Testimony of Beth A. Garvy, 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 2019 Budget for the National Institutes of Health
April 24, 2018

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) 2019 appropriations for the National Institutes of Health (NIH). ***AAI recommends an appropriation for NIH of at least $39.3 billion for FY 2019*** to enable NIH to fund critically important new and ongoing biomedical research, support the next generation of biomedical researchers, and ensure continued robust investment in this national priority area. As a result of generous support from this subcommittee and Congress in recent years, NIH has continued to make great strides in advancing urgently needed medical research, supporting talented scientists and trainees who want to pursue research careers in the United States, and providing hope to all who are afflicted by illness or disability.

Why the Immune System Matters – and Why Immunologists are Essential

The immune system is the body's primary defense against viruses, bacteria, parasites, toxins, and carcinogens. When it performs optimally, it can protect its host from a wide range of infectious diseases, including influenza virus, and from chronic illnesses, such as cancer. But the immune system can underperform, leaving the body vulnerable to disease, such as the common cold, measles, pneumonia, and AIDS; and it can "overperform," attacking normal organs and tissues and causing autoimmune diseases/ conditions such as allergy, asthma, inflammatory bowel disease, lupus, multiple sclerosis, rheumatoid arthritis, and type 1 diabetes. Immunologists study how the immune system works, including ways it can 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 other bacteria (like anthrax and plague) and viruses (like smallpox and Ebola) that could also be used as bioweapons.

Recent Immunological Discoveries and their Impact on Preventing and Fighting Disease

Cancer immunotherapy – Cancer immunotherapy, which harnesses the immune system to fight tumors, is revolutionizing cancer treatment. Because of NIH-funded research, several new immuno-therapeutic agents have recently been developed that offer great hope for cancer patients.[1] In 2017, the Food and Drug Administration (FDA) approved the nation's first gene therapy, CAR-T (chimeric antigen receptor T cell) therapy, tisagenlecleucel (Kymriah™), for treatment of acute lymphoblastic leukemia.[2] In a key clinical trial, this highly effective therapy showed an overall remission rate of 83%. Subsequently, axicabtagene ciloleucel (Yescarta®) received FDA approval for the treatment of B cell lymphoma following a clinical trial that showed a complete remission rate of 51%.[3] These therapies using engineered immune cells offer exciting new approaches to tailoring treatments to individuals (known as "precision medicine"). Another type of immunotherapy (checkpoint inhibitors), previously FDA-approved for the treatment of some solid tumors and blood cancers, was also recently approved for treatment of cancers with a specific genetic feature (biomarker). This recent approval of pembrolizumab (Keytruda®) is significant not only because of the responses that are being achieved (~40% complete or partial response), but also because this was the first FDA approval given to a therapy based on a biomarker rather than on the tumor's original location in the body.[4] Subsequently, nivolumab (Opdivo®) received approval for treatment of colorectal cancer with a specific biomarker.[5] These advances directly result from NIH-funded research demonstrating the sensitivity of tumors harboring these genetic features to immunotherapy.[6]

Hepatitis B vaccine - Hepatitis B is a viral disease of the liver that can become chronic and lead to cirrhosis, liver cancer, and death. An estimated 850,000 – 2.2 million people in the U.S. have chronic hepatitis B, resulting in approximately 1,800 deaths every year.[7] There is no cure, and infections are on the rise. Over the past decade, however, NIH has provided more than $17 million toward the development of vaccine adjuvants (which enhance vaccine efficacy).[8] In 2017, the FDA approved HEPLISAV-B, the first new vaccine for the hepatitis B virus (HBV) in 25 years.[9] Because HEPLISAV-B requires only two doses

over one month, in contrast to previously available vaccines, which require three doses over six months, this new vaccine may be a valuable tool in the effort to improve vaccination rates and therefore prevent infection with, and death from, HBV.

Artificial pancreas for type 1 diabetes – Type 1 diabetes (T1D) is an autoimmune disease that affects over 1.25 million Americans, including 200,000 children.[10] People with T1D are unable to produce insulin because their immune system has destroyed their insulin-producing (i.e., beta) cells, resulting in an uncontrolled rise in blood sugar levels. Complications from T1D include blindness, nerve damage, kidney failure, heart disease, and death. Because changes in diet or lifestyle alone will not treat the disease, diabetic patients must closely monitor their blood sugar levels to ensure that they are taking the needed dose of insulin.[11] Control of blood sugar levels is essential to preventing or delaying T1D complications. NIH-funded researchers from fields including immunology, endocrinology, bio-engineering, and computational biology have developed "closed-loop" artificial pancreas systems, which continuously monitor blood sugar and automatically administer the appropriate amount of insulin when needed; these systems have recently entered clinical trials, and if successful and approved by the FDA, will not only revolutionize T1D treatment, but also dramatically improve the quality of life of these patients.[12]

NIH's Essential Role in the Nation's – and the World's - Biomedical Research Enterprise

As the nation's main funding agency for biomedical research, NIH distributes more than 80% of its budget through approximately 50,000 grants annually, supporting the work of more than 300,000 researchers at universities, medical schools, and other research institutions in all 50 states, the District of Columbia, and several U.S. territories.[13] NIH also utilizes about 10% of its budget to support roughly 6,000 additional researchers and clinicians who work at NIH facilities in Maryland, Arizona, Massachusetts, Michigan, Montana, and North Carolina.[14] NIH funding strengthens the economies of the states where its researchers live and work; in 2017, it supported more than 402,000 jobs across the U.S.[15] NIH-funded research also propels the nation's extraordinarily successful pharmaceutical industry: according to NIH Director Francis

Collins, M.D., Ph.D., a recent study shows that "NIH contributed to published research that was associated with every single one of the 210 new drugs approved by the [FDA] from 2010 through 2016 [and that] [m]ore than 90 percent of that contributory research was basic – that is, related to the discovery of fundamental biological mechanisms, rather than actual development of the drugs themselves."[16]

NIH also provides invaluable scientific leadership both in the U.S. and abroad. The steward of more than $37 billion in taxpayer dollars, NIH advises our nation's elected and appointed leaders on scientific advancements, needs, and threats, and works to ensure that its funds are properly and prudently spent. NIH not only governs the conduct of scientific research at academic institutions in the U.S., it also fosters collaborations between U.S.-based scientists and their invaluable international colleagues; and between government and the pharmaceutical, biotechnology and medical device industries, all of which benefit from NIH-supported research to fuel their own advances.[17] These NIH leadership responsibilities, which include consultation with a broad and diverse stakeholder community, require a sufficient number of skilled personnel. Therefore, AAI urges that NIH be permitted to hire the scientific and administrative personnel needed to ensure the success of what is unquestionably an enormous and complicated enterprise.

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

Strong, decisive action by this subcommittee and the full Congress has resulted in substantial funding increases for NIH over the last several years. With generous, needed increases of $3 billion in FY 2018 and $2 billion each in FY 2016 and FY 2017 (including supplemental funding to support initiatives authorized by the 21st Century Cures Act), Congress has helped restore some of the purchasing power that NIH lost from years of insufficient budgets that were further eroded by biomedical research inflation; this gap, which once reached ~25%, has been reduced to ~11%. Continued efforts to close this gap, and to grow the research enterprise, are needed if we are to ensure a robust research environment that will both facilitate research on discoveries that might lead to new treatments or cures, and encourage promising young people to become the next generation of researchers, doctors, professors, and inventors. Predictable, ample funding increases

for NIH, particularly through the timely passage of annual appropriations bills, would strengthen the nation's biomedical research enterprise and foster needed confidence within the scientific community.

Conclusion

AAI greatly appreciates this subcommittee's longstanding leadership and strong bipartisan support for NIH and biomedical research through regular appropriations and supplementary funds to support 21st Century Cures Act initiatives. AAI urges the subcommittee to continue to strengthen NIH's ability to support research that is critical to human health by appropriating at least $39.3 billion for NIH for FY 2019.

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[1] Maude, S. L. *et al*. 2014. Chimeric antigen receptor T cells for sustained remissions in leukemia. *N. Engl. J. Med.* 371: 1507-1517; Zhong, X. S. *et al*. 2010. Chimeric antigen receptors combining 4-1BB and CD28 signaling domains augment PI3kinase/AKT/Bcl-XL activation and CD8+ T cell-mediated tumor eradication. *Mol. Ther.* 18: 413-420.; Rosenberg, S. A. *et al*. 1988. Use of tumor-infiltrating lymphocytes and interleukin-2 in the immunotherapy of patients with metastatic melanoma. *N. Engl. J. Med.* 319: 1676-1680.

[2] https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm574058.htm

[3] https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm581216.htm

[4] https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm560040.htm [approval for two biomarkers: microsatellite instability high (MSI-H) and mismatch repair deficient (dMMR)]

[5] https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm560040.htm (approval for MSI-H and dMMR)

[6] Le, D. T. *et al*. 2017. Mismatch repair deficiency predicts response of solid tumors to PD-1 blockade. *Science* 357: 409-413.

[7] https://www.cdc.gov/hepatitis/hbv/bfaq.htm

[8] http://investors.dynavax.com/releasedetail.cfm?releaseid=337232

[9] https://www.hhs.gov/hepatitis/blog/2017/11/29/fda-approves-new-hepatitis-b-vaccine

[10] http://www.jdrf.org/about/what-is-t1d/

[11] https://www.cdc.gov/diabetes/basics/type1.html

[12] https://www.nih.gov/news-events/news-releases/four-pivotal-nih-funded-artificial-pancreas-research-efforts-begin

[13] https://www.nih.gov/about-nih/what-we-do/budget; https://report.nih.gov/award/index.cfm

[14] https://www.training.nih.gov/resources/intro_nih/other_locations

[15] http://www.unitedformedicalresearch.com/advocacy_reports/nihs-role-in-sustaining-the-u-s-economy-2018-update/

[16] https://directorsblog.nih.gov/2018/02/27/basic-research-building-a-firm-foundation-for-biomedicine/

[17] http://conservativereform.com/wp-content/uploads/2016/09/CRN_MedicalResearch.pdf