Testimony of Gretchen E. Diehl, Ph.D., Chair of the Committee on Public Affairs of The American Association of Immunologists (AAI), submitted on behalf of AAI to the Senate Appropriations Subcommittee on Labor, Health and Human Services, Education, and Related Agencies, regarding the FY 2025 budget for the National Institutes of Health (NIH)
May 20, 2024

The American Association of Immunologists (AAI), the nation's largest organizations of immunologists and scientists in related disciplines, with a mission to improve global health and well-being by advancing immunology and elevating public understanding about the immune system, respectfully submits this testimony regarding fiscal year (FY) 2025 appropriations for the National Institutes of Health (NIH). AAI recommends an appropriation of at least $51.3 billion for the NIH base budget for FY 2025. In addition, AAI recommends an appropriation of at least $1.7 billion for the Advanced Research Projects Agency for Health (ARPA-H), but emphasizes that this funding must supplement, not supplant, the NIH base budget.

Robust investment in NIH will enable the agency to make substantial investments in research priorities like cancer, Alzheimer's disease, and the vast array of autoimmune diseases, and to commit additional resources to funding the next generation of researchers while continuing to support meritorious researchers at all career stages. Increased funding for ARPA-H will help support its mission to accelerate better health outcomes by supporting high-risk, high-impact research proposals that would not ordinarily be funded by NIH or the private sector.

Exciting Immunological Advances Fueled by NIH Funding

Breakthroughs in the Treatment of Cancer

Pioneered by National Cancer Institute scientists, tumor infiltrating lymphocyte (TIL) therapy has recently received U.S. Food and Drug Administration (FDA) approval for use in patients with advanced melanoma.[1] This is the first cellular therapy to be approved to treat solid tumors, which rarely respond to traditional immunotherapies, providing revitalized hope for harnessing the immune system to combat solid tumors. Another type of solid tumor cancer, pancreatic cancer, is one of the most difficult to treat. It is diagnosed in more than 60,000 Americans every year and carries a five-year survival rate of just 12.5%.[2] Currently, there are limited treatment options for patients with pancreatic cancer; however, researchers funded through the NIH Cancer Moonshot have developed mRNA vaccines that target a patient's unique tumor and stimulate the immune system, leading to decreased recurrence and increased patient survival in a Phase I clinical trial.[3] While this demonstrates that cancer vaccines can be potent tools to elicit immune responses against tumors, they still face a major limitation: cancer-causing genetic mutations vary dramatically across tumor types and among patients, and identifying the best vaccine targets has remained elusive. However, encouraging results have come from research collaborations between NIH funded investigators and tech giants like Amazon that leverage artificial

intelligence and machine learning to better design personalized cancer vaccine therapies.[4]

Treatments for Autoimmune Diseases and Allergies

Chimeric antigen receptor T cell (CAR-T) therapy has revolutionized the treatment of blood cancers and is now being investigated to treat autoimmunity. Recent small-scale clinical trials have shown that patients with three different kinds of autoimmune diseases (systemic lupus erythematosus, idiopathic inflammatory myositis, and systemic sclerosis) who were treated with CAR-T therapy had either long-term remission or major reduction in disease,[5] demonstrating the potential power of this treatment for those suffering from autoimmune diseases.

In the United States, one in 10 adults and one in 13 children have food allergies. More than 50% of adults and 40% of children with food allergies have experienced severe reactions, including anaphylaxis.[6] Recently, in a collaborative effort between the National Institute of Allergy and Infectious Diseases (NIAID) and industry partners, a phase 3 clinical trial called OUtMATCH tested the efficacy of omalizumab (a monoclonal antibody) as an oral immunotherapy treatment for food allergy in children. After treatment with omalizumab, children experienced significant improvement in tolerating foods that normally cause allergic reaction, leading to FDA approval for use in adults and children over one year old.[7] While vigilance in avoiding food allergens remains critical, this treatment may provide protection against severe outcomes and emergencies due to accidental exposure.

Advances in Vaccines and Treatments for Infectious Diseases

Respiratory syncytial virus (RSV) is a highly contagious respiratory illness that normally causes mild, cold-like symptoms, but can pose great risk to infants, young children, and the elderly. Due to decades of research and clinical trials funded by the NIH, there are now multiple FDA-approved interventions to prevent severe disease: vaccines for pregnant people (to pass protective antibodies to their infants) and the elderly, and monoclonal antibodies for infants.[8] Additional advancements have been made for other infectious diseases, including an NIAID-sponsored phase I clinical trial for an HIV vaccine,[9] an NIH-sponsored clinical trial for a vaccine against Epstein-Barr virus (which can cause autoimmune disease and cancer with persistent infection) developed by NIAID scientists, and widespread administration of the first WHO-recommended malaria vaccine, which has shown a 13% reduction in child mortality in Africa.[10]

Antimicrobial resistance represents a significant global threat to human health; development of new antibiotics and alternative therapies is crucial to controlling increasingly hard-to-treat bacterial infections. Gonorrhea, the second most common sexually transmitted infection that affects more than 80 million adults annually, has become fully resistant to all but one treatment. However, Zoliflodacin, a new antibiotic belonging to an entirely new class of antibiotics, is in phase III clinical trials and shows great promise. Another new antibiotic called Zosurabalpin, designed to treat the WHO "priority 1" pathogen carbapenem-resistant *Acinetobacter baumannii* (CRAB), is currently in phase I clinical trials after showing efficacy in preclinical models.

As of March 2024, 17 million people in the U.S. report that they are suffering from long COVID,

a chronic and often debilitating condition that can occur after infection with SARS-CoV-2.[11] People with long COVID experience a wide range of symptoms, including extreme fatigue, brain fog, and shortness of breath. While no definitive cause has been discovered, recent studies suggest several promising hypotheses for why some people develop long COVID, including viral persistence, immune dysregulation, impacts of the infection on the microbiota, latent viral reactivation, and autoimmunity.[12] The NIH RECOVER Initiative, which aims to "understand, prevent, and treat long COVID," is supporting clinical trials to test the efficacy of three treatments for long COVID in patients suffering from autonomic nervous system dysfunction, including an antibody that mitigates inflammation.[13]

The Economic Impact of NIH Research

NIH is the largest public funder of biomedical and behavioral research in the world, creating economic benefits all across the country. Every state and nearly every congressional district in the nation receives NIH funding, which flows to more than 300,000 researchers at roughly 2,500 institutions. In FY 2023, NIH funding supported more than 412,000 jobs and led to nearly $93 billion in economic activity.[14]

About half of the NIH budget is allocated to support basic research, which "helps us understand the principles, mechanisms, and processes that underlie living organisms. Through basic research, scientists try to understand fundamental questions about how life works."[15] Private sector entities, like pharmaceutical companies, are far less likely to fund this type of incremental research because it does not immediately result in marketable products (like drugs and devices). And yet, basic research is a prerequisite to developing these products, which helps explain why a 2023 study published in *JAMA Health Forum* found that NIH funding contributed to 354 of the 356 drugs (99.4%) approved by the FDA from 2010 to 2019.[16]

Investing in the Next Generation of Researchers

NIH recently announced that it is increasing pay for predoctoral scholars to $28,224 (4%) and for postdoctoral scholars to a first-year level of $61,008 (8%), and that it hopes to make additional increases over the next five years.[17] This action was taken in response to a recommendation made by an NIH advisory committee which found that insufficient compensation is the major reason why graduate students are not pursuing scientific careers in academia.

AAI supports increasing compensation for graduate students and postdoctoral scholars and believes that this change is long overdue. It is difficult, however, for NIH to make this vital investment in the research workforce, or in urgently needed basic and translational research, in this fiscal environment. The NIH budget was cut by $378 million in FY 2024 and funding for most NIH Institutes and Centers was held flat. While AAI is deeply grateful that Congress provided substantial funding increases for NIH for eight consecutive years leading up to FY 2024, we urge Congress to provide the sustained, robust funding increases that are required to continue to invest in priorities like funding the next generation of biomedical researchers.

The Exciting Promise of ARPA-H

Modeled after the Defense Advanced Research Projects Agency (DARPA), ARPA-H was created in 2022 to address health-related challenges by supporting high-risk projects that can yield major rewards on a relatively short timeline. ARPA-H has funded myriad bold and transformative projects since issuing its first award in August 2023, including efforts to develop more effective cancer immunotherapies, create a platform for the discovery and development of new antibiotics, and utilize 3D printing technology to print a human heart. Increased funding is required to continue to support as well as scale up this exciting work, including hiring new Program Managers to lead and develop these projects.

Conclusion

AAI greatly appreciates this subcommittee's past support for NIH and urges it to provide NIH with a base budget of at least $51.3 billion for FY 2025. Such a robust increase will enable NIH to invest in a strong portfolio of biomedical research, including immunological research, to address the great health challenges of today and those on the horizon. And it will help NIH make vital investments in the biomedical research workforce, in particular helping to increase compensation for the next generation of researchers and our country's future scientific leaders. AAI also recommends providing at least $1.7 billion for ARPA-H to enable the agency to boldly address urgent challenges in health.

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