

NIAID

National Institute of Allergy
and Infectious Diseases

Strategic Plan 2026-2030



National Institute of
Allergy and
Infectious Diseases



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MISSION

NIAID conducts and supports basic and applied research to better understand, treat, and ultimately prevent infectious, immunologic, and allergic diseases.

VISION

Improve human health through an integrated, person-centered approach to immune-mediated and infectious diseases research.

DIRECTOR'S MESSAGE



The National Institute of Allergy and Infectious Diseases (NIAID) in collaboration with partners within and outside the National Institutes of Health (NIH) has played a pivotal role in **advancing scientific knowledge and transforming human health by supporting and conducting basic, translational, and clinical research on infectious and immune-mediated diseases**. Through rigorous research, NIAID has consistently demonstrated how scientific discovery directly improves health outcomes—reducing morbidity, preventing mortality, and enhancing quality of life for millions of Americans.

I am pleased to present the **NIAID 2026-2030 Strategic Plan**, our roadmap for the next five years. This plan reaffirms our mission to develop patient-centered strategies grounded in rigorous research that safeguard and improve health.

At its core, the plan envisions improving human health through an integrated, person-centered approach to infectious and immune-mediated diseases. It is anchored in advancing our understanding of human immunology to strengthen protective responses that prevent disease, improve health outcomes, and support cures, mitigate harmful immune responses in allergies and autoimmune conditions, and harness insights from the microbiome to develop new host-directed therapies. Through expanding the scope of immunology and infectious disease research, NIAID will generate the foundational knowledge needed to deliver measurable improvements in patient outcomes and reduce the morbidity and mortality of pressing public health challenges.

NIAID remains committed to scientific rigor, reproducibility, and bold innovation—especially ideas from the next generation of researchers. By supporting new investigators and ensuring today's research investments yield exponential future advances, we will continue driving progress to improve outcomes against current and future diseases.

The 2026-2030 Strategic Plan sets ambitious yet achievable goals. We will track progress through regular reviews, evaluate public benefit, and adjust as needed to maintain transparency and maximize impact on health.

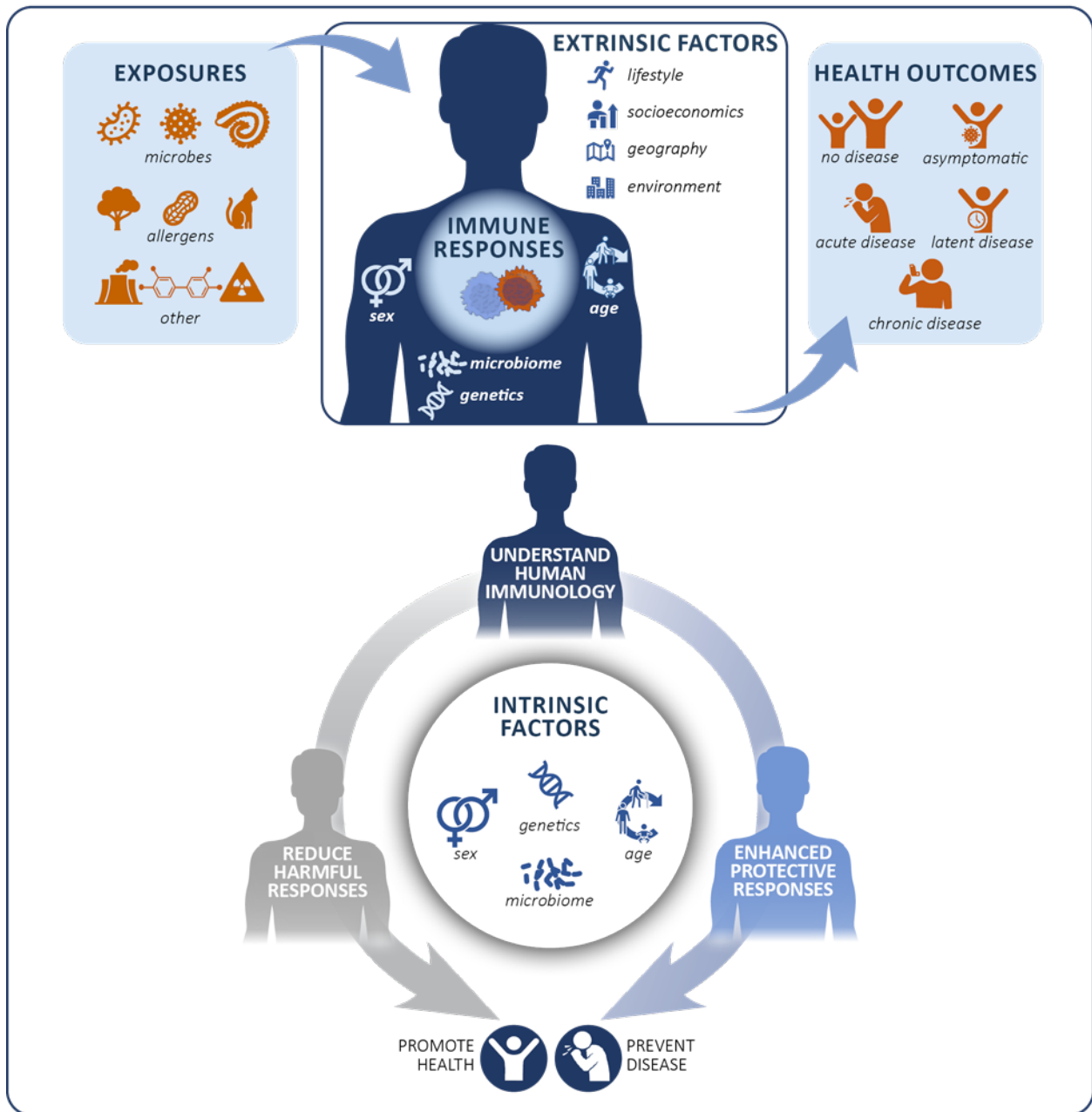
This plan reflects broad collaboration, and I am grateful to all who contributed. Together, we will advance research excellence to address our most pressing health challenges and improve the lives of all Americans.

Best Regards,

John H. Powers, III, M.D.

Acting Director and Principal Deputy Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health

An Integrated Approach to Infectious and Immune-Mediated Disease Research



NIAID's core priority is advancing foundational knowledge of human immunology. This knowledge is needed **to enhance protective immune responses** that prevent disease, while **reducing harmful responses** that lead to disease. Understanding the continuum of immune responses, including how intrinsic factors influence this balance, is essential to achieving these goals. By deepening our insight into both beneficial and detrimental immune mechanisms, NIAID aims to drive the development of innovative prevention strategies, targeted therapies, and precision medicine approaches. Placing immunology at the forefront of our strategic agenda ensures that scientific advances translate into meaningful improvements in Americans' health.

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INTRODUCTION

NIAID Overview and Organization

The National Institute of Allergy and Infectious Diseases (NIAID) is one of the 27 institutes, centers, and offices (ICOs) that comprise the National Institutes of Health (NIH). NIAID supports the broader NIH mission of seeking fundamental knowledge to enhance human health by conducting and supporting biomedical research aimed at understanding, preventing, and treating infectious and immune-mediated diseases. For more than seven decades, NIAID has focused on basic, translational, and clinical research, leading to advances, including novel diagnostics, prevention, and treatment strategies that have significantly improved the health of millions of people in the U.S.

The Institute's organizational framework equips NIAID with the necessary structure and staff to effectively advance the NIAID mission. NIAID is composed of extramural and intramural divisions that guide the Institute's scientific activities, along with the Office of the Director, which provides scientific leadership,

science policy guidance, and comprehensive operational and administrative coordination for the Institute.

NIAID oversees a multifaceted research portfolio aimed at expanding and deepening the understanding of immune system development and function, as well as all aspects of infectious and immune-mediated diseases, including numerous chronic conditions linked to immune dysfunction. In this context, "infectious diseases" includes illnesses that occur when pathogenic microbes interact with the host, while "immune-mediated diseases" encompasses a broad range of disorders related to allergies, asthma, autoimmunity, inborn errors of immunity, secondary immunodeficiencies, and the prevention of transplant organ, tissue, and cell rejection. The Institute will remain a world leader in biomedical research by advancing science through the studies conducted at the Institute and through grants and contracts to academic institutions and other organizations.



NIAID Legislative Authority

42 U.S.C. § 285f: The general purpose of NIAID is to conduct and support research, training, health information dissemination, and other programs with respect to fundamental immunology, allergic and immune-mediated diseases and disorders, and infectious diseases, including tropical diseases. Additional details, including updates to the Institute's authorities, can be found in [Appendix A](#).

Fiscal Years 2026-2030 Strategic Planning Process

NIAID is dedicated to pioneering comprehensive research and innovation to advance strategies to understand, diagnose, prevent, treat, and cure infectious and immune-mediated diseases. The NIAID strategic plan was developed to align goals across the Institute and identify areas where additional efforts are required to advance the Institute's mission.

STRATEGIC PLAN FRAMEWORK

The NIAID Strategic Plan is organized around three **Research Goals** that will advance research related to infectious and immune-mediated diseases: 1) Foundational Research; 2) Diagnostics and Prevention Research; and 3) Treatments and Cure Research. Within each Research Goal, there are distinct research **Objectives** that outline specific, achievable **Approaches**. Together these goals, objectives, and approaches provide a framework for the Institute to work toward advancing gold standard science in support of the NIAID mission.

Additionally, three Operational and five Capacity Goals were identified to provide the NIAID workforce and the larger biomedical research community with opportunities and tools necessary to advance the NIAID mission. The **Operational Goals** include: 1) Community Engagement; 2) Evidence-Informed Decision

Making; and 3) Research Transparency. The **Capacity Goals** include: 1) Biomedical Workforce and Training; 2) Research Tools and Services; 3) Data Science and Data Sharing; 4) Networks and Multicenter Collaborations; and 5) Research Facilities and Infrastructure.

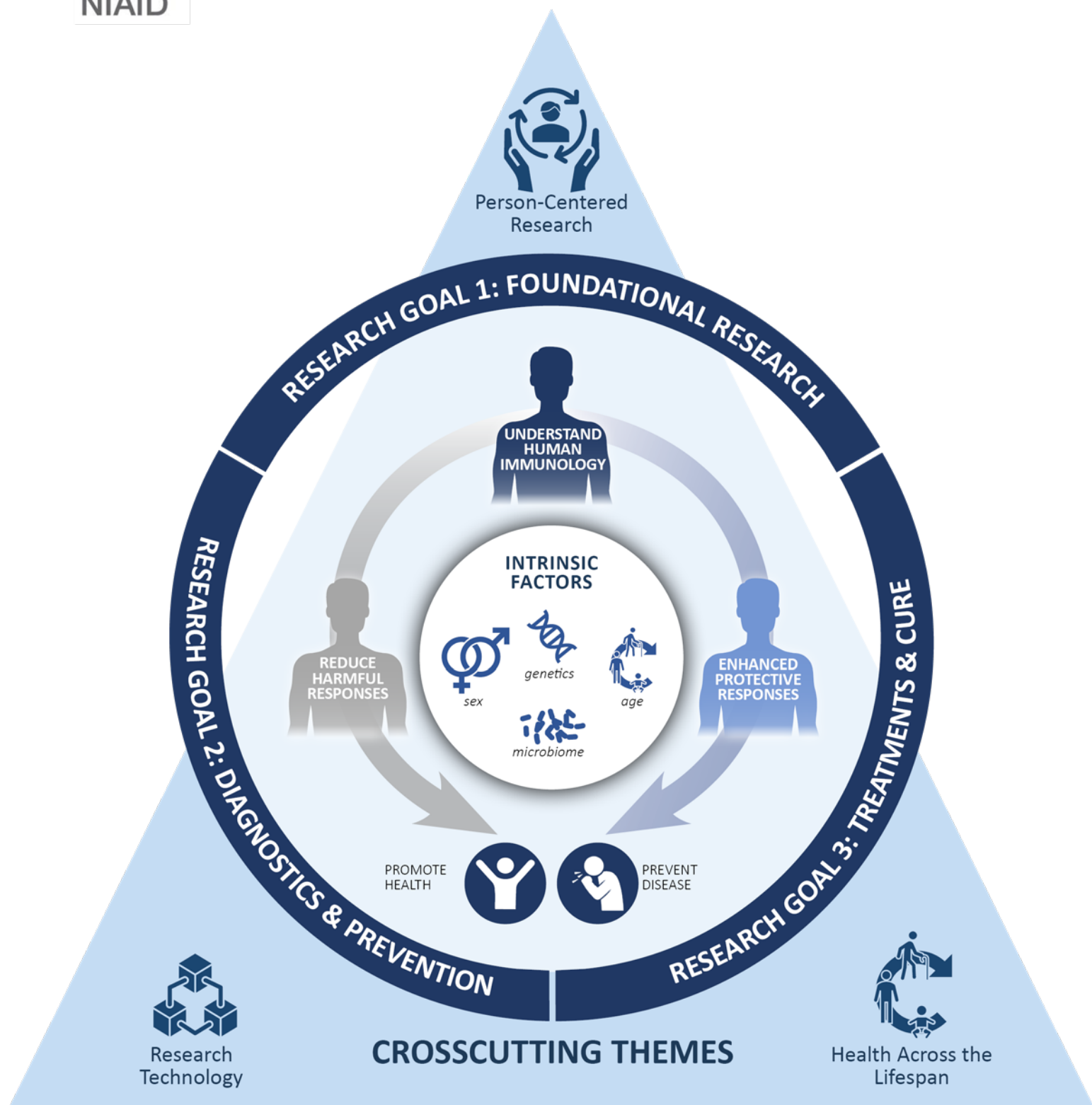
Finally, three **Crosscutting Themes** were identified to highlight topics that are integrated into each of the Research, Operational, and Capacity Goals that are integral to every facet of the Institute's research portfolio: 1) Person-Centered Research; 2) Research Technology and Data Science; and 3) Health Across the Lifespan.

The Plan will guide NIAID for five years with regular assessments to ensure progress across all Goals. An overview of the NIAID Strategic Plan Framework can be found on the following page.

APPROACH TO PRIORITY SETTING AND IMPLEMENTATION

The Institute sets goals by identifying research areas that should be supported to improve health outcomes related to infectious and immune-mediated diseases. In alignment with the Department of Health and Human Services (HHS) and NIH-wide priorities, the new NIAID strategic plan shifts from a pathogen-centric to a person-centered approach, integrating human immunology into infectious and immune-mediated diseases research. For this plan, NIAID engaged with its collaborators, including biomedical researchers, clinicians, other U.S. Government (USG) organizations and community partners, to set goals that address current and future needs.

To implement this plan, NIAID will assess annual progress toward the approaches outlined in the Research, Operational, and Capacity Goals. Additional information on the Institute's approach to goal setting, strategic planning process, and implementation can be found in [Appendix B](#).



OPERATIONAL GOALS

- » Engaging with Communities
- » Evidence-Informed Decision Making
- » Research Transparency

CAPACITY GOALS

- » Biomedical Workforce & Training
- » Research Tools & Services
- » Data Science & Data Sharing
- » Research & Clinical Trial Networks
- » Research Facilities & Infrastructure

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CROSSCUTTING THEMES

NIAID has a broad research portfolio that spans basic, translational, and clinical research in areas including microbial biology, immunology, and infectious and immune-mediated diseases. Multiple crosscutting themes that are essential to the NIAID mission are woven across the research portfolio. These three **Crosscutting Themes** are: 1) Person-Centered Research; 2) Research Technology and Data Science; and 3) Health Across the Lifespan.

Person-Centered Research

Person-centered research at NIAID is grounded in the collection and application of data not only from clinical trials, but also real-world settings. Real-world data are health-related information collected from healthcare and everyday settings outside traditional clinical trials, reflecting the experiences and outcomes of individuals in real-life contexts. By prioritizing this type of research, NIAID ensures that findings are relevant and applicable beyond controlled clinical environments. This approach emphasizes collaboration with healthy individuals, patients, trial participants, at-risk populations, and caregivers to optimize research for the greatest overall benefit. Engaging these partners throughout all phases of the research process enables the collection of real-world data on their needs, concerns, lived experiences, and health outcomes, which is critical for developing interventions that work to improve health in practical, real-life contexts.

NIAID is committed to promoting research focused on scientifically valid, measurable health outcomes that matter to individuals and communities. This includes supporting studies that assess not only biological factors affecting infectious and immune-mediated diseases, but also the environmental, social,

and lived-experience influences on health outcomes. Considering the multiple factors influencing health outcomes is especially important for populations differently affected by infectious and immune-mediated diseases, helping to better understand and address these differences. By emphasizing a person-centered approach that recognizes and responds to these differences, NIAID ensures that scientific advancements are relevant and applicable to all individuals and communities.

Most importantly, person-centered research is about building trust. Focusing on the whole person, not just isolated microbes, diseases, or conditions, enables researchers to conduct impactful, multidisciplinary science that is rigorous, relevant, and grounded in respect and compassion for those affected by infectious and immune-mediated diseases.

Research Technology and Data Science

Advances in research and data science technologies have significantly accelerated progress in biomedical research. Innovations in areas such as assay development, biomarker discovery, structural biology, and imaging are deepening our understanding of human biology and infectious and immune-mediated diseases. This includes their identification, diagnosis, prevention, and treatment. Further, enhanced computational capabilities, such as artificial intelligence and machine learning (AI/ML), are expanding the Institute's capacity to drive scientific discovery and rigorously validate results. NIAID will continue to leverage data science to advance research by adopting emerging technologies, applying computational methods, fostering interdisciplinary research communities, and

expanding data access and sharing. Together, these practices help ensure that research findings are transparent, replicable, and reproducible. In parallel, NIAID will support the responsible governance of AI/ML through risk-based oversight, validation for intended use, transparent documentation of methods and limitations, privacy protections, reproducibility, and appropriate human oversight.

As biomedical science continues to advance, the volume of data being generated has increased substantially. In accordance with NIH data sharing policies, scientific data from NIAID-funded and -conducted research are made publicly available whenever possible, facilitating transparency, independent validation, and reanalysis. This encompasses a wide range of data types, including genomic, transcriptomic, imaging, proteomics, metabolomics, flow cytometry, immunology, and clinical data. While much of this information is stored in public repositories, more sensitive data are housed in controlled-access, NIH-supported repositories to protect participant privacy. Rapid data sharing is crucial for advancing research on human biology and infectious and immune-mediated diseases, and NIAID is committed to supporting these efforts while upholding the highest standards of data stewardship and participant confidentiality.

Health Across the Lifespan

The way an individual's immune system and microbiome respond to external challenges changes over time, which can cause infectious and immune-mediated diseases to present differently across the lifespan. As individuals age, their immune systems may develop less protective immune responses to microbes and vaccines. For example, respiratory syncytial virus (RSV) typically results in a mild infection for many adults, but RSV infections in infants and older adults can result in severe infection, hospitalization, or even death. Most allergic diseases, including food allergy, atopic dermatitis and asthma, begin in the very early years of life. Additionally, major hormonal and biological changes, such as puberty, pregnancy, and menopause, can increase susceptibility to infectious and immune-mediated diseases. Further, clinical trial results may not be generalizable across age groups and life stages. Therefore, it is critical to consider age-related differences across body systems when developing and evaluating a new preventative or therapeutic candidate.

NIAID is committed to researching basic aspects of the immune system as well as infectious and immune-mediated diseases across life phases and will continue to promote the inclusion of people of all ages in clinical trials to improve human health across the lifespan.



RESEARCH GOALS

NIAID conducts and supports biomedical research to better understand, prevent, treat, and cure infectious and immune-mediated diseases. The Institute's research portfolio can be divided into three major areas focused on infectious and immune-mediated diseases with the following goals: 1) **foundational research**; 2) developing and evaluating safety and efficacy of **diagnostic and prevention strategies**; and 3) developing and evaluating safety and efficacy of **treatment and cure strategies**. These three research goals were used to establish the Research Goals covered in this plan. The Goals are structured to focus on scientific approaches that are applicable to diseases across the Institute's broad research portfolio, unless otherwise noted.



Infectious and Immune-Mediated Disease Research at NIAID

NIAID conducts and supports research on a vast number of infectious and immune-mediated diseases. The Institute's efforts are pivotal for understanding, preventing, diagnosing, and treating these diseases and protecting the health of all Americans. In this Plan, the specific goals within the Research Goals highlight approaches that are applicable to a wide array of infectious and immune-mediated diseases covered in the NIAID portfolio, unless otherwise noted. For detailed research goals related to specific infectious and immune-mediated diseases other than human immunodeficiency virus (HIV), please refer to [Appendix C](#), which highlights research goals on the following diseases and conditions:

- » Allergic Diseases
- » Autoimmune Diseases
- » Fungal Infections
- » Inborn Errors of Immunity
- » Neglected Tropical Diseases
- » Respiratory Infections
- » Sexually Transmitted Infections
- » Vector-Borne Diseases, including Malaria
- » Enteric Infectious Diseases
- » Solid Organ Transplantation
- » Viral Hepatitis

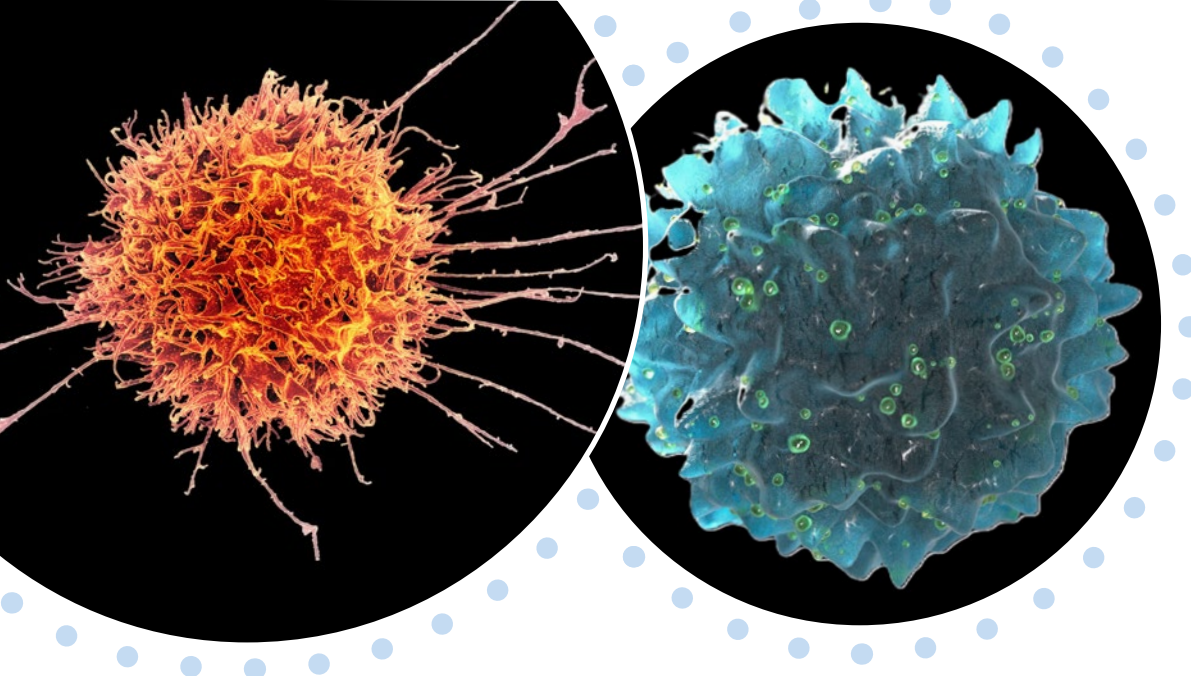




RESEARCH GOAL 1

Advance foundational research of the immune system, microbial biology, and host-microbe interactions.

Basic science research at NIAID encompasses examining the development and function of the immune system, the biology of microbes (bacteria, fungi, viruses, prions, and parasites) and the intricacies of host-microbe interactions. This foundational knowledge informs the development of treatments and preventative strategies for human infectious and immune-mediated diseases. NIAID will continue to support the foundational research necessary to advance the NIAID mission.



Objective 1.1: Increase understanding of the human immune system and microbial biology.

IMMUNE SYSTEM DEVELOPMENT

The immune system begins to develop during fetal growth *in utero* and is comprised of two major components: the innate and the adaptive immune systems. The innate immune system provides a rapid, broadly protective defense against foreign molecules, while the adaptive immune system offers a slower, highly specific response involving lymphocytes and antibody production. The innate and adaptive immune systems both undergo significant changes throughout life. The adaptive immune system matures during childhood and continues to develop through adulthood as it encounters new antigens. However, both the innate and adaptive immune systems may decline with age, environmental exposures, or comorbidities, increasing vulnerability to infections and diseases. NIAID will continue to invest in fundamental research to understand how the immune system develops and adapts in response to internal and external factors throughout the lifespan.

APPROACHES:

- » Determine how inborn errors in immune mechanisms and early life events influence immune system development.
- » Characterize immune system developmental differences by sex and across the lifespan.
- » Identify and characterize immune cell subsets of both the innate and adaptive system to assess their contribution to immune homeostasis and protective immunity.
- » Identify immune mechanisms responsible for the recognition of self vs. non-self (i.e., immune tolerance), including during pregnancy and with transplantation.
- » Characterize the mechanisms that promote trained immunity (i.e., innate immune memory).
- » Investigate how the human microbiome and its interactions with biological and environmental factors influence immune system development, homeostasis, and function across the lifespan.

IMMUNE SYSTEM FUNCTION AND DYSFUNCTION

The immune system is a complex network that carries out immune surveillance in cells, tissues, and organs to defend the body and maintain overall health. When functioning properly, it effectively identifies and neutralizes threats; however, dysfunction in the immune system can lead to a range of issues, from increased susceptibility to infections to tissue damage caused by uncontrolled immune responses to allergens or the body's own tissues. NIAID will continue to invest in foundational research aimed at deepening a basic understanding of immune system function and elucidating mechanisms underlying immune system dysfunction.

APPROACHES:

- » Study how different components of the immune system maintain homeostasis and immune tolerance.
- » Expand understanding of mucosal barrier function, dysfunction, mucosal immune responses, and the role of immune cells at mucosal tissues.
- » Identify drivers of short-lived versus durable immunity.
- » Characterize inflammation, including its role in acute responses to harmful stimuli and the detrimental effects of chronic inflammatory states.
- » Determine the biological, environmental, and lifestyle factors that trigger immune dysfunction.
- » Advance understanding of autoantigens, alloantigens, and allergens that drive immune dysfunction.

DISCOVERY AND BIOLOGY OF MICROBES IN THE CONTEXT OF HUMAN HEALTH

Discovering and characterizing new microbes that impact human health enables scientists to monitor their spread and analyze their genetic and phenotypic properties. Further, understanding the biology of new and known infectious microbes is essential for identifying critical targets for intervention, which can lead to the development of strategies that promote health and protect the public from infectious diseases. NIAID will continue to support foundational research in both microbe discovery and biology to enhance understanding of infectious diseases.

APPROACHES:

- » Advance microbe discovery, characterization, and molecular epidemiology as they relate to the development of infectious disease.
- » Develop robust epidemiological modeling for the emergence of infectious diseases.



ROCKY MOUNTAIN LABORATORIES

Scientists at the NIAID Rocky Mountain Laboratories (RML) in Hamilton, Montana, are at the forefront of studying infectious diseases, including those caused by viruses, bacteria, and other pathogens. The RML facility was established in 1928 originally to combat the spread of Rocky Mountain spotted fever. It has since evolved into a premier biomedical facility. Today, the facility hosts high-containment laboratories that enable specially trained scientists to study organisms that cause severe infectious diseases. These studies are conducted under strict safety regulations to ensure the protection of both the scientists and the community. RML scientists continue to work toward understanding basic pathogen biology and developing strategies to diagnose, prevent, and treat infectious diseases in order to protect the health of all Americans.

- » Investigate the influence of the environment on microbial reservoirs, traits, and geographic distribution.
- » Expand understanding of tropism, receptor and entry requirements, replication mechanisms, structure, and capacity for eliciting antigenic diversity.
- » Utilize advances in technology, such as those in structural biology and reverse genetics systems, to enhance understanding of microbial biology.
- » Identify the stages of both infection and disease and pinpoint key microbe vulnerabilities at each stage.

Objective 1.2: Investigate host-microbe interactions in the context of health and disease.

HOST-MICROBE INTERACTIONS

Interactions between microbes and the host can contribute to acute or chronic diseases. Host and environmental factors influence whether exposure to microbes leads to illness and can determine the severity of disease. Though microbes can cause disease, the human microbiome can also provide important benefits by supporting immune development and regulation, aiding metabolism, protecting

against pathogen colonization, and helping maintain overall health. NIAID is committed to advancing understanding of the dynamic nature of host-microbe interactions to preserve health and inform the development of safe and effective strategies to prevent and treat infectious diseases. A deeper understanding of both the harmful and beneficial effects of host-microbe interactions is essential to reducing disease risk while harnessing microbial functions that support health.

APPROACHES:

- » Examine how pathogenic microbes establish residence in human tissues, as well as adapt to different host environments, thereby contributing to health and disease.
- » Characterize host immune factors, non-immune factors, and microbial factors that influence microbial transmission, pathogenesis, and beneficial host-microbe interactions.
- » Identify beneficial host-microbe interactions, including the microbiome, that can be leveraged to promote health and prevent disease.
- » Characterize how the host microbiome can affect immune homeostasis and alter susceptibility to pathogenic microbial infections.

RESEARCH ON CHRONIC INFECTIONS

Some microbes, including Epstein-Barr virus, cytomegalovirus, varicella-zoster virus, hepatitis B virus, Mycobacterium tuberculosis, and HIV, can cause long-term infections in humans that last months, years, or even a lifetime. Chronic infections can lead to long-term health complications, including cancers, cardiovascular diseases, increased susceptibility to other infections, and immune system dysfunction and autoimmune diseases. Chronic infections occur when microbes have mechanisms that allow them to evade the immune system, establish latency, and persist in the human body, particularly in tissues where the immune system is normally suppressed (e.g., brain, eyes, placenta). Often, these microbes go dormant for extended periods of time and are reactivated by biological or environmental triggers. Understanding the mechanisms that allow microbes to cause chronic infections or escape from latency is essential to develop effective treatments and preventative measures. By funding research initiatives, facilitating collaborations, and providing resources and infrastructure, NIAID accelerates the development of new diagnostics, prevention, and treatment strategies that address the burden of chronic infections and enhance the quality of life for affected individuals.

- » Determine what intrinsic and extrinsic factors modulate host-microbe interactions and contribute to the heterogeneity of health and disease outcomes.
- » Investigate how protective immunity, immune evasion, and other mechanisms can lead to microbial survival and emergence of variants.
- » Examine the microbe and host factors, as well as the mechanisms that contribute to the emergence, transmission, persistence, and poor health outcomes related to antimicrobial resistance.

MICROBE PERSISTENCE AND HOST RESERVOIRS

Persistence refers to the ability of a pathogenic microbe to remain in a host organism for extended periods of time, often by evading the immune system and establishing long-term infections. This persistence can occur through various mechanisms, such as latency, where the microbe remains dormant within host cells, or chronic infection, where the microbe continues to replicate at low levels. Host reservoirs are cells or tissues in which the microbe can persist and maintain its presence over time. Understanding persistence and its relationship to host reservoirs is critical for developing strategies to control and eliminate infections, thereby reducing the risk of transmission and disease recurrence.

APPROACHES:

- » Define cellular and tissue distributions of microbe reservoirs.
- » Develop sensitive and accurate methods to detect and quantify persistent microbe reservoirs in blood and other tissues.
- » Characterize immune system control of microbe resurgence from persistent reservoirs.
- » Advance understanding of post-treatment microbe persistence or disease recurrence.
- » Explore the contribution of microbe persistence to infection-associated chronic conditions and autoimmunity.

IMPACT OF INFECTION ON IMMUNE-MEDIATED DISEASE

Infectious diseases can increase the risk for and severity of immune-mediated diseases by triggering abnormal immune responses, leading to chronic inflammation and tissue damage. Infections can disrupt immune homeostasis, potentially initiating or exacerbating conditions such as autoimmune disorders, allergic diseases, and other chronic illnesses. Additionally, individuals with immune-mediated diseases may demonstrate lowered protective immune responses to infection, making it more difficult to prevent or treat infections. Thus, it is critical to better understand the relationship between infection and immune-mediated disease to develop effective prevention and treatment strategies for all individuals.

APPROACHES:

- » Characterize the commonalities in pathophysiology across different infections observed in individuals with immune-mediated diseases.
- » Understand the contribution of infections and other factors (e.g., microbiome, environment) to the development and exacerbation of allergies and asthma in pediatric and adult populations.
- » Determine whether and how certain pathogens lead to or exacerbate chronic conditions, including autoimmunity.
- » Examine the interplay between infection and the immune response in immunocompromised individuals, including transplant recipients.

ADDRESSING LONG-TERM CONDITIONS FOLLOWING CLEARANCE OF AN INFECTION

Many individuals continue to deal with long-term health consequences following the clearance of an infection. These post-infection long-term conditions can significantly impact an individual's health and quality of life. Specific examples of long-term conditions following the clearance of an infection include:

Long COVID: Many individuals experience debilitating symptoms for months or even years after infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In 2021, NIH launched the Researching COVID to Enhance Recovery (RECOVER) initiative, led by the National Heart, Lung, and Blood Institute (NHLBI) and co-chaired by NIAID and the National Institute of Neurological Disorders and Stroke (NINDS). This initiative identified new drug targets and potential causes of Long COVID and developed extensive clinical trial and research networks. Moving forward, NIAID is leading the second phase of RECOVER, known as RECOVER-Treating Long COVID (RECOVER-TLC), to build on the successes and lessons learned from RECOVER. RECOVER-TLC will leverage new and existing study sites to conduct clinical trials for therapeutics and biologics, and, importantly, will involve people living with Long COVID in each phase of research planning.

Post-Treatment Lyme Disease Syndrome (PTLDS): PTLDS is a set of debilitating symptoms that persist for months or even years after standard antibiotic treatment for Lyme disease. Although the underlying causes remain unclear, ongoing NIH-supported research is working to better understand PTLDS, including its possible links to immune dysfunction and autoimmunity, with the goal of improving diagnosis, prevention, treatment, and quality of life for affected individuals.

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS): ME/CFS is a chronic, multisystem disease characterized by neurological, immunological, autonomic, and metabolic dysfunction. The causes of ME/CFS remain unknown, though it often follows an acute infection and can persist for six months or longer. There is currently no diagnostic test or U.S. Food and Drug Administration (FDA)-approved treatment. In the United States, ME/CFS is estimated to affect up to 3.3 million people, many of whom experience severe disability and never return to their pre-illness level of functioning.

Results from Long COVID studies, as well as ongoing studies addressing conditions like PTLDS and ME/CFS, provide insights into prevention and treatment strategies for similar conditions that are not well understood. NIAID remains committed to supporting research to develop person-centered prevention and treatment strategies that improve the quality of life of those impacted by long-term conditions following clearance of an infection.

Approaches:

- » Identify risk factors for and underlying mechanisms that contribute to persistent symptoms and long-term complications.
- » Define novel immune regulatory mechanisms associated with enhanced protection or disease exacerbation.
- » Understand how infectious diseases influence immunologic memory and vaccine efficacy.

Objective 1.3: Develop and apply *in vitro* and *ex vivo* models, living models, and advanced technologies to further foundational research in infectious and immune-mediated diseases.

IN VITRO AND EX VIVO MODELS AND NEW APPROACH METHODOLOGIES

In vitro and *ex vivo* research models allow for the study of biological processes outside a living organism. These models help scientists dissect complex cellular mechanisms, screen potential therapeutic compounds, and understand disease pathology with greater

relevance to human health. Increasingly, researchers are using new approach methodologies (NAMs), including organoids, microphysiological systems, and computational models, that can complement or even replace animal models. NIAID is committed to advancing the development and validation of *in vitro*, *ex vivo*, and NAM-based models to accelerate the development of prevention and treatment strategies for infectious and immune-mediated diseases.

APPROACHES:

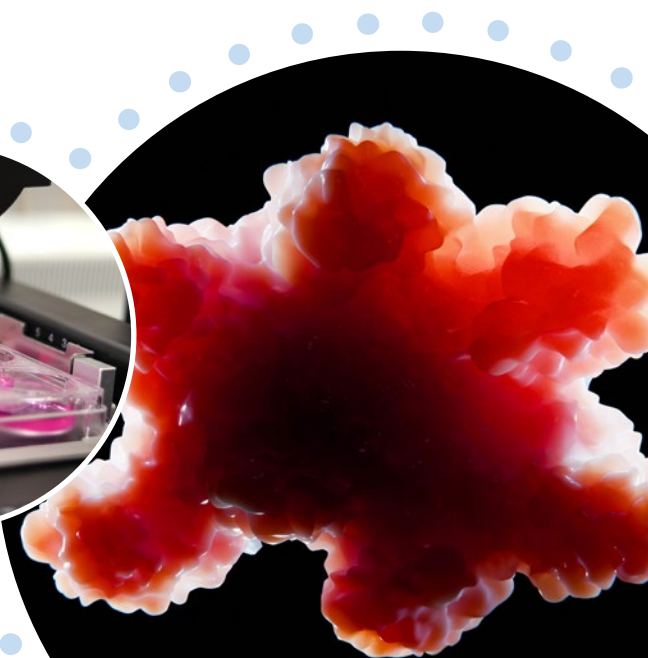
- » Establish novel and enhance existing *in vitro* and *ex vivo* research models to improve accuracy, scalability, relevance, and reliability.
- » Create and validate advanced *in vitro* tissue-structure models, including three-dimensional cell culture, organoid, and organ-on-a-chip platform models that mimic cellular and extracellular architecture and microenvironments for use in infectious and immune-mediated disease research.
- » Develop and utilize *ex vivo* research models, such as tissue and organ explants, to study infectious and immune-mediated diseases in a more physiologically relevant context.
- » Advance predictive *in vitro* and *ex vivo* models to decrease the need for preclinical animal toxicology studies.

LIVING MODELS OF DISEASE

The use of animals in several research areas remains necessary to advance medical and scientific knowledge. This is particularly true for studies leading to treatments and cures for infectious and immune-mediated diseases where the host response plays a major role. Laws, regulations, and policies are in place to ensure the ethical treatment and protection of these animals. NIAID is committed to using the fewest number of animals necessary to definitively answer scientific questions while maximizing the reliability of the results.

APPROACHES:

- » Refine and optimize living models to create human-relatable data for foundational research in microbial biology, immunology, and host-microbe interactions, and to accelerate the transition to novel interventions toward clinical investigation.
- » Develop and further improve small animal models to enhance knowledge of infectious and immune-mediated diseases.
- » Leverage large animal models, only to the extent necessary, to evaluate vaccines and therapeutics for infectious and immune-mediated diseases.
- » Advance development and distribution of immunologic reagents for relevant animal models for use by the research community.



ADVANCED TECHNOLOGIES

Advanced technologies such as artificial intelligence and machine learning (AI/ML) can be used to assist researchers in the analysis of vast datasets from electronic health records, single-cell multi-omics, structure prediction, and imaging, to uncover new insights relating to infectious and immune-mediated diseases. Additionally, computational modeling enables scientists to simulate complex biological systems, rapidly generate hypotheses, model disease progression, and predict prevention and treatment outcomes. These advanced technologies can facilitate interdisciplinary research, streamline experimentation, and reduce research costs.

APPROACHES:

- » Leverage AI/ML to advance development of diagnosis, treatment, and prevention strategies for infectious and immune-mediated diseases.
- » Develop computational models for complex biological systems, including the immune system, to advance research in infectious and immune-mediated diseases.
- » Advance infectious and immune-mediated disease research by integrating large datasets on exposures (e.g., environmental, dietary, pharmaceutical) with immune and microbe biology data.
- » Combine AI/ML with research using *in vitro*, *ex vivo*, and living models to better predict human responses to interventions and accelerate the development of improved prevention and treatment strategies for use across the lifespan.





RESEARCH GOAL 2

Advance and apply foundational knowledge to develop and evaluate diagnostic and prevention strategies against infectious and immune-mediated diseases.

NIAID supports research to advance diagnostic and prevention strategies for a wide range of infectious and immune-mediated diseases. To develop and test innovative approaches, the Institute supports translational, descriptive, and interventional research that draws from foundational knowledge of the human immune system and microbe biology. Through rigorous science and collaborative efforts, NIAID is dedicated to translating research discoveries into tangible health benefits for those at risk of or affected by infectious and immune-mediated diseases.



Objective 2.1: Develop and assess novel strategies for early detection, diagnosis, and improved disease monitoring for infectious and immune-mediated diseases.

BIOMARKER DISCOVERY AND VALIDATION

Biomarkers are biological indicators of disease (e.g., proteins, genes, metabolites) primarily used to identify the presence of a disease (diagnostic biomarkers) and to monitor disease progression (prognostic biomarkers). Biomarkers can provide valuable insights into the underlying mechanisms of diseases and can improve diagnostic accuracy and enable earlier detection. In addition to their role in diagnostics, biomarkers can be used to evaluate effectiveness of treatment and prevention strategies by tracking changes in disease status over time. By advancing biomarker research, NIAID aims to enhance disease identification and monitoring, while also supporting the assessment of therapeutic outcomes.

APPROACHES:

- » Develop improved and novel tools to better understand and identify factors that influence susceptibility to and outcomes of infectious and immune-mediated diseases.
- » Identify and validate biomarkers that improve health outcomes by guiding earlier diagnosis.
- » Investigate potential differences in infectious and immune-mediated disease biomarkers across all populations (e.g., sex, age, geographic region).
- » Advance biomarker discovery for latent infections and for prediction of microbe reactivation.
- » Identify and validate biological signatures of infectious and immune-mediated disease from relevant medical specimen types, including saliva, sweat, breath, tears, and mucosal lesions.

ADVANCED DIAGNOSTIC TECHNOLOGIES

Advanced diagnostic technologies encompass a range of innovative tools designed to enhance the detection and management of infectious and immune-mediated diseases. These tools include pathogen specific multiplex, as well as microbe-agnostic detection platforms that can identify multiple microbes simultaneously with minimal information about the causative agent, high-throughput and low-sample requirement platforms that enable rapid and efficient processing of sparse samples, and point-of-care (POC) and over the counter (OTC) diagnostics that provide immediate results at the healthcare provider's office or in one's home. Additionally, improving sensitivity of detection for low-abundance molecules (e.g., peptides, proteins, nucleic acids) may allow for increased accuracy and reliability of existing and novel diagnostic platforms. These advancements are critical for timely and accurate diagnosis, including in resource-limited regions.

APPROACHES:

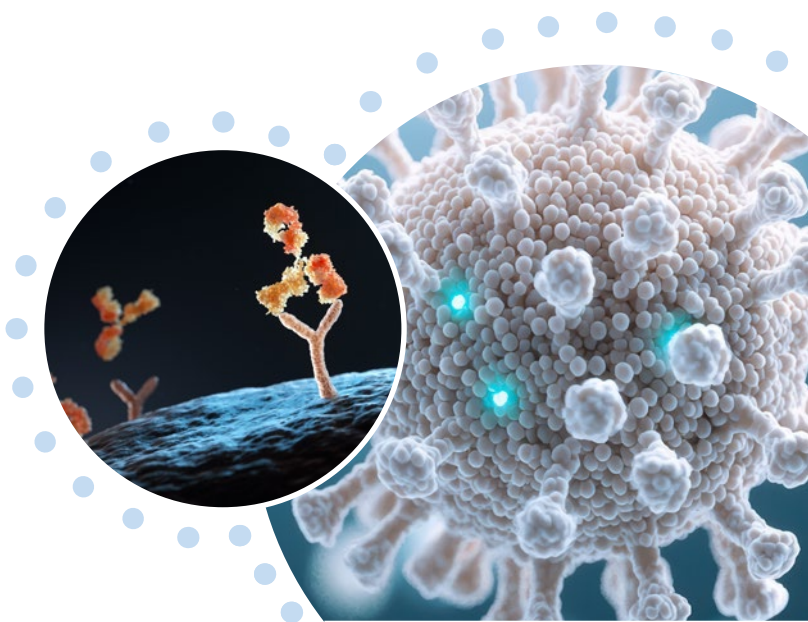
- » Advance pathogen-specific multiplex and microbe-agnostic detection platforms that will provide fast, reliable, and highly sensitive results.
- » Expedite development and validation of serological, cellular, and target tissue screening assay technologies.
- » Develop reagents for high-throughput, low-sample-requirement detection for infectious and immune-mediated diseases.
- » Advance development of detection technologies for more specific and sensitive protein, peptide, nucleic acid, and toxin identification that enable characterization of infection and immune-mediated diseases in the host.
- » Support portable, accurate, and affordable POC and OTC rapid diagnostics development.
- » Optimize POC and OTC diagnostics for vulnerable populations, including rural and resource-limited communities, through implementation research.

DIAGNOSTIC, PROGNOSTIC, AND MONITORING STRATEGIES

The development of diagnostic, prognostic, and monitoring strategies for infectious and immune-mediated diseases enables early detection, accurate prediction of progression, and effective disease management. These strategies can improve health outcomes, reduce healthcare costs, and enhance the quality of life for individuals affected by disease.

APPROACHES:

- » Establish non-invasive and minimally invasive sampling and diagnostic, prognostic, and disease monitoring strategies, including imaging technologies and state-of-the-art medical wearables.
- » Develop predictive risk models, including AI/ML approaches, to identify disease risk and improve diagnostic prediction, accuracy, speed, and efficiency.
- » Advance approaches for at-home use and longitudinal assessment of disease progression, flares, and quiescence.



THE DALE AND BETTY BUMPERS VACCINE RESEARCH CENTER

The intramural NIAID Vaccine Research Center's (VRC) mission is to discover and develop novel vaccines and biologics targeting infectious diseases of public health importance. Established by Executive Order in 1997 and opened for research in 2000, the VRC's original mission was centered on the development of a vaccine against HIV and acquired immune deficiency syndrome (AIDS). Over the past two decades, the VRC portfolio has expanded to include many microbes with major research programs dedicated to HIV, coronaviruses, influenza, malaria, and infectious disease outbreak response. The VRC applies scientific and technological innovation to design, develop, manufacture, and evaluate investigational vaccines and antibody-based products. Through a translational research infrastructure, the VRC advances scientific discovery into practical and accessible public health interventions.



- » Establish new and leverage existing longitudinal cohorts to study natural history, prevention, and response to therapy across infectious and immune-mediated diseases.
- » Advance development of rapid diagnostics that aid clinical decision making, including those that provide actionable phenotypic resistance information and determine drug sensitivity.

Objective 2.2: Develop and evaluate prevention strategies for infectious and immune-mediated diseases.

PREVENTION STRATEGIES FOR INFECTIOUS DISEASES

Development of a comprehensive portfolio of infectious disease prevention strategies is critical to reduce morbidity and mortality rates in the U.S. and worldwide. Preventative medical countermeasures, including vaccines, monoclonal antibodies, and other alternative

prevention methods, play a vital role in protecting individuals and communities from infectious diseases. NIAID support for research and development of a broad range of preventative strategies is critical to protecting the health of all Americans.

APPROACHES:

- » Develop and evaluate prevention strategies, including candidates that leverage beneficial microbiome functions, modulate the immune system, or target pathogen vectors or reservoirs.
- » Advance strategies to interrupt vector-borne disease transmission through the development of vector-targeted interventions.
- » Accelerate the development and validation of protective antigens, including by using de novo protein design tools and technologies.
- » Establish and accelerate safe and ethical human challenge models to facilitate development of prevention strategies.
- » Advance delivery approaches for prevention candidates, including mucosal delivery, new biomaterials, and novel formulations, to improve safety, efficacy, and durability.

- » Improve current vaccine manufacturing platforms for scale-up, alternative delivery, cost reduction, and storage requirements.
- » Optimize strategies for implementation of new and existing prevention methods in all populations, including transplant recipients and other immunocompromised individuals.

ADJUVANT DISCOVERY AND DEVELOPMENT

Adjuvant development involves identifying and creating substances that can enhance the body's protective immune response when added to vaccines. NIAID aims to expand upon the existing versatile toolbox of adjuvants that can be paired with different vaccine antigens and platforms to improve the efficacy and durability of vaccines. By advancing adjuvant research, scientists can develop safer, more effective, and more durable immunizations to protect against a wide range of infectious diseases.

- » Advance the discovery, comparison, characterization, and clinical testing of novel adjuvants and adjuvant combinations to enhance vaccine safety, efficacy, and durability.
- » Define mechanisms of action and immunomodulatory profiles of current and novel adjuvants.
- » Identify and evaluate adjuvants that facilitate the delivery of mucosal vaccines.
- » Increase availability of novel adjuvants and metadata on candidate adjuvants to the broader scientific community.

PREVENTION STRATEGIES FOR IMMUNE-MEDIATED DISEASES

Advancing prevention strategies for immune-mediated diseases is necessary to combat their rising incidence. In addition, these diseases often necessitate long-term management that significantly impacts quality of life and leads to increased healthcare costs, further emphasizing the importance of preventing disease onset. Effective prevention strategies, such as immune tolerance-inducing strategies, lifestyle interventions, and environmental modifications, can help reduce disease incidence, burden, and societal costs.

APPROACHES:

- » Leverage advances in foundational immunology, including understanding of the microbiome, to develop targeted immunomodulatory interventions that prevent the development and progression of immune-mediated diseases.
- » Investigate the impacts of early life exposures, including dietary introduction of allergenic foods, on the prevention and development of food allergies.
- » Develop and conduct clinical trials to evaluate prevention strategies for immune-mediated diseases, including complex and heterogeneous autoimmune diseases.
- » Investigate when and how exposures, including cancer immunotherapy, trigger immune-related adverse events.



Objective 2.3: Advance the development of HIV prevention strategies.

EPIDEMIOLOGY OF HIV

Evaluating the epidemiology of HIV helps identify populations at greatest risk, patterns of transmission, and emerging trends in infection. This information guides biomedical research by informing the design of preventative and therapeutic interventions. NIAID is committed to advancing this foundational understanding to support the development of HIV prevention strategies.

APPROACHES:

- » Advance epidemiologic knowledge of all aspects of the HIV epidemic in the U.S.
- » Identify individuals and populations who are more likely to acquire or transmit HIV and tailor prevention methods to preempt new HIV outbreaks.
- » Characterize host and viral factors contributing to HIV incidence rates and integrate this knowledge into the design of clinical trials and implementation research to ensure research findings are relevant to all individuals.
- » Identify causal pathways and mechanisms of immune dysfunction in people living with HIV (PLWH), such as HIV-induced inflammation, that lead to higher rates and earlier onset of non-infectious comorbidities.

PRE-EXPOSURE AND POST-EXPOSURE PROPHYLAXIS

Pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP) are essential first-line strategies to prevent HIV acquisition, with ongoing research focused on developing new and longer-acting formulations. Continued innovation in PrEP and PEP, including expanding implementation research, is vital to further reduce transmission rates and support the goal of an HIV-free generation.

APPROACHES:

- » Develop ultra-long-acting and next generation PrEP and PEP formulations, including single-dose and on-demand options that provide at least seven days of protection.
- » Assess preferences, uptake, and adherence to various PrEP delivery methods in populations most affected by HIV using implementation studies to guide effective approaches.
- » Examine PEP as a bridge to improved PrEP adherence.
- » Evaluate the safety and efficacy of HIV prevention strategies in children and women, including pregnant and lactating women.
- » Conduct clinical research to optimize postnatal prophylaxis strategies in infants at high risk of HIV acquisition.

PrEP vs. PEP	
PrEP Pre-exposure prophylaxis (PrEP) is taken BEFORE a potential exposure to HIV to prevent acquisition.	PEP Post-exposure prophylaxis (PEP) is taken AFTER a potential exposure to HIV to prevent acquisition.

MULTIPURPOSE PREVENTION TECHNOLOGIES

Multipurpose prevention technologies (MPTs) are innovative products designed to meet multiple reproductive health needs at the same time, such as preventing HIV, unintended pregnancies, and sexually transmitted infections (STIs). MPTs play a crucial role in HIV prevention by offering a comprehensive approach to reproductive health that enhances adherence, thus increasing overall effectiveness in reducing HIV transmission rates. MPTs are a crucial prevention option particularly for women from populations with a high incidence of HIV.

APPROACHES:

- » Identify community-driven priorities for MPT disease targets.
- » Enhance understanding of the overlapping pathology of HIV and STIs to guide MPT development, including potential effects on the healthy microbiome.
- » Identify social and behavioral factors to inform the design of implementation studies and enhance uptake of and adherence to MPTs in PLWH.
- » Collaborate with other NIH ICOs, as well as academia, industry, and community partners, to advance MPT development and clinical trials for populations most affected by HIV and STIs.

ENDING THE HIV EPIDEMIC

The Ending the HIV Epidemic in the U.S. (EHE) initiative is a USG-wide plan that aspires to end or significantly reduce the HIV epidemic in the U.S. by 2030 through targeted interventions and scientific innovation. NIAID-supported research is critical to achieving the goals of the EHE by advancing the science needed to understand, prevent, and treat HIV. In support of the EHE initiative, NIAID is committed to basic, translational, and clinical HIV research focused on long-acting prevention strategies and novel antiviral therapies. Further, NIAID is increasing its focus on implementation research to ensure these innovations reach populations most affected by HIV in the U.S.



HIV VACCINE AND IMMUNE-BASED PREVENTION STRATEGIES

The development of immune-based preventative interventions represents a promising approach to preventing new HIV infections. These interventions include vaccines, antibody-based approaches such as broadly neutralizing antibodies (bNAbs), and other strategies that bolster protective immune responses. Immune-based prevention strategies augment the immune system to recognize and block the virus or rapidly control infection before it becomes established, with the potential to provide protection against diverse HIV strains. NIAID continues to support the advancement of a range of immune-based and complementary HIV prevention strategies as part of a comprehensive effort to reduce HIV acquisition.

APPROACHES:

- » Identify effective anti-HIV immune responses to inform and advance the design, development, and delivery of prophylactic vaccines for broad and durable protection against HIV acquisition.
- » Design and develop HIV vaccine candidates, formulations (e.g., adjuvants), dosing strategies, and administration methodologies to achieve broad and durable protection.
- » Conduct clinical research to assess the safety, acceptability, and efficacy of HIV vaccine candidates to expedite prevention efforts.
- » Advance and assess next generation immune-based prevention strategies, including engineered antibodies and

vectored immunoprophylaxis.

- » Evaluate the safety, efficacy, and effectiveness of bNAb strategies for HIV prevention.
- » Conduct implementation research to assess strategies to optimize uptake, adherence, and access to immune-based HIV prevention strategies across multiple populations.

PREVENTION OF HIV-ASSOCIATED CO-INFECTIONS AND COMORBIDITIES

HIV-associated co-infections and comorbidities are common among PLWH and can significantly impact their health and overall quality of life. Co-infections occur when PLWH are simultaneously affected by other infectious diseases, such as tuberculosis (TB), hepatitis, or herpes simplex virus (HSV) infections, which can accelerate HIV disease progression and complicate treatment. In addition to co-infections, PLWH often experience comorbidities including cardiovascular disease, diabetes, or certain cancers that may be related to long-term HIV infection and treatment. Both HIV-associated co-infections and comorbidities pose significant public health challenges and remain a major research priority at NIAID.

APPROACHES:

- » Enhance understanding of the pathogenesis, immunology, and transmission of co-infections and comorbidities, including how these processes differ by HIV status, to improve prevention.
- » Develop strategies to prevent onset and recurrence of co-infections and comorbidities in PLWH.
- » Improve modalities to enhance vaccination responses among those with immune suppression, including PLWH.
- » Collaborate with relevant NIH ICOs to advance prevention strategies for HIV co-infections and comorbidities.

Community Engagement and Implementation Science

Spanning the Prevention and Treatment of Infectious and Immune-Mediated Diseases

Advancements in diagnostics, prevention, and treatment for infectious and immune-mediated diseases are often slow to reach the communities most affected by these conditions. To bridge this gap, NIAID will prioritize community engagement and implementation science, with a particular focus on preventing diseases. These efforts will help ensure that scientific breakthroughs are accessible, relevant, and impactful for all populations, especially those at greatest risk.

COMMUNITY ENGAGEMENT: BUILDING TRUST AND RELEVANCE

NIAID is committed to collaborating with a range of partners—including community groups, healthcare organizations, industry, clinical laboratories, and advocacy groups—to ensure that new strategies address the specific needs of affected communities.

Community engagement is vital to:

- » **Build trust and respect** in local communities by partnering with health departments and multilateral organizations to address local research priorities.
- » **Promote Good Participatory Practices** by fostering trust and respect, leading to broader implementation and greater impact.
- » **Empower communities** to have a voice in setting research priorities, designing and conducting clinical studies, and disseminating research results.
- » **Encourage participation in clinical research** through specific outreach, ensuring that findings are relevant and applicable to those most affected by diseases.
- » **Address legal, ethical, and regulatory barriers** to include underrepresented groups, such as pregnant women, in research on HIV and its associated co-infections and comorbidities.

IMPLEMENTATION SCIENCE: BRIDGING RESEARCH AND REAL-WORLD IMPACT

Translating research findings into practical applications is critical for delivering novel approaches to those most in need.

Implementation science is vital to:

- » **Promote interdisciplinary collaboration** from the outset of efficacy studies, increasing the success of prevention and treatment programs.
- » **Ensure optimal implementation** of new and existing interventions across the lifespan and in all populations, including pregnant women.
- » **Accelerate outreach and adoption** of new advances through programs like EHE, addressing challenges in prevention, treatment, and care.
- » **Reduce delays** in delivering new advances by identifying and overcoming barriers to implementation, especially for those most in need.
- » **End the HIV epidemic** in the United States.

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RESEARCH GOAL 3

Advance and apply foundational knowledge to develop and evaluate treatment and cure strategies for infectious and immune-mediated diseases.

NIAID research spans the continuum from basic discovery to clinical application, focusing on infectious and immune-mediated diseases. By supporting studies that build on foundational insights into immune mechanisms, microbe biology, and microbe-host interactions, the Institute seeks to advance and rigorously evaluate innovative treatment and cure strategies. Through multidisciplinary collaboration and commitment to scientific excellence, NIAID aims to accelerate the translation of basic research into effective therapies, ultimately improving health outcomes and quality of life for individuals affected by these diseases.



Objective 3.1: Advance existing and novel treatment strategies for infectious and immune-mediated diseases.

THERAPEUTIC DISCOVERY AND DEVELOPMENT

Advancing therapeutic strategies for infectious diseases, including HIV, requires a robust pipeline of innovative interventions to prevent and treat infections and their complications. This includes identifying and optimizing promising therapeutic candidates and advancing them through preclinical and clinical studies. These efforts aim to expand therapeutic options, address unmet medical needs, and improve treatment outcomes across all populations, including those affected by co-infections and other comorbidities.

APPROACHES:

- » Develop, validate, and utilize innovative discovery platforms, including AI/ML, novel assay technologies, and *in vitro* and *in silico* screening tools, to identify and optimize therapeutic candidates for infectious diseases.
- » Advance a broad pipeline of therapeutics for infectious diseases, including small molecules, antibodies, therapeutic vaccines, and antimicrobials.
- » Explore and evaluate non-traditional therapeutic modalities, such as microbiome-based, gene, phage, host-directed, and cellular therapies.
- » Develop immune-based therapies, including human antibodies, to strengthen host defenses against pathogens.

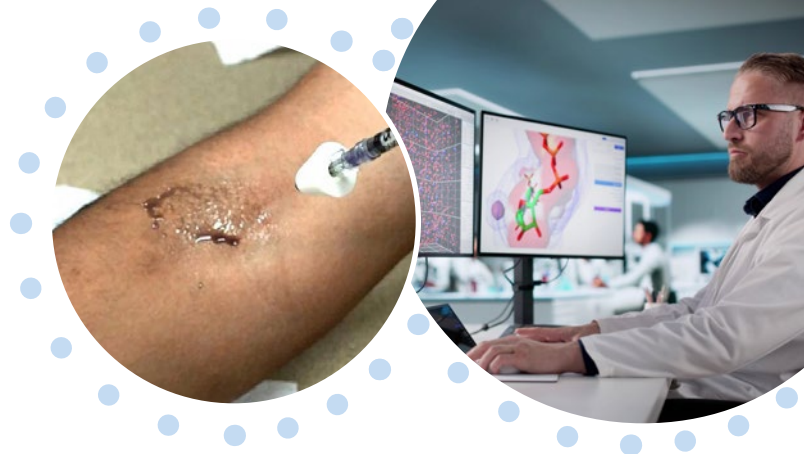
- » Develop effective treatment formulations and drug delivery strategies, including those that are ultra-long-acting and age-appropriate, to improve adherence, continuity of care, and access across adult and pediatric populations.
- » Advance therapeutic strategies for HIV-associated co-infections and comorbidities, including approaches that address overlapping disease burden, drug interactions, and the needs of disproportionately impacted populations.

THERAPEUTIC STRATEGIES FOR IMMUNE-MEDIATED DISEASES

Many immune-mediated diseases are chronic and require long-term treatments to manage symptoms, prevent progression, and improve quality of life. Available options include oral and inhaled medications, immunotherapy, vaccines, biologics, and anti-inflammatory drugs. However, these treatments often come with negative side effects or lose effectiveness over time. Therefore, it is crucial to continue to improve the available therapies to enhance the well-being of individuals living with these disorders.

APPROACHES:

- » Advance and evaluate novel therapeutic approaches for immune-mediated diseases, including small molecules, gene and cellular therapies, vaccines, hematopoietic stem cell transplantation, chimeric antigen receptor T-cell (CAR-T) therapies, and improved allergen immunotherapies.



- » Develop personalized and potentially curative strategies that restore immune tolerance and target human-specific immune mechanisms across disease stages and populations.
- » Identify mechanisms of action and assess the immunoregulatory and immunoinhibitory properties of existing and emerging therapies and adjuvants to inform more effective treatment and prevention strategies.
- » Conduct inclusive clinical trials to evaluate treatment and prevention approaches, improve long-term outcomes, and address the needs of populations disproportionately affected by immune-mediated diseases.

DRUG REPURPOSING

Drug repurposing involves identifying new therapeutic uses for existing drugs, which can significantly accelerate the availability of treatments for both infectious and immune-mediated diseases. This approach also utilizes existing data on safety and efficacy to reduce the time and cost involved in bringing useful therapies to people. By focusing on drug repurposing, NIAID aims to expand treatment options in response to existing and emerging health threats.

IMMUNE TOLERANCE NETWORK

The Immune Tolerance Network (ITN) is a collaborative extramural research initiative largely funded and administered by NIAID. The ITN includes basic scientists and clinical investigators who conduct clinical research to evaluate the safety and efficacy of methods that can induce the immune system to tolerate certain foreign antigens or re-induce tolerance to self to treat immune-mediated diseases. The ITN addresses many immune-mediated diseases, including autoimmune diseases like type 1 diabetes and multiple sclerosis, allergic diseases like asthma and food allergies, and other areas including immune responses and organ transplantation.

APPROACHES:

- » Accelerate the identification and evaluation of repurposed drugs with potential efficacy against infectious diseases through targeted preclinical and clinical studies.
- » Expand collaborative research initiatives to assess the safety and efficacy of repurposed drugs in the management of immune-mediated diseases.
- » Develop AI/ML models to guide drug repurposing for infectious and immune-mediated diseases.

ANTIMICROBIAL RESISTANCE

Many patients will have suboptimal outcomes on current therapies that include antibiotics, antivirals, antifungals, and antiparasitics. This antimicrobial resistance (AMR) is a significant public health problem in the U.S. and around the world, especially in healthcare facilities and in people with weakened immune systems. To address this growing problem, NIAID seeks to understand resistance to treatment in both patients and microbes, and to advance new antimicrobials, vaccines, and novel therapeutics, such as bacteriophages, microbiome therapies, and host-directed therapies. These novel approaches will expand treatment options for patients for whom currently available therapies are ineffective.

APPROACHES:

- » Incorporate a patient-centered perspective in NIAID's AMR strategy, including by ensuring that a comprehensive approach prioritizes interventions that improve real-world patient outcomes.
- » Identify novel traditional (e.g., small molecules) and non-traditional (e.g., phage, microbiome, and host-directed) therapeutics for infectious agents with resistance.
- » Design therapeutics that promote host-mediated elimination of bacterial and fungal microbes and toxins.
- » Leverage advanced technologies, including AI/ML and *in silico* screening, to identify targets to aid development of new therapies and investigate potential compounds for combatting AMR.
- » Support preclinical and clinical studies to comprehensively assess optimal dosing and duration, as well as combinations of approved therapies, to enhance safety, efficacy, ease of treatment, and improve patient outcomes.

PATIENT-CENTERED OUTCOMES IN AMR

Most Americans who die from infections do not do so because of antibiotic-resistant bacteria. A large issue is that most infection-related deaths occur despite the availability of drugs that are biologically active against microbes in vitro, suggesting that factors such as weakened patient immune systems or inadequate diagnoses play a larger role. A comprehensive AMR strategy should not just focus on identifying agents with in vitro activity but should focus on evaluating strategies that improve patient outcomes in real-world settings, including those that consider the patient's immune status, side effects of treatments, and the use of supportive strategies such as steroid or microbiome interventions. Focusing on patient-centered outcomes could have a greater impact on reducing deaths from infections than simply developing new antibiotics alone.



THERAPEUTICS FOR RADIATION AND CHEMICAL INJURIES

NIAID, in coordination with the NIH Office of the Director, supports research and development of therapeutic strategies against mass casualty public health emergencies involving exposure to radiation or highly toxic chemicals. NIAID continues to support the discovery, development, and advancement of therapeutics and tools to diagnose and treat the immediate or long-term injuries caused by radiation or chemical exposure.

APPROACHES:

- » Develop devices to detect validated biomarkers as predictors of radiation-induced injuries for use as triage tools in radiological or nuclear emergencies.
- » Develop novel and repurposed products with demonstrated efficacy for radiation- or chemical-induced injuries.
- » Develop evidence to support regulatory review of products with multi-utility across different types of injuries (e.g., radiation, chemical, thermal burn, multi-tissue and organ trauma).
- » Identify sex- and age-related differences in response to radiation and chemical exposures.
- » Create effective treatments to address radiation or chemical threats for distinct populations, including in utero, neonates, pregnant and lactating women, and older adults.

Objective 3.2: Advance novel therapeutic and curative approaches for HIV.

BROADLY NEUTRALIZING ANTIBODIES

Broadly neutralizing antibodies (bNAbs) are being explored as innovative treatment and curative strategies for PLWH. By targeting multiple HIV variants, bNAbs may help suppress viral replication, enhance immune responses, and potentially reduce the need for lifelong antiretroviral therapy. Ongoing research is focused on optimizing bNAb combinations and delivery strategies to improve treatment outcomes and pave the way toward durable HIV remission. NIAID aims to advance potent, scalable bNAb therapies and delivery strategies that improve access across populations.

APPROACHES:

- » Discover and evaluate novel and more potent bNAbs targeting known and new epitopes.
- » Evaluate the level of pre-existing resistance to bNAb neutralization in currently circulating HIV strains.
- » Examine the efficacy and effectiveness of combination bNAb strategies for HIV treatment and cure.
- » Create cost-effective manufacturing and delivery methods for antibody-based modalities.
- » Explore delivery approaches, combinations, and long-acting bNAb formulations for all populations.

ANTIRETROVIRAL THERAPY DRUG RESISTANCE

Antiretroviral therapy (ART) is an HIV treatment regimen that uses antiretroviral medications to suppress HIV and prevent disease progression. As ART became more widely used, resistance to ART similarly increased. NIAID and the HIV research community are investigating strategies to prevent ART resistance to ensure continuity of HIV treatment options.

APPROACHES:

- » Advance interventions that foster adherence to ART and reduce emergence of HIV resistance.
- » Assess strategies to prevent transmission of drug-resistant HIV variants.
- » Advance basic, descriptive, and clinical studies on HIV drug resistance, particularly in HIV-affected populations.
- » Develop improved assays for HIV resistance detection, including assays that are simple and easy to deploy in all settings.

STRATEGIES TO CURE HIV

Antiretroviral therapy (ART) allows PLWH who adhere to treatment regimens to live longer, healthier lives, but it does not cure HIV. NIAID will continue to invest in HIV cure research that is focused on two broad aims: sustained viral remission and viral eradication.

APPROACHES:

- » Characterize the biology of HIV reservoirs that persist despite ART.
- » Identify strategies to achieve sustained ART-free viral remission, and work toward eradication of viral reservoirs, including gene-therapy approaches.
- » Understand latency mechanisms, persistent antigen expression, immune evasion, reactivation and post-treatment control and rebound, and identify targets for cure strategies.





OPERATIONAL GOALS

NIAID is committed to being a responsible steward of public resources. To fulfill its mission, the Institute has established goals across three **Operational Goals**: 1) engaging with communities; 2) collecting and evaluating evidence to make informed decisions; and 3) promoting research transparency and accountability. Implementing these priorities will enable all NIAID staff to continue supporting the Institute's ability to operate and advance its mission of improving public health through research and innovation.

Goal 1: Engaging with Communities

Community engagement ensures that NIAID research is relevant to the needs and concerns of all populations it aims to serve, including those most affected by disease. Study participants, advocacy organizations, and local, state, and other community groups play an essential role in the research enterprise, offering perspectives that can shape and refine research. NIAID remains steadfast in its commitment to engaging with communities affected by diseases at all stages of research, from initial planning to disseminating findings. Ongoing engagement is vital for maintaining trust in the NIAID mission and ensuring that research outcomes benefit those who need them most.

APPROACHES:

- » Ensure participation of communities most affected by infectious or immune-mediated diseases at all research stages.
- » Clearly communicate NIAID research priorities and educate communities about NIAID operations, including the importance of research facilities such as high containment laboratories.
- » Engage with communities during public health emergencies and infectious disease outbreaks to advance research and foster access to clear, relevant information about prevention and treatment options.

Goal 2: Collecting and Evaluating Evidence to Make Informed Decisions

Evidence-informed decision-making at NIAID involves using reliable data from multiple sources to guide institutional and operational decisions across the Institute. This approach is supported by the development of real-time data tools that give leadership and staff access to financial, research, workforce, and other key trends as they emerge. Rather than making policy, NIAID generates and analyzes the evidence needed to inform its own priorities, planning, and management decisions, while also contributing data that may be useful to others. By creating and maintaining dashboards, reports, and analyses, NIAID promotes transparency and equips leadership with the evidence needed to make informed decisions across the Institute.

APPROACHES:

- » Foster a culture of transparency and accountability in decision-making by formally evaluating research programs and initiatives.
- » Routinely assess biomedical workforce and training needs to inform workforce development.
- » Integrate data systems across NIAID to improve data integrity and create real-time dashboards with forecasting capabilities to anticipate and fill research gaps.

Goal 3: Promoting Research Transparency and Accountability

Clear communication of what the evidence shows and what remains unknown is essential for transparency and maximizing the impact of NIAID-funded research. Timely and context-appropriate dissemination of study results is particularly vital during public health emergencies, when sharing accurate information can inform critical decisions and guide clinical practices. In addition to promoting transparency through open communication of research findings, NIAID also advances transparency and accountability in its funding decisions through implementation of the NIH Unified Funding Strategy. This approach moves NIAID beyond funding based on strict paylines to a system where scientific priorities, strategic goals, career stage, and geographic balance are prioritized.

APPROACHES:

- » Ensure NIAID-supported research informed by the NIH Unified Funding Strategy is made openly accessible to both public and scientific communities in a timely manner.
- » Collaborate with NIH to disseminate the impact of NIAID-funded research to a broad range of audiences, including researchers, healthcare professionals, news outlets, advocates, other federal agencies, Congress, and the public.
- » Ensure the timely release and regular update of relevant and context-appropriate research information to the public during public health emergencies and disease outbreaks.



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CAPACITY GOALS

To remain at the forefront of biomedical research, NIAID empowers its staff and the biomedical workforce by providing the necessary resources and infrastructure to conduct groundbreaking and vital research, drive innovation, and advance the Institute's mission. The Institute has established five **Capacity Goals**: 1) advancing the biomedical workforce; 2) providing research tools and services; 3) promoting data science and data sharing; 4) advancing networks and multicenter collaborations; and 5) supporting research facilities and infrastructure.

Goal 1: Advancing the Biomedical Workforce

Highly trained researchers bring unique perspectives and fresh ideas that provide NIAID with the expertise needed to achieve its mission. Many scientists use NIAID funding and resources to advance basic, translational, and clinical research that supports the health of all Americans. The Institute is dedicated to enhancing the quality of the biomedical research workforce by offering essential support for the research and career development of biomedical scientists, including robust training and mentoring programs. The Institute's efforts aim to empower promising scientists to pursue biomedical research careers.

APPROACHES:

Extramural Researchers

- » Develop and evaluate programs that provide research support for meritorious scientists at all career stages.
- » Achieve targeted success rates for key mentored and career transition awards by expanding and promoting NIAID mentorship and training programs.
- » Provide training and educational resources regarding NIH and NIAID policies and practices to ensure the success of researchers at all career stages.
- » Establish resources for workforce training in specialized topics related to infectious and immune-mediated disease research, including biosafety, biosecurity, and biocontainment.

Intramural Researchers

- » Support biomedical education, training, and mentoring of research fellows in the NIAID intramural research program.
- » Develop and implement training programs for physician-scientists to advance both basic and clinical research skills.
- » Promote recruitment and retention of meritorious talent at all career levels.
- » Provide training and resources for specialized topics, including the ethical use of emerging technologies like AI/ML and technology transfer policies, laws, and skills.

Goal 2: Providing Research Tools and Services

Sharing research tools with the biomedical community allows scientists to rapidly build on research findings. NIAID-supported researchers advance biomedical research by developing novel tools and resources, publishing their developments, and transitioning technologies for future development in collaboration with NIAID partners. These efforts are crucial for fostering research progress and advancing human health.

APPROACHES:

- » Enhance and expand shared and cost-effective research resources, including models, reagents, biorepositories, and common core facilities, to enable broad access to cutting-edge technologies across basic, translational, clinical, and interdisciplinary research.
- » Advance tools and infrastructure to rapidly coordinate and share real-world data within NIAID and with USG collaborators, including support for field studies in remote and resource-limited environments.



- » Develop, validate, and share NAMs and Standardized Organoid Modeling (SOMs) to improve experimental reproducibility and enable more accurate modeling of human biology.
- » Develop and disseminate advanced statistical and computational methods, including AI/ML, to improve the design, monitoring, and analysis of clinical studies.
- » Promote responsible governance of AI/ML in biomedical research by supporting standards for risk-based management, validation for intended use, transparent documentation of methods and limitations, privacy protections, reproducibility, and appropriate human oversight.
- » Develop resources, training programs, and partnerships to support successful commercialization and broader utilization of NIAID-supported technology.
- » Develop and disseminate patient-reported outcome tools to standardize the measurement of direct patient outcomes in clinical research and practice.

Goal 3: Promoting Data Science and Data Sharing

Gold standard data science and data sharing practices play a critical role in supporting biomedical research, including the replication and reproducibility of research findings. By enabling researchers to systematically collect, analyze, and interpret complex datasets, data science provides the tools necessary to accelerate discovery and rigorously validate findings, ensuring results can be reliably reproduced by others. These practices also underpin modern AI/ML approaches, which depend on well-structured, high-quality, and interoperable data for training, validation, and

generalization. Robust data sharing practices are central to this effort, as they ensure high-quality datasets and other resources are openly available to the research community. By championing NIH data sharing policies, NIAID fosters a research environment where reproducibility and replicability are prioritized, ultimately strengthening the integrity and impact of biomedical science.

APPROACHES:

Data Science

- » Develop an interoperable network of data, analytical tools, and services to promote data sharing, ensure privacy compliance, and democratize data access to support infectious and immune-mediated disease research.
- » Develop research, training, and workforce development programs to improve knowledge, skills, and use of data science approaches across career stages and disciplines.
- » Promote multidisciplinary use of data science for infectious and immune-mediated diseases research.
- » Ensure NIAID-funded research data assets adhere to data and repository management principles: FAIR, CARE, and TRUST, including by providing tools to assist researchers.
- » Streamline data integration and access by automating processes and using flexible, standardized data formats and protocols, making it easier to find, use, and analyze data from NIAID-funded studies.

Data Sharing

- » Ensure data derived from human research participants is shared appropriately, securely, ethically, in a timely manner, and in alignment with informed consent documentation.
- » Improve the frameworks, policies, and practices to promote sharing and use of data and computational methods.
- » Define, validate, and employ common data elements in NIAID-sponsored research to maximize their utility in data science applications.
- » Enhance and develop repositories of data, knowledge, and specimens and ensure proper collection, curation, analysis, reuse, and sharing of metadata.
- » Expand data repositories in support of NIH Data Management and Sharing and Genomic Data Sharing policies, while providing investigators with resources to create and follow effective data management and sharing plans.

DATA MANAGEMENT PRINCIPLES

FAIR	CARE	TRUST
F indable A ccessible I nteroperable R eusable	C ollective Benefit A uthority to Control R esponsibility E thics	T ransparency R esponsibility U ser Focus S ustainability T echnology

Goal 4: Advancing Networks and Multicenter Collaborations

NIAID operates and supports robust clinical trials, research networks, and multicenter collaborations that are integral to its overarching mission of understanding, treating, and preventing infectious and immune-mediated diseases. These networks not only foster collaborations, accelerate research, and translate scientific discoveries into practical strategies for public health, but also play a crucial role in enhancing the collection of real-world data. These networks strengthen the Institute's ability to address a wide spectrum of health challenges and ensure that research findings are applicable and impactful in everyday practice.

APPROACHES:

- » Enhance ethical and appropriate recruitment of participants from all populations for clinical trials and ensure communities from which participants will be recruited are involved throughout all stages of the clinical trial planning.
- » Enhance and develop collaborations and consortia that advance infectious and immune-mediated diseases research.
- » Facilitate collaborations and coordination of trials on priority areas of research, streamlining processes to improve research effectiveness and efficiency.
- » Enable clinical studies in collaboration with other NIH ICOs and communities in all geographic locations, including in rural communities.
- » Strengthen partnerships to foster the development and conduct of clinical research protocols by leveraging the NIH Clinical Center.

Goal 5: Supporting Research Facilities and Infrastructure

The cutting-edge research conducted within NIAID-supported laboratories requires facilities capable of meeting the evolving needs of research, technology, and staff. The Institute will continue to ensure existing facilities are safe and capable of supporting collaborative work across the U.S. Additionally, NIAID will continue to support and maintain intramural and extramural biocontainment facilities that are vital for ensuring the safety of researchers and the public while critical research is conducted on infectious microbes of public health concern.

APPROACHES:

- » Ensure facilities are appropriate and suitable for evolving research requirements, including safe and technologically appropriate research spaces.
- » Invest in biocontainment infrastructure to ensure biosafety and biosecurity of infectious disease research, while benchmarking sustainable best practices and incorporating collaborative oversight among maintenance staff, safety officials, and end users.



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APPENDICES

Appendix A: NIAID Statute of Authority and Legislative Timeline

STATUTE OF AUTHORITY

42 U.S.C. § 285f: Purpose of the Institute: The general purpose of the National Institute of Allergy and Infectious Diseases is the conduct and support of research, training, health information dissemination, and other programs with respect to allergic and immunologic diseases and disorders and infectious diseases, including tropical diseases.

LEGISLATIVE TIMELINE

1902: Rocky Mountain Laboratory and Biologics Control Laboratory were founded, later incorporated into the Institute.

1944: Public Health Service (PHS) Act: provided foundational legislative framework for establishing various health institutes at the NIH.

1948: PHS Act: established the National Microbiological Institute and incorporated the Rocky Mountain and Biologics Control laboratories into the new institute.

1955: Omnibus Medical Research Act: renamed the National Microbiological Institute to the National Institute of Allergy and Infectious Diseases (NIAID).

1985: a new statute defined the general purpose of NIAID, emphasizing research, training, health information dissemination, and other programs with respect to allergic and immunologic diseases and disorders and infectious diseases.

1988: Health Omnibus Programs Extension Act: granted additional authorities to NIAID, particularly focusing on AIDS research, information, education, and prevention.

1991: Terry Beirn Community Based AIDS Research Initiative Act: reauthorized the NIAID Community Programs for Clinical Research on AIDS.

1993: Preventive Health Amendments: required NIAID to conduct or support research and research training on tuberculosis; expanded the Institute's mandate to include tropical diseases.

2000: Children's Health Act and the Public Health Improvement Act: required the NIAID Director to both expand research activities concerning juvenile arthritis and related conditions and to establish programs of clinical research and training awards for sexually transmitted diseases, respectively.

2004: Project BioShield Act: authorized NIAID to provide grants for modernization and construction of research facilities and to increase the federal share of these projects.

2008: Tom Lantos and Henry J. Hyde United States Global Leadership Against HIV/AIDS, Tuberculosis, and Malaria Reauthorization Act: authorized NIAID to prioritize research on methods to prevent the transmission of HIV, particularly focusing on women.

2013: HIV Organ Policy Equity Act (HOPE Act): called for development and publication of research criteria and guidelines for the transplant of organs from one person living with HIV to another.

2022: PHS Act Amendment: authorized NIAID to support multidisciplinary research for the discovery and preclinical development of medical products for pathogens of pandemic potential.

Appendix B: Approach to Goal Setting and Strategic Planning Process

PRE-PLANNING

The NIAID Policy, Planning, and Evaluation (PPE) Branch of the Office of Strategic Planning, Initiative Development, and Analysis initiated the strategic planning process by developing a timeline and an initial outline based on current and known future goals.

FRAMEWORK DEVELOPMENT

NIAID leadership reviewed the draft outline and provided comments. PPE integrated leadership feedback to develop the initial strategic plan framework, which provided an overview of the future NIAID research, operational, and capacity goals.

PUBLIC INPUT

To receive feedback on the NIAID strategic plan framework from the public, PPE released a Request for Information (RFI) in the NIH Guide (NOT-AI-24-032). At a summer NIAID planning retreat, PPE facilitated discussions on the RFI responses with NIAID leadership.

DRAFTING

PPE established a strategic plan Working Group to draft the approaches within each goal area in the framework. PPE and the Working Group worked together in multiple review cycles to refine the full draft of the strategic plan.

FINALIZING AND PUBLISHING

PPE shared the full draft of the strategic plan with NIAID leadership prior to approval by the NIH Office of the Director. Following necessary approvals, the plan was released to the public.

IMPLEMENTATION

To assess progress toward the goals outlined in the strategic plan, NIAID will revisit it annually. Progress will be determined based on alignment of activities (e.g., research advances, funding opportunities, awards, workshops, working groups) with the plan.



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Appendix C: Disease-Specific Areas of Emphasis

The topics chosen for inclusion in the disease-specific appendix cover a **broad spectrum of disease areas within the NIAID portfolio**, though they do not encompass every funded area. Notably, HIV is excluded from the appendix as it is comprehensively addressed in the main body of the strategic plan. This approach ensures that **the appendix serves as a focused supplement to the primary document**, highlighting additional areas of interest without redundancy.

Infectious diseases and the microbes that cause them often intersect multiple categories; for instance, dengue virus is classified as a vector-borne disease (VBD) and a neglected tropical disease (NTD). To minimize duplication, each disease/microbe will be listed on a single appendix page. This provides clarity and avoids repetitive information, making it easier to navigate the complex landscape of the Institute's research goals.

In instances where NIAID or its collaborators have published strategic plans or supplemental articles that define approaches for specific microbes or viral families, such as herpes simplex virus (HSV) and Valley fever, the documents will be referenced in the appendix. This ensures continuity and alignment with established objectives. By leveraging existing strategic frameworks, the appendix can effectively complement the overarching NIAID plan, providing a cohesive and comprehensive overview of the Institute's research endeavors.

ALLERGIC DISEASES

Allergic diseases affect nearly one third of the U.S. population. These diseases include asthma, food allergies, eczema, rhinitis and rhinosinusitis, and drug allergies. Allergic diseases occur when the **immune system responds to harmless materials**, mostly proteins, that are part of our natural environment. Some people also have unpredictable allergic reactions to drugs, making treatment of other diseases particularly difficult.



~8% & ~11%

Of U.S. **children and adults**, respectively, have **food allergies**.



8%

Of U.S. **children and adults** are affected by **asthma**.



10-30%

Of U.S. **children** have or have had **eczema**.

NIAID Supports Allergic Disease Research to:

- » Better understand the causes and factors that lead to allergic diseases.
- » Identify and evaluate biomarkers and other tools to enable early diagnosis and intervention.
- » Innovate and enhance therapeutic strategies to prevent and treat allergic diseases.
- » Advance and evaluate therapeutic strategies that may offer a potential cure for allergic diseases.

TYPES OF ALLERGIC DISEASES

ASTHMA



Chronic respiratory disease in which the **airways become inflamed and narrowed**, leading to wheezing, coughing, and difficulty breathing.

FOOD AND DRUG ALLERGY



Condition where the immune system **reacts to certain foods and drugs**, leading to hives, swelling, difficulty breathing, and in severe cases, anaphylaxis.

ATOPIC DERMATITIS



Chronic skin condition, also known as eczema, that leads to **recurring itchy, inflamed, and red patches on the skin**, that can weep clear fluid when scratched.

RHINITIS AND RHINOSINUSITIS



Conditions that cause **inflammation and swelling in the upper airway**, leading to runny and stuffy nose, sneezing, headaches and coughing.

RESEARCH GOALS FOR SELECT DISEASES

ASTHMA



Examine the impact of **genetic, environmental** (e.g., infections, air quality, climate), **immune**, and **mucosal barrier factors** on asthma.



Develop and test **early life interventions** to prevent childhood asthma.

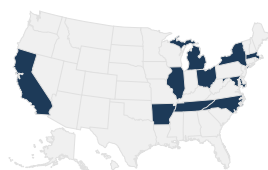


Characterize **asthma pathogenesis** to inform development of novel prevention and treatment strategies.



Evaluate current and new immune-targeting treatments to **improve therapies for severe asthma** and identify potential **asthma cures**.

ALLERGIC DISEASES



The **Consortium for Food Allergy Research (CoFAR)** is a collaborative network of Clinical Research Centers focused on improving the understanding, diagnosis, prevention, and treatment of food allergies.

10

CoFAR Clinical Research Centers
funded by NIAID in FY2026.

FOOD ALLERGY



Characterize the **mechanisms behind allergic sensitization** and **acute allergic reactions** to food.



Identify and test new **immune-mediated** and **non-immune-mediated interventions** to prevent food allergies.



Advance development of **diagnostics** and **epidemiological tools** to identify disease and evaluate treatment responses.



Evaluate **novel therapies** in patients with established food allergy focusing on those with **potential for a cure**.

DRUG ALLERGY



Advance understanding of **pathogenesis** and **factors influencing development** of common drug allergies.



Develop **predictive approaches** to both **prevent** drug allergies and **support** development of less allergenic drugs.



Simplify and **optimize approaches to diagnose drug allergies** to improve accuracy and reduce mislabeling patients.



Improve **management strategies** for severe allergic reactions to drugs.

ATOPIC DERMATITIS



Characterize the **genetic, immune, skin, and environmental factors**, including microbial skin infections or colonization, and **skin barrier functions** that contribute to the **early development** and **outgrowth of atopic dermatitis**.



Test **early interventions** to prevent atopic dermatitis in infants and **evaluate their impact on food** and respiratory allergies.



Develop and evaluate therapies aimed at **treating microbial skin infections** or **colonization** to address atopic dermatitis.



Evaluate the underlying **mechanisms of action** of **existing and new therapeutic modalities** to inform the development of improved **treatment and prevention strategies** for atopic dermatitis.

ALLERGIC RHINITIS AND RHINOSINUSITIS



Identify **phenotypes** and **endotypes** of rhinitis and rhinosinusitis based on factors including **clinical presentation, mucosal inflammation, allergic sensitization, response to infection, and response to treatment**.



Compare **existing therapies** (e.g., immunotherapy, antihistamines) to inform **treatment optimization**.



Design and evaluate novel **immune-modulating therapies**, including injections and other medications.

AUTOIMMUNE DISEASES

Autoimmune diseases occur when the **immune system attacks the body's own organs and tissues**. Though anyone can develop an autoimmune disease, many of these chronic conditions **affect populations differently**. Despite intensive research and advances toward understanding and treating autoimmunity, challenges remain for these incurable diseases, including understanding the immune mechanisms that drive autoimmunity.



≥8%

Of the U.S. population has an **autoimmune disease**.



~80%

Of those with an autoimmune disease are **women**.



>140

Autoimmune diseases have been identified.

NIAID Supports Autoimmune Disease Research to:

- » Expand the understanding of the immunological mechanisms driving and perpetuating autoimmunity.
- » Understand what factors influence a person's risk for and severity of autoimmune disease.
- » Advance diagnostic and prognostic tools to identify and monitor autoimmune diseases.
- » Develop immunomodulatory treatment and prevention strategies.

TYPES OF AUTOIMMUNE DISEASES

AUTOIMMUNE DISEASES OF THE NERVOUS SYSTEM

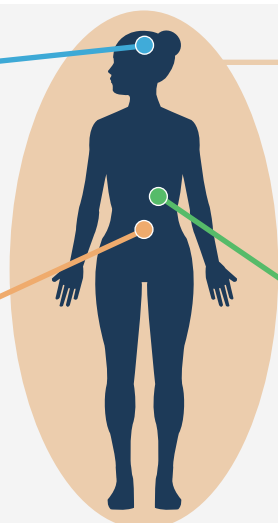


Conditions including **multiple sclerosis** and **myasthenia gravis** that occur when the immune system attacks the body's own neural tissues.

AUTOIMMUNE DISEASES OF THE GUT



Conditions where the immune system attacks gut tissues, leading to diseases like **celiac disease** and **inflammatory bowel diseases**.



SYSTEMIC AUTOIMMUNE DISEASE



Conditions like **systemic lupus erythematosus** and **rheumatoid arthritis** where the immune system attacks multiple tissues, leading to widespread inflammation.

ENDOCRINE AUTOIMMUNE DISEASES



Conditions like **type 1 diabetes** and **Hashimoto's thyroiditis**, where the immune system attacks hormone glands, preventing normal function.

RESEARCH GOALS FOR SELECT DISEASES

AUTOIMMUNE DISEASES OF THE NERVOUS SYSTEM

Autoimmunity can affect **any part of the nervous system**, including the **brain and spinal cord** (e.g., multiple sclerosis) and **neuromuscular junction** (e.g., myasthenia gravis). Many of these conditions affect women more than men.



Examine the **drivers** and **effector mechanisms** of neurologic autoimmune diseases.



Characterize the role of **novel** or **understudied immune cells** in neurological autoimmune disease.



Investigate how **microbial** and **infectious factors** impact immune drivers of neurologic autoimmunity.



Decipher the role of **poorly understood molecular mechanisms** in neurological autoimmunity pathogenesis.

AUTOIMMUNE DISEASES

The NIAID **Autoimmunity Centers of Excellence (ACE)** conduct collaborative basic and clinical research on autoimmune diseases. The ACE program enables close interaction between clinicians and basic researchers to accelerate the discovery, development, and translation of therapies for autoimmune diseases from the lab to use in the clinic.

5

ACE Cooperative Agreements
funded by NIAID in FY2026.

SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

SLE is the most common type of lupus and can cause widespread inflammation. Although SLE affects people of all backgrounds, **some populations are disproportionately affected and have worse outcomes.**



Characterize how the **molecular mechanisms** of SLE vary by **sex, race and ethnicity**, and **age**, and examine how these differences influence disease progression and treatment efficacy.



Examine **molecular variations** in SLE to enhance understanding of the disease and inform treatment development.



Conduct **SLE clinical trials** to evaluate novel therapies and uncover immunologic mechanisms of disease.



Leverage existing cohorts of lupus subjects to **refine our understanding** of infectious triggers and immune processes that lead to lupus.

TYPE 1 DIABETES (T1D)

T1D, caused by autoimmune attack of **pancreatic insulin-producing cells**, is fatal without lifelong insulin therapy and can cause **significant morbidity throughout life.**



Characterize the role of **innate immune responses** in triggering and perpetuating islet-specific autoimmunity.



Develop intervention strategies to **slow or stop the progression** of autoimmune attack of insulin-producing pancreatic cells.



Examine the impact of **infections**, particularly viral infections, on the **onset of T1D.**



Identify the **factors that influence the efficacy of immunomodulatory therapy** for prevention or treatment of T1D.

AUTOIMMUNE DISEASES OF THE GUT

Celiac disease and inflammatory bowel diseases (IBDs) cause **significant inflammation to the digestive system** and severely impact the quality of life of those living with these diseases. There are currently **no prevention or cure strategies** for these debilitating conditions.



Identify **genetic, immune, and microbial profiles** that **predict gluten intolerance** and the development of celiac disease.



Identify **environmental triggers** (e.g., diet, antimicrobials, air quality) involved in IBD onset, progression, and severity.



Autoimmune diseases are **chronic diseases that can impact almost every organ or tissue in the body.** NIAID leverages its expertise in human immunology to understand, prevent, and treat autoimmune diseases, while collaborating with other NIH institutes, centers, and offices to ensure a **robust and comprehensive approach** to autoimmune disease research.

FUNGAL INFECTIONS

Fungal diseases are infections caused by a **diverse group of organisms that include yeasts, molds, and mushrooms**. These diseases can affect various parts of the body, ranging from superficial skin infections like athlete's foot to more severe systemic infections such as histoplasmosis and candidiasis, particularly in people with compromised immune systems.



6.55M

Patients develop life-threatening fungal infections globally every year, of which **3.75 million do not survive**.



~20,000

Cases of **Valley fever** are reported every year in the U.S.

NIAID Supports Fungal Infection Research to:

- » Understand how fungi cause disease and develop antifungal resistance.
- » Determine how the immune system responds to fungal infections and why some people are more susceptible.
- » Improve existing and identify new ways to diagnose, treat, and prevent fungal infections.
- » Characterize mechanisms of antifungal resistance and examine methods to mitigate resistance.

TYPES OF FUNGI THAT CAUSE HUMAN DISEASE

<i>Aspergillus</i>	Common environmental mold that can be found in soil, decaying vegetation, and indoor air that can cause lung infections known as aspergillosis.
<i>Blastomyces</i>	Fungus that can be found in moist soil and decomposing material , such as wood and leaves ; spore inhalation can cause an infection with flu-like symptoms.
<i>Candida</i>	Normal yeast that can be found on the human body (mouth, gut, vagina); overgrowth can cause infections such as oral thrush and yeast infections.
<i>Cryptococcus</i>	Yeast that can be found in soil, bird droppings, and decaying wood that can cause severe lung and central nervous system disease (cryptococcosis).
<i>Coccidioides</i>	Fungus that can be found in arid soil regions including the southwestern U.S.; can cause Valley fever, which presents with flu-like symptoms.
<i>Pneumocystis</i>	Fungus that is spread through the air , from person to person; can cause pneumonia in people with weakened immune systems.

RESEARCH GOALS FOR SELECT DISEASES

ASPERGILLUS



Examine **human immune** and **non-immune mechanisms** that protect against *Aspergillus* infection.



Investigate **virulence mechanisms** of *Aspergillus* that promote human disease.



Advance **therapeutic strategies** to treat aspergillosis, particularly for **immunocompromised individuals**.

FUNGAL INFECTIONS

BLASTOMYCES AND HISTOPLASMA



Advance understanding of **human immune** and **non-immune mechanisms** that protect against *Blastomyces* and *Histoplasma* infections.



Identify **virulence factors** enabling transition to pathogenic yeast form.

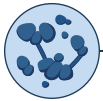


Advance novel strategies for **detection** and **treatment of infection** in low and under-resourced settings.

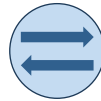
CANDIDA



Develop **personalized approaches** to assessing risk, predicting disease outcomes, and providing treatment for individuals who acquire *Candida* infection.



Determine the **fungal factors** that enable *Candida* species to cause mucosal and systemic candidiasis.



Identify the **factors that promote commensalism** of *Candida* species.



Examine how the **immune system protects** against *Candida* infection.



Investigate mechanisms of and methods to **mitigate antifungal resistance** in *Candida auris*.

CRYPTOCOCCUS



Advance vaccination approaches to **protect populations at higher risk**, including those with weakened immune systems and people living with HIV, against cryptococcal infections.



Characterize the **immune response** to cryptococcal infections in individuals with healthy immune systems.



Identify the **mechanisms** that enable some *Cryptococcus* species to **target the brain**.



Advance treatment strategies for **cryptococcal meningitis**, particularly in people living with HIV.

COCCIDIIOIDES



Advance **fundamental knowledge** to support development of a *Coccidioides* vaccine, including by:

- » Characterizing host immune **mechanisms of protection**.
- » Examining **microbe factors** that aid in infection, survival, and immune evasion.



Develop new therapeutics to treat **neuroinvasive coccidioidomycosis**.



For more information on **Valley fever** vaccine research, see the **NIAID Strategic Plan for Research to Develop a Valley fever Vaccine**.

PNEUMOCYSTIS



Develop **tractable genetic tools** and **culture conditions** for *in vitro* and *ex vivo* analyses.



Identify **fungal virulence factors** contributing to pneumocystis pneumonia.

INBORN ERRORS OF IMMUNITY

Inborn errors of immunity (IEI), also known as primary immunodeficiency disorders, are **disorders where a component of the immune system is missing or does not function properly**. This results in recurrent, unusual, and severe or life-threatening infections. Immune dysfunction in people with IEI also increases the risk of developing other immune-mediated diseases, such as autoimmunity, atopy/allergies, and malignancies.



>500

Types of IEIs have been characterized.



1 in 2,000

People in the U.S. have been **diagnosed with or suspected to have an IEI**.



40-80

Annual diagnoses of **Severe Combined Immunodeficiency (SCID)** in the U.S. and Canada.

NIAID Supports IEI Research to:

- » Pursue new discoveries about the causes and pathogenesis of IEIs.
- » Understand basic immune mechanisms and conduct immune profiling of IEIs.
- » Evaluate safety and efficacy of disease-modifying and tolerance strategies for these diseases.
- » Identify new treatment, prevention, and curative strategies for IEIs.

EXAMPLES OF INBORN ERRORS OF IMMUNITY

PRIMARY IMMUNOREGULATORY DISORDERS (PIRDs)



Genetic conditions that **disrupt immune tolerance**, causing excess inflammation, autoimmunity, and immune cell proliferation.

SEVERE COMBINED IMMUNODEFICIENCY (SCID)



Genetic disorder **diagnosed in infants** that **severely impairs immune function**, leading to vulnerability to infections and failure to thrive.

CHRONIC GRANULOMATOUS DISEASE (CGD)



Genetic disorder diagnosed in infants that **impairs the immune system's ability to fight certain infections**, leading to recurrent bacterial and fungal infections and formation of granulomas.

RESEARCH GOALS FOR SELECT DISEASES

PRIMARY IMMUNOREGULATORY DISORDERS (PIRDs)



Examine the **genetic basis** and other novel mechanisms of PIRDs.



Advance existing and develop **novel diagnostics** and **treatment strategies** for PIRDs.



Investigate the role of PIRDs on **development of other immunologic diseases** (e.g., autoimmunity, atopy).



Evaluate potential curative strategies for PIRDs, including **hematopoietic stem cell transplantation**.

INBORN ERRORS OF IMMUNITY

NIAID aims to improve IEI diagnosis, treatment, and prevention options and facilitate genetic counseling for IEI patients. **NIAID is home to the Primary Immune Deficiency Clinic**, which provides diagnoses and disease management recommendations for patients and their families.

>200

Conditions examined by the **Primary Immune Deficiency Clinic**.

SEVERE COMBINED IMMUNODEFICIENCY (SCID)



Leverage advanced technologies to examine **genetic mechanisms** and **immune dysfunction** in SCID patients.



Develop **optimal gene therapy strategies** that enhance immune function without long-term side effects.



Optimize diagnostic strategies to **rapidly identify SCID** in infants and enable early initiation of therapies.



Advance **hematopoietic cell transplantation** therapies for SCID to ameliorate disease outcomes.

CHRONIC GRANULOMATOUS DISEASE (CGD)



Examine **infectious disease pathology** in patients with CGD to identify potential targets for novel therapeutics.



Refine **genetic** and **cellular therapies** to improve immune function and prevent infection in CGD patients.



Identify and enhance strategies to prevent and treat **complications associated with CGD**.



Investigate long-term outcomes of **gene therapy** or **hematopoietic cell transplantation therapy** for CGD.

IEIs AND SUSCEPTIBILITY TO INFECTION



Expand understanding of **genetic variants** that increase susceptibility to and severity of infection.



Identify **pathogenic microbes**, including microbes that normally do not cause disease, in people with IEIs.



The **NIAID Centralized Sequencing Program** serves as a genomics resource for NIAID study participants. All NIAID study participants are eligible to receive **genome sequencing** and associated services, including **genetic counseling**.

GENERAL IEI RESEARCH GOALS



Characterize **disease** and **symptom progression** and understand the different presentations of disease pathogenesis.



Leverage **partnerships** and **existing data repositories** to develop novel diagnostics and treatments.



Facilitate partnerships to advance **curative transplant** and **gene therapy strategies** for IEIs.

NEGLECTED TROPICAL DISEASES

Neglected tropical diseases (NTDs) encompass a **range of infections prevalent in tropical regions**, primarily affecting impoverished populations. These diseases are considered “neglected” because they generally do not receive as much attention as other diseases. However, **NTDs take a tremendous toll on global health**, and although they are typically found in developing regions of the world, they can also be found in areas of the U.S.



1 billion

People globally are **affected by NTDs**.



179

Countries and territories reported **human NTD infection** in 2021.



120,000

Estimated global deaths annually due to NTDs.

NIAID Supports NTD Research to:

- » Characterize pathobiology of NTD-causing microbes.
- » Identify targets for potential new drugs and vaccines.
- » Develop and evaluate novel strategies to prevent and treat NTDs.
- » Support researchers and research infrastructure in countries where NTDs are endemic.
- » Develop strategies for interrupting transmission of NTDs by the insect vectors and intermediate host organisms responsible for transmission.

NEGLECTED TROPICAL DISEASES



NTD BY TYPE OF MICROBE



Bacteria

- » Buruli Ulcer
- » Leprosy
- » Trachoma
- » Yaws



Fungi

- » Chromoblastomycosis
- » Mycetoma
- » Sporotrichosis



Helminths

- » Cysticercosis
- » Guinea-worm disease
- » Echinococcosis
- » Food-borne trematodiasis
- » Lymphatic filariasis
- » Soil-transmitted helminthiasis
- » Schistosomiasis
- » River blindness



Parasites

- » Scabies
- » Tungiasis



Protozoa

- » Chagas' Disease
- » Leishmaniasis
- » Trypanosomiasis



Viruses

- » Rabies
- » Dengue
- » Chikungunya

NEGLECTED TROPICAL DISEASES

RESEARCH GOALS FOR NTDs

GENERAL APPROACH



Support a **One Health approach** to understanding, controlling, and preventing NTDs.



Characterize the **biology** and **molecular mechanisms** of parasite and helminth development to identify drug targets.



Collaborate with U.S. government partners to **identify novel approaches to vector control**.



Develop **point-of-care tests** for use in all settings to diagnose NTDs and support programs toward their **elimination**.



Advance development of **vaccines, treatments, and therapeutics** for NTDs and other parasitic diseases.



Develop and maintain **sample** and **data repositories** to support NTD research.

HELMINTHS



Identify **biomarkers for advanced disease states** associated with schistosomiasis infection.



Identify and develop novel **vaccines, drugs, and field-deployable diagnostics** for schistosomiasis.

PROTOZOA



Identify new **predictive biomarkers** for chronic Chagas' disease to **enable early intervention** and reduce complications.



Develop **novel diagnostics** to enable detection of infection by any *Leishmania* species that causes disease.



Investigate whether **oral antifungal agents are effective** against the most common *Leishmania* species.



Improve **existing therapeutics** and develop **potential vaccines** against *Leishmania* species.



Advance **early detection** and **diagnosis tools** for all trypanosome infections.



Examine the **mechanisms of drug resistance to treatments and therapeutics** for trypanosomiasis.

VIRUSES



Improve **rabies vaccine strategies** that require **fewer doses** for pre- and post-exposure prophylaxis.



Identify **monoclonal antibodies** directed against the rabies virus that are affordable and have a long shelf life.



Advance development of **antiviral therapeutics** to treat rabies infections.



Develop or identify **therapeutic agents** to reduce the morbidity and mortality of severe dengue infection.

RESPIRATORY INFECTIONS

Respiratory infections cover an **array of infectious diseases that affect the respiratory system**, including the upper airway and the lungs. These infections can be chronic or acute and can significantly impact overall health. Respiratory infections require various treatments and preventative measures to manage a person's symptoms and improve their respiratory functions.



234,180

People died of respiratory infections in the U.S. in 2022.



51 million

Flu-related illnesses in the U.S. in 2025.



>80%

TB cases in the U.S. result from untreated latent TB infections.

NIAID Supports Respiratory Infection Research to:

- » Characterize transmission, biology, pathology, and immunology of viral respiratory diseases.
- » Advance diagnostic, prevention, therapeutic, and vaccination strategies for respiratory infections.
- » Identify strategies to address the needs of all Americans across the lifespan.

ROUTES OF TRANSMISSION OF RESPIRATORY INFECTIONS

DIRECT DEPOSITION

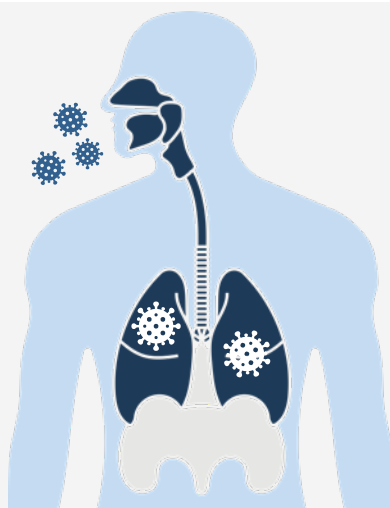


Contaminated particles from an infected person **travel a short distance through** the air and are transmitted through the eyes, nose, or mouth.

DIRECT CONTACT



Contaminated particles from an infected person are **transmitted via touch** and transferred to the eyes, nose, or mouth.



INDIRECT CONTACT



Contaminated particles are **transferred to a surface**, and **when the surface is touched**, are transmitted to the eyes, nose, or mouth.

INHALATION



Contaminated air particles are **transmitted when breathed in** through the nose or mouth, transferring through the respiratory tract.

RESEARCH GOALS FOR SELECT DISEASES

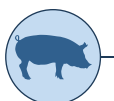
INFLUENZA VIRUSES



Characterize **mechanisms of immune imprinting** to inform development of improved vaccines.



Develop and test **vaccines** and **monoclonal antibodies** to protect against seasonal and emerging strains.



Advance **animal challenge models** for highly pathogenic strains of avian influenza.



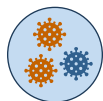
Develop and evaluate candidates for a **universal flu vaccine**.

RESPIRATORY INFECTIONS

CORONAVIRUSES



Identify **human immune mechanisms** that prevent coronavirus infections.



Characterize the **mechanisms driving the emergence of variants** and identify strategies to mitigate these processes.



Advance development of antivirals by identifying **novel small molecules** and **biotherapeutics** that block viral targets.



Develop and test **next generation coronavirus vaccines** that can limit viral infection and transmission and provide broad and durable protection.

RESPIRATORY SYNCYTIAL VIRUS (RSV)



Examine **pathogenesis of** and **adaptive immune responses to RSV** to inform development of treatment and prevention strategies.



Identify strategies to **prevent** and **treat concurrent infections** with RSV and other respiratory viruses.



Develop a vaccine **safe for infants** and **young children** that promotes long-lasting immunity from RSV infection.



Optimize vaccine composition and regimens to **enhance vaccine effectiveness**, in part by examining immunity elicited by existing vaccines.

TUBERCULOSIS (TB)



Enhance understanding of **drivers of TB transmission, asymptomatic TB, and host responses** related to TB progression.



Develop and improve accurate **rapid diagnostics**, including the discovery and validation of novel TB biomarkers.



Support development of preventative vaccine candidates by identifying **immune correlates of protection**.



For additional information related to NIAID-supported TB research, see the **NIAID Strategic Plan for Tuberculosis Research**.



Advance TB prevention and treatment research through **global collaboration** and **community engagement**.

ADDITIONAL APPROACHES



Characterize **transmission mechanisms, biology, pathology, and immunology** of respiratory infections.



Advance development of **broadly protective strategies** to prevent respiratory infections.



Develop strategies to **prevent emergence of microbial resistance**, particularly in vulnerable populations.



Examine **antibacterial resistance mechanisms** to inform development of treatments that mitigate resistance.

SEXUALLY TRANSMITTED INFECTIONS

Sexually transmitted infections (STIs) are caused by **microbes transmitted from person to person through vaginal, oral, and anal sexual contact**. STIs are caused by bacteria, viruses, or parasites and can have a devastating impact on adults and infants. Infection with certain STIs can even increase a person's risk of developing cancer.



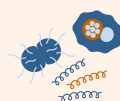
1 in 5

Estimated number of people in the U.S. **diagnosed with an STI** as of 2018.



3,941

Cases of congenital syphilis in 2024, an 82% increase since 2020.



2.2M

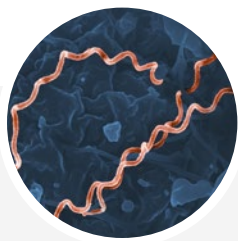
Cases of STIs reported in the U.S. in 2024.

NIAID Supports Sexually Transmitted Infection Research to:

- » Expand knowledge of STI epidemiology and disease progression.
- » Develop and evaluate diagnostic, preventative, and therapeutic approaches for STIs.
- » Address the disproportionate burden of STIs on specific populations.
- » Develop and evaluate interventions for sexual and reproductive health.

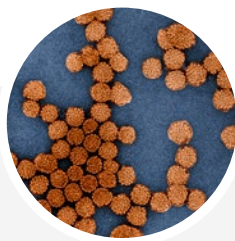
SCOPE OF NIAID STI RESEARCH

STI-CAUSING BACTERIA



- » *Chlamydia trachomatis*
- » *Neisseria gonorrhoeae*
- » *Mycoplasma genitalium*
- » *Treponema pallidum*

STI-CAUSING VIRUSES



- » Hepatitis viruses*
- » Herpes simplex viruses
- » HIV**
- » Human papillomavirus (HPV)

OTHER STI CONCERNS



- » Bacterial vaginosis
- » Cervicitis
- » Pelvic inflammatory disease
- » Trichomoniasis
- » Urethritis

*Hepatitis research is covered on the Viral Hepatitis appendix page.

**HIV research is covered in Research Goals 2 and 3 of the strategic plan.

RESEARCH GOALS FOR SELECT DISEASES

CHLAMYDIA



Evaluate **prophylactic strategies** in all populations, including **those most impacted by STIs** (e.g., women).



Develop and assess novel vaccines and vaccination strategies to **prevent chlamydia**, including during pregnancy.



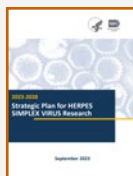
Characterize **immune responses to *Chlamydia trachomatis*** infection to inform development of improved vaccines and therapeutics.

SEXUALLY TRANSMITTED INFECTIONS

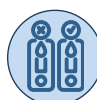
HERPES SIMPLEX VIRUSES

>50% of people in the U.S. between 14-49 years old **live with HSV-1**.

~12% of people in the U.S. **live with HSV-2**.



Herpes simplex virus 1 and 2 (HSV-1 and HSV-2, respectively) are common viral infections in the U.S., with severe cases causing life-threatening or long-term complications. There are currently no vaccine or cure strategies for HSV. For more detailed information on HSV research, see the [NIH Strategic Plan for HSV Research](#).



Develop accurate and convenient **diagnostic tests** for symptomatic and asymptomatic herpes infection.



Advance new technologies aimed at **curing HSV infection** through reducing or eliminating latent HSV.



Develop and evaluate vaccines that **protect against HSV infections**.



Develop therapeutic vaccines and novel antiviral strategies that **decrease outbreaks** and **shedding**.

SYPHILIS



Identify **novel targets associated with syphilis** to inform development of novel medical countermeasures.



Identify and evaluate **alternatives to benzathine penicillin G** for treatment of syphilis.



Evaluate prevention and treatment strategies to **address the rise in congenital syphilis**.



Develop **cutting-edge** and **user-friendly diagnostic technologies** for rapid and reliable syphilis diagnosis.

GONORRHEA



Characterize **cellular and molecular targets associated with gonorrhea** to inform vaccine development.



Evaluate treatments, including novel antibiotics, that **mitigate antimicrobial resistance** and **improve patient outcomes**.



Expand understanding of **antimicrobial resistance mechanisms** and identify strategies to address resistance.



Develop **rapid diagnostic technologies** for detecting infection and identifying antibiotic susceptibility.

ADDITIONAL APPROACHES



Characterize the **mechanisms of STI-related complications** and identify targets for prevention.



Examine **causes of bacterial vaginosis** and the role of the **vaginal microbiome** in infection and treatment.



Identify and evaluate **novel treatment strategies** for trichomoniasis that **prevent breakthrough infections**.



For additional information about the HHS-wide goals for STI research, see the [STI National Strategic Plan](#).



Conduct clinical trials that **include participants representative of at-risk populations**.

VECTOR-BORNE DISEASES, INCLUDING MALARIA

Vectors are organisms that **transmit microbes among humans** or **between animals and humans**. Many of these vectors are biting insects like mosquitoes and flies and biting arthropods like ticks and lice. Vector-borne diseases (VBDs) are **human illnesses caused by microbes transmitted by vectors**. Further, the allergic disease alpha-gal syndrome has been shown to be triggered by the bite of a tick as opposed to transmission of a microbe.



>1 million

Cases of VBDs reported in the U.S. between 2001 and 2023.



>700,000

Deaths every year globally attributed to VBDs.



610,000

Malaria deaths in 80 countries in 2024.

NIAID Supports Vector-Borne Disease Research to:

- » Understand the biology and epidemiology of disease-carrying vectors and reservoirs.
- » Examine the mechanisms by which vectors transmit microbes to humans.
- » Evaluate approaches designed to mitigate disease transmission.
- » Develop and evaluate diagnostic, preventative, and treatment approaches for diseases spread by vectors.

EXAMPLE VBDs BY TYPE OF VECTOR

MOSQUITOES



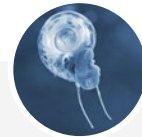
- » Chikungunya virus disease
- » Dengue fever*
- » Lymphatic filariasis
- » Malaria
- » West Nile fever
- » Yellow fever
- » Zika

TICKS



- » Alpha-gal syndrome
- » Babesiosis
- » Crimean-Congo hemorrhagic fever
- » Lyme disease
- » Powassan disease
- » Rocky Mountain spotted fever
- » Tickborne relapsing fever
- » Tularemia**

OTHER



- » Oropouche fever
- » Plague
- » Sandfly fever
- » Schistosomiasis*
- » Typhus
- » Tularemia**

*Disease research covered on Neglected Tropical Diseases page.
**Tularemia has multiple vectors including ticks and wild animals.

RESEARCH GOALS FOR SELECT DISEASES

VECTOR BIOLOGY AND MICROBIAL TRANSMISSION



Better understand how the **climate impacts vectors** and their ability to transmit microbes to humans.



Understand the **skin immune responses to vector bites** for vaccine development and insight into vector allergies.



Identify interventions to **elicit anti-vector immunity** to limit infection risk and reduce community transmission.



Investigate **vector-microbe interactions** that drive transmission to humans.



Use **vector salivary proteins** as a tool to assess risk of transmission or exposure to VBDs.



Facilitate partnerships to **develop vector control tools**, particularly in endemic regions.

VECTOR-BORNE DISEASES, INCLUDING MALARIA

TREATMENT AND PREVENTION OF VBDs



Expand the tools available for **preventing VBDs**, including pre- and post-exposure prophylaxis.



Develop **cost-effective, sensitive, and specific diagnostic tests** that can distinguish between related infections.



Develop and test **vaccines and therapeutic monoclonal antibodies** to prevent VBD infections.



Assess treatment strategies for **persistent symptoms** associated with VBDs.



Identify **immunologic correlates of protection** against VBD infection and vaccination.



Facilitate partnerships to identify causes of and strategies to prevent and treat VBDs.

MALARIA



Characterize the **pathogenesis, persistence, and clinical and public health management** of malaria.



Improve understanding of the **liver stage biology** of the malaria parasite, including the hypnozoite.



Develop long-acting oral or injectable antimalarials that provide **sustained protection** against malaria.



Develop **highly sensitive malaria diagnostics** capable of detecting low density infections.



Better understand the **molecular mechanisms of drug resistance** and continue to develop novel therapeutics.



Develop **vaccines, monoclonal antibodies, and immune prophylaxis** against malaria.

OTHER DISEASE-SPECIFIC APPROACHES



Understand the **causes of chronic illness** associated with Lyme disease and other infections.



Identify ***B. burgdorferi* antigens** that could be used in next generation Lyme disease vaccines.



Develop **genetic tools** to better enable research on tick-borne rickettsial infections.



Develop or identify therapeutic agents to **reduce the morbidity and mortality** of severe dengue infection.



Better understand the factors underlying the development of **alpha-gal syndrome**.



Utilize new approaches to develop **rapid point-of-care diagnostic tests** for Lyme disease.



Increase **availability of reagents** to advance research on tickborne relapsing fever.



Identify **tick-associated biomarkers** to assess risk of transmission of Rocky Mountain spotted fever.



Investigate the **pathology of persistent West Nile virus infection**, associated clinical outcomes, and treatment options.

ENTERIC INFECTIOUS DISEASES

Enteric infections **affect the gastrointestinal tract** and are often caused by bacteria, viruses, or parasites, leading to symptoms such as diarrhea, vomiting, and abdominal pain. In addition to affecting the gastrointestinal tract, many microbes that cause enteric infections have the capacity to involve multiple organ systems.



1.7B

Global cases of **childhood diarrheal diseases** annually.



1.49M

Annual U.S. cases of **bacterial foodborne illnesses**.



3rd

Diarrheal diseases are the **3rd leading cause of death** in children <5.

NIAID Supports Enteric Infectious Diseases Research to:

- » Understand the immune responses to enteric infections and the course of disease development.
- » Investigate the mechanisms by which microbes cause enteric infectious diseases.
- » Develop and advance diagnostics, therapeutics, and vaccines to prevent and treat enteric infectious diseases.

ENTERIC DISEASE BURDEN

Enteric infectious diseases are the **second leading infectious cause of illness and death** worldwide, following respiratory infections. They range from **persistent, low-grade infections** to **severe, acute epidemic infections** like cholera.

Many enteric infections also **worsen the pathogenicity of diseases** like malaria and HIV/AIDS.



EXAMPLES OF MICROBES THAT CAUSE ENTERIC INFECTIONS

- | | |
|--------------------------------|---------------------|
| » Adenovirus | » <i>Listeria</i> |
| » Astrovirus | » Norovirus |
| » <i>Campylobacter</i> | » Rotavirus |
| » <i>Clostridioides</i> | » <i>Salmonella</i> |
| » Diarrheagenic <i>E. coli</i> | » <i>Shigella</i> |
| » <i>H. pylori</i> | » <i>Vibrio</i> |

RESEARCH GOALS FOR ENTERIC INFECTIOUS DISEASES



Identify **immunologic correlates of protection** against enteric diseases like norovirus.



Develop and test vaccines to **protect pediatric populations** against enteric diseases.



Advance the development of **diagnostics that aid clinical decisions** in treating enteric diseases.



Develop vaccine candidates against enteric diseases that cause **significant morbidity**.



Support research that encompasses a **One Health approach** and includes investigating the impact of the environment on enteric infections.



Advance knowledge of enteric disease burden by leveraging **natural immunity studies** in areas with endemic disease.



Investigate **multidrug resistance** mechanisms of microbes that cause enteric infections, particularly *Salmonella*, *Clostridioides difficile*, *Shigella*, and *Vibrio cholerae*.



SOLID ORGAN TRANSPLANTATION

Solid organ transplantation faces **significant challenges**, including long wait times, the risk of transplant rejection, severe side effects from immunosuppressive drugs, and increased vulnerability to infections. Transplant immunology is crucial in **understanding the immune response to transplanted organs**, particularly in allotransplantation, in which organs are transferred between genetically non-identical members of the same species, and xenotransplantation, in which organs are transplanted between different species.



108,000

Number of **men, women, and children** on the U.S. national transplant waiting list in April 2026.



17

People die each day in the U.S. **waiting for an organ transplant.**

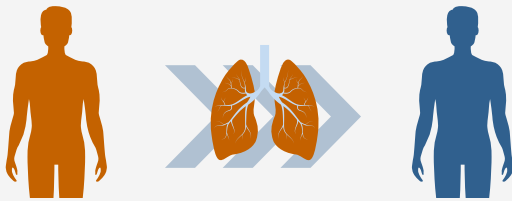
NIAID Supports Transplant Immunology Research to:

- » Improve recipient and graft survival.
- » Enhance the overall quality of life for transplant recipients.
- » Explore novel strategies to improve transplantation outcomes for vulnerable populations.
- » Overcome challenges with xenotransplants.

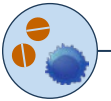
RESEARCH GOALS FOR SOLID ORGAN TRANSPLANTATION

ALLOTRANSPLANTATION

When an organ is transplanted from a **human donor to a human recipient**, often of different genetic backgrounds.



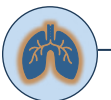
Diminish and ultimately eliminate the need for **long-term pharmacologic immunosuppression** after organ transplantation.



Develop and evaluate **cellular therapeutics** to achieve **immunological tolerance** in organ allotransplantation.



Develop strategies that result in a single organ transplant **restoring normal life expectancy**.



Develop and evaluate strategies that prevent or treat **infection, graft dysfunction, and transplant rejection**.



Identify and advance **biomarkers** and **non-invasive or minimally invasive approaches** to predict rejection and enable early diagnosis and treatment.

XENOTRANSPLANTATION

When an organ is transplanted from a **genetically altered animal donor to a human recipient**. This method is being pursued in part to overcome the shortage of human organs.



Determine the **critical immunologic targets** that limit survival in xenotransplantation and optimize tools to minimize incompatibilities.



Develop comprehensive strategies to detect and prevent **transmission of zoonotic infections**.



Enhance **immunosuppressive regimens** and develop **xeno-immune tolerance** to reduce morbidity and mortality in patients on long-term immunosuppressive agents.



Conduct rigorous clinical trials to **make xenotransplantation a safe, effective, and readily available treatment** for end-stage organ failure.

VIRAL HEPATITIS

Hepatic infections involve the liver and can result from viruses, such as the hepatitis viruses. While some viruses result in acute infections that reduce liver function and cause short-term illness, **hepatitis viruses A, B, C, D, and E** can cause **liver inflammation, cirrhosis, end stage liver disease, and cancer**.



~287 million

People affected by **chronic hepatitis B and C** globally.



5 times

More likely to have hepatitis C if an individual was **born between 1945-1965** compared to other generations.

NIAID Supports Viral Hepatitis Research to:

- » Characterize pathogenesis of each of the five known hepatitis viruses.
- » Enhance understanding of how the immune system responds to hepatic infections.
- » Optimize diagnostics, therapeutics, and vaccines to prevent and treat hepatic infections.

FOCUS ON HEPATITIS B AND C



The NIAID research program on hepatitis viruses focuses **primarily on hepatitis B (HBV) and C (HCV)** due to their significant medical burden.



For more information on goals for viral hepatitis research, see the **Strategic Plan for NIH Research to Cure Hepatitis B 2022 Update** and the **2021-2025 HHS Viral Hepatitis National Strategic Plan**.



HBV causes both short- and long-term liver infections.

HBV is spread through bodily fluids, though infection can be prevented by vaccination. There is currently no cure for HBV infection.



HCV is spread through blood and can cause serious liver damage if left untreated.

HCV is spread through blood and can **cause serious liver damage if left untreated**. There is no vaccine to prevent HCV infection, though there are oral medications for treatment.

RESEARCH GOALS FOR HBV AND HCV



Develop biologics and antivirals for treatment of viral hepatitis in **infants** and **immunocompromised individuals**.



Develop **point-of-care diagnostics** for HBV and HCV, particularly for use in those disproportionately impacted.



Support basic, preclinical, and clinical research to **advance the development of vaccines** for HCV.



Improve diagnostic, prevention, and treatment options for HBV and HCV in **all populations**.



Identify and evaluate **novel therapeutics** for viral hepatitis including **HBV cure strategies**.



Develop **long-acting treatments** for HBV and HCV that improve treatment uptake, particularly in populations most impacted by viral hepatitis.

DISEASE-SPECIFIC AREAS OF EMPHASIS REFERENCES

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Appendix D: Glossary of Terms

Acronym	Definition
ACE	Autoimmunity Centers of Excellence
AI	Artificial intelligence
AIDS	Acquired immunodeficiency syndrome
AI/ML	Artificial intelligence and machine learning
AMR	Antimicrobial resistance
ART	Antiretroviral therapy
bNAbs	Broadly neutralizing antibodies
CARE	Collective benefit, Authority to control, Responsibility, Ethics
CAR-T	Chimeric antigen receptor T-cell
CGD	Chronic granulomatous disease
CoFAR	Consortium for Food Allergy Research
COVID-19	Coronavirus disease 2019
DAIDS	Division of AIDS
DAIT	Division of Allergy, Immunology, and Transplantation
DEA	Division of Extramural Activities
DIR	Division of Intramural Research
DMID	Division of Microbiology and Infectious Diseases
EHE	Ending the HIV Epidemic in the U.S.
FAIR	Findable, Accessible, Interoperable, and Reusable
FDA	U.S. Food and Drug Administration
GRAM	Global Research on Antimicrobial Resistance
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HHS	U.S. Department of Health and Human Services
HIV	Human immunodeficiency virus
HOPE	HIV Organ Policy Equity Act
HSV	Herpes simplex virus
IBD	Inflammatory bowel disease
ICO	NIH Institutes, Centers, and Offices
IEI	Inborn errors of immunity
ITN	Immune Tolerance Network
ME/CFS	Myalgic Encephalomyelitis/Chronic Fatigue Syndrome
ML	Machine learning

Acronym	Definition
MPT	Multipurpose prevention technologies
NAMs	New approach methodologies
NHLBI	National Heart, Lung, and Blood Institute
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
NINDS	National Institute of Neurological Disorders and Stroke
NTD	Neglected tropical disease
OTC	Over the counter
PEP	Post-exposure prophylaxis
PHS	U.S. Public Health Service
PIRD	Primary immunoregulatory disorder
PLWH	People living with HIV
POC	Point of care
PPE	Policy, Planning, and Evaluation Branch
PrEP	Pre-exposure prophylaxis
PTLDS	Post-Treatment Lyme Disease Syndrome
RECOVER	Researching COVID to Enhance Recovery
RECOVER-TLC	RECOVER-Treating Long COVID
RFI	Request for Information
RML	Rocky Mountain Laboratories
RSV	Respiratory syncytial virus
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SCID	Severe combined immunodeficiency
SOM	Standardized organoid modeling
SLE	Systemic lupus erythematosus
STI	Sexually transmitted infections
T1D	Type 1 diabetes
TB	Tuberculosis
TRUST	Transparency, Responsibility, User focus, Sustainability, and Technology
USG	United States Government
VBD	Vector-borne disease
VRC	Vaccine Research Center

Appendix E: Image Credits

FRONT MATTER

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Crosscutting Themes: Sabrina/stock.adobe.com.

RESEARCH GOALS

Research Goals: chokniti/stock.adobe.com, DC Studio/stock.adobe.com, pressmaster/stock.adobe.com.

Research Goal 1: my kids/stock.adobe.com, NIAID, Artur/stock.adobe.com, NIAID, TopMicrobialStock/stock.adobe.com, Juan Gärtner/stock.adobe.com, luchschenF/stock.adobe.com, DC Studio/stock.adobe.com, Gorodenkoff/stock.adobe.com.

Research Goal 2: Hariez Razali/stock.adobe.com, tsuguliev/stock.adobe.com, Syda Productions/stock.adobe.com, Peakstock/stock.adobe.com, Tatiana Shepeleva/stock.adobe.com, Sweettymojidesign/stock.adobe.com, NIAID, Halfpoint/stock.adobe.com, Microgen/stock.adobe.com, Yuliia/stock.adobe.com, Zamrznuti tonovi/stock.adobe.com, Konstantin Yuganov/stock.adobe.com, Davide Agnelini/stock.adobe.com, Rawpixel.com/stock.adobe.com.

Research Goal 3: perfectlab/stock.adobe.com, (JLco) Julia Amaral/stock.adobe.com, Krakenimages/stock.adobe.com, cherryandbees/stock.adobe.com, sushytska/stock.adobe.com, halfpoint/stock.adobe.com, NIAID, Andrey Popov/stock.adobe.com, Krakenimages.com/stock.adobe.com, pantovich/stock.adobe.com, MiaB/peopleimages.com/stock.adobe.com, fizkes/stock.adobe.com.

OPERATIONAL AND CAPACITY GOALS

Operational Goals: fizkes/stock.adobe.com, rawpixel.com/stock.adobe.com.

Capacity Goals: NIAID, deagreez/stock.adobe.com, NIAID.

APPENDICES

Appendix B: Andrii Yalanskyi/stock.adobe.com.

Appendix C: Allergic Diseases: nobeastsofierce/stock.adobe.com, LIGHTFIELD STUDIOS/stock.adobe.com, Ольга Тернавская/stock.adobe.com, Daisy Daisy/stock.adobe.com, fizkes/stock.adobe.com, ad_hominem/stock.adobe.com; **Autoimmune Diseases:** ustas/stock.adobe.com, Dshnrgc/stock.adobe.com; **Enteric Infectious Diseases:** NIAID; Fungal Infections: Dr_Microbe/stock.adobe.com; **Inborn Errors of Immunity:** Artur/stock.adobe.com, Daniel/stock.adobe.com, Odua Images/stock.adobe.com, Synthex/stock.adobe.com, immimagery/stock.adobe.com; **Neglected Tropical Diseases:** NIAID; **Respiratory Infections:** NIAID; **Sexually Transmitted Infections:** NIAID, NIAID, NIAID, Dr Microbe/stock.adobe.com; **Solid Organ Transplantation:** fusebulb/stock.adobe.com; **Vector-Borne Diseases:** NIAID, NIAID, ondreicka/stock.adobe.com, buteo/stock.adobe.com; **Viral Hepatitis:** NIAID.

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National Institute of
Allergy and
Infectious Diseases