sequencing of the human genome—that is the story of scientific progress in America. When government fails to make these investments, opportunities are missed. Promising avenues go unexplored. Some of our best scientists leave for other countries that will sponsor their work. And those countries may surge ahead of ours in the advances that transform our lives."
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> *— President Barack Obama, March 9, 2009*

The Broad Benefits of AIDS Research in Fighting Disease [7,8]

The benefits of HIV/AIDS research extend far beyond helping those people at risk for or living with HIV. Investment in AIDS research has provided scientists worldwide with a model for combating an array of other diseases and conditions. For example, AIDS research has led to:

Promising Experimental Treatments for Cancer

- Various cancers: Several natural body hormones called growth factors promote the activity of HIV. Many of these hormones also promote the growth and spread of cancer cells. Blocking the activity of these hormones is a strategy first used experimentally to treat Kaposi's sarcoma, a cancer found in patients with HIV/AIDS. Now it is also being tested as a therapy in bladder, vulvar, and breast cancers and has shown some exciting recent success in treating colon cancer as well. Anti-HIV protease inhibitors used for HIV/AIDS are being evaluated in clinical trials for possible treatment of breast cancer.
- Immune suppression: The profound immune suppression necessary for a successful bone marrow transplant, required for the treatment of leukemias and other cancers, often leads to devastating, even fatal, infections such as cytomegalovirus (CMV) and pneumocystis pneumonia, which also affect people with AIDS. New drugs to treat and prevent these infections in cancer patients have come directly from AIDS-targeted research.

Potential Benefits for Heart Attack and Stroke Patients

HIV-positive children and adults, both on and off certain anti-HIV medications, can suffer heart attacks and strokes because HIV appears to affect small blood vessels in the heart and the brain, which makes these patients vulnerable to spasm, blood clots, and early atherosclerosis. And in HIV infection, a process of programmed cell death injures the cells that line the small blood vessels of the heart. Inflammation appears to play a significant role in this process, as it is does in non-HIV-infected individuals. Methods to control inflammation and detect it early should limit these damaging processes in all affected individuals.

New Approaches to Treating Hepatitis, Osteoporosis, Heart Damage, and Influenza

- Hepatitis B: Three drugs developed against HIV—lamivudine, tenofovir, and entecavir—are now the mainstays of therapy for hepatitis B virus (HBV) infections. Another antiviral drug called adefovir, which failed as an HIV treatment, was found to suppress HBV at much lower dosages and has been approved for treatment of chronic HBV disease.

1985: The first HIV antibody test is licensed by the U.S. Food and Drug Administration (FDA), and screening of the U.S. blood supply begins.

1987: The first antiretroviral drug to fight HIV is approved by the FDA. The drug is called AZT (or zidovudine) and is in a class of antiretroviral drugs called nucleoside reverse transcriptase inhibitors (NRTI), which act to prevent HIV from reproducing in the body. The FDA licenses the HIV Western blot test, a confirmatory antibody test.

- Hepatitis C, Influenza, Osteoporosis, Heart Damage: Protease inhibitors are being developed to combat infections such as hepatitis C (HCV) and influenza, and medical conditions such as osteoporosis and the heart muscle damage that results from heart attack.

New Hope for Alzheimer's Patients

Profound dementia is commonly seen in the late stages of AIDS, so drugs that are successful in reducing nerve damage and dementia in AIDS, for example, could potentially benefit patients with Alzheimer's. The characteristic plaques that fill the brain cells of an Alzheimer's patient are formed partly by proteases, so scientists are now investigating the use of protease inhibitors to treat this debilitating dementia affecting millions of people in the U.S. and worldwide.

Experimental Treatments for Autoimmune Disorders

HIV-positive people can develop autoimmune problems such as psoriasis or blood abnormalities associated with lupus. For these autoimmune diseases, treatments developed for AIDS may also work when the same conditions occur spontaneously. A new class of anti-HIV drug that blocks a protein known as CCR5, the key co-receptor for HIV's entry into cells, is also being evaluated in inflammatory bowel disease and other autoimmune disorders.

New Technologies for Diagnosing Other Infections

New PCR (polymerase chain reaction) tests, developed for diagnosing HIV, are now routinely used to rapidly detect a number of other infectious diseases including hepatitis C, tuberculosis, chlamydia, influenza, Lyme disease, and many fungal infections. These PCR techniques have also made it possible to measure otherwise undetectable levels of cancer cells in people who appear to have been cured.

New Approaches to the Design and Conduct of Clinical Trials

- Recruiting and Enrolling: AIDS research has resulted in new approaches to the design and conduct of clinical trials, including community-based trials that capture the expertise of community physicians, as well as in recruiting and enrolling patients from diverse populations. These models are now being applied to test diagnostic, prevention, and treatment approaches for other diseases using faster, more efficient, and more inclusive protocols.
- Community Advisory Boards: AIDS clinical studies pioneered the development of community advisory boards to bring community perspectives into the planning, development, and implementation of the research, including recruiting study participants, educating community members about issues of consent, and helping with retention of participants.
- Parallel-Track Mechanism: In 1992, the "parallel-track" mechanism was established to allow select people with HIV to access new and safe drugs prior to the completion of clinical trials and formal approval by the FDA. This mechanism has been lifesaving for people with HIV/AIDS and for individuals suffering from other serious or life-threatening diseases for which existing therapies were either ineffective or failed.

Insights into the Function of Human Systems

- Immune system studies: AIDS research has led to advances in the understanding of the thymus gland, a small endocrine organ that produces a type of white blood cells—T lymphocytes—that help cells in the body to fight infections.
- Neurological studies: Studies of the mechanisms involved when HIV crosses the blood-brain barrier could shed light on how drug therapies can be delivered to the brain and nervous system to fight debilitating neurological disorders.

1992: The FDA approves another NRTI-based antiretroviral drug, ddC (or zalcitabine), for use with AZT, and the first clinical trial of combination antiretroviral therapy begins. The FDA also licenses the first rapid HIV test, which provides results in as little as ten minutes.

1994: An NIH-funded trial demonstrates that AZT can reduce the risk of mother-to-child HIV transmission.

1995: Saquinavir, the first antiretroviral drug in the protease inhibitor class, is approved by the FDA.

Innovative Behavioral, Social, Psychosocial, and Outreach Preventive Interventions

- Behavioral and social interventions: In the case of HIV/AIDS, these include increasing condom use, reducing the number of sex partners, delaying the onset of sexual intercourse, reducing the frequency of needle sharing among injection drug users (IDUs), and referring IDUs to drug treatment programs. These interventions have reduced HIV-related risk behaviors and lowered the incidence of HIV and other sexually transmitted infections (STIs) in a range of population groups and settings. The development and improvement of HIV-related behavioral intervention science has benefited all areas of health promotion and disease prevention, including nutrition, smoking, alcohol and drug use, and unintended pregnancy prevention.
- Psychosocial interventions: These interventions emphasize the development of behavioral skills, such as confidence in one's ability to negotiate with partners about condom use or sexual abstinence. These skills are applicable to other health and social life situations, including unintended pregnancy prevention, avoidance of drug and alcohol abuse, and conflict resolution/violence prevention.
- Outreach interventions: Employing peer leaders and social networks, such as those developed for out-of-treatment drug users to deliver HIV prevention messages and services, are applicable to other health promotion and disease prevention efforts that would benefit from peer outreach, such as nutrition and exercise campaigns.
- Research on enhancing adherence: This area of research among HIV-infected patients has also produced a number of new psychosocial and technological methods that are applicable to other health arenas, especially those that involve taking numerous medications on different schedules such as with advanced cancer and heart disease.

Methodologies for Measuring Behavioral and Social Factors

HIV/AIDS researchers have pioneered the use of qualitative and quantitative techniques for mapping social networks to understand patterns in epidemics. The use of social and biostatistical modeling research has helped to improve understanding of trends in epidemics and their impact at the community level.

Investment in AIDS Research = Money Well Spent

Additional funding for AIDS and other health research is essential if we are to take advantage of significant scientific opportunities to prevent and treat HIV/AIDS and other diseases. The consequences of stepping back on our commitment to AIDS and other health research would result in unnecessary suffering and loss of life in the U.S. and around the world.

Scientific Advances on the Horizon

- Pre-Exposure Prophylaxis (PrEP) is one of the most promising experimental HIV prevention interventions. With PrEP, HIV-negative people would take one or more antiretrovirals (ARVs) on a daily or periodic basis to lower the risk of becoming infected if exposed to HIV. Animal studies and experience with prevention of mother-to-child transmissions suggest that PrEP may be safe and effective as a preventive intervention. Several clinical studies of PrEP are now under way, with efficacy results expected as early as 2010. Additional research is needed to test a variety of candidate drugs for use in PrEP, daily versus periodic use of medications, and the appropriateness of PrEP in various populations, including women of childbearing age and adolescents.
- The search for an AIDS vaccine that would prevent HIV infection has been a holy grail of medical research for

1996: The FDA approves the first antiretroviral drug in the non-nucleoside reverse transcriptase inhibitor (NNRTI) class. Similar to NRTIs and protease inhibitors, NNRTIs prevent HIV from reproducing in the body. The FDA approves the first urine test for HIV as well as the first test that detects the level of HIV in the blood.

1999: Trial results from a study in Uganda first demonstrate that a single dose of an antiretroviral drug, nevirapine, when given to the mother at the onset of labor and to the baby after delivery, roughly halves the rate of HIV transmission.[3, 4]

many years. Just in the last several years, promising new findings have brought new optimism into the AIDS vaccine field. In September 2009, researchers reported that a vaccine combination tested in Thailand showed moderate but statistically significant impact in reducing infection. This is the first possible evidence of an AIDS vaccine providing any level of protection against HIV infection. Though this vaccine is not appropriate for licensure, it may provide valuable clues for the development of an AIDS vaccine that can be used widely. Also in September 2009, scientists announced the discovery of two neutralizing antibodies capable of preventing HIV replication, providing new leads in vaccine development.

- Topical microbicides are preparations in the form of gels, creams, or foams applied to prevent sexually transmitted infections, including HIV. A new generation of microbicides is now entering clinical trials. Further research is needed to find definitive answers about the safety and effectiveness of current microbicide candidates and to develop new candidate products.
- Adult male circumcision has been shown to reduce HIV infection among heterosexual men by up to 60 percent in some settings.[9] Operations research is now needed to help bring male circumcision to scale in order to achieve widespread impact on lowering the number of new infections.

Maintaining the U.S. as a World Leader in Research

New investments in health research at NIH and elsewhere are essential to realizing the exciting and innovative scientific opportunities ahead. The cornerstone of the globally admired U.S. research funding system is the R01 grant. These proposals are initiated by investigators and reviewed by their peers in NIH study sections organized around specific fields of study. Receiving an R01 grant for the first time is considered a milestone in the career of a researcher, providing the freedom to pursue promising research ideas. Many of the major breakthroughs in HIV/AIDS research—and biomedical science generally—can be traced back to R01 grants. Increasing opportunities to secure first-time grants is absolutely critical to fostering a new generation of researchers with innovative ideas. A strong and vibrant research enterprise is crucial to maintaining the status of the U.S. as a world leader in research.

> "We are faced with compelling scientific challenges to develop truly transforming interventions such as a cure for HIV infection and powerful new prevention modalities. Without these interventions, the scope and burden of the HIV pandemic will continue to grow."
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> —*Anthony Fauci, M.D., Director, National Institute of Allergy and Infectious Diseases, and Gregory Folkers, M.S., M.P.H., Chief of Staff to Dr. Fauci.* Health Affairs, *November 2009*

More American Jobs

The NIH is a major employer of Americans across the country. The Federation of American Societies for Experimental Biology (FASEB) noted that "More than 83 percent of NIH funding supports extramural researchers (researchers who work at institutions throughout the U.S.) in every state in the country. The extramural community consists of more than 325,000 scientists and other research personnel affiliated with more than 3,100 universities and organizations nationally and internationally."[10] New NIH Director Dr. Francis Collins brought this point home during his public town hall meeting on September 9, 2009, by

2000: The Centers for Disease Control and Prevention (CDC), the FDA, the NIH, and the U.S. Agency for International Development (USAID) jointly conclude that male condoms significantly reduce the risk of HIV transmission for both men and women during vaginal intercourse when used correctly and consistently.[5]

2002: The FDA approves the first rapid finger-prick HIV diagnostic (or screening) test.

2003: The FDA approves the antiretroviral drug enfuvirtide (Fuzeon), the first entry inhibitor.

2004: The FDA approves the first saliva-based HIV diagnostic (or screening) test.

citing that for every research grant awarded by the NIH, on average seven new jobs are created.[11] With additional dollars, scientists are given valuable opportunities to advance science while creating more jobs to boost the economy.

Roller Coaster Funding for NIH and AIDS Research: A Bad Approach

In 1998, Congress set out to double the NIH budget and within five years increased resources for NIH from $13.7 billion (FY1998) to $27.1 billion (FY2003).[12] The funding increases allowed research institutions to break ground on new facilities and expand their faculties to move forward on ambitious research agendas.[12] In a 2002 survey, the Association of American Medical Colleges (AAMC) found that new construction at medical schools had exploded. From 1998 to 2002, schools invested $3.9 billion in new construction, compared with $2.2 billion between 1990 and 1997. For many young people, this expansion and the attendant growth in employment opportunities demonstrated the viability of a career in the science and research field.[12] By fiscal year 2004, however, Congress had moved on to other priorities. Flat funding of NIH combined with inflation over the past six years has led to a reversal of gains made during the doubling period, and more importantly, has undermined our nation's ability to respond to deadly infectious and chronic health conditions in the U.S. and abroad.[12]

Missed Scientific Opportunities

- The percentage of research proposals supported by NIH has dropped dramatically from 32 percent of proposals received in 2001 to a projected 18 percent in 2009.[14]
- Funded grants are routinely cut by 10 percent or more.[12] At the National Cancer Institute and the National Institute on Aging, funded grants are cut by even more—24 percent and 18 percent on average respectively.[12]
- For AIDS research, flat funding has resulted in an 18 percent decline in NIH's ability to support new research grants.[13]
- Flat funding combined with inflation has resulted in nearly a 20 percent loss in buying power for NIH over the past five years.[14]

Discouraging the Next Generation of Scientists and Researchers

The reality that young researchers face, knowing that the likelihood of receiving funding support is not high, has dampened the energy and enthusiasm of many of those aiming for a career in biomedical research. A 2005 report by the National Academy of Sciences noted that young investigators play a crucial role in bringing novel, potentially breakthrough ideas to the research table. Appropriate funding to nurture their careers is vital to the future of health research.

- New grant applications to the NIH now have a less than 20 percent chance of being funded.[13]
- In 2006, the chance of an established investigator being awarded an NIH grant on the first try was seven percent.[12]
- The intense difficulty in obtaining NIH support is forcing researchers to spend excessive amounts of time writing and resubmitting grants. Some researchers are reporting that their laboratories are in peril as a consequence.[12]
- The average age at which an investigator receives his or her first grant has increased by nearly a decade, from 34 years in 1970 to 42 years today.[15]
- In 2006, the *New England Journal of Medicine* observed that, "as it becomes increasingly difficult for established investigators to renew their grants, their frustration is transmitted to trainees, who increasingly opt for alternative career paths, shrinking the pipeline of future investigators."[16]

2005: Results from a trial in South Africa show for the first time that adult male circumcision significantly reduces the risk of acquiring HIV.[6]

2006: The FDA approves the first single-pill, once-a-day, combination drug for AIDS patients, eliminating the need for complicated, multi-pill treatments. The single pill is called Atripla (a combination of the drugs efavirenz, tenofovir, and emtricitabine) and is considered a major breakthrough in AIDS treatment.

2007: The FDA approves two new types of HIV drugs that block HIV from infecting healthy cells: raltegravir, the first integrase inhibitor, and maraviroc, the first CCR5 blocker.

2010: A growing body of research suggests that provision of antiretroviral therapy, especially early in the course of HIV infection, is associated with reduced community prevalence of HIV.

"Many of us are worrying quite a bit about FY11 and what's going to happen after the Recovery Act two-year support comes to an end and I'm sure you are thinking about that too. I hope you are."

— Dr. Francis Collins, NIH Director
September 9, 2009

Loss of U.S. Competitive Edge

The *2006 American Competitiveness Initiative* report of the Domestic Policy Council of the White House Office of Science and Technology Policy begins by stating that "keeping our competitive edge in the world economy requires policies that lay the groundwork for continued leadership in innovation, exploration, and ingenuity." When a career in science appears unachievable and insecure, the research industry suffers and top-tier U.S. researchers are increasingly tempted to migrate to countries that provide greater opportunities to test innovative ideas. In January 2010, the National Science Foundation released a report[17] on science and technology investments by countries around the world, noting the "gradual erosion" of the U.S. leadership position in this area given rapidly increasing investments by Asian and European Union countries. Through increased and consistent opportunities to foster new research, the U.S. can maintain its competitive edge.

The Time-Limited Promise of the American Recovery and Reinvestment Act of 2009 (ARRA)

After years of stagnant funding at the NIH, the American Recovery and Reinvestment Act of 2009 (ARRA) was a welcome infusion of resources—but with some strings attached. Congress allocated $10.4 billion to NIH for FY09–FY10 as part of ARRA, more commonly referred to as the "stimulus bill." These increased resources led to the protection and creation of tens of thousands of jobs as researchers went to work in communities nationwide. They also led to a higher than expected demand for funding to support potentially groundbreaking research. NIH was only able to support approximately three percent of the 21,000 ARRA-supported challenge grant applications that it received.[18]

ARRA funds are intended to be used in a two-year time frame and will not increase the ongoing (base) support for NIH. It is estimated that if NIH funding returns to the FY09 level after stimulus funds dry up, it could mean a 40 percent reduction in the number of research project grants awarded by NIH.[19]

The NIH's long-term vision cannot be realized without a consistent and robust investment strategy. This is key to securing the NIH's future global competitiveness as well as realizing its potential for powering biomedical innovation and economic growth, and improving health in the U.S. and worldwide.

The bottom line: In FY2011 and future years, Congress must redress five years of flat funding for NIH by significantly increasing overall NIH appropriations to take advantage of growing scientific opportunity in health research.

References

1 Food and Drug Administration (FDA). Timeline/History. Available at: http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/HIVandAIDSActivities/ucm117935.htm. Accessed October 8, 2009.
2 Kaiser Family Foundation. The Global HIV/AIDS Epidemic: A Timeline of Key Milestones. Available at: http://www.kff.org/hivaids/aidstimeline/timeline.cfm. Accessed October 8, 2009.
3 Connor, EM, et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. *NEJM*. 1994; 331(18). Available at: http://www.ncbi.nlm.nih.gov/pubmed/7935654?dopt=Citation.
4 Guay, LA, et al. Intrapartum and neonatal single-dose nevirapine compared with zidovudine for prevention of mother-to-child transmission of HIV-1 in Kampala, Uganda: HIVNET 012 randomised trial. *Lancet*. 1999; 354(9181). Available at: http://www.ncbi.nlm.nih.gov/pubmed/10485720?dopt=Abstract.
5 Globalhealthreporting.org. Available at: http://www.globalhealthreporting.org/diseaseinfo.asp?id=273. Accessed October 4, 2009.
6 Centers for Disease Control and Prevention. Male Circumcision and Risk for HIV Transmission and Other Health Conditions: Implications for the U.S.. Available at: http://www.cdc.gov/hiv/resources/factsheets/circumcision.htm#ref11. Accessed October 8, 2009.
7 *The Broad Benefits of AIDS Research: Better Health for All*. amfAR, The Foundation for AIDS Research. 2009.
8 Research on AIDS Benefits Efforts Against Other Diseases. 2009. Available at: http://www.oar.nih.gov/hivaids/crossoverbenefits.asp.
9 Katz, IT, Wright, AA. Circumcision—A Surgical Strategy for HIV Prevention in Africa. *NEJM*. 2008; 359: 2412–2415. Available at: http://content.nejm.org/cgi/content/full/359/23/2412#R1. Accessed October 8, 2009.
10 Federation of American Societies for Experimental Biology (FASEB). Federal Funding for Biomedical and Related Life Sciences Research FY2008. Available at: http://opa.faseb.org/pdf/final_funding_fy2008.pdf. Accessed October 4, 2009.
11 Constituents Meeting with NIH Director Francis Collins [webcast]. NIH. September 9, 2009. Available at: http://videocast.nih.gov/Summary.asp?File=15263.
12 Couzin J, Miller, G. Boom and bust. *Science*. 2007; 316(5823):356–61.
13 American Association for the Advancement of Science (AAAS). AAAS Report XXXIII Research and Development FY 2009. Intersociety Working Group. Available at: http://www.aaas.org/spp/rd/09pch7.htm. Accessed October 6, 2009.
14 Steinbrook, R. Opportunities and Challenges for the NIH — An Interview with Francis Collins. *NEJM*. 2009. Available at: http://healthcarereform.nejm.org/?p=1808. Accessed September 26, 2009.
15 Weinberg, RA. Lost Generation. *Cell*. 2006;126: 9–10.
16 Loscalzo, J. The NIH Budget and the Future of Biomedical Research. *NEJM*. 2006;354(16): 1665–67
17 National Science Foundation, Science and Engineering Indicators, 2010. Available at: http://www.nsf.gov/statistics/seind10/.
18 Constituents Meeting with NIH Director Francis Collins. Available at: http://videocast.nih.gov/Summary.asp?File=15263.
19 Federation of American Societies for Experimental Biology (FASEB). Investing in Our Future: A Stronger NIH for a Healthier America. Available at: http://opa.faseb.org/pages/PolicyIssues/NIHfundingtrends/Investing_In_Our_Future.pdf. Accessed September 15, 2009.

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