Testimony of Elizabeth J. Kovacs, Ph.D., on behalf of
The American Association of Immunologists (AAI),
Submitted to the House Appropriations Subcommittee on Labor, Health and Human Services, Education and Related Agencies,
Regarding the Fiscal Year (FY) 2015 Budget for the National Institutes of Health
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The American Association of Immunologists (AAI), the world's largest professional society of research scientists and physicians who study the immune system, respectfully submits this testimony regarding fiscal year (FY) 2015 appropriations for the National Institutes of Health (NIH). ***AAI recommends an appropriation of at least $32 billion for NIH for FY 2015*** to support important ongoing research, fund a reasonable number of outstanding new grant applications, and restore NIH funding to a level that can sustain a robust and dynamic biomedical research enterprise in the United States.

NIH's Crucial Role in Advancing Biomedical Research

NIH is essential to the advancement of biomedical research in the United States, where virtually all biomedical scientists rely on NIH leadership and funding.[1] Academic scientists, many of whom conduct research while teaching the next generation of doctors and scientists, depend on NIH grants to support their research at universities, colleges and research institutions all around the country. NIH intramural scientists require funding to do their own research as well as collaborate with their private sector colleagues.[2] And scientists employed by industry, who generally do not receive NIH grants or awards, depend on NIH-funded scientific discoveries to develop products that bring research to the bedside. A strong NIH budget, therefore, is essential to all sectors of the U.S. biomedical research enterprise, and has enabled NIH to remain the key international leader influencing biomedical research around the globe.

NIH Budget Woes Slow Research and Threaten U.S. Preeminence

The slow growth of the NIH budget in recent years, exacerbated by the impact of biomedical research inflation,[3] has significantly reduced NIH's purchasing power, and in turn, the purchasing power of its

grantees. According to the Congressional Research Service (CRS),"[i]n constant 2003 dollars, FY2014 funding is 22% lower than the FY2003 level."[4] *How many avenues of research have not been followed because of this reduction? How many potential treatments and cures have been delayed or not discovered?* These are questions that cannot be answered definitively, but we do know that NIH budget reductions have already caused real and lasting damage: the loss of grant funding, even among the most highly qualified scientists; the closure of labs; the termination or interruption of important research; and the emigration of talented scientists to other countries. And we do know that too many scientists are spending too much time in a constant chase for funding, rather than conducting research and mentoring the nation's future researchers, inventors and innovators. These budget woes threaten America's preeminence in advancing basic biomedical research, discovering urgently needed treatments and cures, and "growing" brilliant young scientists.

Research on the Immune System: Essential to our Health, Crucial to our Future

The immune system is the body's primary defense against viruses, bacteria, and parasites that cause disease in millions of people every year. When the immune system is operating properly, it provides powerful protection against a wide variety of illnesses, including cancer, Alzheimer's disease, and cardiovascular disease. The immune system can, however, perform poorly, leaving the body vulnerable to infections, including influenza, HIV/AIDS, tuberculosis, malaria, and the common cold. It can also become overactive, damaging normal organs and tissues, and causing autoimmune diseases, such as allergy, asthma, inflammatory bowel disease, lupus, multiple sclerosis, rheumatoid arthritis, and type 1 diabetes. Research scientists and clinicians are working to harness this powerful system to protect people and animals from infectious diseases, cancer, and many other illnesses, and to protect against natural or man-made infectious organisms (including plague, smallpox and anthrax) that could be used for bioterrorism.[5]

Recent Immunological Advances and Their Promise for Tomorrow

1. Cancer Immunotherapies: Offering Hope of Conquering Cancer

NIH-funded scientists recently identified inhibitory receptors which suppress immune cell activation.

Blocking these receptors can allow the immune system to destroy tumor cells.[6] Today, therapeutics targeted against inhibitory receptors like CTLA4 are undergoing rigorous clinical trials against a variety of cancers. The success rates for these therapies have been astounding and unprecedented: for example, rates of tumor regression in patients with metastatic melanoma have increased from ~10% to ~50%.[7] With this level of success, immunotherapy is one of the most exciting and promising areas of cancer treatment.

2. ***Early Antiretroviral Therapy: Eliminating HIV, Ending AIDS?***

NIH-funded researchers have discovered that early administration of antiviral medication, known as anti-retroviral therapy (ART), can have lasting effects on an HIV-infected patient's long-term prognosis. In one study,[8] an infant born to an HIV-infected mother began receiving ART within hours of birth. The infant tested positive for HIV and continued treatment for 18 months. Despite the HIV diagnosis and subsequent discontinuation of ART, the child remained virus-free one year later. A second baby with a similar history also showed an absence of HIV.[9] Together with several additional unconfirmed cases of babies "cured" of HIV infection, these findings offer hope to the ~250,000 babies born each year infected with HIV.[10]

3. Gut (Intestinal) Bacteria: The Microbiome Role in Autoimmune Disease

NIH-funded research has shown that gut bacteria (the intestinal "microbiome"), which aid in food digestion, may impact the development of autoimmune diseases, including rheumatoid arthritis, type 1 diabetes, multiple sclerosis and inflammatory bowel disorders.[11] Current research is exploring changes in gut bacteria from diet, hormones, antibiotics, and infections, and the effect of gut bacteria based therapeutics [for example, the ingestion of healthy gut bacteria (probiotics) in yogurt]. One study involving fecal transplantation (which includes the transfer of intestinal bacteria from one person to another) has found that such transplantation in pill form is well tolerated and is 98-100% efficacious in curing infections with *Clostridium difficile*, a bacterium linked to ~14,000 diarrheal deaths in the U.S. per year. [12]

4. RSV Vaccine: Saving Infants' Lives

Millions of infants are hospitalized and 160,000 children die each year each from pneumonia and other lung

diseases caused by respiratory syncytial virus (RSV).[13] Until recently, however, a vaccine for RSV has been elusive. In an important breakthrough, scientists at the NIH discovered antibodies – protective molecules produced by the immune system – that helped identify a key protein for use in vaccine development.[14] The NIH scientists were then able to engineer this protein and demonstrate its ability to produce a strong protective immune response against RSV in animals.[15] This molecule is expected to be ready soon for testing in humans. Importantly, the approach developed in this case can be applied to vaccine design for numerous other viruses, such as HIV, hepatitis C, dengue, and West Nile viruses, that have evaded the body's protective immune responses, and will provide insight into how viruses evade the immune system.

Conclusion

AAI thanks the members and staff of the subcommittee for their ongoing, strong bipartisan support for biomedical research, and recommends an appropriation of *at least $32 billion* for NIH for FY 2015 to fund important ongoing research, strengthen the biomedical research enterprise, and ensure that the brightest scientists, trainees, and students are able to pursue careers in biomedical research in the United States.

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[1] After a highly competitive peer review process, which includes comprehensive review by panels of extramural scientists, NIH awards more than 80% of its ~$30.1 billion budget to "more than 300,000 researchers at more than 2,500 universities, medical schools, and other research institutions in every state and around the world." About 10% of its budget supports the work of the approximately 6,000 scientists who work in NIH's own laboratories. (http://www.nih.gov/about/budget.htm)

[2] AAI is concerned that a federal policy limits government scientists' ability to attend privately sponsored scientific meetings and conferences. (See http://www.hhs.gov/travel/policies/2012_policy_manual.pdf) AAI believes that "the rules have had an unintended and deleterious effect … [and] made government scientists feel cut off from the rest of the scientific community, wreaked havoc with their ability to fulfill professional commitments, and undermined the morale of some of the government's finest minds." *Testimony (Amended) of Lauren G. Gross, J.D., on behalf of The American Association of Immunologists (AAI), Submitted to the Senate Homeland Security and Governmental Affairs Committee for the Hearing Record of January 14, 2014: "Examining Conference and Travel Spending Across the Federal Government"* (http://aai.org/Public_Affairs/Docs/2014/AAI_Testimony_to_Senate_HSGAC_01142014.pdf)

[3] The Biomedical Research and Development Price Index (BRDPI) "is developed each year for NIH by the Bureau of Economic Analysis of the Department of Commerce. It reflects the increase in prices of the resources needed to conduct biomedical research, including personnel, services, supplies, and equipment.

It indicates how much the NIH budget must change to maintain purchasing power." Johnson, Judith A., "A History of NIH Funding: Fact Sheet," Congressional Research Service, R43341, p. 2 (2014)

[4] Ibid

[5] NIH should robustly fund and primarily rely on individual investigator-initiated research, in which researchers working in institutions across the nation submit applications to, and following independent peer review, receive grants from, NIH. Biomedical innovation and discovery are less likely to be achieved through "top-down" science, in which the government specifies the type of research it wishes to fund.

[6] Couzin-Frankel, Jennifer. "Cancer Immunotherapy." *Science* 342.6165 (2013): 1432-433

[7] Wolchok, J. D. et al. "Nivolumab plus Ipilimumab in Advanced Melanoma." *N Engl J Med* 369.2 (2013): 122-33

[8] Deborah, Persaud et al. "Absence of Detectable HIV-1 Viremia after Treatment Cessation in an Infant." *N Engl J Med* 369 (2013): 1828-835

[9] Conference on Retroviruses and Opportunistic Infections, March 3 - 6, 2014, Boston, MA (http://www.croi2014.org/) (See also http://www.nytimes.com/2014/03/06/health/second-success-raises-hope-for-a-way-to-rid-babies-of-hiv.html)

[10] A clinical trial following 60 babies born infected with HIV and being treated with antiretroviral medication will begin soon. (See http://www.nytimes.com/2014/03/06/health/second-success-raises-hope-for-a-way-to-rid-babies-of-hiv.html) A second study found that adult HIV-infected patients who were treated with ART within four months of infection display significantly improved response to treatment. [See Le, Tuan, et al. "Enhanced CD4+ T-Cell Recovery with Earlier HIV-1 Antiretroviral Therapy." *N Engl J Med* 368 (2013): 218-30]

[11] Sorini, C., and M. Falcone. "Shaping the (auto)immune Response in the Gut: The Role of Intestinal Immune Regulation in the Prevention of Type 1 Diabetes." *Am J Clin Exp Immunol* 2.2 (2013): 156-71

[12] Infectious Diseases Society of America. "Fecal Transplant pill knocks out recurrent C. diff infection," *Science Daily* (2013) (See http://www.cdc.gov/hai/organisms/cdiff/cdiff_infect.html)

[13] Couzin-Frankel, Jennifer. "Cancer Immunotherapy." *Science* 342.6165 (2013): 1432-433

[14] McLellan, J. S. et al. "Structure of RSV Fusion Glycoprotein Trimer Bound to a Pre-fusion Specific Neutralizing Antibody." *Science* 340.6136 (2013): 1113-117

[15] McLellan, J. S. et al. "Structure-Based Design of a Fusion Glycoprotein Vaccine for Respiratory Syncytial Virus." *Science* 342.6158 (2013): 592-98