Testimony of Beth A. Garvy, Ph.D., on behalf of The American Association of Immunologists (AAI), Submitted to the Senate Appropriations Subcommittee on Labor, Health and Human Services, Education, and Related Agencies, Regarding the Fiscal Year 2018 Budget for the National Institutes of Health
May 25, 2017

The American Association of Immunologists (AAI), the nation's largest professional society of research scientists and physicians who study the immune system, respectfully submits this testimony regarding fiscal year (FY) 2018 appropriations for the National Institutes of Health (NIH). ***AAI recommends an appropriation of at least $35 billion for NIH for FY 2018 (in addition to any funding provided to support the 21st Century Cures Act)*** to fund promising new and important ongoing research; to encourage the world's most talented scientists, trainees, and students to pursue biomedical research careers in the United States; and to enable NIH to continue to serve as an independent voice for, and strong leader of, the nation's biomedical research enterprise.

Why the Immune System – and Immunology Research – Matters

As the body's primary defense against viruses, bacteria, parasites, toxins, and carcinogens, the immune system can protect its host from a wide range of infectious diseases, including influenza, and from chronic illnesses, such as cancer. But the immune system can underperform, leaving the body vulnerable to disease, such as those caused by human immunodeficiency virus (HIV) and Zika virus; and it can go awry, attacking normal organs and tissues and causing autoimmune diseases including allergy, asthma, inflammatory bowel disease, lupus, multiple sclerosis, rheumatoid arthritis, and type 1 diabetes. Immunologists study how the immune system works; how it may be harnessed to help prevent, treat, or cure disease; and how it can be used to protect people and animals from infectious organisms, including antibiotic resistant bacteria, and others, such as anthrax, smallpox, and plague, that could be used as bioweapons.

Recent Discoveries Harness the Power of the Immune System to Prevent and Fight Disease

1. Using the immune system to treat cancer - Immunotherapy, which uses a patient's own immune system to fight disease, is transforming the treatment of cancer. NIH-funded basic researchers identified inhibitory receptors on immune cells that can be blocked, facilitating the immune system's ability to destroy tumor cells; clinical researchers then discovered that immunotherapy could fight cancer with much less toxicity than standard chemotherapy or radiation.[1] This research has contributed to the development of checkpoint inhibitor drugs, such as pembrolizumab (Keytruda®) and nivolumab (Opdivo®), which have recently received Food and Drug Administration (FDA) approval for the treatment of several cancer types, including melanoma, lymphoma, kidney, and head and neck cancer.[2] In October 2016, Keytruda® was approved by the FDA for the treatment of lung cancer, marking the first time that immunotherapy could be used as the initial treatment option for these patients (before standard options such as chemotherapy).[3]
In another promising approach to immunotherapy, NIH-supported clinical trials are examining the use of genetically engineered immune cells to treat many cancers, including kidney, bone, brain, and skin, as well as leukemia and lymphoma.[4] When combined with conventional approaches, these immune cells can enhance treatment results and permit the use of lower doses of conventional therapies, reducing harmful side effects and providing a treatment option for cancers that do not respond solely to conventional drugs.[5]

2. New way to prevent and treat allergies - Peanut allergies, which occur in 1-2% of people in the United States, continue to increase.[6] Death due to peanut allergy remains the number one cause of food-related anaphylaxis, and no treatment or cure exists. An NIH-funded study showed that the early intro-

duction of peanut-containing foods significantly decreased the development of peanut allergy among children at high risk.[7] For individuals who already have peanut allergies, an ongoing NIH-sponsored clinical trial testing a wearable patch that delivers a small amount of peanut protein through the skin is showing great promise. The treatment, called epicutaneous immunotherapy or EPIT, trains the immune system to tolerate peanut-containing foods and has been shown to be safe and well-tolerated.[8] These studies have revealed new insight into the prevention and treatment of peanut - and potentially other - allergies.

3. Development of vaccines and treatments for emerging infectious diseases - NIH-funded research plays a key role in the development of vaccines and treatments to combat epidemics and other major public health threats. Researchers are working urgently to develop a vaccine to protect against the Zika virus, which can hamper fetal development and cause birth defects (including microcephaly).[9] To contain this virus, which continues to spread (with over 41,000 cases reported within the U.S. and its territories as of May 2017), NIH-funded researchers have developed a promising DNA-based vaccine that is now being tested in a clinical trial.[10] Progress has also been made in developing a therapeutic strategy to protect against Ebola virus, which recently killed more than 11,300 individuals in West Africa.[11] In pre-clinical studies, NIH-funded scientists identified an antibody cocktail that was able to neutralize Ebola and protect against disease, even when administered after viral exposure.[12] Advances have also been made in efforts to protect against the Dengue virus: a vaccine candidate developed by NIH researchers has shown protection against infection and is now being tested in a multi-center Phase 3 clinical trial.[13]

NIH's Essential Role in the Biomedical Research Enterprise

As the nation's main funding agency for biomedical research, NIH supports the work of "more than 300,000 members of the research workforce" located at universities, medical schools, and other research institutions in all 50 states, the District of Columbia, and several U.S. territories.[14] More than 80% of its budget supports the work of these scientists through about 50,000 grants; about 10% of its budget supports roughly 6,000 researchers and clinicians who work at NIH facilities in Maryland, Arizona, Massachusetts, Michigan, Montana and North Carolina.[15] NIH funding strengthens the economies of the states where these researchers live and work; in 2015, it supported nearly 380,000 jobs across the United States.[16]

NIH also provides invaluable scientific leadership. Through congressional testimony and frank dialogue, NIH advises our nation's elected and appointed leaders on scientific advancements, needs, and threats. This open exchange is essential to ensuring that urgent and long-term scientific needs are addressed, and that taxpayer funds directed to NIH are well-spent. In addition, as the leader of our nation's biomedical research enterprise and the steward of more than $34 billion in taxpayer dollars, NIH governs the conduct of scientific research and fosters collaborations between government and academia; between U.S.-based scientists and their international colleagues, who are invaluable to our nation's research enterprise; and between government and industry, which depends on the innovative and sometimes high-risk basic research supported by NIH to fuel their own advances in drug and medical device development.[17] These NIH leadership responsibilities, which include consultation with, and notice to, a broad and diverse stakeholder community, require skilled personnel. Therefore, AAI is deeply concerned that NIH continues to be adversely affected by an ongoing government hiring freeze. Although NIH is apparently able to hire for "essential patient care staff vacancies," the *Washington Post* reported that there are numerous staffing prohibitions and that "some support positions," including those that impact patient care, "remain vacant."[18] This same report indicated that some personnel "spoke on the condition of anonymity for fear of funding retaliation." Both the hiring freeze and the inability of NIH personnel to speak freely about its adverse impact on patient care or on the advancement of research are deeply troubling.

Recent Funding Increases Have Eased, Not Eliminated, Erosion of NIH Purchasing Power

Recent NIH funding increases, including $2 billion in both FY 2016 and FY 2017, have helped restore some of the purchasing power that NIH lost from years of inadequate budgets that were eroded further by biomedical research inflation.[19] Although AAI is extremely grateful to Congress for these funding increases (and for the Cures Act's FY 2018 authorization of $496 million to supplement regular NIH appropriations), AAI remains concerned that NIH's purchasing power is still estimated to be about 16% below what it was in FY 2003. In addition to limiting ongoing and promising new research and delaying discoveries that might lead to new treatments or cures, these funding constraints have a deleterious impact in other ways, forcing some productive researchers to lay off staff, close their labs, or move overseas, where support for biomedical research continues to grow.[20] Perhaps most importantly, inadequate or uncertain funding is deterring many promising young people from pursuing careers in biomedical research, threatening the viability of the next generation of researchers, doctors, professors, and inventors. Regular, predictable, and robust funding increases for NIH, through the timely passage of annual appropriations bills, would strengthen and stabilize NIH and the biomedical research enterprise.

Trump Budget would Devastate NIH and the Biomedical Research Enterprise

AAI is extremely alarmed that President Trump's FY 2018 budget proposal for NIH includes, among many other concerns, the following:1) an unprecedented and disastrous budget cut of about 21% that would cause irreparable damage to NIH and to ongoing research across the nation; 2) the elimination of the Fogarty International Center, which would seriously impede NIH's ability to promote global health and prevent pandemics and other international health crises;[21] and 3) the implementation of an immediate 10% cap on indirect costs to research institutions, which could drive many independent research institutions out of business and cause fiscal havoc at many others.[22] We urge Congress to prevent all budget cuts to NIH and to consider carefully, following stakeholder input, any proposed changes to NIH to ensure that they would benefit – and not harm – the world's most respected biomedical research agency and its *de facto* leader.

Conclusion

AAI greatly appreciates the subcommittee's continued strong bipartisan support for NIH and biomedical research through annual appropriations and additional appropriations to support the 21st Century Cures Act initiatives. We urge Congress to continue to engage in frank dialogue with both NIH leaders and stakeholders to ensure that the best science continues to be funded. For FY 2018, AAI recommends a regular appropriation of *at least $35 billion* for NIH and additional funding for the 21st Century Cures initiatives.

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[1] Chen, L. and Han, X. 2015. Anti-PD-1/PD-L1 therapy of human cancer. *J. Clin. Invest.* 125: 3384-3391.

[2] See https://www.cancer.gov/about-cancer/treatment/drugs for list of drug approvals

[3] https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm526430.htm

[4] https://clinicaltrials.gov/ (NCT01218867, NCT02107963, NCT00924326, NCT02153580); Johnson, L.A., *et al*. 2017. Driving gene-engineered T cell immunotherapy of cancer. *Cell Research* 27: 38-58.

[5] Deniger, D.C., *et al. 2017.* A Pilot Trial of the Combination of Vemurafenib with Adoptive Cell Therapy in Patients with Metastatic Melanoma. *Clin. Cancer Res.* 23: 351-62.; Zhang, W., *et al*. 2016. Treatment of CD20-directed Chimeric Antigen Receptor-modified T cells in patients with relapsed or refractory B-cell non-Hodgkin lymphoma. *Sig. Transd. Tar. Ther.* 1: 16002.

[6] Togias, A., *et al.* 2017. Addendum guidelines for the prevention of peanut allergy in the United States: Report of the National Institute of Allergy and Infectious Diseases-sponsored expert panel. *J. Allergy Clin. Immunol.* 139: 29-44.

[7] Du Toit,G. *et al.*2015.Randomized Trial of Peanut Consumption in Infants at Risk for Peanut Allergy.*N.Engl.J.Med.*372:803-13.

[8] Jones, S.M., *et al*. 2016. Epicutaneous immunotherapy for the treatment of peanut allergy in children and young adults. *J. Allergy Clin. Immunol.* DOI: 10.1016/j.jaci.2016.08.017.; https://www.niaid.nih.gov/news-events/skin-patch-treat-peanut-allergy-shows-benefit-children

[9] Singh, M.V., *et al*. 2017. Preventive and therapeutic challenges in combating Zika virus infection:are we getting any closer? *J. Neurovirol.* DOI:10.1007/s13365-017-0513-4.

[10] https://www.cdc.gov/zika/index.html; Dowd, K.A., *et al.* 2016. Rapid development of a DNA vaccine for Zika virus. *Science* 354: 237-240.; https://www.nih.gov/news-events/news-releases/phase-2-zika-vaccine-trial-begins-us-central-south-america

[11] http://www.who.int/csr/disease/ebola/en/

[12] Corti, D., *et al*. 2016. Protective monotherapy against lethal Ebola virus infection by a potently neutralizing antibody. *Science* 351: 1339-1342.

[13] Kirkpatrick, B.D., *et al.* 2016. The live attenuated dengue vaccine TV003 elicits complete protection against dengue in a human challenge model. *Sci. Transl. Med.* 8: 330-336.; https://www.niaid.nih.gov/news-events/dengue-vaccine-enters-phase-3-trial-brazil

[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; https://report.nih.gov/award/index.cfm?ot=&fy=2016&state=&ic=&fm=&orgid=&distr=&rfa=&om=n&pid=#tab1

[15] See footnote 14; https://www.training.nih.gov/resources/intro_nih/other_locations

[16] Ehrlich, Everett. NIH's Role in Sustaining the U.S. Economy – 2017 update. United for Medical Research, http://www.unitedformedicalresearch.com/advocacy_reports/nihs-role-in-sustaining-the-u-s-economy-2017-update/

[17] http://www.help.senate.gov/imo/media/Innovation_for_Healthier_Americans.pdf; http://conservativereform.com/wp-content/uploads/2016/09/CRN_MedicalResearch.pdf

[18] Sun, Lena H. *Washington Post*. https://www.washingtonpost.com/news/to-your-health/wp/2017/05/19/nearly-700-vacancies-at-cdc-because-of-trump-administration-hiring-freeze/?utm_term=.c3e741d8eee1 According to Sun, the Centers for Disease Control and Prevention (CDC) has nearly 700 vacancies as result of the freeze. Although AAI is not submitting testimony on the CDC budget, we note that NIH and CDC work very closely together on many urgent domestic and international public health matters, and that a crippled, understaffed, or underfunded CDC, in addition to the damage this would cause to CDC and public health, will almost certainly cripple related efforts at NIH.

[19] Federation of American Societies for Experimental Biology. NIH Research Funding Trends: FY 1995-2016 http://www.faseb.org/Portals/2/PDFs/opa/2017/NIH%20Grants%20Slideshow.pptx

[20] Moses, H., *et al.* 2015. The Anatomy of Medical Research: US and International Comparisons. *JAMA* 313: 174-189.

[21] Despite its relatively small budget, Fogarty's mission (to "[support] and [facilitate] global health research . . . and [train] the next generation of scientists to address global health needs") is essential in a world where disease knows no borders. (See https://www.fic.nih.gov/About/Pages/mission-vision.aspx) With more than 80 percent of Fogarty's extramural grant budget providing salary and other support to U.S. scientists (and all grants engaging U.S. investigators), providing continued funding for Fogarty is a wise investment in advancing global health security and emergency preparedness. (See https://www.fic.nih.gov/About/Pages/role-global-health.aspx)

[22] AAI would support a review of the formula used to determine the level of indirect costs appropriate for each institution, but believes that a uniform cap of 10%, or any cap implemented immediately, could be disastrous for many research institutions.