Testimony of Peter E. Jensen, M.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 Fiscal Year 2023 Budget for the National Institutes of Health May 2, 2022

The American Association of Immunologists (AAI), the nation's largest professional association of research scientists and physicians who are dedicated to understanding the immune system through basic, translational, and clinical research, respectfully submits this testimony regarding fiscal year (FY) 2023 appropriations for the National Institutes of Health (NIH). *AAI recommends an appropriation of at least $49 billion for NIH's base budget for FY 2023. In addition, AAI recommends providing substantial funding for the Advanced Research Projects Agency for Health (ARPA-H), though it is crucial that this funding supplements, and does not supplant, NIH's base budget.* Robust investment in NIH will support needed research to prevent and treat dangerous infectious and debilitating chronic diseases, fund meritorious research proposals and scientists at all career stages, and ensure the continuity of our nation's robust, preeminent biomedical research enterprise. Because the COVID-19 pandemic continues, AAI also strongly supports an infusion of supplemental funds to address ongoing COVID-19 needs, help scientists whose work was adversely impacted by pandemic-related interruptions, and prepare for future pandemics.

How Investment in Immunological Research Transformed the COVID-19 Response

Immunological research, including understanding how vaccine-induced immunity and memory are formed, has been vital to the development and use of safe and effective vaccines to protect against coronavirus disease 2019 (COVID-19). While the current vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes COVID-19, continue to provide strong protection against severe disease, hospitalization, and death, the emergence of variants like delta have resulted in surges of infections, leading to significant morbidity and mortality and placing great strain on our health care system. Although the latest variants (omicron and its subvariants) spread much more easily, they have generally caused less serious disease. Nevertheless, we must be vigilant and prepared for new variants and continue to invest significantly in research aimed at understanding the immune response to the virus and whether – and when – these new variants are able to evade vaccine-induced immunity.

As a result of three substantial coronavirus outbreaks across the globe [SARS, Middle East respiratory syndrome (MERS), and COVID-19] in the last two decades, scientists are working to discover new approaches for vaccinating against coronaviruses. One such approach currently being explored by NIH is the development of universal coronavirus ("pan-coronavirus") vaccines that could protect against these and other types of coronaviruses and viral variants.[1] Another approach that shows great promise is an intranasal vaccine, currently being tested against COVID-19. Delivering the vaccine intranasally could generate robust mucosal immunity at the site of infection, potentially resulting in long-term protection from infection. There are over a dozen intranasal vaccine candidates in various stages of clinical trials; preliminary data from one recent preclinical study showed the potential utility of using an intranasal vaccine as a booster dose to our current COVID-19 vaccines to induce long lasting, protective immune responses.[2]

Advances have also been made in the development of effective treatments for active COVID-19. Various

therapeutics are now available to those who test positive for COVID-19, often preventing the development of serious disease. In other areas, treatment is lacking. There are few therapeutics available for those who experience post-acute sequelae of SARS-CoV-2 (PASC, or "long COVID"), a chronic condition that can affect almost every part of the body and incapacitate individuals who have recovered from initial infection. While research is ongoing, particularly through the NIH Researching COVID to Enhance Recovery (RECOVER) Initiative,[3] there is currently limited understanding of what causes long COVID and why only some patients develop the condition. Some individuals, even those who had mild infections, experience lingering health problems that can severely limit their activity for months. More research is needed to investigate the cause and pathology of long COVID and discover treatments for this enigmatic and often debilitating condition.

Other Important Vaccine Advances

Malaria: Every year, malaria infects millions and kills hundreds of thousands of vulnerable people around the world, in particular young children living in poor countries with inadequate health systems. The development of the first World Health Organization (WHO)-recommended vaccine for malaria represents a major scientific advance with the potential to significantly improve health outcomes and was the result of decades of basic research funded in part by NIH.[4] In addition, an NIH-funded phase 1 clinical trial found that a novel monoclonal antibody conferred unprecedentedly high levels of durable protection against malaria.[5]

Influenza: The Centers for Disease Control and Prevention (CDC) estimates that influenza has caused between 9 and 41 million infections, 140,000 and 710,000 hospitalizations, and 12,000 and 52,000 deaths each year in the United States over the last decade.[6] Annual vaccination is currently the most effective way to prevent illness due to flu; however, these vaccines must be updated annually and their ability to protect against infection varies widely from year to year due to seasonal shifts in the type of influenza viruses that circulate. NIH is currently supporting research to develop new types of vaccines, including universal flu vaccines (currently in phase 1 clinical studies), that would protect more broadly and effectively against multiple strains of flu, including newly emerging strains that pose a pandemic risk.[7]

Tuberculosis (TB): In 2020, 10 million people were infected with, and 1.5 million people died from, TB.[8] Although TB is the second leading infectious cause of death in the world, the only available vaccine against TB is the BCG (Bacillus Calmette-Guerin) vaccine, which has variable efficacy against pulmonary disease. NIH-supported research is seeking to understand how the TB bacterium interacts with its human host. Recently, NIH-funded researchers identified a method to dramatically improve the efficacy of the BCG vaccine in non-human primates by changing the route of administration.[9]

Opioid use disorder: The opioid epidemic has devastated families and communities across America, with 1.6 million people diagnosed with opioid use disorder and more than 70,000 people dying from opioid-related overdoses in the past year alone.[10] NIH is currently funding cutting-edge research seeking to prevent addiction by generating antibodies to block opioid molecules from entering the brain and by developing a vaccine that could combat opioid use disorder.[11]

Alzheimer's disease: Alzheimer's disease, which afflicts more than six million Americans, is a devastating illness that deprives its victims of their lifelong memories and ultimately destroys their brain function.[12] NIH-funded basic research has revealed how the immune system can contribute to the formation of amyloid

plaques in the brains of Alzheimer's patients, causing irreversible neuronal damage. Currently, there are multiple novel vaccine candidates, all currently in different stages of clinical studies, that aim to prevent Alzheimer's disease from ever developing.[13]

Immunology and Other Diseases, Including Cancer

While immunology has been in the news because of its extraordinary role in understanding and combatting COVID-19, critically important immunological research continues – and is advancing – in many other areas. Research on the immune system is improving our understanding of how to treat chronic conditions such as multiple sclerosis and cardiovascular disease; how to ensure successful organ or tissue transplantation; and how to protect against natural or man-made agents of bioterrorism.

Cancer research is also advancing, as immunologists have been able to effectively leverage the immune system's ability to recognize and eliminate tumor cells into treatments called immunotherapies. Scientists continue to unravel the complicated interaction between immune cells and cancer, with the hope that this will lead to the discovery of effective new cancer treatments. Recently, the Food and Drug Administration (FDA) approved the first KRAS inhibitor (sotorasib) to treat advanced *KRAS* G12C-mutant non-small cell lung cancer (NSCLC), which accounts for 82% of all lung cancer cases.[14] With lung cancer one of the three most common cancers diagnosed in U.S. adults, and with mutations to the *KRAS* gene one of the most common genetic alterations observed in NSCLC, this approval marks a major breakthrough in oncology.[15]

The Role of a Robust NIH in the Nation's Biomedical Research Enterprise

The nation's major funding agency for biomedical research, NIH is also a key source of economic activity in every U.S. state and in countries around the world. More than 80% of its $45 billion budget is distributed, following a competitive peer review process, to more than 300,000 researchers at more than 2,500 universities, medical schools, and other research institutions across the nation,[16] while approximately 10% of its budget supports ~6,000 researchers and clinicians who work at NIH facilities around the country.[17] This funding supports both scientific research and local economies; in 2021, NIH funding supported more than 552,000 jobs and accounted for $94 billion in economic activity across the U.S.[18] The basic research that NIH funds is also critical to the biomedical research pipeline; it contributed to the discovery of all 210 new drugs that were approved by the FDA from 2010-2016.[19]

NIH is the indisputable leader of biomedical research in the world, and its scientists play an indispensable role in responding to both emerging and ongoing health threats. Together with scientists from the CDC and other federal health and science agencies, NIH scientists have been essential to guiding the nation through the coronavirus pandemic, in part by providing timely and candid scientific advice to the President, Congress, and the American public.

For many years, strong bipartisan support for biomedical research has led to substantial increases in the NIH budget. Although these increases have largely restored the purchasing power that NIH had lost to inflation and inadequate budgets since 2003, meaningful budget growth is needed to enable NIH to invest not just in important research priorities across its Institutes and Centers, but also in its most valuable resource: the research workforce. While NIH should continue to support meritorious senior scientists, it is essential that it have the ability to support a sufficient cadre of trainees and early to mid-career scientists who are able to both address increasingly complex scientific challenges and eventually lead the research enterprise.

Congress must, therefore, provide NIH with the resources needed for the training, development, and support of our next generation of researchers, doctors, professors, and inventors – and give them the dynamic research environment they need to pursue these careers.

Conclusion

AAI greatly appreciates the subcommittee's strong, continuous, and bipartisan support for NIH and urges an NIH base budget of at least $49 billion for FY 2023 to help the agency invest in vital immunologic research, support meritorious biomedical scientists at all career stages, and help researchers and doctors discover new ways to prevent, treat, and cure disease. In addition, AAI recommends the appropriation of substantial funding for ARPA-H, which has the potential to greatly advance human immunology in an era of unprecedented scientific opportunity.

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[1] https://www.nih.gov/news-events/news-releases/niaid-issues-new-awards-fund-pan-coronavirus-vaccines

[2] https://www.nytimes.com/2022/02/02/health/covid-vaccine-nasal.html

[3] https://recovercovid.org/

[4] https://www.nih.gov/news-events/news-releases/investigational-malaria-vaccine-gives-strong-lasting-protection; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7227679/

[5] https://www.nih.gov/news-events/nih-research-matters/monoclonal-antibody-prevents-malaria-early-trial

[6] https://www.cdc.gov/flu/about/burden/index.html

[7] https://www.niaid.nih.gov/news-events/nih-launches-clinical-trial-universal-influenza-vaccine-candidate

[8] https://www.who.int/news-room/fact-sheets/detail/tuberculosis

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[10] https://www.hhs.gov/opioids/about-the-epidemic/index.html

[11] https://heal.nih.gov/news/stories/OUD-vaccine; https://www.gao.gov/assets/gao-19-706sp.pdf

[12] https://www.nia.nih.gov/health/alzheimers-disease-fact-sheet

[13] https://www.beingpatient.com/there-are-9-alzheimers-vaccines-in-trials-right-now/

[14] https://www.cancer.net/cancer-types/lung-cancer-non-small-cell/statistics

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