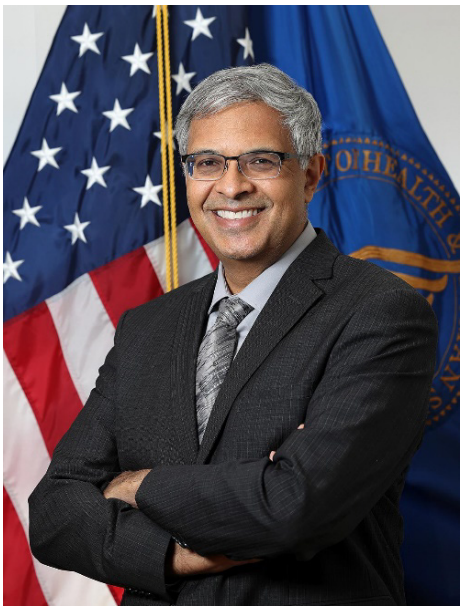
National Institutes of Health

NIH-WIDE STRATEGIC PLAN FOR AUTOIMMUNE DISEASE RESEARCH

FISCAL YEARS 2026–2030

FOREWORD



Jay Bhattacharya, M.D., Ph.D.
Director, National Institutes of Health

I am pleased to introduce the inaugural *NIH-Wide Strategic Plan for Autoimmune Disease Research, Fiscal Years 2026–2030*. This comprehensive blueprint is a manifestation of the National Institutes of Health (NIH)'s unwavering commitment to address the chronic disease crisis in the U.S. and to improve the health of the American people.

Autoimmune diseases influence every system in the body and pose significant risks to human health throughout the lifespan. Between 23.5 and 50.0 million people in America live with one or more autoimmune diseases; collectively, autoimmune diseases represent some of the most common chronic diseases affecting the U.S. population. Beyond their own substantial morbidity and mortality, autoimmune diseases commonly co-occur with other debilitating chronic conditions. These findings reinforce the observation that autoimmune diseases touch the lives of every person in America.

Autoimmune diseases also carry substantial costs, estimated at more than $100 billion per year for health care in the U.S. Accounting for indirect costs, such as lost productivity and the broader impact on dependents, families, and society, the costs to the American people are likely much higher.

The study of autoimmune diseases intersects with the mission of every Institute and Center (IC) at NIH. While significant progress has been and continues to be made in autoimmune disease research across NIH, more work is needed to improve diagnostics and therapeutics and to bring scientific discoveries to the bedside. This strategic plan proposes a coordinated approach that will foster a synergistic environment where collaboration and innovation can flourish.

The plan will prioritize research that addresses the health needs of the American people. By integrating the perspectives and experiences of those living with autoimmune diseases, scientific inquiry will be tailored to focus on their most pressing needs. This holistic approach will not only enhance understanding of disease pathogenesis but also expedite the development of novel therapies.

By enhancing reproducibility and rigor in research, as well as cultivating a culture of research safety, transparency, and academic freedom, this plan underscores the importance of harnessing cutting-edge technologies to advance science. Recent innovations in technology and bioinformatics offer unprecedented opportunities to dissect the molecular underpinnings of autoimmune diseases at a scale never previously achievable. Leveraging these tools, we hope to optimize collaborative autoimmune disease research efforts; bolster infrastructure and resource allocation; and support basic, clinical, translational, epidemiologic, and implementation sciences. This strategic approach will create a robust infrastructure to support interdisciplinary research consortia pivotal for accelerating scientific breakthroughs and supporting future autoimmune disease researchers.

The plan is a testament to NIH's dedication to advance human health. Through a collaborative approach, innovative thinking, and a steadfast focus on outcomes that impact human health, we are poised to make significant strides in the fight against autoimmune diseases. It is our hope that this plan will serve as a catalyst for transformative change, ultimately improving the lives of all people living with and at risk of autoimmune diseases.

Jay Bhattacharya, M.D., Ph.D.
Director, National Institutes of Health

Autoimmune Diseases: Why Research Matters

>140 autoimmune diseases have been identified, affecting every organ system

25% of people living with autoimmune diseases have **more than one autoimmune disease**

>80% of individuals with an autoimmune disease are **women**

>23.5 million Americans are living with an autoimmune disease

50% of people living with autoimmune diseases **experience a delay in diagnosis**

Partnerships Drive Progress

2022
Epstein-Barr virus (EBV) identified as a potential trigger for the development of multiple sclerosis

2022
Anti-CD3 monoclonal antibody, teplizumab, approved to delay progression to type 1 diabetes in people at risk

2020
Monoclonal antibody, teprotumumab, approved as first treatment for thyroid eye disease

2020
First precision cellular immunotherapies entered clinical trials for autoimmunity

2012
First oral JAK inhibitor, tofacitinib, approved as a novel targeted therapy for autoimmunity

2000
T cell function and memory discovered to be intimately connected to metabolism

1998
First tumor necrosis factor (TNF) inhibitor, infliximab, approved for autoimmune disease treatment

1997
Anti-tissue transglutaminase antibody identified as a biomarker of celiac disease

1987
Immune tolerance mechanism elucidated in the developing thymus

1975
Autoimmunity research catalyzed by large-scale production of monoclonal antibodies

1971
Cyclophosphamide reported to improve outcomes of lupus nephritis

1965
Antibody structure first described; a crucial step to understanding the immune system

1957
Immune signaling pathways clarified with the discovery of the first cytokine, interferon

1956
Paradigm of autoimmunity conceptualized with the identification of disease-specific autoantibodies in Hashimoto's thyroiditis

1949
Corticosteroid treatment observed to significantly improve mobility in rheumatoid arthritis

People with Autoimmune Diseases | **Community Partners** | **Philanthropic Partners** | **Academic Partners** | **NIH Institutes, Centers, and Offices** | **Federal Partners** | **Industry Partners** | **Health Providers and Organizations** | **Caregivers**

National Institutes of Health
Office of Autoimmune Disease Research
Office of Research on Women's Health

OADR-ORWH supports high-priority autoimmune disease research, identifies emerging areas of innovation, and fosters collaboration across NIH.

To learn more, visit https://orwh.od.nih.gov/OADR-ORWH

TABLE OF CONTENTS

OVERVIEW OF AUTOIMMUNE DISEASES

The human immune system operates in a state of balance. It increases activity in response to external threats, such as the many infections and external stimuli encountered over the life course, and decreases activity when the infectious trigger or stimulus has resolved. The immune system constantly surveys for external and internal threats such as infections and malignant cells—trafficking into all organs and systems and distinguishing self from non-self, which is a concept termed "tolerance."

Autoimmunity occurs when the body's immune tolerance breaks down and the immune system generates autoreactive antibodies, cells, cytokines, and other molecules that react against components of healthy cells and tissues. The development of autoimmunity may occur years prior to clinical signs and symptoms of autoimmune disease; yet some individuals with evidence of autoimmunity never develop clinical disease.

Autoimmune diseases develop when autoreactive antibodies, cells, and molecules cause damage to organs or tissues that results in signs and symptoms. Autoimmune diseases are an incredibly diverse group of conditions, affecting almost any part of the body and manifesting across the life course. More than 140 known autoimmune diseases have been identified, and symptoms vary extensively based on the organs involved and disease type.[1] Because the immune system traffics into every organ, autoimmune diseases may impact any system in the body and may also affect multiple systems simultaneously.

Most autoimmune diseases are chronic, but the presentation may be acute. They may be organ- or life-threatening. Symptoms of many autoimmune diseases wax and wane over time. The unpredictability of flares, periods during which symptoms worsen, can be extremely challenging to manage, and although many autoimmune diseases are now treatable, most autoimmune diseases do not have curative interventions.

Autoimmune diseases are believed to affect 7% to 8% of the U.S. population, between 23.5 and 50.0 million Americans are estimated to be living with autoimmune diseases. Rates of autoimmunity are increasing; however, the exact prevalence of autoimmune diseases in the U.S. is unknown because of the absence of comprehensive longitudinal data.[2-4]

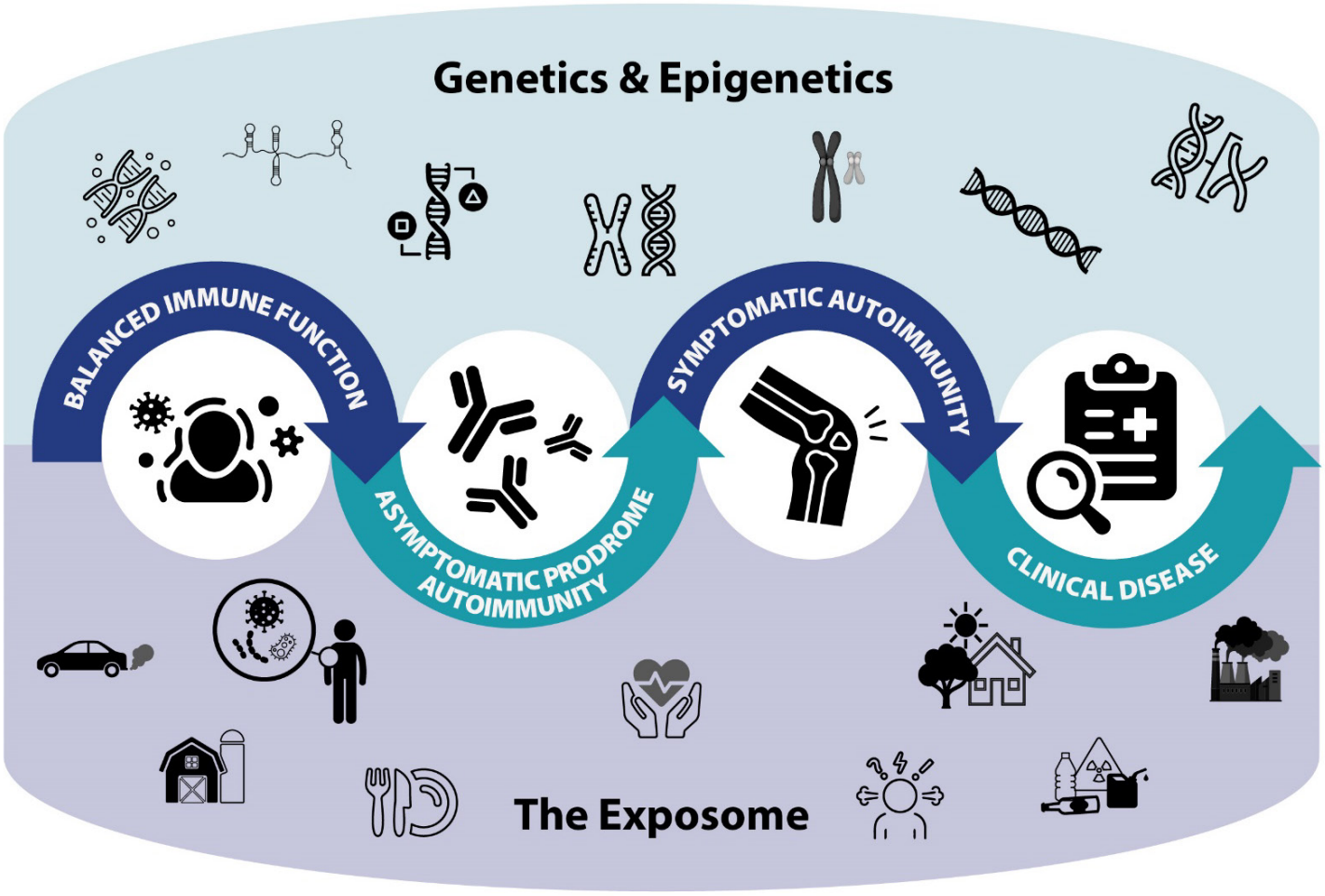
Because of their breadth and complexity, the study of autoimmune diseases intersects with the mission of every National Institutes of Health (NIH) Institute and Center (IC), underscoring the need for an NIH-wide approach for strategic planning for autoimmune disease research.

The mission of the NIH-wide Strategic Plan for Autoimmune Disease Research is to coordinate and advance efforts to support rigorous, high-priority, innovative, and collaborative autoimmune disease research.

Preclinical Autoimmunity

A common feature of many autoimmune diseases is a period of asymptomatic autoimmunity—the prodrome—typically manifested by detection of autoantibodies or other markers of immune activation. This period is followed by development of symptoms, which may be initially nonspecific, and then progress to clinical disease (Figure 1). The duration of the prodrome varies. Research has shown that autoantibodies may predate clinically definable disease by more than five years in people who ultimately are diagnosed with systemic lupus erythematosus and other autoimmune diseases.[5,6] Similarly, in diseases such as multiple sclerosis, the prodrome may last a decade or longer before an individual meets criteria for a formal diagnosis. During this period, autoimmunity can be pathogenic and cause organ damage. In some diseases, such as type I diabetes in children, the prodrome tends to be shorter. The period of asymptomatic autoimmunity presents a unique opportunity to evaluate immunomodulatory therapies before disease fully develops. Recent groundbreaking research has led to the approval of a new therapy for delaying progression to type I diabetes in high-risk individuals.[7] This marks the first Food and Drug Administration-approved treatment for delaying progression in preclinical autoimmunity. Importantly, this success offers tantalizing evidence that a similar preventative approach might be possible for other chronic autoimmune diseases.

Figure 1. Many autoimmune diseases have a period of asymptomatic or preclinical autoimmunity, known as the prodrome, prior to the development of clinically definable disease.



Living with Autoimmune Diseases

In addition to managing the chronicity of autoimmune disease, people living with autoimmune diseases and their caregivers face challenges that extend beyond the disease itself. Reaching an accurate autoimmune disease diagnosis is challenging and may take months to years, despite frequent office visits to experienced physicians. The long timeline to diagnosis is due to many factors, including the nonspecific prodromal symptoms seen early in autoimmune disease and lack of robust diagnostic tests for autoimmunity. Extended diagnostic uncertainty contributes additional mental and psychosocial stress over and above that caused from the chronicity of autoimmune diseases. However, studies show that timely diagnosis and early targeted treatment typically result in better outcomes for people with autoimmune diseases.[8] Therefore, advancing research into improving diagnostic testing for autoimmunity is essential.

Even with an accurate diagnosis, many people with autoimmune diseases face a lifetime of disease flares and treatments, with associated side effects and complications. Disease flares can occur without warning. These sudden, unpredictable increases in disease activity can impair physical, mental, and cognitive functioning, both for the person experiencing the flares and their support network. Recommended lifestyle and dietary changes can be arduous and difficult to navigate. Improving understanding of flares in autoimmune diseases is a crucial step in advancing autoimmune disease research.

Many treatments for autoimmune diseases involve complex regimens, including pills and injectable therapies. Treatment can lead to side effects such as becoming immunocompromised, which makes the person receiving these treatments vulnerable to infections. Treatments also carry other complications and necessitate significant time and costs. For many autoimmune diseases, treatment options remain extremely limited and may not fully halt disease progression. However, recent scientific advances have demonstrated that targeted treatment is possible for some autoimmune diseases, and more research is needed to accelerate the development of additional therapies, drug combinations, dosing regimens, and delivery methods to improve treatment, prevention, and cure.[9]

Efforts are needed across the research continuum to improve outcomes and reduce the challenges experienced by people living with autoimmune diseases. Moving forward, research is warranted in several key areas: improving diagnostics; predicting disease progression and flares; addressing the psychosocial impacts of living with an autoimmune disease; and accelerating development of new treatments and preventative interventions, including optimizing drug combinations, dosing regimens, and delivery methods.

Co-Occurring Autoimmune Diseases

People living with one autoimmune disease have a high likelihood of developing additional autoimmune diseases.[4] It is also common for multiple individuals within the same family to be affected with different autoimmune diseases. The reasons for these phenomena are unknown, but the observation inherently suggests the existence of commonalities in disease pathogenesis and shared risk factors that predispose to autoimmunity. Traditional research paradigms challenge the ability of investigators to study co-occurring conditions because people living with multiple autoimmune diseases are often excluded from research trials. Studies of co-occurring autoimmune diseases often fall outside of a single NIH Institute's scientific mission area, which highlights the unmet need for a coordinated *NIH-Wide Strategic Plan for Autoimmune Disease Research*.

Risk Factors for Autoimmune Diseases

Although many autoimmune diseases occur in genetically susceptible individuals, inherited genetics alone cannot explain the rapidly increasing incidence and prevalence of autoimmune diseases.[2,10] The importance of somatic mutations has recently become apparent,[11-13] and experts generally agree that exposures and triggers throughout the life course likely contribute to development of autoimmunity.[14]

Exposome research is the study of the various exposures experienced by humans throughout their lives.[15,16] The exposome encompasses internal and external exposures, such as diet, stress, hormones, alcohol, drugs, medication, cigarette smoke, chemicals, heavy metals, ultraviolet radiation, air and water pollutants, and indirect health indicators, such as education, social conditions, or job security (Figure 2). The microbiome, which is the collection of all microbes (including bacteria, fungi, viruses, and parasites) that live on and inside our bodies, also contributes to the exposome and may affect how autoimmune diseases develop and manifest. The unique and dynamic composition of microbes that are present or absent during an individual's life course influences their immune function in health and disease.

In 2010, an NIH-convened expert panel established consensus on the associations between autoimmune diseases and various environmental exposures such as crystalline silica, solvents, and other chemical exposures as well as smoking and radiation.[17,18] However, the study of environmental exposures in autoimmune diseases is challenging, in part because of exposure latency and the spatiotemporal variability in exposures and because exposures may have different influences depending on the life stage of the individual. For example, exposures during childhood and adolescence may have a more pronounced impact than those later in life, or vice versa, depending on the agent involved. The influence of psychosocial stressors and behavioral factors may also play a role in autoimmunity, either independently or in conjunction with other environmental factors. The study of cumulative and time-varying exposures, along with their interactions over the life course, requires complex analytic modeling. These dynamic, interconnected components of the exposome can be very difficult to integrate into research but are critically important to understand—especially because their impact may be disproportionate in different groups.

Studying cohorts of people at risk of autoimmunity, and people with different autoimmune diseases, over time is important to inform understanding of the interplay of time-varying exposures on the immune system. Cross-sectional studies of individuals with rare diseases can also help to reveal how the immune system functions in health and disease. A coordinated approach to autoimmune disease research would enable integration and analysis of the interactions between various environmental exposures and biologic systems over the lifespan. Through advances in predictive modeling and other data analytics, such research will improve identification of individuals and populations at risk of autoimmunity and help identify new strategies for intervention.

Figure 2. The exposome encompasses many exposures experienced across the lifespan, including those from the physical environment, social environment, and lifestyle. Figure adapted from the National Institute of Environmental Health Sciences.

Exposomics

Our environment—from the air we breathe, food we eat, and water we drink to the chemicals we ingest and stress we experience—influences health. Scientists strive to measure the exposome, which is the totality of these exposures and the body's response to them. The study of the exposome, called exposomics, will enable scientists to discover how exposure mixtures drive health and disease, so people can take steps to modify their individual exposures and improve their health.

Physical Environment

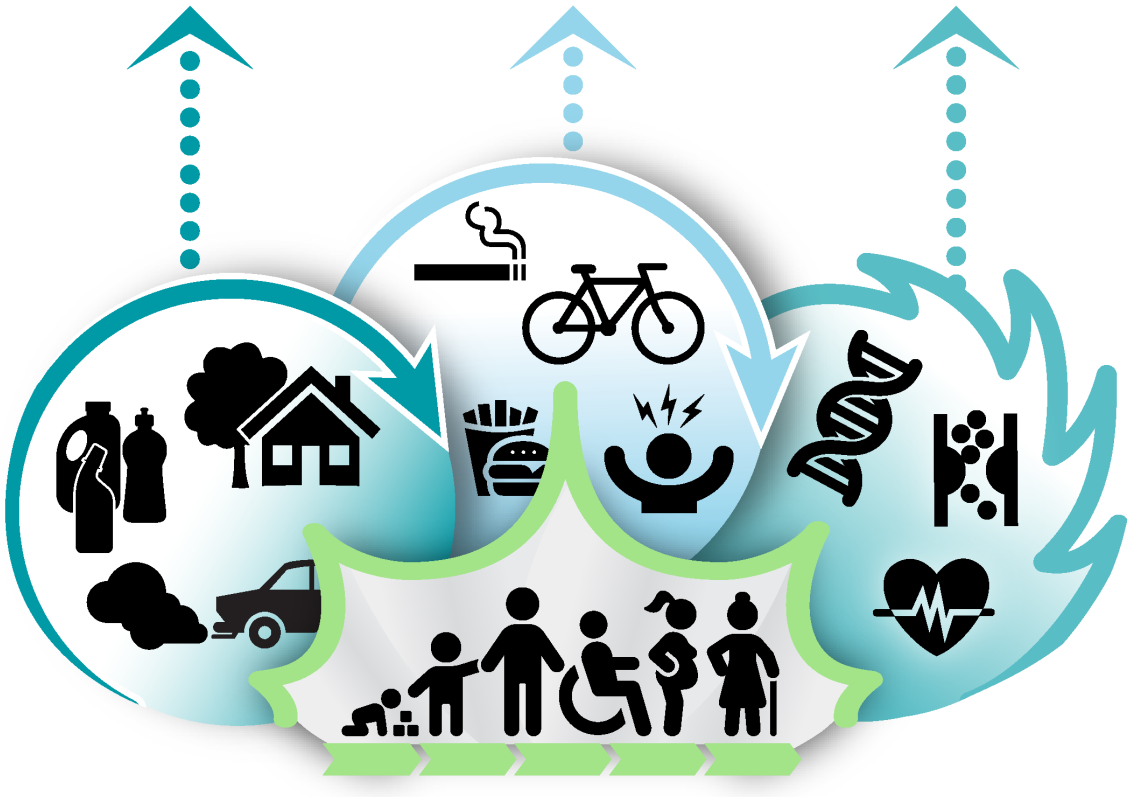
The human immune response can be affected by UV light, radiation, pesticides, atmospheric dust, water and soil impurities, chemical exposures at home and work, as well as the surrounding natural environment.

Social Environment and Lifestyle

Diet, exercise, sleep habits, stress, smoking, and alcohol and drug use, along with socioeconomic conditions, may also influence the human immune response.

Biologic Pathways

Environmental exposures can cause biological changes that affect DNA, protein levels, signaling pathways, and metabolism, all of which can result in immunologic changes.



Variations in Autoimmune Diseases

Autoimmune diseases are more common in women and individuals with chromosomal abnormalities including trisomy-21 (also known as Down syndrome) and other aneuploidies;[19] greater than 80% of those affected are female. Autoimmune diseases also occur in men, and in some cases, men experience more severe disease course and a higher risk of mortality.[20,21] There are multiple biologic reasons for these differences. Women are known to exhibit more robust immune responses to pathogens.[22] Recent data also suggest that the biologic inactivation of additional X-chromosomes by long noncoding ribonucleic acid molecules, including the X-inactive specific transcript (XIST), may play a role in the observed sex-specific variation across autoimmune diseases.[23] The biology of autoimmunity needs further research to better understand autoimmune disease pathogenesis.

Autoimmune Disease Across Different Populations

Although most autoimmune diseases affect people of all backgrounds, some populations are disproportionately affected and have worse outcomes.[24,25] The reasons for this disproportionate burden are not fully understood; to ensure that scientific discoveries benefit all populations, research studies should enroll individuals from all communities.[26-28] In addition, environmental exposures and life events also differ over the life course and across geographical areas. These variables should be incorporated into autoimmune disease research[29] so that the scientific knowledge gained is widely applicable.

Autoimmunity as a Risk Factor for Other Comorbid Conditions

The effects of autoimmunity are numerous and can have wide-reaching consequences. For example, chronic inflammation, part of the pathophysiology of many autoimmune diseases, is an independent risk factor for cardiovascular disease.[30] In addition, many people with autoimmune diseases develop mental health disorders such as depression and anxiety.[31] Data increasingly signal that these comorbidities are not simply related to the difficulties of living with a chronic disease; rather, inflammation may contribute to the development of systemic complications.[32,33] Thus, the proposed coordinated approach to advancing autoimmune disease research, outlined in this NIH-wide plan, may catalyze scientific understanding in other complex diseases and have far-reaching impact across all communities.

Patient Partnership for Autoimmune Disease Research

The engagement of people living with autoimmune diseases has been an essential component in the development of this strategic plan and will remain a priority for NIH. People living with autoimmune diseases, individuals and organizations advocating for patients, caregivers, and autoimmune disease-focused clinicians and scientists all bring unique perspectives and contribute to the goal of advancing fundamental knowledge and applying that knowledge to improve the lives of people living with autoimmune diseases. NIH is dedicated to synergizing efforts to advance scientific discovery for autoimmune diseases and translating those findings into meaningful interventions for prevention, diagnosis, treatment, and cure of autoimmune diseases.

Community Networks for Autoimmune Disease Research

The many existing community networks and disease-specific advocacy groups are a unique and important resource for people living with autoimmune diseases and those engaged in autoimmune disease research and care. Across the research continuum, engagement with community networks is essential to enhancing innovation, catalyzing breakthroughs, and disseminating and implementing new findings in the community. Many autoimmune diseases are also considered rare diseases because they affect fewer than 200,000 people in the U.S. As exemplified in the rare disease community, networks are an incredible resource—often serving a synergistic role of supporting people living with autoimmune diseases and supporting research through expanding clinical trial access, advancing understanding of diseases and their complications through coordinated natural history studies, and disseminating research findings. Dissemination and implementation research is important to enhance uptake of evidence-based, person-centered research findings. Developing and

strengthening relationships with community networks is a cornerstone to ensuring that autoimmune disease research is person-centered and reaches all communities.

Enhancing Capacity for Autoimmune Disease Research

Training and retaining the autoimmune disease research scientific workforce will remain critically important for supporting the future of autoimmune disease research. Pre-COVID-19 data from the American College of Rheumatology Workforce Survey demonstrated that multiple regions of the U.S. will have a critical shortage of rheumatologists by 2030,[34] and the pressures of the pandemic and its aftermath will only exacerbate these shortfalls. Similar trends have been observed in other autoimmune disease-focused specialties and impact the ability to not only advance fundamental research but also conduct the clinical trials needed to translate new discoveries into clinical practice.[35] A strategic approach is needed to dovetail initiatives that support training, sustaining, and re-engaging the autoimmune disease research workforce across the research continuum in parallel with advancing the science.

Advancing Autoimmune Disease Research

NIH is committed to advancing progress in autoimmune disease research and care. NIH will continue to support the fundamental research that is essential for identifying new therapeutic targets and translating these discoveries into clinical treatments that ultimately improve the health of people living with autoimmune diseases. Through the implementation of this strategic plan, NIH will support all phases of the scientific process, adopting a coordinated approach to autoimmune disease research and integrating fundamental, translational, epidemiological, clinical, and implementation science. As the research accelerates, NIH will continue to build capacity for autoimmune disease research through the development of advanced tools, techniques, and methods, as well as a skilled workforce to deftly deliver new discoveries to the bedside. These priorities are essential for advancing and translating scientific discoveries into practical applications that improve outcomes for people living with and at risk of autoimmune disease. Through a collaborative and coordinated approach, encompassing scientific integrity and rigor, this *NIH-Wide Strategic Plan for Autoimmune Disease Research* will serve as a framework for priority setting for autoimmune disease research across NIH over the next five years.

The Office of Autoimmune Disease Research

The Consolidated Appropriations Act, 2023 (Public Law 117-328) provided the National Institutes of Health (NIH) with funds to establish the Office of Autoimmune Disease Research in the Office of Research on Women's Health (OADR-ORWH) to enhance coordination across NIH autoimmune disease research efforts.

In addition to calling upon NIH to establish OADR, Congress set out the following six directives for the new office:

1. Coordinate the development of a multi-IC strategic research plan with concrete, meaningful milestones to set priorities
2. Identify emerging areas of innovation and research opportunity
3. Coordinate and foster collaborative research across ICs
4. Annually evaluate the autoimmune disease research portfolio to determine progress made across NIH
5. Provide resources to support planning, collaboration, and innovation
6. Develop and oversee a publicly accessible central repository for autoimmune disease research

Coordinating Committee for Autoimmune Disease Research (CCADR)

The Coordinating Committee for Autoimmune Disease Research (CCADR) is an NIH committee convened in support of autoimmune disease research at NIH. CCADR members include NIH Institute, Center, and Office (ICO) representatives nominated by ICO Directors (Appendix A).

PRIORITY SETTING AND STRATEGIC PLANNING PROCESS

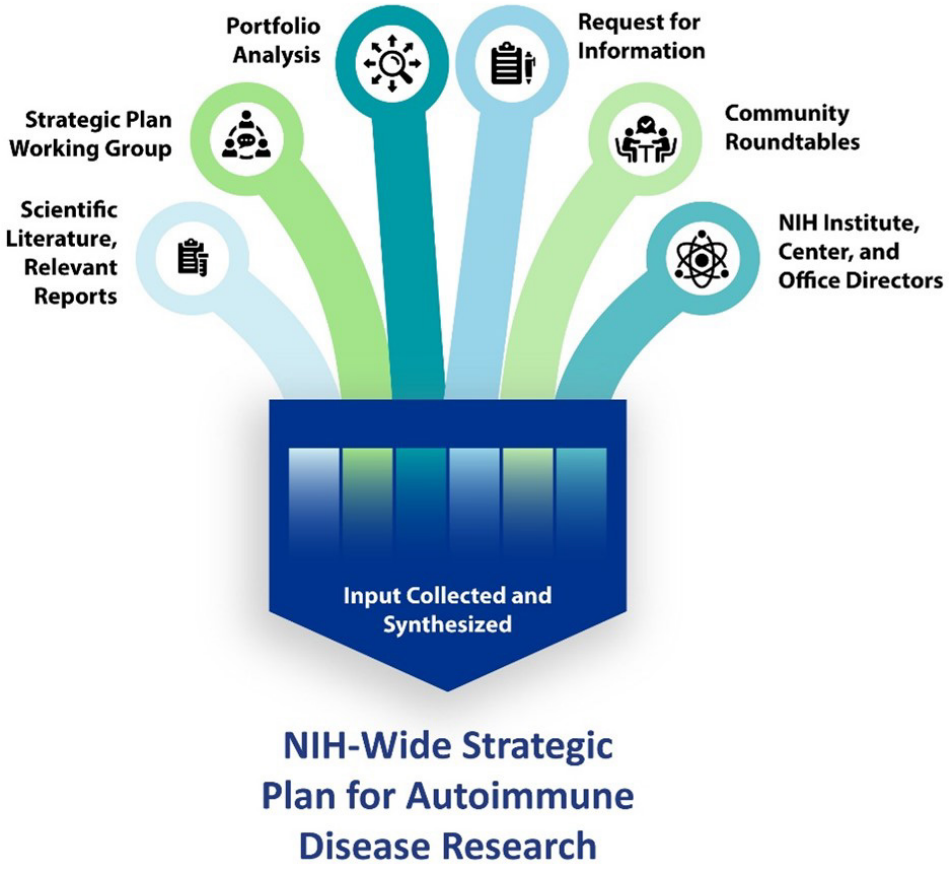
Development of the *NIH-Wide Strategic Plan for Autoimmune Disease Research* began in 2023 with the formation of the Office of Autoimmune Disease Research in the Office of Research on Women's Health (OADR-ORWH). In the Joint Explanatory Statement accompanying the Consolidated Appropriations Act, 2023, Congress also directed the Office to coordinate the development of this NIH-wide strategic plan. OADR-ORWH convened an internal NIH Coordinating Committee for Autoimmune Disease Research (CCADR) with representatives from across NIH Institutes, Centers, and Offices (ICOs), which then formed a Strategic Plan Working Group (SPWG, Appendix B).

OADR-ORWH's process for strategic planning and priority setting emphasized input from autoimmune disease communities. In December 2023, in coordination with the SPWG, OADR-ORWH developed and issued a Request for Information (RFI; NOT-OD-24-049) that requested input from the public on the development of the strategic plan. OADR-ORWH also hosted two community roundtables in February 2024 to garner input from academic and patient advocacy partners.

The SPWG met regularly to establish the priorities, objectives, and crosscutting themes. SPWG members evaluated and integrated data from multiple sources including (a) responses to the RFI, (b) dialogues at the community roundtable sessions, (c) input from NIH ICO representatives and directors, (d) data from public health organizations, (e) analysis of the existing NIH autoimmune disease research portfolio, and (f) recommendations from the National Academies of Sciences, Engineering, and Medicine (NASEM) report on *Enhancing NIH Research on Autoimmune Disease* and other reports (Figure 3).

The NIH common template was used to guide the strategic planning process and to identify and develop research priorities, capacity priorities, and operational priorities, as well as crosscutting themes.

Figure 3. Strategic planning and priority setting emphasized input from multiple sources including the autoimmune disease community.



NIH supports a broad range of basic to clinical research on autoimmunity and autoimmune diseases. Autoimmune disease research is conducted and supported across various NIH ICOs in alignment with their mission areas.

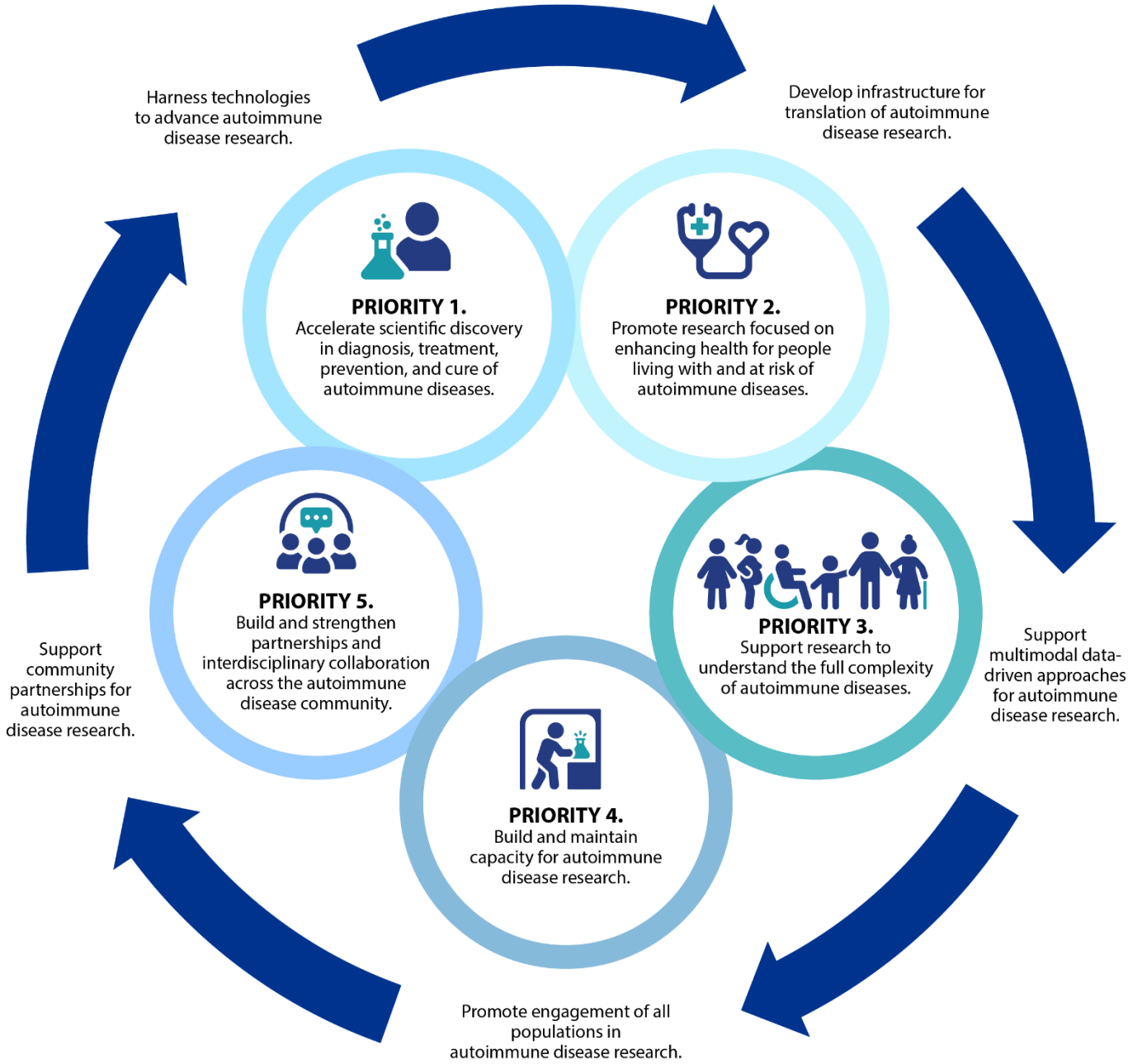
To support the development of the *NIH-Wide Strategic Plan for Autoimmune Disease Research*, OADR-ORWH conducted a baseline landscape analysis of NIH's autoimmune disease research portfolio. For the purposes of this analysis, more than 140 diseases and conditions (Figure 4) included in the NASEM report and considered to be either autoimmune or to coexist with autoimmune diseases were reviewed.[1] An additional crosscutting category of fundamental immunology research has been included in the analysis because understanding autoimmune diseases requires a holistic view of the immune system, which cannot be achieved without studying relevant fundamental immune mechanisms. This analysis informed the strategic priorities by providing data-driven insights on gaps within the portfolio and fostered consensus on strategic objectives.

Although NIH's investment in autoimmune disease research increased from $800 million in Fiscal Year (FY) 2018 to more than $1 billion in FY22,[36] continued and sustained funding is necessary to fully address the breadth and depth of the autoimmune disease research portfolio. The current funding levels are not proportional to the rising prevalence of autoimmune diseases, highlighting a significant gap that must be addressed. The autoimmune disease research portfolio serves as a vital reference for pinpointing areas that require additional investment to ensure comprehensive advances and impactful progress in the field of autoimmune disease research.

Figure 4. The autoimmune disease research portfolio encompasses more than 140 different diseases and conditions across 15 disease areas aligned by organ system and/or mechanism as well as a crosscutting category of fundamental immunology research (see also Appendix B).

Five strategic priorities, each supported by four objectives, constitute the foundation of the *NIH-Wide Strategic Plan for Autoimmune Disease Research*. The priorities and objectives were identified through input from across the autoimmune disease community and refined by NIH ICO representatives and subject matter experts in autoimmunity and autoimmune diseases. The five priorities and their respective objectives as well as five crosscutting themes will guide NIH-wide autoimmune disease research and are intended to supplement relevant ICO mission areas (Figure 5).

Figure 5. The *NIH-Wide Strategic Plan for Autoimmune Disease Research* consists of five strategic priorities and five crosscutting themes that will guide NIH-wide autoimmune disease research in FY26–FY30.



PRIORITY 1. Accelerate scientific discovery in diagnosis, treatment, prevention, and cure of autoimmune diseases

Advances in basic science research are critical to improving fundamental understanding of autoimmunity and autoimmune diseases, catalyzing novel clinical research, and translating knowledge into meaningful results for people living with autoimmune diseases, at-risk populations, and their communities. Disease pathogenesis and the mechanisms that drive autoimmune disease development, symptoms, and flares are poorly understood. Exploring these areas with a critical appreciation for commonalities across and differences within autoimmune diseases will illuminate new approaches to advance the diagnosis, treatment, prevention, and cure of autoimmune diseases.

OBJECTIVES

1.1 Support research into fundamental mechanisms of autoimmunity and autoimmune disease

Understanding autoimmune disease mechanisms, pathways, and crosscutting characteristics is critical to progressing scientific discovery and innovation in autoimmune disease diagnostics, prevention, and intervention. Supporting fundamental research into mechanisms of disease initiation and progression, including genetic and environmental drivers, disease subsets, biomarkers, and potential treatment targets, will advance opportunities to inform therapies and precision medicine, better understand disproportionate risk among populations, and apply knowledge and clinical developments across multiple autoimmune diseases.

1.2 Advance understanding of drivers of autoimmune disease signs, symptoms, and flares

Autoimmune disease signs and symptoms are wide ranging and often wax and wane over time. Many autoimmune diseases are characterized by flares—episodes during which the severity of symptoms worsens dramatically. Mechanisms of flares are not well understood, and frequency and severity of flares may vary in different populations. Research that includes representation from all populations and age groups is needed to understand the pathogenesis of disease manifestations and the mechanisms and drivers of flares. Furthermore, a life-course perspective will support the examination of factors that fluctuate over time and may contribute to autoimmune disease flares, such as hormonal changes and environmental influences.

1.3 Optimize development of research models for studying autoimmune disease

Representative, accurate research models that mimic human structure and function are critical for studying the basics of autoimmunity and autoimmune disease. Animal models are often used to study autoimmunity; however, these models are an imperfect representation of human disease. The development and refinement of research models for studying autoimmune diseases is crucial to advance autoimmune disease research. This effort may include the use of animal and non-animal models, organoids, and enhanced computational modeling, such as digital twins. Naturally occurring genetic abnormalities and drug-induced autoimmunity also offer a unique opportunity for studying the inception of autoimmunity in humans.

1.4 Improve understanding of predictors and risk factors for autoimmunity across the lifespan

Autoimmune diseases are affected by numerous variables, including individual biology, environment, geographic factors, infections, and life events, which may evolve, fluctuate, and compound over time. Accelerating autoimmune disease research requires integration of multiomic data from multiple sources. Multidimensional and longitudinal analysis of autoimmunity from pre-disease through clinical disease is needed to understand the progression, coexisting morbidities, and long-term outcomes of autoimmune diseases. Such analytics will enable scientists to integrate complex time-varying exposures, such as indirect health indicators and risks and exposures across the lifespan; identify common characteristics of autoimmune diseases; and understand the complex relationships driving autoimmune diseases.

PRIORITY 2. Promote research focused on enhancing health for people living with and at risk of autoimmune diseases

For people living with autoimmune diseases, early diagnosis, treatment, and intervention are crucial. Autoimmune diseases are chronic and may cause irreversible damage to multiple tissues and organs, with debilitating physical, psychosocial, and mental effects. Early intervention may help delay or prevent progression and reduce tissue and organ damage. However, delays in diagnosis and treatment of autoimmune diseases are common. To support tangible improvements in health for people living with autoimmune diseases, research focused on developing accurate diagnostics and effective treatments that are accessible and deployable in real-world settings are needed.

OBJECTIVES

2.1 Support research investigating preclinical autoimmunity

Autoimmunity often develops years prior to presentation of clinical symptoms. This asymptomatic period is known as the prodrome of autoimmune disease. The prodrome offers scientists a window to understand human immune responses to exposures and other triggers, advancing scientific knowledge of disease pathogenesis and offering opportunities to intervene before disease manifests. Research focused on examining preclinical autoimmunity and drivers of autoimmune disease in all populations will be crucial to prevent and reverse autoimmunity and promote health.

2.2 Advance research to accelerate accurate diagnosis of autoimmune disease

An accurate autoimmune disease diagnosis may take years to reach and involve multiple health care interactions. Delays in diagnosis allow disease to progress unchecked, sometimes causing irreparable damage. Research is needed to develop novel diagnostics that reduce the time to diagnosis and tools to predict complications and flares. It is essential to support biomarker discovery and the development of new technologies, such as point-of-care testing, imaging technology, sensors, and wearable technologies. Additionally, integrating predictive modeling tools into longitudinal and epidemiologic studies is important for improving disease diagnosis.

2.3 Bolster research focused on improving treatment for autoimmune disease

Treatments for autoimmune diseases may carry side effects and are frequently complex, involving time-consuming therapies, complicated medication regimens, and often with intravenous or injectable delivery methods. These factors contribute to nonadherence, which ultimately reduces treatment efficacy. To advance this field, research is needed into innovative therapies, tools and tests that help predict treatment responses, and improved drug delivery options. It is also critical to support research into the impact of psychosocial factors on health, and to study interventions that may improve quality of life—including therapeutic and nonmedical interventions—to enhance health and longevity for people living with autoimmune diseases.

2.4 Support implementation science for autoimmune disease research across all populations

Implementation science, focused on the uptake of research into clinical practice, is essential for ensuring that scientific findings are applied effectively and efficiently in a real-world setting. Studies are needed to assess how treatments for autoimmune diseases are implemented in practice, examine factors that contribute to low disease activity and remission, and to reduce direct and indirect costs associated with autoimmune diseases.

PRIORITY 3. Support research to understand the full complexity of autoimmune diseases

The incidence of autoimmune diseases is rising globally, and there are many gaps in understanding of how autoimmune diseases affect health across the lifespan. Longitudinal, cross-sectional, and other epidemiologic study of populations from before disease manifests through the course of disease are needed to advance understanding of autoimmune disease development, progression, and impact across all facets of daily life. Short- and long-term outcomes are influenced by numerous variables, including access to and complications from treatment. Genetics, microbiome, hormonal changes, internal and external environmental exposures, and indirect health indicators may all play a role in autoimmunity inception and long-term outcomes.

OBJECTIVES

3.1 Support the study of human cohorts for autoimmune disease research

Longitudinal and cross-sectional cohorts provide opportunities to follow groups of people with autoimmune diseases over time and to study differences between individuals that develop disease and those that do not. Cohorts enable investigators to study disease-specific phenotypes and the natural history of disease progression and complications over time. Through multidimensional analysis, researchers will gain insights into the complex interaction of genomics and exposomics across the lifespan that contribute to autoimmune disease development, progression, complications, and flares. These interactions may include genetic factors, environmental exposures, microbial factors, indirect health indicators, and other variables. The study of different cohorts will provide a foundation for development of predictive models to identify individuals and populations at risk of autoimmune disease, with a view to enabling strategic approaches to alter disease progression.

3.2 Promote research to understand how different populations are affected by autoimmune diseases

Prevalence of autoimmune diseases varies across populations. Autoimmune diseases also occur in children, presenting unique challenges in both diagnosis and care. Improved understanding of the differences in disease across and within populations may identify opportunities for prevention, treatment, and cure of autoimmunity. It is important to study new and established cohorts of people encompassing the spectrum of autoimmune diseases and individuals from all backgrounds and ages. Data generated through these studies will advance understanding of the complex, bidirectional relationships observed in autoimmunity, including between clinical profiles, health indicators, and life events, such as adolescence, pregnancy, midlife, menopause, and aging.

3.3 Advance research that will facilitate clinical trials for autoimmune diseases

Clinical trials are essential to bringing discoveries from the laboratory to the clinic and to accelerating the development of new treatments for autoimmune diseases. Data from observational, cross-sectional, and longitudinal cohort studies in autoimmune diseases can aid the design of clinical trials for novel therapies and preventive strategies. Harnessing the use of data science modalities and of adaptive, pragmatic clinical trial designs, including basket trials, adaptive trials, cluster trials, parallel randomized trials, and registry-embedded trials, will enable more efficient recruitment and completion of clinical trials in autoimmune diseases.

3.4 Expand autoimmune disease research focused on co-occurring and comorbid conditions

People living with an autoimmune disease often develop co-occurring autoimmune diseases and are at risk for other comorbidities. Research that examines new and known co-occurring and comorbid conditions, risk factors for developing comorbidities, their impact on autoimmune disease progression, and long-term outcomes for people living with autoimmune diseases is crucial to understanding how these coexisting and comorbid relationships vary in populations, and how autoimmunity progresses across the lifespan.

PRIORITY 4. Build and maintain capacity for autoimmune disease research

Development of infrastructure and the scientific workforce are important to ensure that high-priority autoimmune disease research can be executed and to further accelerate the translation of scientific discoveries into improvements in health. Scaling infrastructure to growing needs and adapting to rapid advancements in science on an ongoing basis will be crucial for the future of autoimmune disease research.

OBJECTIVES

4.1 Prioritize and support development of infrastructure for autoimmune disease research

Infrastructure is needed to support autoimmune disease research from discovery to implementation. Building and maintaining research pipelines and collaborative networks will facilitate the management and coordination of all aspects of research including molecular discovery, drug development, deployment of biologic and cellular therapies, and recruitment and retention in longitudinal registries and population cohorts. By prioritizing the development of research infrastructure and ensuring its continued support, the discovery of new mechanisms, biomarkers, and therapeutic targets will be accelerated.

4.2 Integrate clinical trial networks and registries in autoimmune disease research

Clinical trial networks are organized systems of clinicians, scientists, and institutions that span multiple sites and have a shared goal to accelerate scientific progress. Development of new networks as well as expansion and integration of existing clinical trial networks and registries, will support research to advance progress in autoimmune disease prevention, diagnosis, treatment, and cure. Supported research may include studies that validate biomarkers, deploy novel therapeutics, conduct imaging studies, identify best clinical practices, and identify important commonalities across autoimmune diseases. Clinical trial and other networks encourage interaction between researchers, clinicians, people living with autoimmune diseases, caregivers, and community organizations—facilitating multidisciplinary collaboration and reducing barriers to access clinical trials. Expanding network infrastructure will provide a foundation to accelerate autoimmune disease research and to promote preclinical and clinical progress.

4.3 Develop data science and computational tools to accelerate autoimmune disease research

Although large quantities of autoimmune disease data exist, they are often under-utilized for many reasons. Robust data science and advanced computational tools are necessary to collect, manage, integrate, analyze, and further utilize substantial amounts of autoimmune disease data. Foundational components of data integration include defining ontologies and common data elements to harmonize datasets and leveraging computational models to integrate multiomic profiles across diseases over time to better understand the human immunome and autoimmunity across the lifespan. Investing in foundational data platforms for autoimmune disease research will enable NIH to support development of modeling pipelines, federated data platforms and analytical tools such as machine learning, and other computational approaches to accelerate autoimmune disease research.

4.4 Support efforts to develop and sustain the scientific workforce

Developing a scientific workforce is imperative to drive autoimmune science forward. A skilled workforce includes basic, translational, clinical, computational, and multidisciplinary scientists capable of supporting novel interventions. Bolstering the research workforce pipeline requires training and support for new investigators, efforts to retain established scientists, and ongoing efforts to ensure that the workforce adapts to evolving scientific progress. This is necessary to enable NIH to gather varied perspectives, catalyze innovation, and support building trust in the scientific community.

PRIORITY 5. Build and strengthen partnerships and interdisciplinary collaboration across the autoimmune disease community

Developing and maintaining partnerships and opportunities for collaboration across the autoimmune disease community is crucial to stimulate innovation in the research process. Autoimmune disease research inherently benefits from interdisciplinary expertise because of complex risk factors, shared crosscutting characteristics, and the fact that autoimmune diseases are often systemic and commonly co-occur. Scientific advances require engagement and collaboration across the autoimmune disease community, including people living with autoimmune diseases, advocates, caregivers, academic researchers, health care professionals, philanthropic organizations, industry partners, and federal entities. NIH is committed to supporting these partnerships to advance autoimmune disease research.

OBJECTIVES

5.1 Leverage public–private partnerships to support autoimmune disease research

Public–private partnerships bring unique opportunities to autoimmune disease research, including access to new resources and technologies, increased logistical support, and opportunities to advance interdisciplinary research. By building on current and fostering new partnerships, innovations in biomarker discovery, therapies, imaging and sensor technology, and predictive tools for autoimmune disease will be accelerated.

5.2 Engage people living with autoimmune diseases, patient advocacy groups, and caregivers in research

People living with autoimmune diseases, patient advocacy groups, and caregivers are all essential community partners in science, providing unique perspectives that add value to all stages of autoimmune disease research. Incorporating community input throughout the research process accelerates research that is relevant, accessible, and implementable. Dialogues with the autoimmune disease community will be established and maintained through regular updates, research seminars, virtual roundtables and formal RFIs. This engagement will ensure that high-priority research is supported to enhance outcomes for people with and affected by autoimmune diseases.

5.3 Partner with people and communities disproportionately affected by autoimmune disease outcomes

Building strong community partnerships that include populations that are disproportionately affected by autoimmune diseases is essential to establishing a robust research network. Prioritizing new and existing partner engagement, will ensure involvement of all individuals and perspectives in research by addressing challenges and barriers experienced by these communities. Strengthening community networks will both support the implementation and dissemination of research findings and benefit public health.

5.4 Coordinate and foster collaborative research

To amplify existing research efforts and create new opportunities, interdisciplinary collaborations through NIH-wide and federal interagency partnerships will be fostered, along with opportunities for cross-ICO partnership in autoimmune disease research through research events, and other interdisciplinary activities.

CROSSCUTTING THEMES

Five crosscutting themes representing foundational concepts interwoven through the strategic plan were developed with input from the autoimmune disease community to complement the strategic priorities and objectives. The crosscutting themes echo the importance of rigorous and collaborative autoimmune disease research and dovetail with the *NIH-Wide Strategic Plan for Fiscal Years 2021–2025*.

THEME 1: Harness technologies to advance autoimmune disease research

Advancing and harnessing technologies to drive scientific progress is important to stimulate research and improve autoimmune disease outcomes. Advanced technologies, including artificial intelligence and systems biology approaches, can support efforts to improve how scientists define and classify autoimmune diseases at a molecular level, and can stimulate groundbreaking discoveries, such as targeted and cell-based therapies. Imaging, sensor, and wearable technologies can aid in reducing time to diagnosis and help predict disease flares. New point-of-care technology can increase accessibility for patients with limited access to health care, and predictive modeling can be influential in devising individualized approaches to patient screening and therapy. By supporting technologies in research, new scientific discoveries for autoimmune disease research will be catalyzed.

THEME 2: Develop infrastructure for translation of autoimmune disease research

Translational science bridges fundamental discovery into clinical applications and supports real-world adoption of discovery into practice. Optimizing the autoimmune disease research environment and accelerating translation of discovery into practice is essential for delivering improved outcomes for people living with and affected by autoimmune disease. Autoimmune disease research infrastructure needs will grow with scientific advances, and will likely include clinical trial infrastructure, workforce training and re-entry initiatives, and programmatic opportunities dedicated to promoting translational research. Digital infrastructure to manage, share, and analyze data from population cohorts to accelerate new therapeutic interventions will also be critical for supporting autoimmune disease research.

THEME 3: Support multimodal data-driven approaches for autoimmune disease research

Autoimmune diseases are impacted by multiple factors. Individual biology, including genetics and epigenetics, play a role in autoimmunity. It is also well established that the exposome, which encompasses the many variables external to an individual that fluctuate and change over time, also plays a role in the development of autoimmune disease. Integrative analysis of these complex interrelated and time-varying factors requires innovative analytic approaches including artificial intelligence and systems biology methodologies. Integration of high-throughput data analytic platforms and innovative approaches to advance understanding of the complex multidimensional data generated will be critical to support autoimmune disease research.

THEME 4: Promote engagement of all populations in autoimmune disease research

Effective research helps confirm that scientific discoveries are applicable across all populations. Dedicated efforts are needed to ensure that all populations are accounted for during data analysis. Women and certain racial and ethnic groups develop autoimmune diseases at disproportionate rates yet are historically underrepresented in research. In contrast when men develop autoimmune diseases, they often have worse outcomes. Rates of autoimmunity are also increasing in children, a population often excluded from research. Environmental exposures and life events differ across populations and over the lifespan, and the relationships of exposures to autoimmune disease merit further study. Rigorous research will support a clearer understanding of differences in autoimmunity across populations, the epidemiology of autoimmune diseases, and the complex factors that influence autoimmune disease inception and progression.

THEME 5: Support community partnerships for autoimmune disease research

Ongoing partnerships and multidisciplinary collaborations, across and within autoimmune disease communities, are vital to stimulate new perspectives, innovation, and exchange of information and resources for autoimmune disease research. Collaboration across all phases of research will incorporate different perspectives, resources, and expertise to drive high-priority scientific advances.

IMPLEMENTATION VISION: NIH-WIDE STRATEGIC PLAN FOR AUTOIMMUNE DISEASE RESEARCH

The *NIH-Wide Strategic Plan for Autoimmune Disease Research* sets forth a unified approach to accelerate scientific discovery, expand capacity, and catalyze critical partnerships and collaborations for autoimmune disease research. This plan will serve as a framework to guide priority setting across NIH for the next five years, with the voices of people living with autoimmune diseases remaining paramount. Implementing this strategic plan will accelerate discoveries in autoimmune disease research leading to improved health outcomes and better well-being for all people living with or at risk of autoimmune diseases. Figure 6 illustrates a schema for implementation through sustaining and expanding ongoing activities, employing a unified approach to accelerate progress, and achieving bold initiatives. Working in partnership with ICs, OADR-ORWH will monitor and evaluate progress toward achieving the objectives outlined in this strategic plan and will collaborate to create opportunities, fill gaps, and emphasize cross-disciplinary endeavors.

Figure 6. Building on existing programs, implementation of the *NIH-Wide Strategic Plan for Autoimmune Disease Research* centers on accelerating research progress and innovation and catalyzing bold initiatives.

REFERENCES

1. National Academies of Sciences, Engineering, and Medicine. *Enhancing NIH Research on Autoimmune Disease: Consensus Study Report*. National Academies Press; 2022.

2. Miller FW. The increasing prevalence of autoimmunity and autoimmune diseases: an urgent call to action for improved understanding, diagnosis, treatment, and prevention. *Curr Opin Immunol*. doi:10.1016/j.coi.2022.102266.

3. Jacobson DL, Gange SJ, Rose NR, Graham NM. Epidemiology and estimated population burden of selected autoimmune diseases in the United States. *Clin Immunol Immunopathol*. 1997;84(3):223-243. doi:10.1006/clin.1997.4412.

4. Conrad N, Misra S, Verbakel JY, Verbeke G, Molenberghs G, Taylor PN, Mason J, Sattar N, McMurray JJV, McInnes IB, Khunti K, Cambridge G. Incidence, prevalence, and co-occurrence of autoimmune disorders over time and by age, sex, and socioeconomic status: a population-based cohort study of 22 million individuals in the UK. *Lancet*. 2023;401(10391):1878-1890. doi:10.1016/s0140-6736(23)00457-9.

5. Arbuckle MR, McClain MT, Rubertone MV, Scofield RH, Dennis GJ, James JA, Harley JB. Development of autoantibodies before the clinical onset of systemic lupus erythematosus. *N Engl J Med*. 2003;349(16):1526-1533. doi:10.1056/NEJMoa021933.

6. Sahin D, Di Matteo A, Emery P. Biomarkers in the diagnosis, prognosis and management of rheumatoid arthritis: A comprehensive review. *Ann Clin Biochem*. 2024:45632241285843. doi:10.1177/00045632241285843.

7. Herold KC, Bundy BN, Long SA, Bluestone JA, DiMeglio LA, Dufort MJ, Gitelman SE, Gottlieb PA, Krischer JP, Linsley PS, Marks JB, Moore W, Moran A, Rodriguez H, Russell WE, Schatz D, Skyler JS, Tsalikian E, Wherrett DK, Ziegler AG, Greenbaum CJ. An anti-CD3 antibody, teplizumab, in relatives at risk for type 1 diabetes. *N Engl J Med*. 2019;381(7):603-613. doi:10.1056/NEJMoa1902226.

8. McInnes IB, Schett G. The pathogenesis of rheumatoid arthritis. *N Engl J Med*. 2011;365(23):2205-2219. doi:10.1056/NEJMra1004965.

9. Schett G, McInnes IB, Neurath MF. Reframing immune-mediated inflammatory diseases through signature cytokine hubs. *N Engl J Med*. 2021;385(7):628-639. doi:10.1056/NEJMra1909094.

10. Hocaoglu M, Casares-Marfil D, Sawalha AH. Genetic analysis of asymptomatic antinuclear antibody production. *Arthritis Rheumatol*. 2024. doi:10.1002/art.43032.

11. Grayson PC, Patel BA, Young NS. VEXAS syndrome. *Blood*. 2021;137(26):3591-3594. doi:10.1182/blood.2021011455.

12. Young NS. Aplastic anemia. *N Engl J Med*. 2018;379(17):1643-1656. doi:10.1056/NEJMra1413485.

13. Brodsky RA. Paroxysmal nocturnal hemoglobinuria. *Blood*. 2014;124(18):2804-2811. doi:10.1182/blood-2014-02-522128.

14. Selmi C, Lu Q, Humble MC. Heritability versus the role of the environment in autoimmunity. *J Autoimmun*. 2012;39(4):249-252. doi:10.1016/j.jaut.2012.07.011.

15. Vermeulen R, Schymanski EL, Barabási AL, Miller GW. The exposome and health: where chemistry meets biology. *Science*. 2020;367(6476):392-396. doi:10.1126/science.aay3164.

16. Wild CP. Complementing the genome with an “exposome”: the outstanding challenge of environmental exposure measurement in molecular epidemiology. *Cancer Epidemiol Biomarkers Prev*. 2005;14(8):1847-1850. doi:10.1158/1055-9965.

17. Miller FW, Alfredsson L, Costenbader KH, Kamen DL, Nelson LM, Norris JM, De Roos AJ. Epidemiology of environmental exposures and human autoimmune diseases: findings from a National Institute of Environmental Health Sciences Expert Panel Workshop. *J Autoimmun*. 2012;39(4):259-271.

18. Parks CG, Miller FW, Pollard KM, Selmi C, Germolec D, Joyce K, Rose NR, Humble MC. Expert panel workshop consensus statement on the role of the environment in the development of autoimmune disease. *Int J Mol Sci*. 2014;15(8):14269-14297. doi:10.3390/ijms150814269.

19. Whitacre CC. Sex differences in autoimmune disease. *Nat Immunol*. 2001;2(9):777-780. doi:10.1038/ni0901-777.

20. Sumelahti ML, Verkko A, Kytö V, Sipilä JOT. Stable excess mortality in a multiple sclerosis cohort diagnosed 1970-2010. *Eur J Neurol*. 2024:e16480. doi:10.1111/ene.16480. PubMed PMID: 39258870.

21. Singh RR, Singh DR, Yen EY. Worsening premature death burden gap from systemic sclerosis in men and black persons: a US nationwide population-based study. *J Scleroderma Relat Disord*. 2023;8(1):20-26. doi:10.1177/23971983221140538.

22. Klein SL, Flanagan KL. Sex differences in immune responses. *Nat Rev Immunol*. 2016;16(10):626-638. doi:10.1038/nri.2016.90.

23. Forsyth KS, Jiwrajka N, Lovell CD, Toothacre NE, Anguera MC. The conneXion between sex and immune responses. *Nat Rev Immunol*. 2024. doi:10.1038/s41577-024-00996-9.

24. Buie J, McMillan E, Kirby J, Cardenas LA, Eftekhari S, Feldman CH, Gawuga C, Knight AM, Lim SS, McCalla S, McClamb D, Polk B, Williams E, Yelin E, Shah S, Costenbader KH. Disparities in lupus and the role of social determinants of health: current state of knowledge and directions for future research. *ACR Open Rheumatol*. 2023;5(9):454-464. doi:10.1002/acr2.11590.

25. Chang JC, Liu JP, Berbert LM, Chandler MT, Patel PN, Smitherman EA, Weller EA, Son MBF, Costenbader KH. Racial and ethnic composition of populations served by freestanding children's hospitals and disparities in outcomes of pediatric lupus. *Arthritis Care Res (Hoboken)*. 2024;76(7):926-935. doi:10.1002/acr.25314.

26. Public Health Service Act, 42 USC §289a-2 (2011).

27. Amendment: NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research [cited 2024 12/4/2024]. Available from: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-014.html.

28. 21st Century Cures Act, 42 USC §241(d)(4) (2016).

29. Parks CG, Costenbader KH. The exposome: what is it, really, and does it help to understand environmental influences on human health and rheumatic disease? *Arthritis Rheumatol*. 2024. doi:10.1002/art.42816.

30. Conrad N, Verbeke G, Molenberghs G, Goetschalckx L, Callender T, Cambridge G, Mason JC, Rahimi K, McMurray JJV, Verbakel JY. Autoimmune diseases and cardiovascular risk: a population-based study on 19 autoimmune diseases and 12 cardiovascular diseases in 22 million individuals in the UK. *Lancet*. 2022;400(10354):733-743. doi:10.1016/s0140-6736(22)01349-6.

31. Sparks JA, Malspeis S, Hahn J, Wang J, Roberts AL, Kubzansky LD, Costenbader KH. Depression and subsequent risk for incident rheumatoid arthritis among women. *Arthritis Care Res (Hoboken)*. 2021;73(1):78-89. doi:10.1002/acr.24441.

32. Howren A, Sayre EC, Avina-Zubieta JA, Puyat JH, Da Costa D, Xie H, Davidson E, De Vera MA. "What came first?" Population-based evaluation of health care encounters for depression and anxiety before and after inflammatory arthritis diagnosis: disentangling the relationship between mental health and arthritis. *Arthritis Care Res (Hoboken)*. 2024;76(5):743-752. doi:10.1002/acr.25294.

33. Brock J, Basu N, Schlachetzki JCM, Schett G, McInnes IB, Cavanagh J. Immune mechanisms of depression in rheumatoid arthritis. *Nat Rev Rheumatol*. 2023;19(12):790-804. doi:10.1038/s41584-023-01037-w.

34. Battafarano DF, Ditmyer M, Bolster MB, Fitzgerald JD, Deal C, Bass AR, Molina R, Erickson AR, Hausmann JS, Klein-Gitelman M, Imundo LF, Smith BJ, Jones K, Greene K, Monrad SU. 2015 American College of Rheumatology Workforce

REFERENCES

Study: Supply and Demand Projections of Adult Rheumatology Workforce, 2015-2030. *Arthritis Care Res (Hoboken)*. 2018;70(4):617-626. doi:10.1002/acr.23518.

35. Hartman AL, Weigand LA, Korn SJ, Wright CB. Training clinical scientists: at all career stages. *Neurology*. 2024;103(3):e209612. doi:10.1212/wnl.0000000000209612.

36. NIH Reporter 2024 [cited 2024 September 6]. Available from: https://reporter.nih.gov/search/jaM-OeL5Z06RdyOZdknCgg/projects/charts

APPENDIX A:
COORDINATING COMMITTEE FOR AUTOIMMUNE DISEASE RESEARCH

Coordinating Committee for Autoimmune Disease Research

The Coordinating Committee for Autoimmune Disease Research (CCADR) is an internal National Institutes of Health (NIH) committee convened in support of autoimmune disease research at NIH. CCADR members include NIH Institute, Center, and Office (ICO) representatives nominated by ICO Directors, the Office of Autoimmune Disease Research in the Office of Research on Women's Health (OADR-ORWH) and ORWH leadership, and program management staff. Together these individuals bring broad subject matter expertise and experience in autoimmune disease research, priorities, and policy. Members discuss programmatic, scientific, and operational focus areas as well as action plans to leverage ongoing NIH investments in autoimmune disease research.

Strategic Plan Working Group

The Strategic Plan Working Group (SPWG) is an internal NIH-wide working group created under CCADR. With representation from 21 out of 27 Institutes and Centers (ICs), the SPWG provides subject matter expertise in immunology and autoimmune disease research as well as NIH operations and strategic planning. The SPWG drove the development of the inaugural *NIH-Wide Strategic Plan for Autoimmune Disease Research*, evaluating and integrating numerous sources of data to identify gaps, opportunities, and high-priority research areas to create the framework to advance autoimmune disease research across NIH. The SPWG was organized in September 2023, met monthly through July 2025, and continues to meet as needed. OADR-ORWH coordinates the SPWG and related activities. In the CCADR member list, SPWG Members are denoted with an asterisk (*) and SPWG Co-Chairs are denoted with a double asterisk (**).

CCADR Primary Representatives (as of December 2024)

Janine A. Clayton, M.D., FARVO
Co-Chairperson
Associate Director for Research on Women's Health
Director
Office of Research on Women's Health

Victoria Shanmugam, MBBS, MRCP, FACR, CCD**
Co-Chairperson
Director
Office of Autoimmune Disease Research in the Office of Research on Women's Health

Nandini Arunkumar, Ph.D.*
Program Director
Office of Strategic Development and Partnerships
Division of Neuroscience
National Institute on Aging

Preethi Chander, Ph.D.*
Director
Salivary Biology and Immunology Program
Division of Extramural Research
National Institute of Dental and Craniofacial Research

Elaine Collier, M.D.
Senior Advisor to the Director
Office of Translational Medicine
National Center for Advancing Translational Sciences

Tuba Fehr, Ph.D.*
Program Director
Division of Discovery Science and Technology (Bioengineering)
National Institute of Biomedical Imaging and Bioengineering

APPENDIX A:
COORDINATING COMMITTEE FOR AUTOIMMUNE DISEASE RESEARCH

Stacy Ferguson, Ph.D.*
Chief
Autoimmune and Primary Immunodeficiency Diseases Section
National Institute of Allergy and Infectious Diseases

Nataliya Gordiyenko, Ph.D.*
Program Director
Angiogenesis and Immunology
National Eye Institute

Dan Kastner, M.D., Ph.D.**
NIH Distinguished Investigator, Medical Genetics Branch
Head, Inflammatory Disease Section
National Human Genome Research Institute

Hye-Sook Kim, Ph.D.*
Program Director
Basic and Mechanistic Research in Complementary and Integrative Health Branch
Division of Extramural Research
National Center for Complementary and Integrative Health

Lillian Kuo, Ph.D.*
Program Director
Cancer Immunology, Hematology, and Etiology Branch
Division of Cancer Biology
National Cancer Institute

Li Lin, Ph.D.*
Program Director
Division of Metabolism and Health Effects
National Institute on Alcohol Abuse and Alcoholism

Lynne S. Padgett, Ph.D., FAPOS*
Program Director
Division of Clinical and Health Services Research
National Institute on Minority Health and Health Disparities

Lisa Rider, M.D.*
Head and Senior Clinician
Environmental Autoimmunity Group
National Institute of Environmental Health Sciences

Sergio D. Rosenzweig, M.D., Ph.D.*
Chief, Immunology Service
Senior Investigator, Department of Laboratory Medicine
NIH Clinical Center

Richard Scheuermann, Ph.D.*
Scientific Director
National Library of Medicine

Susana A. Serrate-Sztein, M.D.*
Associate Director for Strategic Initiatives
Office of the Director
National Institute of Arthritis and Musculoskeletal and Skin Diseases

Ross Shonat, Ph.D.*
Director
Division of Physiological and Pathological Sciences
Center for Scientific Review

Lisa M. Spain, Ph.D.*
Program Director
Division of Diabetes, Endocrinology, & Metabolic Diseases
National Institute of Diabetes and Digestive and Kidney Diseases

Candace Tingen, Ph.D.*
Chief
Gynecologic Health and Disease Branch
Division of Extramural Research
Eunice Kennedy Shriver National Institute of Child Health and Human Development

APPENDIX A:
COORDINATING COMMITTEE FOR AUTOIMMUNE DISEASE RESEARCH

Leonardo Tonelli, Ph.D.*
Chief
Neuroendocrinology and Neuroimmunology Program
Molecular and Cellular Neuroscience Research Branch
Division of Neuroscience and Basic Behavioral Science
National Institute of Mental Health

Ursula Utz, Ph.D., M.B.A.*
Program Director
Neural Environment Cluster
Division of Neuroscience
National Institute of Neurological Disorders and Stroke

Louis Vuga, M.D., M.P.H., Ph.D.*
Program Director
Granulomatous and Interstitial Lung Disease Program
Division of Lung Diseases
National Heart, Lung, and Blood Institute

Bracie Watson, Ph.D.*
Hearing and Balance
Division of Scientific Programs
National Institute on Deafness and Other Communication Disorders

CCADR Secondary Representatives (as of December 2024)

Beena Akolkar, Ph.D.*
Senior Advisor, Immunopathogenesis and Genetics of Diabetes Programs
Division of Diabetes, Endocrinology, & Metabolic Diseases
National Institute of Diabetes and Digestive Kidney Diseases

Larissa Aviles-Santa, M.D., M.P.H.*
Director
Division of Clinical and Health Services Research
National Institute on Minority Health and Health Disparities

Inna Belfer, M.D., Ph.D.*
Deputy Branch Chief
Basic and Mechanistic Research in Complementary and Integrative Health Branch
Program Director
Division of Extramural Research
National Center for Complementary and Integrative Health

William P. Daley, Ph.D.*
Program Director
Division of Neuroscience
National Institute of Neurological Disorders and Stroke

Nichole Daringer, Ph.D.*
Program Director
Division of Discovery Science and Technology (Bioengineering)
National Institute of Biomedical Imaging and Bioengineering

Margaret M. Grisius, D.D.S.*
Director
Oral & Comprehensive Health Program
Clinical Technologies Research Program
National Institute of Dental and Craniofacial Research

Mireia Guerau, Ph.D.*
Program Officer
Autoimmunity and Mucosal Immunology Branch
Division of Allergy, Immunology, and Transplantation
National Institute of Allergy and Infectious Diseases

Michael Humble, Ph.D.*
Health Scientist Administrator, Basic Science
Genes, Environment, and Health Branch
National Institute of Environmental Health Sciences

APPENDIX A:
COORDINATING COMMITTEE FOR AUTOIMMUNE DISEASE RESEARCH

Ruth Kirby, R.N., B.S.*
Program Officer
Clinical Trial Management/Operations
Autoimmune and Cardiovascular Diseases
National Heart, Lung, and Blood Institute

Yin Liu, Ph.D.*
Program Director
Cancer Immunology, Hematology, and Etiology Branch
Division of Cancer Biology
National Cancer Institute

Marie Mancini, Ph.D.*
Program Director
Systemic Autoimmune Disease Biology Program
National Institute of Arthritis and Musculoskeletal and Skin Diseases

Yael Mandelblat-Cerf, Ph.D.*
Chief
Molecular and Cellular Neuroscience Research Branch
Division of Neuroscience and Basic Behavioral Science
National Institute of Mental Health

George A. McKie, D.V.M., Ph.D.*
Program Officer
Division of Extramural Sciences Program
National Eye Institute

Joan Davis Nagel, M.D., M.P.H.*
Medical Officer and Program Director
Clinical and Translational Science Awards Program Branch
Division of Clinical Innovation
Initiatives & Consortium Wide Activities Section
National Center for Advancing Translational Sciences

Amanda Alise Price, Ph.D.*
Program Officer
Office of the Director
Eunice Kennedy Shriver National Institute of Child Health and Human Development

Mulualem Tilahun, D.V.M., Ph.D.*
Program Officer
Aging Physiology Branch
Division of Aging Biology
National Institute on Aging

H. Joe Wang, Ph.D.*
Program Director
Division of Metabolism and Health Effects
National Institute on Alcohol Abuse and Alcoholism

SPWG Guests (as of December 2024)

Sarah Rhodes, Ph.D.
Assistant Director for Planning and Reporting
Office of Evaluation, Performance, and Reporting

Kelly Singel, Ph.D.
Health Science Policy Analyst
Office of Evaluation, Performance, and Reporting

APPENDIX B:
DISEASES INCLUDED IN PORTFOLIO ANALYSIS

Auditory/Ear

Autoimmune inner ear disease
Cogan's syndrome
Meniere's disease

Complex Comorbid Conditions

Autoimmune dysautonomia
Chronic Lyme disease
Fibromyalgia
Interstitial cystitis
Narcolepsy

Dermatologic/Mucosa

Alopecia areata
Autoimmune urticaria
Benign mucosal pemphigoid
Bullous pemphigoid
Cicatricial pemphigoid
Hidradenitis suppurativa
Lichen planus
Lichen sclerosus
Pityriasis lichenoides et varioliformis acuta (PLEVA or Mucha-Habermann disease)
Pemphigus
Pyoderma gangrenosum
Vitiligo

Endocrine

Addison's disease
Graves' disease
Hashimoto's thyroiditis
Polyglandular syndromes types I, II, III
Thyroid eye disease
Type 1 diabetes

Gastrointestinal

Autoimmune hepatitis
Autoimmune pancreatitis
Celiac disease
Crohn's disease
Dermatitis herpetiformis
Eosinophilic esophagitis
Primary biliary cholangitis
Primary sclerosing cholangitis
Ulcerative colitis

Gynecological and Fertility

Autoimmune oophoritis
Autoimmune orchitis
Herpes gestationis
Progesterone dermatitis
Endometriosis

Hematology

Agammaglobulinemia
Amyloidosis
Autoimmune angioedema
Autoimmune hemolytic anemia
Autoimmune neutropenia
Autoimmune thrombocytopenic purpura
Castleman disease
Cold agglutinin disease
Essential mixed cryoglobulinemia
Paroxysmal nocturnal hemoglobinuria
Pernicious anemia
POEMS syndrome
Pure red cell aplasia

APPENDIX B:
DISEASES INCLUDED IN PORTFOLIO ANALYSIS

Lupus/Scleroderma/Myositis

Antiphospholipid syndrome
Congenital heart block
CREST syndrome (Limited scleroderma)
Dermatomyositis
Discoid lupus
Eosinophilic fasciitis
Evans syndrome
Inclusion body myositis
Juvenile myositis
Mixed connective tissue disease
Myositis/Polymyositis
Neonatal lupus
Progressive hemifacial atrophy
Raynaud's phenomenon
Scleroderma
Sjögren's disease
Systemic Lupus Erythematosus

Neurologic/Myelin-related

Autoimmune encephalitis
Baló disease
Chronic inflammatory demyelinating polyneuropathy
Complex regional pain syndrome
Guillain-Barré syndrome
Lambert-Eaton syndrome
Multifocal motor neuropathy
Multiple sclerosis
Myasthenia gravis
Myelin oligodendrocyte glycoprotein antibody associated disease (MOGAD)
Neuromyelitis optica
Optic neuritis
Paraneoplastic cerebellar degeneration
Brachial neuritis (Parsonage-Turner syndrome)
Perivenous encephalomyelitis
Stiff person syndrome
Transverse myelitis

APPENDIX B:
DISEASES INCLUDED IN PORTFOLIO ANALYSIS

Ocular/Eye

Autoimmune retinopathy
Autoimmune uveitis
Pars planitis
Scleritis
Sympathetic ophthalmia
Tolosa-Hunt syndrome

Pulmonary

Erythema nodosum
Fibrosing alveolitis
Pulmonary Alveolar Proteinosis
Sarcoidosis

Renal

Glomerulonephritis
Goodpasture's syndrome
Henoch-Schonlein purpura
IgA nephropathy
Linear IgA disease

Rheumatoid Arthritis and Seronegatives

Ankylosing spondylitis
Juvenile idiopathic arthritis
Palindromic rheumatism
Psoriasis
Psoriatic arthritis
Reactive arthritis
Rheumatoid arthritis

Systemic Inflammatory Conditions

Adult Still's disease
Chronic recurrent multifocal osteomyelitis
Giant cell myocarditis
Kawasaki disease
Myocarditis
PANDAS or PANS (Pediatric autoimmune neuropsychiatric disorders associated with streptococcus infections)
Postmyocardial infarction syndrome (Dressler's syndrome)
Rheumatic fever

Vasculitis

Autoimmune vasculitis
Behçet's disease
Churg-Strauss syndrome
Giant cell arteritis
Granulomatosis with polyangiitis
IgG4-related sclerosing disease
Microscopic polyangiitis
Polyarteritis nodosa
Polymyalgia rheumatica
Relapsing polychondritis
Retroperitoneal fibrosis
Susac's syndrome
Takayasu's arteritis
Vogt-Koyanagi-Harada disease

National Institutes of Health

U.S. Department of Health & Human Services
National Institutes of Health
9000 Rockville Pike
Bethesda, Maryland 20892
https://www.nih.gov/