

WHY IMMUNOLOGY RESEARCH MATTERS

A publication of
The American Association of Immunologists

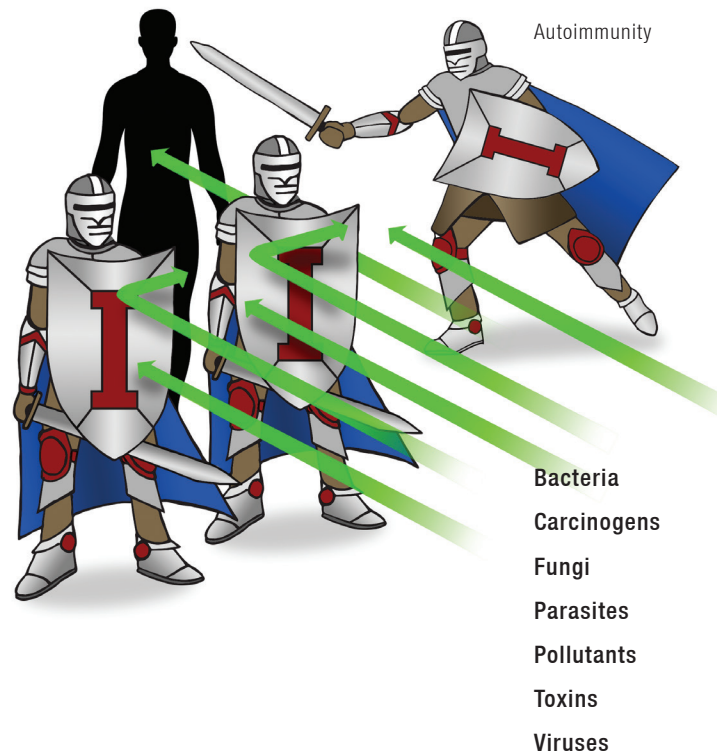


The Importance of the Immune System

The immune system is the body's primary defense against viruses, bacteria, and parasites that cause disease in millions of people every year. In addition, the immune system helps the body resist the development of cancer and other illnesses.

When the immune system is operating properly, it provides powerful protection against a variety of diseases. It can, however, be a double-edged sword. When it is underactive, it can leave the body vulnerable to infection. And when it is overly active, it can damage normal organs and tissues, causing illnesses such as allergy, asthma, inflammatory bowel disease, lupus, multiple sclerosis, psoriasis, rheumatoid arthritis, type 1 diabetes, and other autoimmune diseases.

Research scientists and clinicians are working to harness this powerful defense system to protect people and animals against naturally occurring infectious diseases, potential bioterrorism agents, cancer, and autoimmune diseases. Basic research focused on understanding and controlling the immune system is essential to discovering better ways to prevent and treat disease.



Autoimmunity

Bacteria

Carcinogens

Fungi

Parasites

Pollutants

Toxins

Viruses

Major Immunological Advances in Preventing and Treating Infectious Diseases

Vaccines

Vaccines help train the immune system to protect against an encounter with harmful bacteria or viruses that can cause life-threatening illnesses. A critical public health strategy, vaccination has led to the eradication of smallpox worldwide, the elimination of polio from the United States, and the control of many childhood diseases (including measles, mumps, and rubella) that once routinely sickened or killed millions of infants and children. Use of vaccines against high-risk forms of human papillomavirus (HPV), which cause about 91% of cervical and anal cancers, have reduced the U.S. incidence of HPV in female teenagers by more than 80%. Vaccines can also prevent or reduce the severity of many diseases for older adults, including shingles, pneumonia, and influenza.

Recently, the FDA approved vaccines against respiratory syncytial virus (RSV) for adults over 60 and pregnant women, and a monoclonal antibody treatment to prevent RSV in infants. Exciting progress is also being made in the development and use of vaccines against other infectious diseases, including Ebola, dengue, norovirus, and meningitis, and research is underway to develop a universal flu vaccine.

COVID-19

Scientists responded rapidly to the COVID-19 pandemic, caused by the SARS-CoV-2 virus, by developing several vaccines in record time, including the first FDA-approved vaccines that utilized messenger RNA (mRNA) technology. As variants have emerged over time, scientists have updated booster formulations to match the circulating variants. COVID-19 vaccines remain highly effective at preventing severe disease, hospitalization, and death. Scientists also developed novel therapies, such as monoclonal antibodies and antiviral drugs, that can significantly reduce COVID-19 severity.

Researchers are also working to develop a universal coronavirus vaccine, that could protect against many types of coronaviruses (including SARS-CoV-2), as well as mucosal vaccines which aim to block infection and/or extend the durability of the immune response. To help the millions of Americans currently suffering from Long COVID (persistent symptoms after SARS-CoV-2 infection), scientists are working to find ways to diagnose and treat Long COVID, including through the NIH RECOVER Initiative.

HIV and AIDS

Left untreated, the highly infectious HIV virus, which attacks and disables a critical part of the immune system, leads to the deadly disease AIDS. Decades ago, a person with HIV/AIDS was unlikely to live longer than a few years. Today, a person living with HIV who receives antiretroviral therapy can expect to live a nearly normal lifespan with little risk of sexually transmitting the virus. Because current therapies only suppress the virus, NIH is supporting research on new strategies to prevent infection, reduce transmission, and eradicate the virus in persons living with HIV. For example, NIH scientists are currently testing a promising mRNA vaccine against HIV, and have reported the successful remission (no detectable virus) through stem cell transplantation in a fifth person.

Influenza

Influenza (flu) is a respiratory virus that can cause serious illness, particularly in the elderly, leading to the hospitalization and/or death of hundreds of thousands of people in the U.S. each year. Influenza mutates rapidly, leading to multiple strains that may circulate each year. Newly emerging strains, like the recent H5N1 “bird flu” that has been circulating globally in birds, poultry, and mammals, have the potential to spill over into humans. Such strains can be more contagious and deadly, due to a lack of prior immunity, and have the potential to cause a pandemic. NIH-funded influenza research has driven several recent advances in vaccines, including a phase 1 study testing a new way to administer flu vaccines, and the first phase 1 clinical trial of a vaccine designed to provide universal protection against many different strains of influenza.

Malaria and Tuberculosis

Malaria and tuberculosis (TB) are leading global causes of death. An estimated 13 million Americans are infected with TB, and locally-acquired cases of malaria were recently reported in the U.S. for the first time since 2003. NIH-funded research has led to several recent breakthroughs, including the distribution of the first licensed and World Health Organization (WHO)-recommended malaria vaccine; WHO endorsement of a second malaria vaccine, R21/Matrix-M; clinical trials which demonstrate protection against malaria by a monoclonal antibody; and a new vaccination method (intravenous) that provides the most effective protection ever achieved against TB.



Immunological Advances that Have Changed the Course of Cancer, Autoimmune Diseases, and More

Cancer

Cancer research continues to focus on understanding the complex interactions between tumor cells and healthy (including immune) cells in the tumor microenvironment. Scientists are also utilizing vast, comprehensive genetic and metabolic data to advance our understanding, diagnosis, and treatment of cancer.

Numerous advancements have been made in the field of cancer immunotherapy, in which the patient's own immune system is stimulated or suppressed to fight cancer, including CAR-T cell therapy (engineered immune cells that can identify and eliminate tumor cells); cancer vaccine research (including testing mRNA vaccines); and better understanding the microbiome's influence on tumor growth. Immunotherapies and targeted therapies (drugs that inhibit cancer cell growth) have resulted in long-term remission for some cancer patients, including those who previously had limited options for successful treatment.

Autoimmunity

Autoimmune diseases are chronic illnesses in which a person's own immune system attacks their body. There are more than 100 autoimmune diseases that afflict over 50 million people in the U.S., 80 percent of whom are women. Autoimmunity can affect any region of the body, including the gastrointestinal system (e.g., inflammatory bowel disease), the musculoskeletal system (e.g., rheumatoid arthritis), the brain (e.g., multiple sclerosis), the metabolic systems (e.g., type 1 diabetes), and multiple organ systems at once (e.g., systemic lupus erythematosus).

NIH-supported research has identified the immune cells and molecules that cause some of these diseases, enabling the development of needed therapeutics. These medicines, including immunotherapies (treatments that utilize parts of a patient's immune system to fight disease), have been used with some success to treat rheumatoid arthritis, multiple sclerosis, and inflammatory bowel disease. However, more research is needed to better understand and treat these and other autoimmune diseases, including allergies and asthma.

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The Deleterious Impact of Inflammation on the Heart and Brain

Inflammation is the immune system's normal response to injury and infection, as immune cells rush to the affected site to protect or facilitate repair. Excessive or chronic inflammation, however, can cause or exacerbate disease. For example, inflammation in the cardiovascular system can lead to heart attacks and strokes. New research has shown that age-associated mutations in immune cells can cause inflammation that is correlated with damage to heart tissue.

NIH-funded research has recently revealed a link between brain inflammation and memory deficits, including Alzheimer's disease (AD). Scientists are testing the efficacy of several vaccines and treatments, including a way to teach the immune system to clear out harmful plaques in the brain, to combat AD. NIH research on the role of a harmful plaque called amyloid led to the development and recent Food and Drug Administration (FDA) approval of lecanemab, a monoclonal antibody, for the treatment of AD.

Organ Transplantation

Organ, tissue, and bone marrow transplantation have been utilized successfully as therapeutic options for patients suffering from kidney, liver, lung, and heart failure; for certain cancers and genetic diseases; and after significant injury. Scientists are optimizing ways to prevent the immune system from rejecting the transplant without compromising its ability to fight infections. Research has greatly improved rates of survival and the quality of life of transplant patients, particularly by better matching patients and donors to prevent transplant rejection and graft versus host disease. Scientists have recently made significant strides in xenotransplantation (using organs from other species) and 3D tissue printing [including through the HEART Initiative at the Advanced Research Projects Agency for Health (ARPA-H)], both of which could help overcome the major hurdle of insufficient organ availability.



Economic Benefits of Biomedical Research

High Quality Jobs

Discoveries funded by the National Institutes of Health (NIH) make possible a vibrant and innovative U.S. life sciences industry which directly supports about 2.1 million high-quality scientific jobs at 127,000 business establishments with an average annual salary of \$126,000.¹ These jobs are the economic engine for many communities around the nation.

In fiscal year (FY) 2022, NIH funding directly or indirectly supported more than 568,000² jobs at approximately 2,500 academic and research institutions across the U.S.³

Return on Investment

Every \$1 of NIH funding produces \$2.64 in economic output.⁴ Investment in NIH contributed almost \$97 billion to the U.S. Gross Domestic Product in 2022.⁵

Impact on Industry

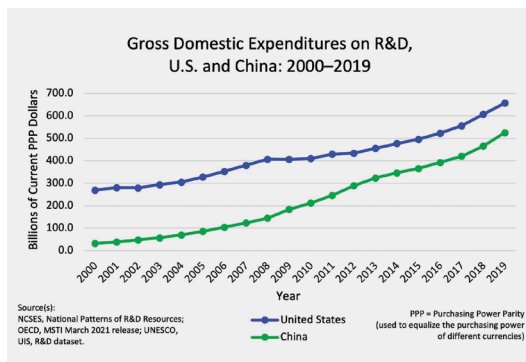
The basic discoveries of NIH-supported researchers are crucial to industry success in developing new products, including vaccines and other drugs, to prevent and treat disease. According to a bipartisan Senate Health, Education, Labor, and Pensions Committee report, “early stage research is high-risk—prone to high failure rates—making it less attractive to industry investment or undertaking, but these basic research findings form the foundation of the biomedical research continuum. NIH plays a vital role in its support of basic research. ...”⁶

A 2023 study, published in *JAMA Health Forum*, found that NIH funding contributed to 354 of the 356 drugs (99.4%) approved by the U.S. Food and Drug Administration from 2010 to 2019. This builds on previous evidence demonstrating that basic research funded by NIH is an essential and irreplaceable part of the biomedical research pipeline that leads to lifesaving and life-changing new drugs.

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Global Competitiveness

Despite recent increases in federal biomedical research funding, the growth rate for U.S. research and development (R&D) spending remains relatively low, especially in comparison with some of our economic competitors. For example, from 2010-2019, China’s R&D spending increased by 10.6% annually, compared to an average annual increase of 5.4% in the U.S.⁸ Due to China’s strong and consistent investment in R&D, it has already surpassed the U.S. in key metrics, including the number of patents granted and the total number of scientific publications each year.⁹



Increased investment in U.S. R&D will bolster innovation, strengthen our economy, and give the U.S. a competitive edge, enabling the U.S. to maintain its preeminence in biomedical research.

¹ https://www.bio.org/sites/default/files/2023-06/BIO_CSBA_Best_Practices_Report_2023.pdf

² https://www.unitedformedicalresearch.org/wp-content/uploads/2023/03/UMR_NIHs-Role-in-Sustaining-the-U.S.-Economy-2023-Update.pdf

³ <https://www.nih.gov/about-nih/what-we-do/budget>

⁴ See endnote 2

⁵ See endnote 2

⁶ http://www.help.senate.gov/imo/media/Innovation_for_Healthier_Americans.pdf

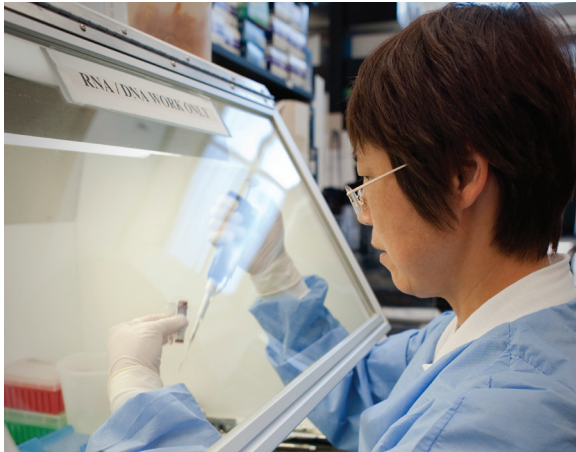
⁷ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10148199/>

⁸ <https://nces.nsf.gov/pubs/nsb20221/u-s-and-global-research-and-development>

⁹ <https://nces.nsf.gov/pubs/nsb20221/u-s-and-global-science-and-technology-capabilities>



The National Institutes of Health (NIH): At a Glance



Source: National Institute of Allergy and Infectious Diseases, NIH

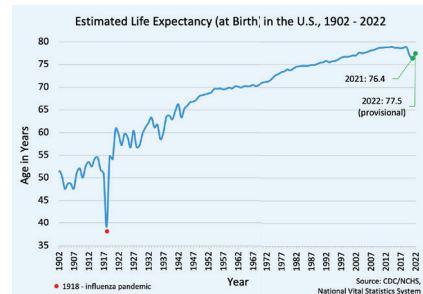
NIH's mission is "to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability."

NIH is comprised of 27 Institutes and Centers, most of which fund and conduct research on diseases or body systems. While about 10% of its budget supports the research of nearly 6,000 scientists in its own laboratories, more than 83% of its budget funds the work of about 300,000 extramural scientists at 2,500 universities, medical schools, and other research institutions in every state across the nation.¹ Importantly, this includes support for the training of more than 35,000 graduate students and nearly 29,000 postdoctoral fellows in FY 2022.²

A History of Success

NIH-supported researchers have received almost 170 Nobel Prizes and more than 210 Lasker Awards.³

NIH-funded biomedical research has helped to dramatically lengthen—and improve—the lives of millions of Americans. In 2019, then-NIH Director Francis Collins, M.D., Ph.D., explained that "[l]ife expectancy for a baby born in the U.S. has risen from 47 years in 1900 to more than 78 years today. Among the advances that have helped to make this possible are a 70% decline in the U.S. death rate from cardiovascular disease over the past 50 years, and a drop of more than 1% annually in the cancer death rate over the past couple of decades."⁴



Life expectancy in the U.S. has slightly declined in recent years due to several public health crises, including the COVID-19 pandemic. NIH-funded research, which has led to the development of new vaccines and treatments, is helping to reverse this trend, with estimated life expectancy increasing by more than one year in 2022.

¹ <http://www.nih.gov/about-nih>

² <https://nexus.od.nih.gov/all/2023/03/02/number-of-postdoctoral-researchers-supported-by-nih-grant-awards-fy-2017-fy-2022/>

³ <https://www.nih.gov/about-nih/what-we-do/impact-nih-research/revolutionizing-science/scientific-breakthroughs>

⁴ <https://time.com/5709207/medical-science-age-of-discovery/> (2019)



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AAI Funding Recommendation for NIH

The American Association of Immunologists (AAI) recommends an appropriation of at least \$51.3 billion for the base budget of the National Institutes of Health (NIH) for fiscal year (FY) 2025

to enable NIH to invest robustly in the next generation of biomedical researchers while providing ample support for established investigators who lead laboratories, train and teach aspiring scientists and medical students, and bring the latest scientific discoveries to patients' bedsides. Immunologists rely heavily on NIH funding to support their research and maintain their laboratories at institutions across the country. While NIH-funded research has resulted in remarkable scientific discoveries, continued progress is contingent on strong and consistent federal support.

AAI thanks Congress for its strong bipartisan support for NIH, which has enabled the agency's budget to grow significantly over the past eight years. However, this investment in NIH follows many years of insufficient funding; it was only recently that the NIH budget, after adjusting for inflation, was restored to its FY 2003 level. Robust, sustained, and predictable funding increases are needed to ensure adequate investment in health priorities including cancer, Alzheimer's disease, autoimmune diseases, and infectious diseases, and in a talented, diverse biomedical research workforce.



For more details on AAI funding priorities, please visit:
<http://www.aai.org/Public-Affairs/Advocacy-Center>

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Advanced Research Projects Agency for Health

AAI supports the Advanced Research Projects Agency for Health (ARPA-H), which funds high-risk, high-reward research projects with the potential to lead to transformative biomedical and health breakthroughs. Though part of NIH, ARPA-H is designed to operate independently with its own mission and culture, a higher tolerance for risk, and significantly different processes for identifying and funding research proposals.

ARPA-H funded its first project in August 2023, a collaboration among five different institutions which aims to reprogram dysfunctional immune cells to treat cancer, autoimmune diseases, and other common maladies. The agency has since funded many subsequent projects with similarly ambitious goals.



Credit: National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health

AAI believes that ARPA-H, which received an appropriation of \$1.5 billion in FY 2023, needs substantial, continued investment to meet its full potential. It is vital, however, that any funding provided to ARPA-H supplement, and not supplant, the NIH base budget. Funding ARPA-H at the expense of the NIH base budget could do great harm to the core functions of NIH, including its investigator-initiated basic research portfolio.



About AAI

AAI is the nation's largest professional association for immunologists. Since 1913, AAI has been dedicated to advancing the work of our members — research scientists and physicians who are the world's leading experts on the biology of the immune system and whose discoveries lead to the prevention, treatment, and cure of many life-threatening and debilitating diseases.

AAI represents immunologists from every state and around the globe. Our members include principal investigators, staff scientists, postdoctoral fellows, graduate students, lab managers, and other professionals who support our mission: to advance knowledge within immunology and related disciplines, foster the interchange of ideas and information among scientists, and promote a better understanding of the field of immunology.

AAI is the owner and publisher of *The Journal of Immunology* (*The JI*), which has published novel, peer-reviewed findings in all areas of experimental immunology since 1916. AAI also owns and publishes *ImmunoHorizons*, an open access, fully peer-reviewed journal committed to advancing the knowledge of immunology by publishing articles that cover all areas of basic and clinical immunology.

AAI is a founding member of the Federation of American Societies for Experimental Biology (FASEB), which is comprised of more than 20 professional scientific societies and over 100,000 researchers and is the largest coalition of biomedical research associations in the United States.

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