Testimony of Clifford V. Harding, M.D., 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) 2017 Budget for the National Institutes of Health
April 11, 2016

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) 2017 appropriations for the National Institutes of Health (NIH). ***AAI recommends an appropriation of at least $35 billion for NIH for FY 2017*** to fund new and ongoing research, stabilize and strengthen the biomedical research enterprise, and encourage the world's most talented scientists, trainees, and students to pursue biomedical research careers in the United States.

The Importance of Immunology and the Immune System

"[I]mmunology kind of transcends it all." So said Senator Richard Shelby (R-AL), a senior member of the Senate Appropriations Committee and its subcommittee on Labor, Health and Human Services, Education, and Related Agencies, during the committee's April 2, 2014, hearing on the FY 2015 budget request for NIH.[1] What Senator Shelby correctly noted is the extraordinary importance – and nearly unlimited potential – of the immune system. And the more we learn, the more we realize that what was true in 2014 is even more true today.

As the body's primary defense against viruses, bacteria, parasites and carcinogens, the immune system can protect its host from a wide range of infectious diseases and from many chronic illnesses, including cancer, Alzheimer's disease, and cardiovascular disease. But the immune system can underperform, leaving the body vulnerable to infections such as influenza, Zika virus, HIV/AIDS, tuberculosis, malaria, and the common cold. It can also become overactive, attacking normal organs and tissues, and causing autoimmune diseases including allergy, asthma, inflammatory bowel disease, lupus, multiple sclerosis, rheumatoid arthritis, and type 1 diabetes. Understanding how the immune system works and how it may be harnessed to help prevent, treat, or cure disease: this is the mission of immunologists as we strive to protect people and animals from chronic and acute diseases and from natural or man-made infectious organisms (including plague, smallpox and anthrax) that could be used as bioweapons.

Recent Immunological Advances Provide Great Hope for Tomorrow

1. New potential treatments for hard-to-treat cancers
Cancer immunotherapies mobilize an individual's immune system to destroy cancer cells without harming healthy cells. Less toxic than standard chemotherapy and radiation, immunotherapies have already been approved for some cancers, including lymphoma and melanoma. Until recently, however, immunotherapy had not shown great efficacy against some hard-to-treat cancers, like non-small cell lung cancer. The 2015 approval of Nivolumab

and Pembrolizumab (anti PD-1 therapy)[2] was, therefore, a landmark event for the treatment of lung cancer. Because this therapy specifically blocks the PD-1/PD-L1 pathway that prevents T cells from killing tumor cells, it improves the immune system's ability to combat cancer.[3]

2. Using the immune system to control HIV infection in HIV-positive patients

A recent NIH-funded study demonstrated how the immune systems of HIV-positive "elite controllers," people whose natural immunity controls HIV infection, produce antibodies that have the potential to be developed to treat others infected with HIV.[4] In this Phase I clinical trial, copies of the protective antibodies produced by elite controllers successfully reduced HIV viral levels when transferred to other HIV-positive patients. This method of harnessing "broadly neutralizing antibodies"[5] can potentially be used more widely against other viruses, protecting whole populations from dangerous infections until vaccines are available.

3. Preventing and treating emerging infectious diseases

With increased globalization and worldwide travel, emerging infectious diseases can create a serious health threat locally as well as an international public health crisis, as evidenced by the recent Ebola virus epidemic in Africa, outbreak of dengue fever in Hawaii,[6] and Zika virus outbreaks in Latin America, Central America, the Caribbean, and the U.S. territories.[7] It is essential, therefore, that NIH continually fund basic research on pathogens and the host response to pathogens, as well as potential medical interventions, in order to be able to prevent and respond to both current and future epidemics.

Because NIH has long supported such basic and clinical research, we have made progress on a vaccine against the Ebola virus,[8] which killed more than 11,300 people in West Africa in 2014-2015.[9] Last month, NIH announced that an experimental vaccine against dengue fever had protected all of its recipients, an important advance in the fight against a disease that infects 390 million people worldwide each year.[10] And because the dengue virus is in the same virus family as the Zika virus, scientists are applying what they have learned from dengue to their efforts to develop a vaccine for Zika,[11] which is linked to both microcephaly and Guillain-Barré syndrome.[12] Zika is of increasing international concern due to a recent surge in the number of cases, particularly in Brazil, where more than 3,000 newborns have been affected thus far.[13]

NIH's Essential Role in the Research Enterprise

As the nation's main funding agency for biomedical and behavioral research, NIH supports the work of "more than 300,000 members of the research workforce, including 35,000 principal investigators" located at universities, medical schools, and other research institutions in all 50 states and the District of Columbia.[14] More than 80% of its budget supports the work of these "extramural" scientists through almost 50,000 grants, while about 10% of the budget supports roughly 6,000 "intramural" researchers and clinicians who work at NIH research and clinical facilities in Maryland, Arizona, Massachusetts, Michigan, Montana and North Carolina.[15]
NIH funding strengthens the economies of the communities and states where these researchers live and work; in 2014, it supported more than 400,000 jobs across the United States.[16]

NIH also provides irreplaceable scientific leadership to the national and international biomedical research communities. NIH personnel and policies are essential to the coordination of scientists and scientific projects from academia and government,[17] and to fostering important collaborations with industry, whose own advances in drug and medical device development rely heavily on NIH-funded discoveries.[18]

Recent Funding Boost Eased, But Did Not Eliminate, Erosion of NIH Purchasing Power

A $2 billion boost in NIH funding in FY 2016, generously provided by this subcommittee and the Congress, has helped restore some of the loss in NIH's purchasing power that had resulted from years of inadequate budgets eroded further by biomedical research inflation.[19] Although AAI is extremely grateful for this funding increase, NIH's purchasing power remains more than 19% below what it was in FY 2003.[20] In addition to limiting the advancement of important research and the potential treatments or cures that might have been discovered, these funding constraints continue to have a deleterious impact on many productive researchers: some are being forced to lay off staff or close their labs entirely, while others are moving overseas, where support for biomedical research continues to grow.[21] Perhaps most importantly, inadequate funding is deterring many of our most promising young people from pursuing careers in biomedical research; they witness their mentors' unrelenting and time consuming search for funding, rather than their conduct of research or teaching of the nation's future researchers, doctors, inventors and innovators. Regular and predictable funding increases for NIH would provide the stability that science, scientists, and the scientific enterprise urgently need.

Conclusion

AAI greatly appreciates the subcommittee's strong bipartisan support for NIH and biomedical research, and for the reasons described above, recommends an appropriation of ***at least $35 billion*** for NIH in FY 2017.

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[1] http://www.appropriations.senate.gov/hearings/fy15-nih-budget-request.

[2] http://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm466576.htm; http://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm465650.htm.

[3] Chen, L and Han, X. 2015. Anti–PD-1/PD-L1 therapy of human cancer: past, present, and future. *The Journal of Clinical Investigation* 125: 3384-3391.

[4] Caskey, M. *et al*. 2015. Viraemia suppressed in HIV-1 infected humans by broadly neutralizing antibody 3BNC117. *Nature* 522: 487.

[5] "In first human study, new antibody therapy shows promise in suppressing HIV Infection." *Newswire.* http://newswire.rockefeller.edu/2015/04/08/in-first-human-study-new-antibody-therapy-shows-promise-in-suppressing-hiv-infection/.

[6] Dengue "is endemic in Puerto Rico and in many popular tourist destinations in Latin America, Southeast Asia and the Pacific islands." http://www.cdc.gov/dengue/.

[7] http://www.cdc.gov/zika/geo/index.html.

[8] http://www.niaid.nih.gov/news/newsreleases/Archive/2003/pages/ebolahumantrial.aspx; https://www.niaid.nih.gov/news/newsreleases/2016/Pages/CROI-ZMapp.aspx.

[9] http://www.cdc.gov/vhf/ebola/outbreaks/2014-west-africa/case-counts.html.

[10] http://www.nih.gov/news-events/news-releases/experimental-dengue-vaccine-protects-all-recipients-virus-challenge-study. The experimental vaccine was developed primarily by NIH scientists at the NIAID Laboratory of Infectious Diseases, with assistance from scientists at the FDA Center for Biologics Evaluation and Research.

[11] Ibid.

[12] http://www.cdc.gov/zika/about/gbs-qa.html; http://www.cdc.gov/zika/pregnancy/question-answers.html.

[13] Maron, Dina Fine. Surge in Babies Born with Small Heads. *Scientific American.* http://www.scientificamerican.com/article/what-s-behind-brazil-s-alarming-surge-in-babies-born-with-small-heads/.

[14] http://www.nih.gov/sites/default/files/about-nih/strategic-plan-fy2016-2020-508.pdf; http://www.nih.gov/about-nih/what-we-do/budget.

[15] Ibid; https://www.training.nih.gov/resources/intro_nih/other_locations.

[16] Ehrlich, Everett. NIH's Role in Sustaining the U.S. Economy. *United for Medical Research,* http://www.unitedformedicalresearch.com/wp-content/uploads/2015/10/UMR-NIH-FY2014-Economic-Update-10.01.15.pdf.

[17] AAI strongly opposes policies that limit government scientists' ability to attend privately sponsored scientific meetings and conferences and believes that "the rules have … 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." *Written 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).

[18] According to Dr. Marc Tessier-Lavigne, former chief scientific officer at Genentech and current president of The Rockefeller University, "if we invest adequately in basic biomedical research, we can create the knowledge that will in turn trigger private-sector investment to develop therapies to conquer such diseases….For every drug approved by the FDA at the top of the pyramid, the foundation consists of dozens of insights into diseases generated over a period of decades, largely through federal funding of basic, knowledge-driven research." *Written Testimony of Dr. Marc Tessier-Lavigne, Submitted to the House Committee on Science, Space, and Technology, Subcommittee on Research and Technology, for the Hearing Record of July 17, 2014: "Policies to Spur Innovative Medical Breakthroughs from Laboratories to Patients."* https://science.house.gov/sites/ republicans.science.house.gov/files/documents/HHRG-113-SY14-WState-MTessierLavigne-20140717.pdf

[19] Federation of American Societies for Experimental Biology. U.S. Biological and Medical Research Fell for Over a Decade. http://www.faseb.org/Portals/2/PDFs/opa/2016/Factsheet_Restore_NIH_Funding.pdf

[20] Federation of American Societies for Experimental Biology. NIH Research Funding Trends: FY 1995-2015. http://www.faseb.org/Science-Policy-and-Advocacy/Federal-Funding-Data/NIH-Research-Funding-Trends.aspx

[21] Moses, H., *et al.* 2015. The Anatomy of Medical Research: US and International Comparisons. *JAMA* 313: 174-189. According to Moses *et al.*, while U.S. funding for biomedical and health services research increased at a rate of 6 percent per year from 1994-2004, it decreased to just 0.8 percent annually from 2004-2012.