EXHIBIT 22

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

AMERICAN PUBLIC HEALTH ASSOCIATION; IBIS REPRODUCTIVE HEALTH; INTERNATIONAL UNION, UNITED AUTOMOBILE, AEROSPACE, AND AGRICULTURAL IMPLEMENT WORKERS (UAW); BRITTANY CHARLTON; KATIE EDWARDS; PETER LURIE; and NICOLE MAPHIS *Plaintiffs*, v. NATIONAL INSTITUTES OF HEALTH; JAY BHATTACHARYA, *in his official capacity as Director of the National Institutes of Health*; UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES; and ROBERT F. KENNEDY, JR., *in his official capacity as Secretary of the United States Department of Health and Human Services*, *Defendants*.	Case No. 1:25-cv-10787

DECLARATION OF PETER LURIE, MD, MPH

I, Peter Lurie, MD, MPH, pursuant to 28 U.S.C. § 1746, depose and say as follows:

1. I am the Executive Director and President of the Center for Science in the Public Interest, a 501(c)(3) nonprofit organization based in Washington, D.C. that advocates for improving public health through science-based policies and promoting scientific integrity.

2. I am offering this Declaration in my individual capacity and not on behalf of my employer.

3. I obtained a Bachelor of Arts Degree in Chemistry from Cornell University in 1982. In 1987, I obtained my Doctor of Medicine degree from the Albert Einstein College of Medicine, and I completed residencies in Family Medicine in 1990 and Preventive Medicine in 1992. I was an Assistant Professor of Epidemiology and Biostatistics and of Family and Community Medicine at the University of California, San Francisco from 1993-1998 and a Visiting Assistant Research Scientist at the University of Michigan Institute for Social Research from 1997-1999. I hold an adjunct faculty position at the Johns Hopkins School of Public Health and previously did so at the George Washington University School of Public Health and Health Sciences.

4. I have conducted research on HIV infection since the late 1980s. My main areas of interest are needle exchange programs, HIV vaccine trials, clinical trial ethics, HIV testing, the impact of foreign aid on the HIV epidemic, the epidemiology of HIV infection in developing countries, and post-exposure prophylaxis.

5. In the mid-1990s, I was the recipient of a grant from the National Institute of Drug Abuse to study the efficacy of needle exchange programs to prevent HIV infection. In 1998, I submitted a grant to the National Institute on Drug Abuse on the same topic, but it was not funded.

6. From 2014-2017, I was an Associate Commissioner at the U.S. Food and Drug Administration where I worked on a range of regulatory and analytical issues across the agency, including HIV pre-exposure prophylaxis and a potential switch to over-the-counter status for the opioid-reversal drug naloxone.

7. I was an advisor/consultant on an NIH-funded R21 grant titled "Over-the-Counter PrEP: Acceptability, Feasibility, and Potential Impact of Access without a Prescription (OFFSCRIPT)," which aimed to "evaluate the acceptability, feasibility, and potential impact of over-the-counter PrEP," or pre-exposure prophylaxis to reduce the risk of HIV transmission. The grant began on

July 1, 2024, and was a 2-year grant for $489,120. Of this, $277,552 was paid before it was terminated.

8. The Principal Investigators for this grant were Julia Marcus and Douglas Krakower, both of whom are Associate Professors at Harvard Medical School. Due to my decades of experience in HIV research and drug regulation, I was contacted by the Principal Investigators and asked to be an advisor/consultant on the grant and agreed to do so. In this role, I received and was to continue receiving a small amount of compensation under the grant for my services. I participated in some meetings about the grant.

9. The OFFSCRIPT grant was originally awarded based on an application responsive to a posting by the National Institute of Mental Health's Division of AIDS Research, which called specifically for projects that "advance innovative research to optimize HIV prevention and care."

10. The NIH-Wide Strategic Plan for Fiscal Years 2021-2025 lists thirty-five Bold Predictions, one of which is "NIH-wide research will lead to new implementation strategies for pre-exposure prophylaxis that will significantly reduce the number of new HIV infections and to new longacting therapies to improve viral load suppression among people with HIV to levels that prevent transmission." *See* Ex. A, NIH-Wide Strategic Plan for Fiscal Years 2021-2025, at 35, Bold Prediction no. 15.

11. The OFFSCRIPT grant scored in the top 3% of applications during the NIH review process and was funded in part by Innovation Funds from the NIH Office of the Director.

12. However, on March 21, 2025, the grantee institution received a notice from NIH stating that the OFFSCRIPT grant had been terminated. That letter asserted that the award "no longer effectuate[d] agency priorities" and stated that the basis for termination was that the grant was "based on gender identity." At no time before receiving this termination letter did I or the

Principal Investigators receive any notice that this grant was being considered for termination. In addition, no guidance was provided about how to close out the study and how to manage study participants who had already agreed to participate.

13. Despite the assertions in the termination letter, in actuality, the OFFSCRIPT grant was not "based on gender identity," but rather focused on the efficacy of increasing access to preventative HIV drugs for all patients. Though the grant plan included an assessment of "diverse cohorts of cisgender MSM [men who have sex with men], transgender women, and cisgender women on interest in use of OTC PrEP," such an assessment is a necessary tool to evaluate the potential impact of expanding access to PrEP on the population groups most likely to benefit from it. It was not the grant's primary purpose. To my knowledge, this is the first grant to ever look at OTC PrEP.

14. I found the termination letter vague. I do not know exactly what makes a research project to be "based on gender identity," or which NIH priorities this award "no longer effectuates." Similarly, due to the vagueness of the termination letter, I do not know what public health topics might be funded by NIH in the future. Even though I understand that an administrative appeal will be filed concerning this termination, this is likely to be a futile exercise.

15. There were three main study aims, described in this paragraph, and we were mid-way in making progress on these study aims. First, we were in the midst of collaborating with others who had appropriate cohorts to assess subjects' interest in PrEP. Second, we had begun conducting interviews with key stakeholders on attitudes toward PrEP and were starting to analyze those transcripts. Third, we had built a mathematical model to estimate the impact of OTC PrEP on new HIV infections and relevant safety outcomes. As a result of the termination of this grant, work on all three of the study aims was largely stopped.

16. In addition, before the termination, we presented preliminary research at a national conference and were preparing a manuscript describing our findings.

17. As a result of the termination of the OFFSCRIPT grant, the research into PrEP access being conducted under the grant has been largely discontinued, resulting in harms to public health in the form of reduced knowledge about how to effectively reduce the spread of HIV. This is a loss to the American public because PrEP is highly effective but greatly underutilized, a gap this research might have bridged.

18. I will no longer benefit from either financial disbursements under the grant, nor will I be able to conduct the work I set out to complete in assisting in the evaluation of potential HIV prevention measures, a topic of great personal and professional interest to me given my decades of research on HIV and AIDS prevention.

I declare under penalty of perjury that the foregoing is true and correct.

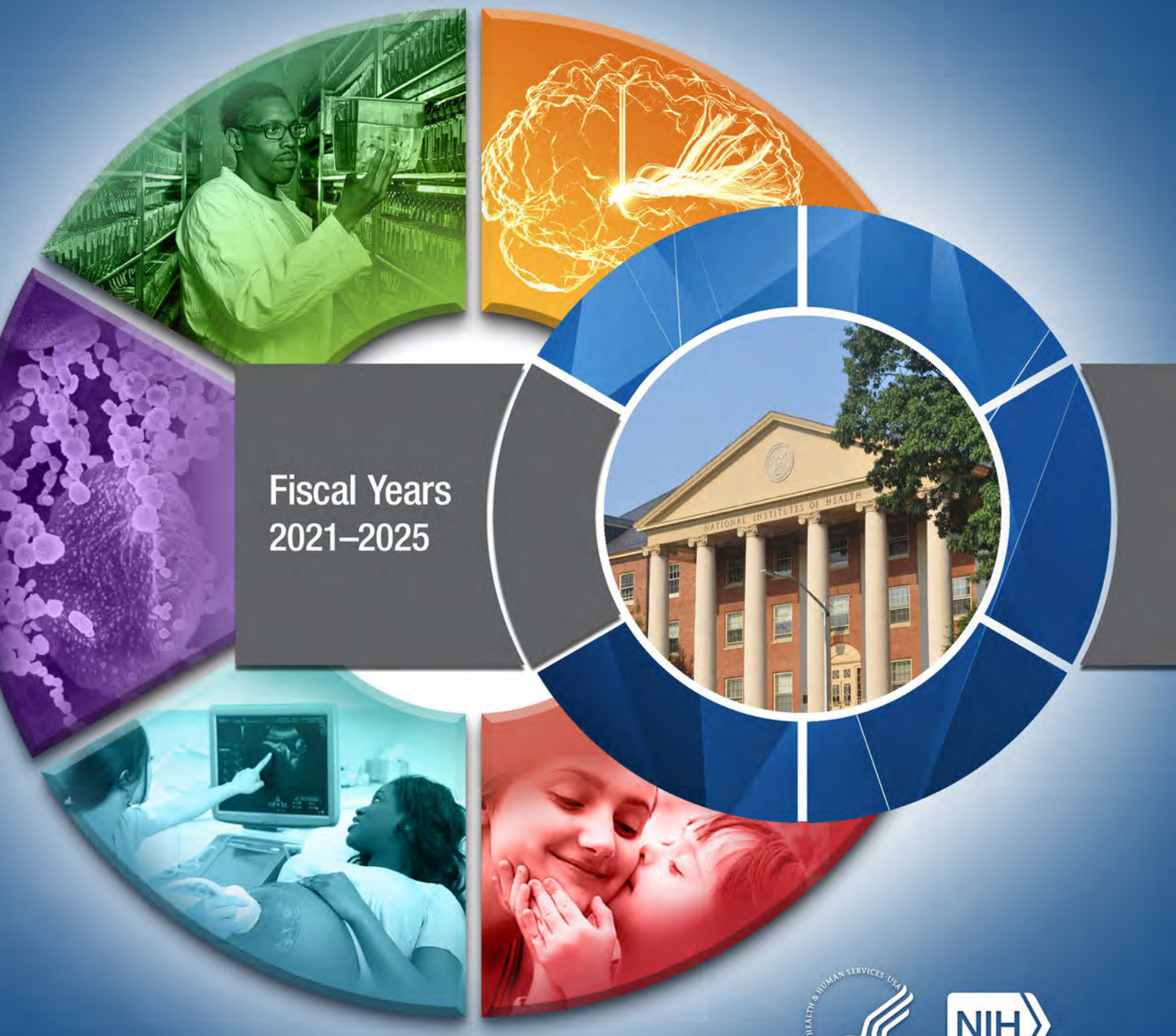
Executed this 7th day of April, 2025.

Peter Lurie

Peter Lurie, MD, MPH

EXHIBIT A

NIH-WIDE STRATEGIC PLAN



Fiscal Years
2021–2025

DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

NIH

Photo page ii: Cell-to-Cell Communication.
Credit: NCATS, NIH.

Photo page vi: Enzyme Repairing DNA.
Credit: Tom Ellenberger, Washington University School of Medicine in St. Louis, and Dave Gohara, Saint Louis University School of Medicine.

Photo page 41: Neurons.
Credit: Leterrier, NeuroCyto Lab, INP, Marseille, France.

Director's Message

To the American People,

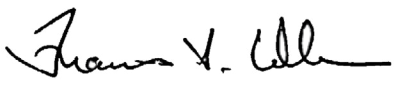
As our nation's biomedical research agency, the National Institutes of Health (NIH) has been the driving force behind many of the recent innovations in science and technology that are improving the health of all humankind. The coming years are certain to offer many exciting new opportunities for scientific exploration—and to pose some serious new challenges for human health. To rise to those opportunities and challenges, it is imperative that NIH, along with all sectors of society, work together in unprecedented ways with unprecedented speed.

Indeed, science is moving faster than ever before. To fuel this engine of discovery, NIH must continue to support the highest caliber research throughout the country and the world, while at the same time take vigorous steps to uphold the ethical conduct of science. NIH will further enhance the science of tomorrow by continuing its efforts to build a next generation of researchers that better reflects the rich, creative diversity of our great nation. The increasingly complex scientific questions that our society will face in the future will require not only diversity of scientific disciplines, but also diversity of thought, experience, and demographics.

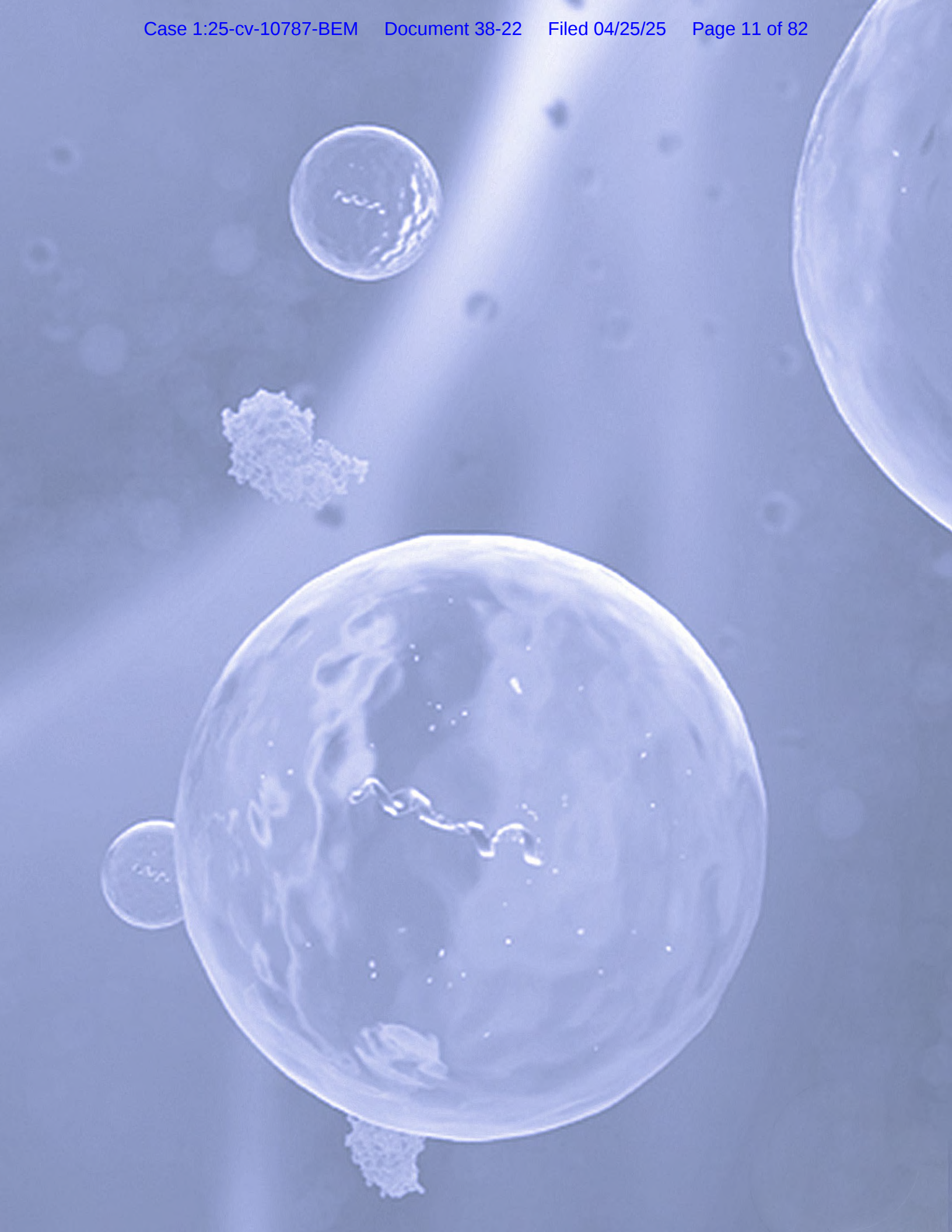
As a publicly funded agency, NIH has a responsibility to be a good steward of the funds entrusted to us by the U.S. taxpayers. NIH will do this by investing efficiently and effectively in a wide range of basic, translational, clinical, and applied research, while at the same time supporting the workforce and infrastructure required for a sustainable research enterprise. As outlined in this Strategic Plan, this approach will enable NIH to build a solid foundation of fundamental knowledge about living systems that will serve to accelerate research aimed at addressing our most pressing health needs.

NIH's mission is to turn discovery into health. We thank you for your strong and steadfast support of this crucial mission, and we look forward to your continued support as we strive to use the power of science to create a healthier and more productive life for all.

With sincere appreciation,



Francis S. Collins
Director, National Institutes of Health



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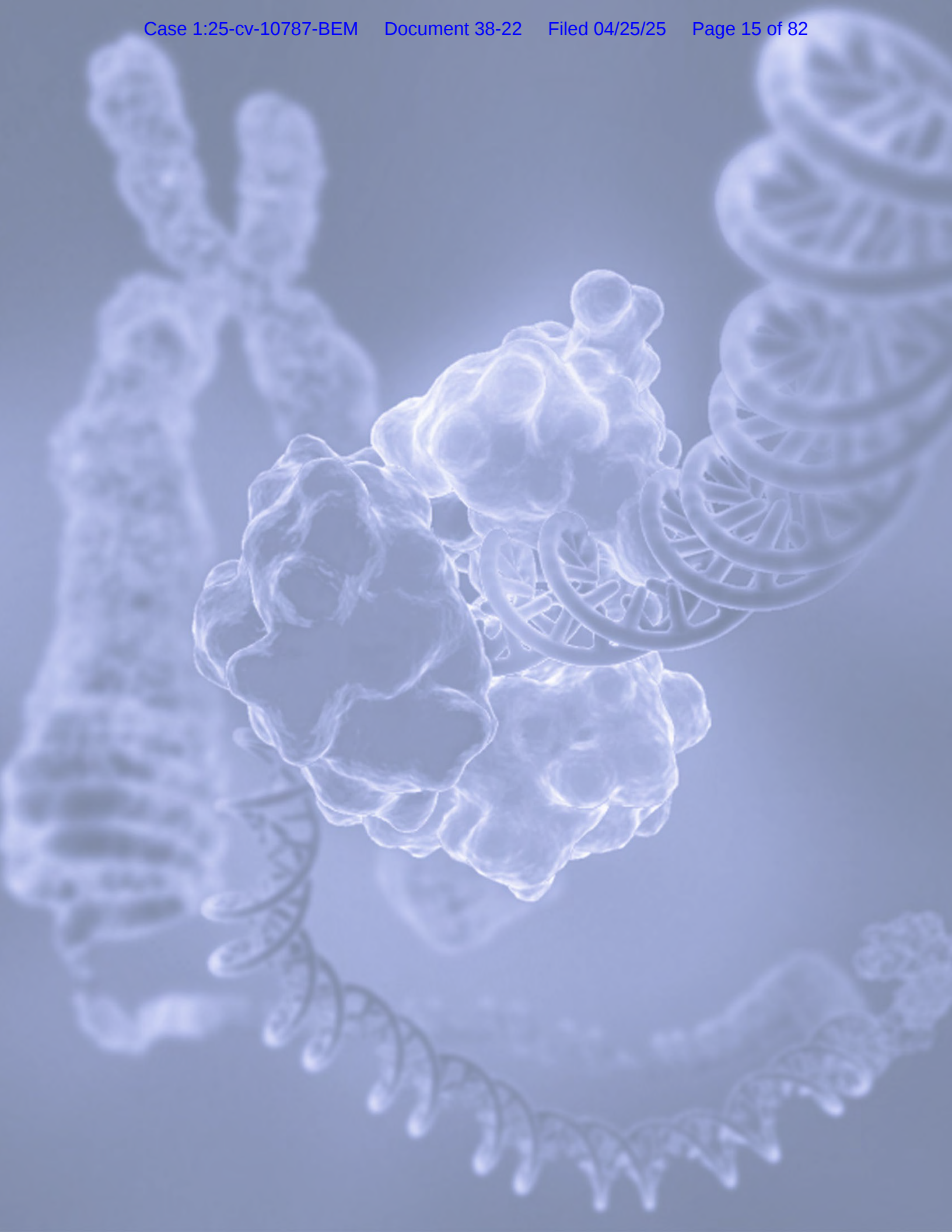


NIH-Wide Strategic Plan Framework

OVERVIEW OF NIH

MISSION:
To seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to **enhance health**, **lengthen life**, and **reduce illness and disability**

ORGANIZATION: 27 Institutes and Centers and the Office of the Director
- Extramural program: supporting research across the U.S. and beyond
- Intramural program: supporting research on NIH campuses

NIH'S STRATEGY

OBJECTIVES

Research Areas
- Foundational Science
- Disease Prevention and Health Promotion
- Treatments, Interventions, and Cures

Research Capacity
- Workforce
- Infrastructure and Resources

Research Conduct
- Stewardship
- Partnerships
- Accountability and Confidence
- Management and Operations

CROSSCUTTING THEMES

- Minority Health and Health Disparities
- Women's Health
- Public Health Challenges Across the Lifespan
- Collaborative Science
- Data Science

NIH National Institutes of Health

Figure 1. NIH Main Campus

Credit: NIH.

The James H. Shannon Building (Building One) at the NIH main campus in Bethesda, MD.

Overview of NIH

Mission and Goals

At the National Institutes of Health (NIH), "Turning Discovery into Health" is what its tens of thousands of employees—and the hundreds of thousands of scientists it supports—strive to accomplish every day. As the foremost agency for funding biomedical research[a] in the U.S., NIH's mission is to seek fundamental knowledge about the nature and behavior of living systems and to use that knowledge to enhance health, lengthen life, and reduce illness and disability (Figure 1).[1] To achieve this mission, NIH works to support innovative research ultimately aimed at protecting and improving human health; train the biomedical research workforce and develop scientific infrastructure; contribute to the nation's economic growth by expanding the biomedical knowledge base; and promote integrity, public accountability, and societal responsibility in scientific research. As an operating division of the U.S. Department of Health and Human Services (HHS), NIH is responsible for carrying out the Department's goal of advancing scientific knowledge and innovation. NIH catalyzes life-saving research breakthroughs by providing critical funding to eligible research institutions throughout the nation and the world, and through the research conducted in NIH laboratories.

While NIH's primary mission is the conduct of research, the agency is also a trusted resource for accurate and timely biomedical information. NIH's biomedical information platforms are among the most visited websites in the federal government, giving researchers, health care professionals, and the public highquality information and data necessary to make informed decisions.

Organization

NIH is made up of 27 Institutes and Centers (ICs), and the NIH Office of the Director (OD).[2] Each IC has its own mission and research priorities focused on specific diseases, body systems, life stages, or fields of science. The NIH OD sets policy and provides guidance, in addition to serving as a resource for planning, managing, and coordinating the programs and activities of all of NIH.

NIH receives its annual funding, or appropriation, from the U.S. Congress. More than 80 percent of this funding is passed on to researchers and research institutions around the country—the extramural research community—through a rigorous, competitive process, while about 11 percent of NIH's budget supports intramural projects conducted by scientists in its own laboratories, which are subject to an equally rigorous review.[3]

Supporting Researchers and Universities Through the Extramural Research Program

Every year, NIH receives more than 54,000 research project grant applications[4] and funds almost 50,000 new and continuing grants. These grants support more than 300,000 researchers at all career stages, including more than 43,000 principal investigators at approximately 2,500 universities, medical schools, and other research institutions in every state of the U.S. and around the world. This enterprise is managed by NIH staff who facilitate and administer scientific programs, consult with scientific experts to inform priority setting, and act as agency experts for specific scientific areas.

NIH's funding decisions are made through a highly competitive, rigorous dual-level peer review process that emphasizes fairness and accountability and prioritizes support of the best scientific ideas.[5] NIH relies on the expertise of more than 25,000 external reviewers annually to assess the scientific merit of incoming grant applications in the first stage of peer review, which is followed by a second-level review for mission relevance by members of national advisory councils for ICs and the OD.[6] Final funding decisions are made by IC Directors, taking into consideration their IC's research program priorities in the context of the existing funding portfolio.

A variety of funding mechanisms—including grants, cooperative agreements, research contracts, prize competitions, and other less frequently used

[a] For the purposes of this Strategic Plan, the term biomedical is used broadly to include biological, behavioral, and social scientific perspectives.

mechanisms—are used to support NIH's broad scientific portfolio,[7] allowing maximum flexibility to fund the rapidly advancing needs of the biomedical research community. These mechanisms are used to support a wide range of efforts—from individual research projects, to international consortia and networks, to training opportunities—each of which may be tailored to meet specific goals. For example, to create innovative technologies that advance its mission and move them toward uptake in the market, NIH supports the Small Business Innovation Research and Small Business Technology Transfer programs.

Research in Action in the NIH Intramural Research Program

The NIH Intramural Research Program conducts NIH's in-house research and is the largest institution committed to biomedical and behavioral research, research training, and career development in the world.[8] The mission of the Intramural Research Program is to conduct distinctive, high-impact laboratory, clinical, and population-based research; facilitate new approaches to improve health through prevention, diagnosis, and treatment; respond to public health emergencies; and train the next generation of biomedical researchers. The program supports approximately 8,000 basic, translational, and clinical researchers at NIH research facilities located across the U.S., including the main NIH campus in Bethesda, Maryland; Research Triangle Park in North Carolina; Johns Hopkins Bayview Medical Center in Baltimore, Maryland; Frederick National Laboratory for Cancer Research in Frederick, Maryland; Rocky Mountain Laboratories in Hamilton, Montana; the Perinatology Research Branch in Detroit, Michigan; and the Phoenix Epidemiology and Clinical Research Branch in Phoenix, Arizona. Scientists in the Intramural Research Program include an estimated 1,200 principal investigators, 1,800 staff clinicians and staff scientists, and 5,000 trainees. Many important medical breakthroughs take place in the intramural research laboratories.

Pioneering Clinical Research at the NIH Clinical Center

The NIH Intramural Research Program includes the NIH Clinical Center,[9] the world's largest hospital devoted exclusively to clinical research. The NIH Clinical Center is designed to rapidly transition scientific observations and laboratory discoveries into clinical studies and bedside cures by bringing together talented investigators and specialized infrastructure, including unique patient cohorts, state-of-the-art equipment, and specialized services. Since its opening in 1953, more than half a million patients have been active partners with NIH in medical discovery. This partnership has resulted in a long list of medical milestones, including the development of chemotherapy for cancer; the development of some of the earliest artificial heart valves; the demonstration that lithium treats depression; and the first treatment of HIV/AIDS with azidothymidine.[10]

About 1,600 clinical research studies are in progress at the NIH Clinical Center. Approximately half are studies of the natural history of disease, while most of the other studies are clinical trials, often the first tests of new drugs and therapies in people. Participants come from all 50 U.S. states and around the world. With its unique ability to assemble cohorts of participants with rare diseases, the NIH Clinical Center plays an important role in fostering new multidisciplinary collaborations that study and find treatments for rare diseases, often revealing insights into common diseases, as well.

NIH's Strategy

To carry out its mission and optimize return on public investment, NIH has designed a strategic *Framework* that includes three key *Objectives* that align with the agency's goals. These three Objectives outline NIH's priorities in (1) biomedical and behavioral research areas, (2) research capacity, and (3) research conduct. Across all of these priorities, NIH emphasizes several *Crosscutting Themes*—approaches that are common to all Objectives of the Strategic Plan—including improving minority health and reducing health disparities; enhancing women's health; addressing public health challenges across the lifespan; promoting collaborative science; and leveraging data science for biomedical discovery. Examples of these important crosscutting topics are located throughout the three Objectives.

OBJECTIVE 1 Advancing Biomedical and Behavioral Sciences

The NIH portfolio is designed with the breadth and flexibility to address current public health needs, emerging areas of scientific opportunity, and public health emergencies, such as the coronavirus disease 2019 (COVID-19) pandemic (Figure 2). Over the next 5 years, NIH will drive cutting-edge biomedical and behavioral sciences forward on three interrelated fronts—foundational science, disease prevention and health promotion, and treatments, interventions, and cures.

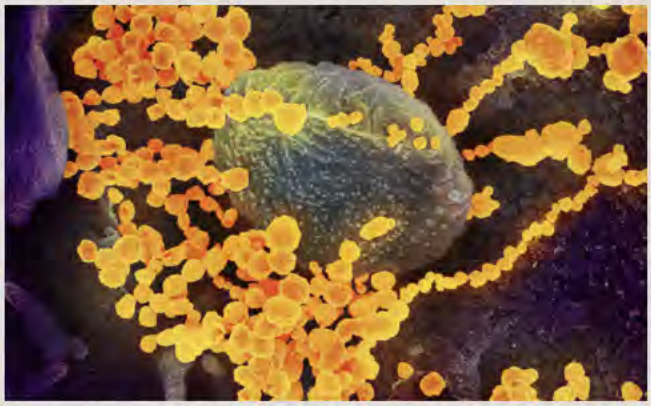
Driving Foundational Science

NIH supports a broad range of foundational scientific research to provide the building blocks for future diagnostics, treatments, and cures across the entire spectrum of health, diseases, and conditions, including those that are emerging, rare, or have yet to be discovered.

Foundational science includes basic biological, behavioral, and social research that generates the knowledge of how living systems work at the molecular, cellular, organismal, behavioral, and social levels.[11] Basic research can be experimental or observational and may involve manipulating molecules in test tubes and cells in culture dishes, studying animal models of disease (Figure 3), or conducting studies to understand human health and disease processes. Basic research also includes epidemiological studies

Figure 2. COVID-19 Research

Coronavirus disease 2019 (COVID-19) is an emergent human disease caused by a naturally arising novel coronavirus, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This scanning electron microscope image shows SARS-CoV-2 (round gold objects) emerging from the surface of cells cultured in the laboratory. NIH supports research to understand SARS-CoV-2 and mitigate the threat of COVID-19 for the health of all people by building on existing and accelerating the development of new research initiatives focused on five research priorities detailed in the *NIH-Wide Strategic Plan for COVID-19 Research*. NIH is improving basic understanding of SARS-CoV-2 and COVID-19 and developing the necessary tools and approaches to better diagnose, prevent, and treat this devastating disease. Pandemics recur, and NIH is also considering how to enhance preparedness for the next one.



Credit: Rocky Mountain Laboratory, NIAID, NIH.

to examine disease burden, distribution, and potential risk and protective factors in specific populations, as well as natural history studies that follow individuals over time to observe early stages and progression of a disease. NIH-supported research serves as the world's leading source of foundational knowledge of relevance to both the public and private sectors of biomedicine.[12]

Figure 3. Animal Research Models

Both people and animals have unique and important roles as research subjects. Many medical advances that enhance the lives of both humans and animals originate from animal studies. NIH supports research using a wide variety of animal models, from the familiar fruit flies, rodents, and nonhuman primates to more unexpected animal models, such as fish, frogs, and yeast. The types of animals used in research are chosen for their similarity to humans in anatomy, physiology, or genetics. For example, zebrafish (pictured) are frequently used in research because of their small size, rapid breeding, and transparent bodies. Approximately 70 percent of human genes are also found in the zebrafish, and zebrafish and humans share many critical developmental pathways. Not only can we learn how to prevent, treat, and cure human diseases by studying animals, but often the treatments developed can also be used to improve the health of animals. In addition, NIH is acting to reduce the number of animals needed for research by using other approaches, such as tissue chips.

Credit: Grimes DT, Boswell CW, Morante NF, Henkelman RM. Used with the permission of Rebecca D. Burdine, Ph.D.

Much of the research process is carefully planned and conducted, but serendipitous discoveries can also drive progress. Because science explores the unknown, it is not always possible to predict where research will lead. This concept is especially true for basic research, which integrates biology, behavior, environment, medicine, physics, chemistry, engineering, and data science to pioneer novel technologies capable of exploring the individual components of life. Investments in basic science result in unexpected breakthroughs and new fields of inquiry that could not have been envisioned when the original experiments were designed. For example, scientists leveraged the discovery of the CRISPR system, a component of the bacterial immune system that responds to viral infection, to develop a molecular tool for editing genes with exquisite precision. This technology has revolutionized the ability to study genes and holds great promise for treating numerous genetic disorders. By investing in foundational science, NIH is laying the groundwork for important future advances that will improve the nation's health.

Building Data Resources to Enable Research Progress

NIH supports the creation of foundational data resources that enable basic research and improve understanding of the biological and environmental factors that contribute to human health and disease. NIH achieves this effort by funding investigators who are studying and cataloging molecules that are the basic building blocks of life—such as DNA, RNA, and proteins—as well as researchers who are establishing and collecting data from large cohorts of research participants. The resulting datasets have the potential to catalyze whole fields of research, as well as lead to the development of new diagnostic tools and therapies.

The 21st century opened with a crowning achievement of basic science, sequencing the human genome—the complete collection of genetic information within an individual. This achievement became the foundation for the branch of science that studies genomes across individuals to find patterns in health and disease and to uncover mechanisms to understand how genes interact with one another and with a person's environment. The immense amount of data produced by genomic studies is helping researchers understand how the complex interactions among different regions of the genome influence human development, aging, and health. One major genomic data resource is the ENCyclopedia of DNA Elements (ENCODE), which is aimed at identifying the function of all parts of the human and mouse genomes and has already been cited by thousands of research publications.[13] The Clinical Genome (ClinGen) Resource catalogues the physical, clinical, and genetic characteristics of individuals to better understand how small changes, or variants, in a person's genome are related to their health.[14] NIH will continue to support the expansion of these databases and improvement of the tools researchers use to generate and analyze genomic data through the development of new DNA-sequencing technologies and computational methods. NIH will also support new efforts to ensure the inclusion of genomes of individuals from

groups that have been historically underrepresented in genomics research.[15]

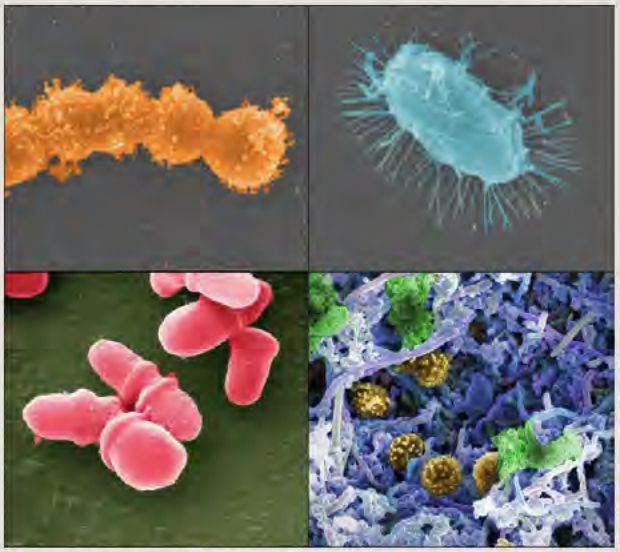
Harnessing the power of DNA-sequencing technologies, NIH-funded scientists have also created fundamental datasets important to microbiome research, or the study of the microbes—including bacteria, viruses, and fungi—that live on and in the human body. The average healthy adult is host to trillions of microbes that live in the gut, in the mouth, or on the skin, for example. The composition of the microbiome influences human health and response to treatment, contributes to early development, affects the immune system, and plays a role in metabolism. The NIH Common Fund's[b] Human Microbiome Project (HMP), conducted from 2007 to 2016, was the first large-scale effort to map and identify the thousands of species of microbes in the human microbiome (Figure 4).[16] HMP generated a comprehensive profile of the microbiome from multiple body sites from more than 300 healthy people and created computational tools and resources to enable more research. HMP also collected microbiome and human data from three longterm cohort studies centered on pregnancy and preterm birth, inflammatory bowel disease, and type 2 diabetes.

Ongoing studies supported by NIH are investigating how the microbiome of pregnant women may affect the risk of preterm birth;[17] exploring the possibility of using complementary foods—foods given in addition to those regularly consumed in the diet—to boost the gut microbiome and treat childhood malnutrition;[18] understanding how beneficial microbes in the mouth protect against periodontal disease or other oral infections;[19] and uncovering how the microbiome influences cancer development and response to therapy.[20] One particularly promising area of research is exploring the role of the microbiome in the onset of chronic conditions involving immune system dysfunction, such as cardiovascular disease and inflammatory diseases of the gut.[21]

Studies that generate large datasets from diverse participants provide vital fundamental research resources. The Adolescent Brain Cognitive Development (ABCD)[22] study is the largest long-term study of brain development and child health in the U.S. This study has recruited more than 11,000 children 9 to 10 years of age, who will be followed into adulthood to explore how childhood experiences affect brain development and a variety of health-related outcomes. Data collection is ongoing, and researchers from within and outside the ABCD study are using the data generated to conduct research on such topics as the link between screen time and brain structure,[23] effects of prenatal exposure to cannabis use,[24] and the relationship between sleep and brain structure and function.[25]

Figure 4. Human Microbiome Project

The Human Microbiome Project, which was launched by NIH in 2007, provided the first glimpse of the microbial diversity of healthy humans and is exploring the possible relationships between particular human diseases and the microbiome.



Credits: Composite image, Jonathan Bailey, NHGRI, NIH. Individual images (Clockwise from top left), Streptococcus, *Tom Schmidt; microbial biofilm of mixed species, from human body, A. Earl, Broad Institute/ Massachusetts Institute of Technology;* Bacillus, *Tom Schmidt;* Malassezia lopophilis, *J.H. Carr, CDC.*

Many NIH-funded projects span multiple areas of research and include both basic and applied science. The ambitious Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) Initiative aims to answer fundamental questions about how brain circuits work; how they become impaired in neurological, psychiatric, and substance use disorders; and how to improve the function of these circuits to treat brain disorders (Figure 5).[26] Components of the BRAIN Initiative® include studies to record, image, and manipulate brain circuits with the aim of developing treatments for brain disorders; development and dissemination of informatics tools to allow

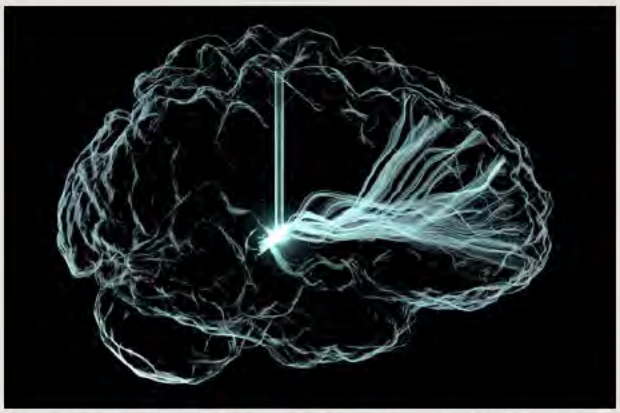
[b] For more information on the NIH Common Fund, see Appendix IV.

widespread sharing and interpretation of research data; and efforts to discover and catalogue the multitude of types of brain cells.

The complexity of the nearly 170 billion cells in a human brain presents a formidable challenge to understanding how different cell types work in brain circuits, their role in disease, and how they might be targeted directly by new therapies. Advances in engineering and highthroughput methods to classify individual cell types have enabled new opportunities to tackle this challenge. The BRAIN Initiative® Cell Census Network is developing a comprehensive mouse brain cell atlas and applying cell type identification methods to studies of human brain tissue.[27]

Figure 5. BRAIN® Initiative

First-place photo winner from the Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) Initiative's 2019 "Show Us Your Brains" photo and video contest for BRAIN investigators. "Light Me Up!" is a light-based rendering of deep brain stimulation's electrical excitation of neuronal fiber pathways to treat patients who have traumatic brain injury.



Credit: Andrew Janson, Graduate Student Research Assistant, Scientific Computing and Imaging Institute, The University of Utah.

Scientists have begun to use these methods to determine precisely which human brain cells are affected in a range of conditions, including Alzheimer's disease and related dementias, autism spectrum disorder, and Zika virus infection.

Inventing Tools and Technologies to Catalyze Discovery

Fundamental research includes the creation of advanced biomedical research tools and technologies for scientists to answer questions about biology and human health. For example, imaging technology has transformed science, allowing researchers to "see" individual molecules interacting, measure brain function, study internal tissues, visualize cell functioning in 3-D in real time, and locate specific molecules in the body using chemical tags.

Certain NIH programs are initiated specifically to spur the development of new tools and technologies for research use. The NIH Common Fund's Single Cell Analysis Program (SCAP) focused on developing tools to explore the behavior of single cells, including new ways to track cells in living multicellular organisms, new imaging techniques and technologies, and sequencing of the genome and transcriptome—the collection of all gene readouts present in a cell.[28] Resources developed through SCAP have paved the way for research that may lead to breakthroughs in understanding the human body at the level of individual cells, rather than groups or populations of cells. Such resources include the NIH Common Fund's Human BioMolecular Atlas Program (HuBMAP), a collaborative effort to develop a global open platform to map the approximately 37 trillion cells in the human body to understand how the relationships between cells can affect a person's health.[29]

New technologies are yielding data in quantities and at a level of complexity that requires increased capacity for storage, management, and analysis. Artificial Intelligence (AI) is being used on big datasets to augment human ability to detect patterns and predict outcomes, thus offering significant promise to advance research. NIH will build a large and diverse set of programs to foster machine learning (a subset of AI), support the generation and management of large-scale datasets, convene multidisciplinary teams of researchers, and develop a set of ethical principles for NIH-funded researchers to follow when using AI (Figure 6).[30] Advances in data science facilitate data processing and sharing, but concomitantly raise concerns regarding privacy, security, ethics, and bias. NIH is proactively engaging data and computer scientists, engineers, clinicians, research participants, ethicists, and the public in its plans to address future challenges and opportunities.

Studies are beginning to demonstrate the potential AI has for revolutionizing medical practice. For example, NIH researchers developed a novel data-driven approach for automated diagnosis and prognosis of Age-related Macular Degeneration (AMD), highlighting the potential of these systems to assist early disease detection and enhance clinical decision-making

Figure 6. ELSI Research at NIH

The term *ELSI* refers to the consideration of Ethical, Legal, and Social Implications of research, particularly in emerging biomedical fields; ELSI has its roots in the genomics community, but has expanded to include other areas of NIH research. ELSI complements scientific research by identifying, analyzing, and addressing the ethical, legal, and social implications of research as it is being conducted. NIH supports ELSI research to facilitate the responsible integration of science into society. Today ELSI initiatives are underway across NIH in several areas of biomedical and behavioral research, such as neuroscience, epidemiology, environmental health, new and emerging technology development and use, precision and personalized medicine, clinical research and care, and special and vulnerable population research. Key to NIH's approach to ELSI is collaboration with its multiple stakeholders.

processes.[31,32] The U.S. Food and Drug Administration (FDA) also approved the first automated medical device to use AI to detect diabetic retinopathy.[33] NIH will continue to explore and expand further uses of AI.

Understanding Biological, Behavioral, and Social Determinants of Population Health

Building the foundation for science includes constructing an overall picture of how physiological, behavioral, and social factors alone and in combination may determine human health. Conditions in which an individual is born, lives, learns, works, and ages combined with the behaviors that they engage in can affect a wide range of health outcomes.[34] Understanding how these factors interact with an individual's biological make-up is a vital area of research. The epigenome consists of chemical compounds and proteins that can attach to DNA and turn genes on and off. These changes in gene expression can occur in response to social experiences (both positive and negative) and environmental exposures and may be passed from one generation to the next. NIH supports research on social epigenomics, the study of how social experiences throughout a person's lifetime can affect biology and health status through changes to the epigenome. Similarly, NIH supports research on environmental epigenomics, which looks at how an individual's exposure to factors in the physical environment—such as air, water, and soil—may also impact gene expression. Studies designed to elucidate how social experiences and environmental exposures—such as those experienced through structural racism and lower economic status—affect the individual epigenome among racial and ethnic groups can provide a unique opportunity to identify the changes that occur within and between populations. This knowledge can be used to increase understanding of minority health and decrease health disparities.

Social and behavioral research is crucial to understanding the health and developmental effects of using digital technology and electronic media that have become integral parts of daily life. Findings from the ABCD study and the NIH Intramural Research Program have demonstrated that a significant proportion of children across a wide age range exceed the daily limits on screen time recommended by the American Academy of Pediatrics.[35,36] In light of the COVID-19 pandemic, screen time has dramatically increased for children of all ages, the effects of which will need to be investigated. To assess how technology and media use affect early childhood health and development—as well as the nature of social interactions among families, peers, and society—NIH will support an initiative to study the impact of technology and media exposure on early childhood development and health outcomes. This effort will support coordinated research projects using existing and newly collected data, as well as determining measures for exposure, usage, development, and health outcomes, including neuroimaging, language development, physical activity, and hormone levels.

Integrating different types of research to address health needs for specific populations can improve the health of these populations and also provide insights into common conditions. For example, Down syndrome is the most common genetic disease of mild to moderate intellectual disability, occurring in 1 out of every 700 babies born in the U.S. In 2018, NIH launched the INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndromE (INCLUDE) project, which studies conditions that affect the general population and often co-occur (i.e., are comorbid) with Down syndrome, such as Alzheimer's disease and related dementias, autism, cataracts, celiac disease, cardiovascular disease, and diabetes (Figure 7). The program focuses on targeted, high-risk/high-reward basic science studies on the causes of Down syndrome comorbidities, cohort studies of individuals with Down syndrome, and inclusion of individuals with Down syndrome in new and existing clinical trials.

Understanding the fundamental processes underlying human health is a key step in determining how to promote and restore health and identify, prevent,

and treat disease. Over the next 5 years, NIH will continue to invest in fundamental research projects that provide new insights into basic biological, behavioral, and social processes across the spectrum—from molecules to cells to humans to communities. These investments will undoubtedly lay the groundwork for unimaginable breakthroughs that will lead NIH one step closer to improving human health.

Figure 7. INCLUDE Project

The INCLUDE (INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndromE) project is an NIH-wide research initiative involving 18 Institutes and Centers that aims to understand critical health and quality-of-life needs for individuals with Down syndrome. Down syndrome is the most common genetic cause of mild to moderate intellectual disability and occurs in one out of every 700 babies born in the U.S.

Credit: The INCLUDE Project, NIH.

Preventing Disease and Promoting Health

Disease prevention and health promotion are core components of NIH's research mission to improve the health of all Americans. NIH research strengthens the evidence base on which national public health objectives and related disease prevention and health promotion strategies are built. Prevention research targets biological, social, and environmental factors, individual behaviors, and health services and informs health-related guidelines, policies, and regulations. NIH supports a broad portfolio of research that examines the best way to bring effective disease prevention and health promotion strategies into communities.

Developing New and Improved Vaccines

Vaccines provide a safe, cost-effective, and efficient means of preventing illness, disability, and death from infectious diseases. NIH supports a comprehensive spectrum of immunology and infectious disease research focused on developing improved or novel vaccines. This includes study of pathogen–host interactions and technological advancements in vaccine development that have led to innovative and exciting vaccine research strategies. For example, NIH-supported researchers are working to identify new platforms to deliver vaccine components and explore how adjuvants (i.e., vaccine components that enhance the immune response) affect the potency, durability, and other aspects of vaccine-induced immunity.[37]

An important remaining need is the rapid development of new vaccines to mitigate emerging infectious disease outbreaks, such as COVID-19, Ebola virus disease (EVD), and influenza (flu). NIH, in collaboration with its industry partner, developed an experimental vaccine for COVID-19 in just weeks using the genetic sequence of SARS-CoV-2 (i.e., the virus that causes COVID-19).[38] As of late 2020, the vaccine co-developed by scientists at NIH and Moderna was granted an Emergency Use Authorization by the FDA, after rigorously testing its safety and ability to protect against infection. Other vaccines are still being tested.[39] Recent outbreaks of the Ebola virus spurred the development of multiple vaccine candidates for EVD, including the rVSV-ZEBOV vaccine, which through significant federal government support was brought to market by the private sector, licensed in 2019, and is now widely available.[40] Preliminary data from an outbreak in the Democratic Republic of the Congo (DRC) has shown that this vaccine is highly effective in preventing disease and death.[41] In the U.S., seasonal influenza causes 12,000–61,000 deaths annually,[42] and emerging influenza strains pose a pandemic risk. A key focus of the NIH influenza research program is developing a universal vaccine[43] that provides robust, long-lasting protection against multiple subtypes of influenza (Figure 8), eliminating the need for a seasonal flu vaccine each year and providing protection against newly emerging strains with pandemic potential. Several flu vaccine clinical trials are being conducted, including an NIH-sponsored trial of a universal vaccine candidate that uses a nanoparticle technology to display portions of the influenza virus that are the same or very similar among different influenza strains.[44]

Figure 8. Universal Flu Vaccine

A healthy volunteer receives an experimental universal influenza vaccine known as H1ssF_3928 as part of a Phase 1 clinical trial at the NIH Clinical Center in Bethesda, Maryland. Scientists at the Vaccine Research Center developed the vaccine.

Credit: NIAID, NIH.

In addition to furthering the development of vaccines against specific pathogens, NIH supports the development of technologies that enable scientists to apply a standardized manufacturing process to develop candidate vaccines against various pathogens and create a collective database with information on their safety. This streamlined approach can shorten the preclinical development period from years to months and is important for rapid response to emerging infectious disease threats.

Addressing Risk and Burden of Disease

NIH is committed to supporting research to reduce the impact of disease by identifying and improving understanding of risk factors (e.g., inadequate nutrition, low physical activity, built environment, tobacco use, alcohol or drug misuse) and protective factors (e.g., weight management, regular exercise, daily tooth brushing and flossing) alone and in combination with genetic factors. An important goal of prevention is to alter the balance between risk and protective factors so that protective factors outweigh risk factors. Screening, health promotion, counseling, behavioral change, stress management, and preventive medications are all potential strategies for reducing individual risk. NIH investments have helped lead to advances in screening for cardiovascular disease, lung cancer, abnormal blood glucose, type 2 diabetes, oral cancer, and intimate partner violence, as well as interventions to address obesity and tobacco use in children and adolescents.

One example of NIH's investments in risk identification is in suicide prevention (Figure 9). Suicide remains one of the top 10 leading causes of death in the U.S., claiming the lives of more than 48,000 people each year.[45] Although it impacts all ages and in all parts of the country, some specific groups are disproportionately affected, such as sexual and gender minority (SGM) populations (especially transgender and gender non-conforming youth) and American Indian or Alaska Native populations (who have the highest suicide rates of any racial or ethnic group in the U.S.[46]). NIH-supported suicide prevention research illustrates how improvements in care can save lives. Universal screening for suicide risk in emergency departments has been shown to be effective and feasible.[47] Building on these findings, NIH-supported researchers are testing brief interventions and follow-up care to prevent recurring self-harm and related comorbidities, such as substance use disorder.

NIH-supported studies have demonstrated how long-term, multigenerational studies of chronic diseases can give rise to innovative prevention and intervention strategies. For example, the Framingham Heart Study,[48] launched in 1948, continues to inform tobacco cessation, nutrition, physical activity, and blood pressure control strategies that are used all over the world to reduce the risk of chronic disease. High blood pressure, or hypertension, is common over the age of 50 years and is a leading risk factor for cardiovascular diseases like heart disease and stroke. It may also increase the risk of dementia later in life. Data from several NIH-funded observational studies suggested that cardiovascular disease risk increases when systolic blood pressure rises beyond a certain level. NIH's Systolic Blood Pressure Intervention Trial (SPRINT)[49] assessed whether aggressively lowering blood pressure can prevent these conditions. SPRINT found that maintaining systolic blood pressure at less than 120 mm Hg reduced the combined risk of heart attack, heart failure, and stroke by 25 percent and reduced the risk of death by 27 percent compared to the standard blood pressure target at the time (140 mm Hg).[50] These findings helped change the national guidelines for treating hypertension, which now use 120 mm Hg as the standard blood pressure target.[51] If successfully adopted into clinical practice across the U.S., these guidelines are expected to prevent about 107,500 deaths per year among people at high risk for fatal cardiovascular disease.[52]

Figure 9. Suicide Prevention

"Five action steps for helping someone in emotional pain": Infographic.

Credit: NIMH, NIH.

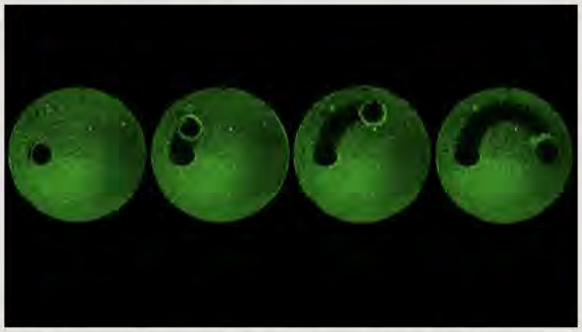
Harnessing Technology to Inform Decision-Making

NIH supports the development of new or improved interventions and technologies along with repurposing existing technologies to monitor and reduce disease risk, enhance protective factors, and restore health (Figure 10). Coupled with advances in data science that enhance analytical capacity and speed, these technologies and tools will help aid decision-making by patients and providers and improve disease prevention and health promotion strategies at the individual, family, community, and population health levels.

Most information used to make decisions in current medical practice is collected at a specific moment in time and in a clinical setting, such as taking blood pressure, providing a limited view of an individual's health and disease risk. Heart rate and motion sensors in smart watches and other wearable devices are examples of consumer technologies that can provide continuous feedback to help people improve their health. These devices detect underlying signs of illness and response to interventions, including medications and lifestyle changes, faster than conventional methods that often require weeks or months to provide actionable feedback. NIH-supported researchers have developed a wearable sensor made of stretchable microelectronics that uses ultrasound to measure blood pressure continuously, whether the wearer is resting or active. Such devices may help identify people at risk of stroke and heart disease by

Figure 10. Nanorobots for Dental Health

NIH supported a collaboration among biomedical researchers and engineers to build microscopic nanorobots to target, destroy, and remove dental plaque, a harmful community of bacteria that grow on teeth. The nanorobots, which contain an antibacterial compound, are controlled using tiny magnets to perform micro-scale precision cleaning, including hard-to-reach spaces. This technology could be used to prevent dental caries and periodontal disease, in addition to cleaning other surfaces susceptible to biofilms, such as metal implants and catheters or hospital equipment.



Credit: Geelsu Hwang and Edward Steager, University of Pennsylvania.

providing patients and physicians with more frequent and accessible information on blood pressure, including fluctuations that occur during the wide variety of activities that people engage in every day.[53]

Designing Research for Everyone

NIH prioritizes research that addresses the needs of underserved populations to address the factors that contribute to health disparities. NIH-wide efforts will continue to focus on developing and testing interventions to reduce health disparities, identifying key gaps in prevention science related to health disparities, and promoting targeted research on appropriately tailored public health, clinical, and community preventive services in diverse settings and contexts. For example, the NIH *All of Us* Research Program[54] has been designed to reflect the diversity of the U.S., with a special focus on including participants from groups that have been underrepresented in health research (Figure 11).

The Collaborative Minority Health and Health Disparities Research with Tribal Epidemiology Centers initiative supports research on topics related to minority health and health disparities in American Indian or Alaska Native populations, with emphasis on areas where there are significant gaps in data and knowledge. Current research projects include examining the impact of the Navajo Nation Tax on Junk Food on health outcomes, identifying the incidence and prevalence of arthritis and autoimmune disease among Alaska Natives, and understanding determinants of motor vehicle injuries and deaths among the Northwest Tribes.[55]

Sex and gender also influence health and disease. *Sex* refers to biological differences between females and males, including chromosomes, sex organs, and endogenous hormonal profiles. *Gender* refers to socially constructed and enacted roles and behaviors, which occur in a historical and cultural context and vary across societies and over time.[56] Considering the effects of sex and gender in study design, data collection and analysis, and dissemination of findings will help to inform the development of prevention strategies and interventions for everyone.

Developing and Optimizing Treatments, Interventions, and Cures

Building on the solid foundation of fundamental discoveries in biology, health and disease, and behavior, as well as innovations in data science and emerging technologies, NIH-supported scientists continue to develop new and improved treatments and cures, including for diseases that were considered intractable even a decade ago.

The path to a new treatment often begins not in the clinic or community but in the laboratory, where basic researchers refine our understanding of disease and identify aspects of disease causation or progression

Figure 11. *All of Us* Research Program

The NIH *All of Us* Research Program is a historic effort to collect and study data from 1 million or more people living in the U.S. The program's goal is better health for all of us, and its aim is to gather data on genetics, lifestyle, and environmental exposures. The *All of Us* Research Program is unique because it is disease agnostic, meaning that it will not focus on one disease, risk factor, or group of people, instead enabling researchers to evaluate multiple risk factors that are associated with outcomes across different diseases. This unprecedented scientific resource will enable research on numerous diseases and conditions across populations and the lifespan, with a special focus on outreach to groups that have been underrepresented in health research, to reflect the diversity of the U.S. The *All of Us* Research Program has already begun to make an early, non-finalized version of its Researcher Workbench available, an important milestone toward creating a publicly accessible platform to increase research on understudied areas, including wellness and resilience.

Credit: NIH.

that could be targeted therapeutically. Investigators use this information to design candidate treatment approaches using cell or tissue samples, animal models, or computer simulations. If the candidate approaches appear to be safe and effective in this preclinical setting, they are moved into human trials, where they are tested for safety and efficacy. Finally, new and improved methods to promote the adoption of effective and proven interventions are identified and refined through implementation research. This process is rarely straightforward. In fact, sometimes the process even circles back on itself in a "virtuous cycle," with applied research informing new ideas in basic research.

To illustrate, NIH-supported basic science was a springboard for the development of a ground-breaking new cystic fibrosis treatment. Cystic fibrosis is an inherited disorder that causes mucus to accumulate in the airways and digestive tract. The identification of the *CFTR* gene, which is mutated in affected individuals, along with additional discoveries over several decades, has enabled a variety of progressively more effective drug therapies for the disease. Recent NIH-supported clinical trials demonstrated that a novel triple-drug therapy could compensate for the effects of a *CFTR* mutation that occurs in 90 percent of affected individuals.[57] Now, instead of being a fatal disease, there is promise that cystic fibrosis in many individuals could soon be a chronic condition that can be managed over a long lifetime.

NIH supports randomized controlled clinical trials—studies conducted under "ideal" research conditions in which participants are randomly placed into one of two or more groups that receive different interventions or a placebo (i.e., a treatment with no therapeutic effect). Outcomes from each group are then analyzed and compared. Such studies are considered the gold standard by which clinical researchers determine the safety and effectiveness of interventions. NIH also supports pragmatic trials, which are designed to evaluate interventions in real-world settings and situations. To support and facilitate pragmatic trials, NIH established a Health Care Systems Research Collaboratory[58] under the NIH Common Fund to engage with health care delivery organizations as key research partners. The Collaboratory disseminates best research practices, provides education and coordination, and supports pilot projects involving a variety of diseases and conditions in community settings.

Giving the Right Treatment to the Right Patient at the Right Time

Advances in molecular medicine have allowed health professionals to move toward a precision medicine approach for targeted treatment and prevention that considers an individual's genes, environment, and lifestyle. In contrast to a one-size-fits-all approach, in which disease treatment and prevention strategies are developed for the average person, precision medicine will allow doctors and researchers to predict more accurately which treatment and prevention strategies will work best in an individual. Unlike research studies that focus on one disease, risk factor, or group of people, the *All of Us* Research Program is building an unprecedented scientific resource that will enable research on numerous diseases and conditions across populations and the lifespan.

Patients with certain types of cancer are already benefiting from precision medicine approaches. For example, an NIH-supported clinical trial showed that a molecular test for the expression of 21 genes associated with breast cancer recurrence could determine whether patients with the most common type of breast cancer would benefit from chemotherapy in addition to surgery.[59,60] The researchers found that most of these women can safely avoid chemotherapy and its toxic side effects.

The promise of precision medicine is exemplified by the development, built on decades of research, of new therapies that harness patients' own immune systems to attack their cancer. Among them are chimeric antigen receptor (CAR) T-cell therapies that are made by genetically engineering a patient's own immune cells so they will bind to specific proteins on cancer cells and kill them. Approved by the FDA in 2017, these biologic products have resulted in remarkable benefits to children and adults with certain types of leukemia and lymphoma.[61] Unfortunately, some patients initially respond to these treatments but then relapse, some patients' cancers do not respond at all, and the treatments can cause serious side effects. Scientists are working to understand the mechanisms underlying these challenges and to develop additional approaches for patients. Hundreds of clinical trials for new CAR T-cell therapies are ongoing, signaling the continued promise of this innovative new treatment for patients with cancer and HIV/AIDS.

Another area of NIH-supported research on personalized approaches to medical treatment has been to develop artificial pancreas technologies to automatically link individualized glucose monitoring and insulin delivery to improve the health and quality of life of people with type 1 diabetes (Figure 12). In the 1.6 million Americans estimated to have type 1 diabetes, the immune system destroys the pancreatic insulin-producing cells, leaving the body unable to absorb or use glucose. Significant progress toward artificial pancreas technologies—which consist of a continuous glucose monitor, an insulin pump, and a computer algorithm that, in some cases, can be run from the user's smartphone—has been made through extensive collaboration among NIH ICs, other federal agencies, private funders, academic investigators, and industry. In 2016, the FDA approved the first commercial hybrid artificial pancreas device[62] and in 2019, the FDA approved the first interoperable system[63] that could give patients the ability to choose the individual components that work best for them. Studies have shown that these technologies result in better control of blood glucose levels compared to standard treatment, potentially lowering the risk of diabetic complications.[64] NIH continues to support research to develop next-generation and novel devices that are smaller, easier to use, and available to all.

Figure 12. Artificial Pancreas

The Control-IQ artificial pancreas system was derived from research done at the Center for Diabetes Technology at the University of Virginia.

Catalyzing Cell Engineering, Bioengineering, and Regenerative Medicine

NIH is at the forefront of remarkable technological advances, such as innovations in cell engineering, bioengineering, and regenerative medicine. These advances are not only accelerating research but also creating the possibility of new treatments that previous generations of clinicians could only imagine. For example, scientists supported by the NIH BRAIN Initiative®[65] have pioneered a new technology that converts brain signals into audible speech—a potentially life-altering breakthrough for individuals who are unable to speak due to a stroke, injury, or other neurological condition. Next, researchers will design a clinical trial involving paralyzed, speech-impaired participants to determine how to best gather brain signal data, which can then be used to refine the previously trained computer algorithm.

Biotechnology is bringing us closer to a cure for AMD, a leading cause of visual impairment among older Americans. By 2050, the estimated number of people with AMD is expected to more than double from 2 million to 5 million.[66] The discovery of induced pluripotent stem cells (iPSCs)—adult cells that have been genetically reprogrammed to a developmental stage such that they can be turned into any cell type in the body—opened the door for transformative regenerative medicine therapies. Researchers at NIH were able to derive iPSCs from participants with advanced AMD and convert them into healthy retinal tissue. The newly developed tissue replaced damaged tissue and prevented blindness in animal models.[67] NIH received FDA approval to begin the first-ever clinical trial using replacement tissue derived from iPSCs in humans.[68]

Therapeutic development for many human diseases and conditions could become faster and more accurate due to the expanding use of tissue chips, or "organs-on-chips." These devices consist of 3-D platforms that support living human tissues or cells to model the structure and function of human organs, such as the lung, liver, and heart. Working closely with the pharmaceutical industry and FDA, the Tissue Chip for Drug Screening program[69] supports research using tissue chips to test new drugs and predict whether they will be safe and effective in humans. In collaboration with the International Space Station National Laboratory (ISS-NL) and the National Aeronautics and Space Administration (NASA), NIH is funding nine tissue chip projects in which different types of tissues are being sent to the ISS-NL to determine how human tissues behave in space when

exposed to reduced gravity,[70] which models aging in an accelerated manner (Figure 13). Researchers are also developing interconnected tissue chips that could model the entire human body's response to candidate therapeutics and are being deployed to address emerging health challenges, such as the opioid crisis and COVID-19 pandemic. In addition, current efforts are focused on the use of tissue chips to inform the implementation of clinical trials.

Figure 13. Tissue Chips in Space

An astronaut in a National Aeronautics and Space Administration spacesuit is shown with a kidney tissue chip in hand. When traveling in space, astronauts experience physiological changes normally associated with aging, such as bone loss, muscle deterioration, and altered immune systems. When the astronauts return to Earth, the changes often reverse. To better understand the relevance of the astronauts' experience to human health—both on the ground and in space—NIH partnered with the International Space Station U.S. National Laboratory to send tissue chips, a research technology that reflects the human body, into space.

Credit: NASA.

Meeting Emerging Public Health Needs

A critical focus of the NIH mission is readiness to address new and emerging public health needs rapidly, comprehensively, and efficiently. From the emergence of HIV/AIDS in the 1980s to the more recent outbreaks of infectious diseases—such as Zika virus disease, EVD, and COVID-19—to conducting research during an unfolding disaster like the Deepwater Horizon oil spill, NIH has been at the forefront of the global research response. NIH's role in combatting emerging threats involves identifying and understanding the responsible pathogens and their effects on the body, treating affected patients in the NIH Clinical Center as part of research studies, and conducting and supporting clinical trials throughout the nation and around the world.

The NIH Clinical Center is specially equipped with high-level respiratory isolation capabilities to handle patients with highly infectious diseases. In addition, the staff includes infectious disease and critical care specialists who have received training in strict infection control practices to prevent the spread of potentially transmissible agents. The Special Clinical Studies Unit is used for cutting-edge investigational clinical studies and treatments, ranging from EVD to universal influenza vaccine studies to treating patients affected by the COVID-19 pandemic.[71]

NIH can also swiftly mobilize its flexible infrastructure and collaborative research partnerships to help advance new and promising treatments, even in areas of armed conflict and tenuous security. NIH and the Institute of Biomedical Research in the DRC conducted the Pamoja Tulinde Maisha (PALM) clinical trial, meaning "Together Save Lives," in Kiswahili. The preliminary results were so compelling that the trial was halted, and the results were promptly made public to help save lives and stem the latest EVD outbreak.[72] All EVD patients in the DRC treatment centers are now treated with one of two treatment options based on the PALM trial results. Through this collaborative research conducted in a region of civil unrest during an ongoing outbreak, the U.S. and its partners have provided the world with two new effective treatments for an emerging disease. Additionally, this experience demonstrated the efficacy of promising therapeutics to treat EVD and serves as a potential guide for conducting future clinical trials in outbreak settings.

NIH's role in safeguarding the public health extends beyond infectious disease. For example, at this writing, opioid misuse and addiction continues to be a rapidly evolving U.S. public health crisis. Although more than 50 million Americans suffer from chronic pain, safe non-opioid options for pain management are unavailable.[73] In 2018, more than 46,000 Americans died of opioid overdose, making it one of the most common causes of non-disease-related deaths for adolescents and young adults.[74] More than 2 million Americans live with an opioid use disorder. To address this national crisis, NIH launched the Helping to End Addiction Long-term℠ (HEAL) Initiative,[75] an aggressive, NIH-wide effort to provide scientific solutions and offer new hope for individuals, families, and communities affected by this devastating crisis (Figure 14).

Figure 14. HEAL Initiative℠

Credit: NIH.

The NIH Helping to End Addiction Long-term℠ Initiative, or NIH HEAL Initiative℠, launched in April 2018, is an aggressive NIH-wide effort to provide scientific solutions to the national opioid overdose crisis, including improved treatment strategies for both pain and opioid use disorder. Notably, a series of highly focused studies has been launched to accelerate the development of new medications to treat all aspects of opioid use disorder, from new formulations of existing drugs to creating new therapies aimed at novel targets to novel devices for the treatment of substance use disorder and pain. Working across scientific disciplines and care settings, the NIH HEAL Initiative seeks to match the seriousness of the crisis and offers new hope for individuals, families, and communities affected by this devastating crisis. In partnership with the Substance Abuse and Mental Health Services Administration (SAMHSA), in 2019 NIH launched the HEALing Communities Study to investigate how tools for preventing and treating opioid misuse and opioid use disorder are most effective at the local level.

Partnering to Advance Treatments and Cures

Collaboration is essential to accelerating progress in developing effective prevention and treatment interventions, as well as ensuring that the benefits of research are available to all Americans. For example, the Partnership for Access to Clinical Trials is a collaborative effort that connects health care providers and their patients in the Washington, D.C., metropolitan area to NIH researchers conducting clinical trials at the NIH Clinical Center.[76] By serving as a bridge between research participants, their health care providers, and NIH researchers, this program serves as a successful model for increasing diversity in research participation, particularly among those who are underrepresented in clinical trials, and expanding access to the benefits of NIH research.

NIH facilitates collaboration with industry and federal partners to advance treatment science. In 2017, in collaboration with 12 leading biopharmaceutical companies and advocacy organizations, NIH launched the Partnership for Accelerating Cancer Therapies,[77] a 5-year public–private research collaboration, as part of Cancer Moonshot℠. The initial focus of the partnership is the development, validation, and standardization of biomarkers to better predict response to immunotherapy—a type of biological therapy that turns on or off the immune system to help the body fight cancer, infection, and other diseases. Immunotherapies have resulted in dramatic clinical benefit in certain types of cancer; however, existing immunotherapies do not work for all patients and are associated with substantial toxicity in some individuals.[78] A better understanding of why immunotherapies work in some patients and not others is needed to help target this treatment to the people most likely to benefit.

NIH is also transforming treatment of sickle cell disease (SCD) through collaborations (Figure 15). SCD is a group of inherited disorders characterized by the buildup of an abnormal protein in red blood cells. It can cause pain, fatigue, and damage to organs throughout the body. People of African ancestry have the highest prevalence of SCD; it is estimated that the disease affects up to 100,000 Americans.[79] Although treatments are available to relieve symptoms and extend lifespan, a bone marrow transplant is currently the only cure for SCD.[80] Unfortunately, a transplant is not feasible for most patients, because it requires bone marrow from an immune-matched sibling.

In 2016, NIH established the Sickle Cell Disease Implementation Consortium (SCDIC), the first

Figure 15. Sickle Cell Disease

Credit: Janice Haney Carr and the CDC Public Health Image Library.

In sickle cell disease, red blood cells make an abnormal protein that causes them to take on a sickle shape. These cells are inflexible and can stick to blood vessel walls, interrupting blood flow.

research program to use implementation science—the scientific study of how best to ensure the uptake of evidence-based practice—to identify and address barriers to quality care in SCD.[81] The SCDIC has created a registry of more than 2,400 patients. In 2018, NIH established the Cure Sickle Cell Initiative, an innovative collaboration among researchers in academia and industry, clinicians, patients, and advocates to identify and support the most promising genetic therapies for SCD.[82] Their goal is to bring new therapies to the point of FDA approval within the next 5–10 years.

NIH facilitates collaboration on complex scientific questions requiring the intersection of disciplines, methodologies, and knowledge by supporting a variety of funding mechanisms that are focused on collaborative or team-based work. Such opportunities for investigator-initiated research extend from serving as co-primary investigators on a grant award to participating in highly complex networks of investigators and institutions charged with advancing science in new directions. NIH looks forward to reaping the scientific benefits of continuing and expanding its partnerships in the next 5 years.

OBJECTIVE 2 Developing, Maintaining, and Renewing Scientific Research Capacity

NIH not only funds innovative biomedical and behavioral research but also pursues its mission by ensuring that the biomedical research workforce is well trained and diverse and conducts its work within an infrastructure that enables groundbreaking results at a rapid pace. Over the next 5 years, NIH is poised to enhance its support of research capacity to maximize the potential of the research that the agency sustains.

Enhancing the Biomedical and Behavioral Research Workforce

NIH recognizes that its mission will be met only through the continued efforts of a talented and dedicated biomedical research workforce. The strength of the NIH workforce depends on its sustainability and diversity (Figure 16), which NIH supports through both intramural and extramural focused training programs.

Sustainability is achieved by maintaining an appropriate balance of researchers at different career stages, ensuring that investigators early in their careers are given every opportunity to excel, even in times of limited funding. Intense competition for funding can pose a challenge for researchers trying to embark upon and sustain independent research careers. NIH's Next Generation Researchers Initiative (NGRI) aims to enhance opportunities for early-stage researchers by prioritizing funding of independent research applications for investigators who are within 10 years of completing postgraduate clinical training or their highest advanced research degree.[83] Through this initiative, NIH has more than doubled the number of early-stage researchers supported—from less than 600 in 2013 to 1,316 in 2019. Moving forward, NIH will continue to explore novel approaches to expand pathways for funding early-stage researchers and assess how NGRI policies affect women and individuals from groups that are underrepresented in biomedical and behavioral sciences.

To encourage early-stage researchers to explore new research avenues, NIH recently created the Stephen

Figure 16. Minority Women in Science

Alma Levant Hayden was one of the first minority women scientists in the federal government and worked at NIH as a biochemist. Photo taken around 1952.

Credit: NIH.

Ira Katz Award, in memory of the longtime director of the National Institute of Arthritis and Musculoskeletal and Skin Diseases. This award is designed to support earlystage researchers who propose innovative and unique ideas that represent a significant change in research direction from their past research or training experience.

Ground-breaking, impactful biomedical and behavioral research depends upon a diverse workforce, composed of people trained in multiple disciplines and from different backgrounds, who can provide a richness of perspectives necessary to inspire new ideas. Recognizing the need to advance talent in muchneeded fields of study, NIH supports training programs in a wide variety of areas, such as bioinformatics, scientific rigor and reproducibility, and data science. To illustrate, NIH supports 16 University-based Biomedical Informatics and Data Science Training Programs,[84] including more than 200 Ph.D.- and postdoctoral-level researchers. Notably, NIH also partners with high schools, minority-serving institutions, and others to support bioinformatics training.

Given the role that interdisciplinary approaches and team science play in fostering innovation, NIH has developed a number of initiatives to encourage collaborative research. One such example is NIH's Building Interdisciplinary Research Careers in Women's Health (BIRCWH), which connects junior and senior faculty with shared interests in interdisciplinary research on women's health.[85] Since 2000, BIRCWH has helped more than 700 junior faculty pursue their career goals, thereby expanding the pipeline of women's health researchers and benefiting the health of women.

NIH supports numerous programs designed to foster research environments that encourage participation from a full and diverse range of talent. NIH's Maximizing Opportunities for Scientific and Academic Independent Careers (MOSAIC) program[86] facilitates the transition of promising postdoctoral researchers from diverse backgrounds, including those from underrepresented groups, to academic faculty positions at institutions throughout the country. The Native American Research Internship (NARI) program supports diverse student researchers, including American Indian and Alaskan Native students, from across the country in paid summer research internships. NARI researchers benefit from cultural and professional mentorship from American Indian or Alaskan Native elders, community organizations, and renowned faculty scientists.

Reflective of the high priority that NIH places on workforce diversity, the NIH Common Fund manages several training programs targeted on diversity. Launched in 2014, the Enhancing the Diversity of the NIHFunded Workforce Program[87] (also called the Diversity Program Consortium or DPC) encourages the inclusion of talent across the career span. Through integrated initiatives, DPC has supported thousands of trainees in biomedical and behavioral research careers by providing funding for institutional infrastructure, student support, and research mentoring. Within 4 years of launch, 1,116 students were appointed to research-training positions through DPC's Building Infrastructure Leading to Diversity (BUILD) program, with 68 percent of BUILD students from underrepresented groups.[88] Moreover, half of DPC member institutions (59 of 113) are either historically Black colleges and universities or institutions with a track record of training Hispanic or Latinx students. BUILD funding enables supported scientists to pursue research focused on understanding health disparities within and across underrepresented groups.

Plans are in place to launch the Faculty Institutional Recruitment for Sustainable Transformation (FIRST) initiative.[89,90] Modeled on the NIH's Distinguished Scholars Program,[91] FIRST aims to transform culture at NIH-funded institutions through the recruitment of faculty cohorts who have a demonstrated commitment to diversity and inclusion. As it enters Phase II of its 10-year program, the DPC will continue to closely monitor the impact of these programs on the careers of individuals from backgrounds underrepresented in NIH-funded research.

NIH recognizes that women scientists often face institutional and environmental barriers that restrict their potential to advance their careers. The NIH Working Group on Women in Biomedical Careers aims to identify and remove barriers to the entry, recruitment, retention, and career development of women biomedical and behavioral scientists.[92] The working group contributed to such recommendations as extended periods for the consideration of tenure and parental leave, a grant program for research on causal factors and interventions that affect the careers of women in science and engineering, and workshops on mentoring women and best practices for women's career success. The Women of Color Committee within the

working group ensures that the unique career barriers faced by women of color are addressed.

Public health needs extend far beyond geographical borders. For example, deadly infectious diseases, such as EVD and COVID-19, can spread rapidly across international borders and continents. Recognizing that scientific research capacity is not equally distributed across the globe, potentially hampering the ability to combat such challenges, NIH develops international training programs. One such program, the Global Infectious Disease Research Training Program, builds infectious disease expertise and research capacity across the world and has prepared more than 1,200 researchers to conduct independent and locally relevant infectious disease research in their home countries.[93] The program connects U.S. institutions with institutions in low- and middle-income countries to provide degree programs, trainings, workshops, and mentoring on topics related to infectious diseases.

The COVID-19 pandemic has also shown the need for local epidemiological modeling capability to provide actionable information for policy makers to make public health decisions during outbreaks. NIH builds capacity for in-country analysis of COVID-19 in low- and middle-income countries by training modelers to track and analyze the progress of the pandemic. These activities include longstanding NIH partners who have well-established epidemiological and surveillance sites in Africa, South America, and South Asia, but lack analytical capacity.

Supporting Research Resources and Infrastructure

For the biomedical research workforce to succeed in moving discovery forward, it requires a scientific infrastructure that is expansive, durable, and capable of quickly integrating state-of-the-art resources that are available to all. To achieve this goal, NIH develops a number of programs and policies designed to provide the biomedical research workforce with stability and flexibility, broad access to innovations in tools and technologies, materials, and knowledge repositories necessary for the design of impactful research programs (Figure 17).

NIH's support of modern technology platforms and high-performance computing capabilities enables innovation in scientific research in several areas, particularly genomics, computational chemistry, and cryo-electron microscopy imaging. Cryo-electron microscopy is a cutting-edge technology that enables researchers to determine the structures of biological molecules to identify therapeutic targets for vaccines and drugs. NIH Common Fund's Transformative High Resolution Cryo-Electron Microscopy program[94] aims to broaden access to cryo-electron microscopy through the support of national service centers, improvement of technology, and training.

NIH is also investing in the data infrastructure necessary to accommodate rapid advances in biomedical and behavioral research. Research progress has produced an explosion of human health data that exceeds current abilities to capture and interpret them (Figure 18). To promote data sharing in high-priority research areas, NIH creates a number of different data repositories. For example, NIH has built a data repository to maximize publication availability and data sharing for NIH HEAL Initiative℠ research projects.[95] This effort promotes dissemination of new knowledge, enhances reproducibility, and will accelerate the ability of researchers to build upon research to make new discoveries. In addition, the Data and Biospecimen Hub (DASH) is a centralized resource that allows researchers to share and access deidentified data, and for many studies, linked biospecimens are available to researchers.[96]

Figure 17. Zebrafish Facility

At the largest zebrafish facility on NIH's campus, Kevin Bishop, NIH Zebrafish Core staff member, holds up a tank of zebrafish to observe their behavior and physiology. Using molecular techniques, researchers alter the zebrafish's genome to mimic what is seen in human patients in the clinic.

Credit: Ernesto del Aguila III, NHGRI, NIH.

Figure 18. Modern Data Environments to Accelerate Research

Rapid advances in data generation and computing power provide extraordinary potential for accelerating biomedical research. However, researchers face technical hurdles to accessing, sharing, and analyzing within and across large biomedical datasets. NIH is tackling this challenge through multiple initiatives to build modern technology platforms, collaborative workspaces, tools, and applications necessary for researchers to securely find, access, share, store, and analyze data across diverse datasets. Two examples are the Genomic Data Science Analysis, Visualization, and Informatics Lab-space and the Cancer Research Data Commons. These platforms enable researchers to efficiently combine and analyze diverse data types, which can lead to new discoveries in disease prevention, diagnosis, and treatment. Several programs seek to provide researchers with state-of-the-art, high-performance computing, such as the Biowulf cluster, which is the world's most powerful supercomputer completely dedicated to advancing biomedical and behavioral research.

Credit: Ernesto del Aguila III, NHGRI, NIH.

Much of NIH's efforts in resource building focuses on providing researchers with the underlying evidence needed to design impactful research programs. These efforts include the development of resources for understanding public health needs of the general population and specific populations, resources that will assist in providing access to patient populations, and resources for better understanding the factors affecting such health conditions as Alzheimer's disease and related dementias (Figure 19).

A widely available tool in which NIH invests to help guide prevention and treatment efforts is the Global Burden of Disease (GBD) enterprise.[97] GBD is the world's largest scientific effort to systematically quantify health loss from all diseases, injuries, and risk factors by age, sex, and geographic location over time. NIH and GBD collaborated to improve the way that disease causes and risk factors are identified. As a result of this collaboration, NIH and the research community can identify and track the causes and risk factors of premature death and disability in the U.S. over time (both historically and projecting up to 25 years in the future). Because premature death is often preventable, the availability of these data not only improves understanding of the burden of disease and key health outcomes in the U.S., but also enhances the ability to focus on the most pressing health challenges facing the nation.

The ability to monitor cancer in the U.S. is an important step toward determining how best to prevent and treat cancer in specific, disproportionately affected populations. The NIH Surveillance, Epidemiology, and End Results (SEER)[98] Program provides information on cancer statistics based on race, gender, and geography to guide efforts to reduce the cancer burden among the U.S. population. SEER currently reflects 35 percent of the U.S. population, and NIH

Figure 19. Alzheimer's Disease Research Infrastructure

More than 5.8 million Americans age 65 and older are living with Alzheimer's disease (AD), the most common form of dementia. Many others younger than age 65 have developed the less common early-onset form of AD. Still more are affected by AD-related dementias (ADRDs). Although the underlying pathology may differ among these conditions, their ultimate outcome is the same: the inexorable, relentless loss of memory, thought, and function. At present, no intervention has been reliably proven to prevent, slow, or reverse the effects of AD/ADRD. Under the auspices of the National Plan to Address Alzheimer's and Related Dementias, NIH develops and supports a robust infrastructure for discovery that supports activity across the full spectrum of AD/ADRD research, including, but not limited to, the Dominantly Inherited Alzheimer's Network, an international consortium of researchers who are working with individuals from families with a rare form of the disease to identify the sequence of brain changes before symptoms appear; the NIH Blueprint Neurotherapeutics Network, NIH's preclinical/early clinical drug development program that provides support for drug discovery and development; and the Alzheimer's Disease Education and Referral Center, NIH's primary source for consumer information on AD/ADRD research and care.

will expand the program to cover 50 percent of the U.S. population.

The medical advances and new technologies that have allowed Americans to live longer and healthier lives have not helped everyone equally. To build capacity at institutions with a historical and current commitment to educating underrepresented students and providing health care in underserved communities, NIH created the Research Centers in Minority Institutions (RCMI) Program.[99] The goals of RCMIs are to enhance institutional research capacity, enable investigators to become more successful in obtaining competitive funding, foster environments conducive to career enhancement, promote research on minority health and health disparities, and establish sustainable relationships with community-based organizations.[100]

NIH is also working to promote health equity in rural populations. NIH's Clinical and Translational Science Awards (CTSA) Program[101,102,103] is engaging with patients, community members, and nonprofit organizations to develop and disseminate best practices for patient-focused research in rural health.[104] Project areas include improving access to clinical trials for rural communities, harnessing technology to deliver effective care, and enhancing rural community outreach. The CTSA Program is also partnering with other NIH ICs and federal agencies to support rural health.

To further support rural communities, NIH is harnessing the Institutional Development Award (IDeA) Program, which aims to broaden the geographic distribution of NIH funding and to build research capacity in states that historically have had low levels of NIH funding. NIH is building on the research capacity within IDeA states to help address the medical needs of children living in rural and underserved areas. Similarly, the Environmental influences on Child Health Outcomes (ECHO) Program also leverages IDeA to expand pediatric research capacity in the IDeA States Pediatric Clinical Trials Network.[105] Beginning in 2018, IDeA also collaborated with NIH's Shared Instrumentation Grant (SIG) Programs to improve access to modern technologies for researchers in underresourced institutions in IDeA-eligible states. SIG supports the acquisition of modern scientific instruments that must be used on a shared basis.[106]

Many NIH Common Fund projects focus on developing resources that can be useful for research communities focused on a particular topic. The NIH Common Fund Molecular Transducers of Physical Activity Consortium (MoTrPAC)[107,108] is building a map of the molecular responses to exercise, both immediate and over the long term. Data are being made widely available to the entire research community so that investigators from anywhere can use this map to develop and test hypotheses about how exercise improves health and ameliorates disease. The program is scheduled to run through 2023 and released its first dataset through the MoTrPAC Data Hub in 2019.

Another valuable resource for the research community includes improved understanding of the biological and behavioral mechanisms of symptoms, which can improve patient outcomes. The NIH Intramural Research Program launched the Symptom Science Center (SSC)[109] to address the need for a more comprehensive approach to understanding the complex mechanisms underlying symptoms. Increased knowledge in this area can help develop precision health interventions to treat patients more effectively. Furthermore, the SSC serves as a nexus for collaboration among investigators from multiple ICs and is committed to training scientists and clinicians in symptom science.

OBJECTIVE 3 Exemplifying and Promoting the Highest Level of Scientific Integrity, Public Accountability, and Social Responsibility in the Conduct of Science

As a steward of public resources, NIH has a responsibility to uphold public trust and confidence in the agency. In addition to fostering innovative research, NIH must endeavor to ensure that all of its operations and the research it supports are conducted efficiently, responsibly, ethically, and with integrity. Over the next

5 years, NIH is committed to taking additional steps to maintain and strengthen the processes by which it governs the conduct of science.

Fostering a Culture of Good Scientific Stewardship

This *NIH-Wide Strategic Plan* positions the agency to meet its mission by pursuing scientific opportunities when they arise, responding to ongoing and emerging public health needs, and addressing rare diseases. NIH research efforts also align with and reflect HHS's priority goals.[110] The agency promotes policies and programs that foster and ensure a strong foundation and culture of good scientific stewardship. As critical research needs arise, NIH will respond by ensuring that the scientific community has flexibility to quickly adapt to and address urgent public health issues.

Setting Priorities

Scientific priority setting at NIH encourages input from a range of sources, including the research community; public forums; the Advisory Committee to the NIH Director; U.S. Congress; Administration objectives; and consultation with advocacy groups, professional societies, and research participants. The NIH Director provides overall leadership to the ICs and OD offices, especially on efforts involving several components of the agency. Strategic plans developed by individual ICs and OD offices, committees composed of representatives from multiple ICs, and interagency working groups describe a multitude of scientific priorities and themes of interest to the agency.[111]

NIH demonstrates effective stewardship by supporting the most meritorious biomedical and behavioral research possible. The NIH peer review process assesses research grant applications for overall scientific and technical merit and ensures that applications receive fair, independent, expert, and timely reviews.[112] Scientific review panels are strategically formed to include reviewers who possess both broad and specialized expertise and who can address stability and recent trends in the field. NIH makes efforts to ensure that review panels reflect diversity in career stage, geographic region, and demographic characteristics. NIH staff seek input from a variety of sources to identify reviewers for panels, including NIH program staff and advisory councils, as well as scientific literature, meetings, and professional organizations.

The relative merit of applications as determined through peer review, in conjunction with input on mission relevance from IC Advisory Councils, informs IC Directors as they make funding decisions that consider mission focus, portfolio balance, scientific opportunity, emerging and ongoing public health needs, and stakeholder priorities. Balancing research with training and infrastructure—as well as distribution across basic, translational, and clinical research—are key factors taken into consideration in maintaining a diverse portfolio. NIH also considers the vital role of rare diseases research, through which unique biological insights are possible. This research is less likely to be supported by private funders than research into more prevalent disorders.

To maintain a peer review process of the highest caliber, NIH has developed an ongoing systematic multimethod evaluation that will objectively assess most peer review study sections over a 5-year cycle.[113] The aims of the system are to keep study sections aligned with the current state of the science, confirm NIH is attracting applications that propose cuttingedge science, and ensure that study sections are functioning efficiently with a balanced workload. Additional programs, such as the Early Career Reviewer Program,[114] help NIH refresh and diversify its pool of reviewers, while also helping investigators improve their grant-writing skills, develop research evaluation capacity, and strengthen critique-writing skills.

NIH proactively pursues scientific opportunities through a variety of programs that promote innovative research concepts and exploration of scientific hypotheses that could steer science in new directions. Additionally, NIH encourages team science and cross-disciplinary collaboration to propel research progress. NIH will continue to look for additional ways to capitalize on the intersection of scientific fields to further scientific progress and improve human health.

Monitoring Expenditures and Scientific Progress

NIH requires regular reporting from grant and contract award recipients on research progress, spending, and findings. NIH staff review these reports to ensure proper stewardship of federal funds and that supported research is fulfilling all terms of the funding agreement.

Another aspect of NIH stewardship is to provide the public with transparent and easily accessible information about NIH research awards and allow interested individuals to monitor NIH's support of research. The *NIH Research Portfolio Online Reporting Tools Expenditures and Results (NIH RePORTER)*[115] tool, for example, provides public access to information on the grants, contracts, and intramural research that NIH supports. Additionally, the *NIH Data Book*[116] provides quick access to key annual statistics, such as application success rates, workforce and training trends, the peer review process, and small business awardees. NIH will continue enhancing these and other tools in the suite of *NIH RePORTER* tools[117] to better meet information and communication needs in the coming years.

Making Evidence-Informed Decisions

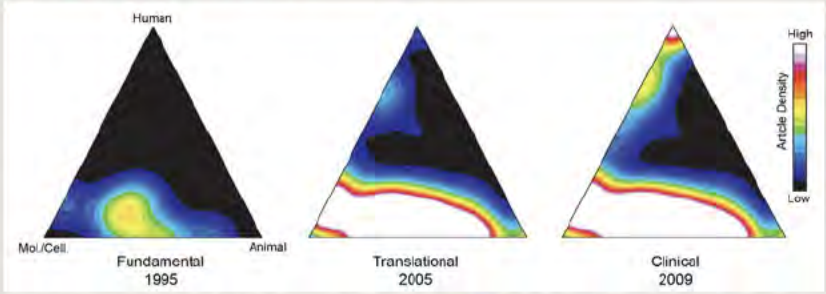
NIH is committed to enhancing scientific stewardship by optimizing approaches that generate evidence used to inform programmatic, operational, and policy decisions. To further these efforts, NIH has developed several tools, available to its staff and to the broader scientific community, that can identify and analyze current and emerging areas of research that will advance NIH's mission. For example, the *iCite*[118] suite of tools is a public resource that enables users to examine validated metrics regarding the impact of NIH-funded research articles (Figure 20). These tools, which are informed by the judgment of subject-matter experts, help users examine the NIH portfolio's productivity, balance, and priorities across the spectrum of research—from basic to clinical and across the diverse areas of biomedical and behavioral research.

NIH shares common interests with many agencies across the federal government and often coordinates with other science agencies to promote collaboration among researchers and manage research portfolios. NIH supports *Federal RePORTER*,[119] a collaborative effort among federal funders to provide a central database for certain grant information. In addition, NIH is partnering with the National Science Foundation and the General Services Administration to develop and implement computational tools to identify overlap between grant proposals across agencies in real-time, reducing the risk of unnecessarily duplicative research.[120] Collectively, these efforts promote transparency and enable efficiency through data-driven decision-making.

Assessing Programs, Processes, Outcomes, and Impact

The NIH *Report on Approaches to Assess the Value of Biomedical Research by NIH*[121] found that a better understanding of all aspects of NIH's work is key to increasing the efficiency and effectiveness of the agency. NIH uses a variety of approaches—including monitoring, performance measurement, analysis, and evaluation—to assess the progress and effectiveness of its programs, policies, and operations and to generate information for decision-making. To increase the use of these tools, NIH is enhancing the quality of administrative data, making it an increasingly strategic source of information that, when coupled with other tools, could improve the agency's

Figure 20. Predicting Translational Progress of Research



Credit: Hutchins BI, Davis MT, Meseroll RA, Santangelo GM. Predicting translational progress in biomedical research. PLOS Biol *2019;17(10):e3000416.* https://doi.org/10.1371/journal.pbio.3000416.

Fundamental research can take decades to translate into clinical outcomes. To capture the translational potential of publications, NIH researchers created a machine learning model that maps papers on a trilinear graph using three Medical Subject Heading (MeSH) terms: Human, Animal, and Molecular/Cellular. Almost all NIH-funded papers (> 96 percent) are assigned at least one of the MeSH terms and can be plotted somewhere on "the triangle of biomedicine." The graph pictured depicts the accumulation of fundamental, translational, and clinical research that led to cancer immunotherapy drugs like Opdivo (nivolumab). This visualization was generated using the *iCite* web tool developed by NIH.

effectiveness. Under HHS's guidance, NIH will engage in capacity- and evidence-building activities to support the Department's implementation of the *Foundations for Evidence-Based Policymaking Act of 2018*[122] and further develop its data-driven, results-oriented culture.

Communicating Results

NIH fosters scientific stewardship by ensuring that the products and processes of scientific research, such as research data and scientific publications, are available in accord with the FAIR principles that all research data should be findable, accessible, interoperable, and reusable (Figure 21). NIH communicates research findings to the public in numerous ways, including through press releases on recent scientific advances on the *NIH News & Events*[123] website, the *NIH Director's Blog*,[124] and the *Impact of NIH Research* pages,[125] which have examples illustrating the downstream impact of NIH research on public health and society. Additionally, NIH ICs and OD offices develop and disseminate a range of publicfriendly health- and disease-specific educational materials on a host of topics. NIH provides evidence-based and authoritative biomedical information in highly expeditious and proactive ways. This vital function is especially important during public health emergencies, such as infectious disease or foodborne illness outbreaks.

Figure 21. FAIR Principles

NIH is working to align the research that it supports with the FAIR principles (findable, accessible, reusable, interoperable) to ensure that the results of NIH investments can be leveraged by the entire research enterprise. NIH organizes its data science efforts around five themes: advancing data infrastructure to increase connectivity across systems and platforms; defining strategies to help researchers better store and share their data; adopting and adapting data science tools to enhance research; engaging with stakeholder communities and enabling citizen scientists to support the biomedical data enterprise; and increasing the capacity of computational and data science workers in biomedical research through new and existing workforce programs.

Credit: Office of Data Science Strategy, NIH.

Research results are also communicated through such NIH resources as *PubMed* and *ClinicalTrials.gov*. In 2020, NIH launched the new *PubMed*,[126,127] the most heavily used biomedical literature citation database in the world, which enables the communication and discovery of scientific literature around the world. NIH's *PubMed Central* (PMC)[128] provides public access to the full text of more than 6 million peer-reviewed research articles (Figure 22). PMC facilitates linking between articles and associated data; supports discovery of these data by aggregating data citations, data availability statements, and supplementary materials; and contains a subset of about 3 million articles available for bulk retrieval for text mining and other research purposes.

Reports from clinical studies are made available through *ClinicalTrials.gov*, the largest public clinical research registry and results database in the world. This NIH resource provides patients and their caregivers, health care providers, and researchers with information on more than 330,000 active and complete registered studies, including studies with summary results, many of which are not otherwise available through published literature. A multiyear effort is underway to modernize *ClinicalTrials.gov* to deliver an improved user experience on an updated platform that will accommodate growth and improve efficiency.

In response to the COVID-19 pandemic, NIH partnered with researchers and leaders from universities and industry to rapidly mobilize and create the *COVID-19 Open Research Dataset* (CORD-19)[129] of scholarly literature about COVID-19, SARS-CoV-2, and other coronaviruses. *CORD-19* provides immediate, machinereadable access to the full text of pre-print and peer-reviewed articles to assist researchers worldwide in finding answers to high-priority scientific questions related to the COVID-19 response. NIH also developed the COVID-19 portfolio tool[130] as a complement to *CORD-19*. This tool provides powerful search functionality and interactive

Figure 22. PubMed Central

As a free archive of full-text biomedical and life sciences journal literature, *PubMed Central* is an authoritative source of scholarly information that ensures the insights gained through biomedical discovery are made openly available to research and clinical care communities, as well as to the public at large.

Credit: National Library of Medicine, NIH.

visualizations to support cutting-edge analytics of the literature to identify gaps and opportunities in COVID-19-related research. In addition, to assist researchers working on the genomics of the novel coronavirus, the COVID-19 Genome Sequence Dataset on Registry of Open Data on Amazon Web Services[131] is a centralized sequence repository for strains of SARS-CoV-2.

Leveraging Partnerships

Expanding fundamental knowledge of biological systems and applying that knowledge to the advancement of health requires strategic partnerships with a range of organizations, including other federal agencies, international governments, the private sector, and the public. These partnerships bring enhanced coordination, critical expertise, pooled resources, and novel stakeholder connections to augment NIH efforts.

Federal Partnerships

NIH values collaboration with its federal partners and partners extensively with other federal agencies. Interagency collaborations address critical public health needs and facilitate coordination, communication, and resource-sharing. For instance, the Tobacco Regulatory Science Program (TRSP),[132] a partnership between NIH and FDA, funded research on youth tobacco use; toxins and nicotine concentration in e-cigarettes; and the Population Assessment of Tobacco and Health (PATH) Study, a longitudinal examination of tobacco product use.[133] Data from TRSP studies provide valuable evidence to inform government-wide policymaking. Research results from the Tobacco Centers of Regulatory Science, a centerpiece of TRSP, will provide further insight into who is using these products, what health outcomes result from product use, and how to implement interventions to target health outcomes.[134]

Another key federal collaboration is the Interagency Pain Research Coordinating Committee (IPRCC),[135] chaired by NIH with members from several agencies within HHS, including FDA, Centers for Disease Control and Prevention (CDC), Agency for Healthcare Research and Quality (AHRQ), Department of Defense (DoD), and U.S. Department of Veterans Affairs (VA). IPRCC coordinates federal activities to enhance pain research efforts and promote collaboration across the government, with the ultimate goals of advancing the fundamental understanding of pain and improving pain-related treatment strategies. NIH also partners with DoD and VA on the NIH-DoD-VA Pain Management Collaboratory, which supports the development, implementation, and testing of cost-effective, large-scale, real-world research on nonpharmacologic approaches for pain management and related conditions in military and veteran health care delivery organizations.[136]

The *21st Century Cures Act* established the HHS Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC) to advise the HHS Secretary regarding gaps in knowledge and research on safe and effective therapies for pregnant women and lactating women (Figure 23).[137] Led by NIH, other

Figure 23. Research for Pregnant and Lactating Women

The *21st Century Cures Act* established the Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC) to advise the Secretary of Health and Human Services regarding gaps in knowledge and research on safe and effective therapies for pregnant women and lactating women. PRGLAC was tasked with identifying these gaps and reporting its findings to the Secretary.

Credit: NICHD, NIH.

federal members include CDC, FDA, AHRQ, Health Resources and Services Administration (HRSA), VA, and HHS Office on Women's Health. Non-federal members include representatives from medical societies, nonprofit organizations, and industry. More than 6 million women are pregnant in the U.S. each year, many taking medications or dietary supplements. PRGLAC identified the lack of scientific evidence on the safety and efficacy of these compounds during pregnancy or breastfeeding as a substantial knowledge gap in maternal health.

Public-Private Partnerships

Public–private partnerships (PPPs) provide a mechanism to strategically accelerate advances and accomplish goals that NIH cannot readily achieve by acting alone. For example, to hasten the development of interventions for COVID-19, NIH is leading the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)[138] PPP (Figure 24). PPP activities focus on the shared goals and mandates of the partners and leverage knowledge, skills, resources, and services to achieve synergy. For example, NIH—together with FDA, biopharmaceutical companies, and nonprofit organizations—launched the Accelerating Medicines Partnership (AMP).[139] The goal of AMP is to increase the number of new diagnostics and therapies and reduce the time and cost of developing them. Four AMP initiatives are underway: AMPAlzheimer's Disease (AMP-AD), AMP-Parkinson's Disease (AMP-PD), AMP-Rheumatoid Arthritis/Lupus (AMP-RA/Lupus), and AMP-type 2 diabetes (AMP-T2D). After successfully meeting program milestones, AMP-AD and AMP-T2D are finalizing research plans for the next phase of the program. New AMP initiatives have been launched for schizophrenia[140] and are in development for gene therapy.

To capitalize on dramatic advances in genetics, NIH and the Bill and Melinda Gates Foundation have expanded their cooperation toward an audacious goal: to develop affordable, gene-based cures for SCD and HIV within a decade. The intention is for these cures to be made globally available, especially in lowresource settings where people are most affected by these conditions.

Figure 24. ACTIV: An Unprecedented Partnership for Unprecedented Times

In April 2020, NIH launched the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) public–private partnership to develop a coordinated research strategy for prioritizing and speeding the clinical evaluation of the most promising vaccines for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and treatments for coronavirus disease 2019 (COVID-19). Through ACTIV, NIH has partnered with more than 15 biopharmaceutical companies, as well as its sibling agencies and offices within the U.S. Department of Health and Human Services, other government agencies, the European Medicines Agency, and representatives from academia and philanthropic organizations. Through the ACTIV partnership, NIH is pursuing four fast-track focus areas most ripe for opportunity: (1) developing a collaborative, streamlined forum to standardize and share evaluation methods and testing of preclinical therapeutics and vaccines; (2) prioritizing and accelerating clinical testing of the most promising treatments for all stages of the disease; (3) leveraging clinical trial capacity and effectiveness; and (4) accelerating the evaluation of vaccine candidates to enable rapid authorization or approval.

Credit: NIH.

The NIH Science and Technology Research Infrastructure for Discovery, Experimentation, and Sustainability (STRIDES) Initiative[141]—one of many NIH-wide efforts underway to implement the *NIH Strategic Plan for Data Science*—provides NIH and its funded researchers with cost-effective access to state-of-the-art cloud-based data storage and computational capabilities, tools, and expertise. Through STRIDES, NIH has established PPPs with commercial providers, such as Amazon Web Services and Google Cloud. NIH anticipates forming additional industry partnerships through STRIDES to broaden access to services and tools, including training and professional services for researchers on how to use the latest cloud tools and technologies. These partnerships will allow academic researchers and industry to come together to create a data ecosystem that maximizes the use of NIH-supported biomedical and behavioral research data for the greatest benefit to human health.

During the next 5 years, NIH will continue to expand partnership opportunities focused on increasing diagnostics and therapies for particular conditions, curing intractable diseases, and making the vast amount of data generated by biomedical research accessible to as many researchers as possible.

International Partnerships

As the world grows increasingly connected, NIH remains committed to developing and sustaining relationships with partners around the globe. Recent events, including the COVID-19 pandemic, have illuminated the importance of a coordinated approach to global health aligned with humanitarian and scientific values. Geographic boundaries do not prevent infectious disease spread, nor should they prevent the advancement of research on such diseases. For this reason, NIH collaborates internationally with foreign governments and organizations.

In collaboration with the Office of the U.S. Global AIDS Coordinator and Health Diplomacy, NIH supports the African Forum for Research and Education in Health (AFREhealth)[142,143] Program and the Health-professional Education Partnership Initiative,[144] both of which are designed to enhance the quality, quantity, retention, research engagement, and networking of an interprofessional health workforce across Africa. NIH also supports the Human Heredity and Health in Africa Consortium (H3Africa) via the NIH Common Fund.[145] This partnership includes the Wellcome Trust and the African Academy of Sciences and seeks to build African research capacity in the genomic sciences and contribute to improving understanding of health and disease in underrepresented and underserved populations.

NIH participates in the Global Alliance for Chronic Diseases (GACD),[146] a consortium of the world's largest public research funding agencies. GACD's mission is to reduce the burden of chronic noncommunicable diseases (NCDs) in low- and middle-income countries and in populations facing conditions of vulnerability in high-income countries, by building evidence to inform national and international NCD policies. NIH funds GACD research in the areas of cancer prevention, mental health, lung disease, type 2 diabetes, hypertension, and scaling-up evidence-based interventions.

In addition to working with international partners on disease, NIH also supports other types of international health initiatives. For example, the NIH Disaster Research Response (DR2) Program, which supports research to inform disaster and public health emergency preparedness, response, and recovery, serves as a compelling model for addressing crises. DR2 has partnered with Japan's National Institute for Environmental Studies and Health Canada to begin developing similar programs in those countries.[147] Early outcomes include translation of data collection tools to Japanese, using DR2 tools in response to Typhoon Hagibis, collaboration on DR2 workshops and training exercises, and international outreach.

Public Engagement

Public engagement is vital to NIH research. Patients, research participants, disease advocacy organizations, and local, state, and cultural communities have a leading role to play in the research enterprise. During study design, these groups can highlight important knowledge gaps impeding community-level programs, policies, and practices. During data collection and analysis, they advise researchers on the challenges of applying new knowledge in different local and cultural contexts.

As part of its commitment to public engagement, NIH will continue providing underrepresented groups with equal access to research in an ethical and responsible manner that protects privacy and respects cultural sensitivities. NIH facilitated a data sharing and use agreement between the Navajo Nation

and NIH grantees of the ECHO Program.[148] The agreement was created to advance the Navajo Birth Cohort Study while respecting Navajo Nation cultural beliefs, Tribal sovereignty, and community values.[149] It is the first Tribal data-sharing agreement for a large-scale database as part of a nationwide research consortium. This achievement lays the groundwork for discussion of similar agreements with other Tribal Nations considering participation in biomedical and behavioral research programs.

Public engagement is also key to NIH's maternal health efforts. The NIH Task Force on Maternal Mortality developed Implementing a Maternal health and PRegnancy Outcomes Vision for Everyone (IMPROVE), an NIH-wide research initiative. IMPROVE was informed by input from a variety of sources, including the public and NIH-convened meetings for scientists and clinicians to solicit recommendations on health disparities underlying maternal mortality, as well as gaps and opportunities for future research. IMPROVE will focus on women beginning in pregnancy and continuing up to 1 year postpartum and will include community-focused social and biobehavioral research, as well as research to accelerate discovery and advance technologies to reduce maternal health risks.

Ensuring Accountability and Confidence in Biomedical and Behavioral Sciences

To foster confidence in NIH-funded research and results, NIH must ensure that both its operations and its supported research are conducted efficiently, responsibly, ethically, and with integrity. NIH is committed to taking steps to maintain and strengthen the processes by which it governs the conduct of science, continuing to be accountable for the public funds it invests in research.

Enhancing Reproducibility Through Rigorous and Transparent Research

Two cornerstones of scientific research are rigor in the design and conduct of experiments and the ability to reproduce research findings. The application of scientific rigor ensures robust and unbiased experimental design, methodology, analysis, interpretation, and reporting of results. When a result can be reproduced by multiple scientists working independently, it validates the original result and indicates readiness to progress to the next phase.

NIH has collaborated with scientific journal publishers to identify shared opportunities to enhance transparency, rigor, and reproducibility in published literature. NIH has also convened working groups and workshops focused on rigor, developed training modules for the research community on good experimental design, enhanced requirements for the content and review of grant applications, and developed specific funding opportunities aimed at improving rigor and reproducibility. Moving forward, NIH will continue working closely with researchers, publishers, and federal partners to develop and share recommendations and best practices. Along these lines, NIH has convened a working group of the Advisory Committee to the Director to explore ways to enhance reproducibility and rigor in laboratory animal research.[150]

Improving Stewardship of Clinical Trials

NIH invests more than $3 billion each year in clinical trials. NIH must ensure these trials investigate high-priority questions, do not needlessly duplicate previous trials, recruit and maintain sufficient participants, are completed in a timely manner, and are likely to advance knowledge and improve health. NIH has launched a series of efforts to enhance accountability and transparency in clinical research,[151] as well as address challenges and shortcomings in the design, efficiency, and timeliness of reporting clinical trial results. These efforts included dedicated funding opportunities, Good Clinical Practice training, a single Institutional Review Board for multisite research policy, and an optional template that guides investigators through the systematic development of a comprehensive clinical protocol and required registration and reporting of clinical trial results. In addition, by ensuring that summaries of results of NIH-supported clinical trials are widely and freely available, *ClinicalTrials.gov* promotes transparency and helps ensure that research findings are contributing to the advancement of public health.

Assuring Ethical and Equitable Conduct of Research Through Inclusion

More women and underrepresented and underserved groups are participating in clinical research than ever before, in large part thanks to NIH policy. NIH's goal is to ensure that these trends continue so that

the knowledge gained from research is applicable to everyone affected by the disease or condition under study (Figure 25). To this end, NIH has taken critical steps to ensure the scientifically appropriate enrollment of women and underrepresented and underserved groups in clinical research and is engaged in efforts to increase inclusion of children, older adults, pregnant and lactating women, and individuals with disabilities as appropriate. NIH requires researchers who propose research involving human subjects to include plans for how participants from these groups will be enrolled, unless there is a scientific or ethical justification for their exclusion. Once a grant is awarded, researchers must annually report deidentified individual-level demographic data so that NIH can continue to monitor inclusion.

Figure 25. Clinical Center Research

An NIH researcher examines a pediatric patient in the NIH Clinical Center.

Credit: Richard Clark, NIAMS, NIH.

NIH will continue its focus on challenges to recruiting and retaining underrepresented populations in clinical studies and will add data on the age at enrollment of participants to the Research, Condition, and Disease Classification (RCDC) *Inclusion Statistics Report*, which allows users to view trends over time. In addition, NIH will train researchers to include women, underrepresented and underserved populations, and individuals of all ages in studies as part of its efforts to increase the diversity of study populations.

Maintaining Transparency Through Data Access and Sharing

NIH is committed to making findings from the research that it funds accessible and available in a timely manner, while also providing safeguards for privacy, intellectual property, security, and data management. For instance, NIH-funded investigators are expected to make the results and accomplishments of their activities freely available within 12 months of publication. NIH also encourages investigators to share results prior to peer review, such as through preprints, to speed the dissemination of their findings and enhance the rigor of their work through informal peer review.

A robust culture of data sharing is critical to continued progress in science, maximizing NIH's investment in research, and assurance of the highest levels of transparency and rigor. To this end, NIH will continue to promote opportunities for data management and sharing while allowing flexibility for various data types, sharing platforms, and strategies. Additionally, NIH is implementing a policy requiring that all applications include data sharing and management plans that consider input from stakeholders.[152,153]

Fostering a Safe and Harassment-Free Work Environment

NIH has an imperative to transform the culture of science to prevent harassment (sexual, gender, and other) and mitigate its detrimental impacts, whether it is in the agency or anywhere NIH-funded activities are conducted. In 2019, NIH established the Advisory Committee to the NIH Director Working Group on Changing the Culture to End Sexual Harassment.[154] Following this group's recommendations, NIH is taking actions within the agency's authority to change the scientific workplace to make it safer and more welcoming (Figure 26). NIH issued several new policies, guidelines, and requirements on this topic and communicated them widely to make expectations clear to NIH-funded organizations and the workforce at NIH.[155]

NIH expects recipients of federal funds to have policies and practices in place that foster a safe and harassment-free environment.[156] For instance, NIH must be notified if a principal investigator or other key personnel named on an NIH grant award is unable to

Figure 26. NIH *Harassment Does Not Work Here* Campaign

An image stating "Harassment Doesn't Work Here" as part of NIH's campaign to create a safe and civil workplace wherever NIH-funded research is conducted.

Credit: NIH Civil Program.

fulfill their obligations to conduct research because they are under investigation or have been removed from the workplace because of sexual harassment concerns. NIH expects recipients requesting changes in investigator, key personnel, or recipient institution to mention whether these requests are related to concerns about the safety and/or work environment, including issues related to sexual harassment or bullying.[157] Internally, NIH has undergone a workplace climate and harassment survey to inform policy and practice and has expanded its human resources program to foster civility throughout the NIH community.[158]

NIH's efforts have led to increased scrutiny and awareness of harassment, centralized mechanisms for reporting harassment, and new anti-harassment policies. NIH will continue working with its partners and exploring policymaking options based on recommendations from the Advisory Committee to the NIH Director and findings from internal studies to change the scientific culture, prevent sexual harassment, and promote a civil, safe, and respectful workplace for everyone.

Managing Risks to the Research Enterprise

NIH is committed to proactively managing risks that may impede the NIH mission. Such risks have the potential to affect patient and laboratory safety, the peer review process, laboratory animal welfare, conflict of interest disclosures, closeout of grant awards, data security, and more. Understanding the need to identify and manage risks, NIH incorporated Enterprise Risk Management (ERM) capabilities into its strategic planning, performance management, and resource allocations (see Figure 27). Going forward, NIH is better prepared to respond to emerging risks that may undermine its research activities and are inconsistent with its research values and principles.

Figure 27. Managing Risks to the Research Enterprise

The NIH Risk Management Program provides NIH with a framework for systematically identifying and addressing risks that might adversely affect NIH's ability to fulfill its mission. Risk management is a continuous process that requires all NIH staff and researchers to proactively identify and mitigate risk as part of their daily jobs. Understanding the need to identify and manage risk, NIH has incorporated Enterprise Risk Management (ERM) capabilities into its strategic planning, performance management, and resource allocations. ERM is a strategic discipline that seeks to deliberately and proactively understand the full spectrum of risks, including opportunities across an entire organization, and integrates them into an enterprise-wide, strategically aligned, and interrelated risk portfolio view. By incorporating ERM, NIH can proactively address emerging threats and opportunities and deliver results to the public in a transparent and accountable manner, all in an effort to further support NIH's mission.

Credit: NIH Risk Management Program.

As a part of its commitment to a culture of health and safety for people conducting NIH-funded research, and to mitigating the effects of emergencies on the research enterprise, the NIH Extramural Response to Natural Disasters and Other Emergencies policy allows NIH to provide resources and assistance to those in the NIH community affected by public health emergencies.[159] Under such circumstances, NIH will provide administrative flexibilities and additional funding using a number of mechanisms to support the continuation of research, as demonstrated during the COVID-19 pandemic.[160]

NIH and the research community have a vested interest in mitigating any breaches of trust and confidentiality that undermine the integrity of U.S. biomedical research, while continuing the tradition of scientific collaboration, including international collaboration. NIH recognizes the importance of these collaborations to advancing its mission. However, some researchers at NIH-funded institutions have taken advantage of these collaborations through failing to disclose contributions of resources from foreign organizations, diverting proprietary information to foreign governments, and sharing confidential information obtained from NIH peer review meetings or otherwise trying to influence the peer review process.

NIH works with other federal agencies to take strong actions in response to these breaches of integrity which appear to be, at least partly, instigated by foreign governments.[161] NIH has increased the visibility of this issue and reminds grant recipients to be transparent and disclose all affiliations, financial conflicts of interest, and other support (including from foreign entities) and contacts recipient institutions about any concerns.[162] NIH has also bolstered its internal processes and systems and increased awareness among its own staff.

Looking to the future, NIH will continue careful monitoring and extensive outreach with academia, professional societies, and federal partners to reinforce the importance of research security and integrity, as well as to hold people and institutions accountable for inappropriate actions.[163] NIH will continue to work closely with federal partners to protect the safety, integrity, and inclusivity of U.S. research and looks forward to continuing to work with institutions and researchers to strengthen values that underpin research integrity and protect the nation's biomedical innovations.[164]

Reducing Administrative Costs and Work Throughout the Grants Process

Reducing administrative burden increases the amount of time that investigators can spend on research and that administrators can spend supporting the research enterprise. NIH works to streamline grants policies and processes to reduce administrative work and costs. Recent changes include automating the issuance of certificates of confidentiality that protect participants in NIH-funded research, creating the Application Submission System & Interface for Submission Tracking (ASSIST) as an option for preparing and submitting applications, developing a tool that reduces the need to develop clinical trial protocol text de novo, simplifying the appendix and other material in grant applications to help during the review process, and reducing the need for multiple biographic profiles across different systems to help people find information and simplify reporting and analysis.[165] NIH will continue to work with stakeholders to further streamline the grant application process, while promoting rigor and fostering compliance.

Optimizing Operations

NIH seeks to continually optimize operations across an array of business, administrative, and scientific functions, as well as to improve its physical and technological infrastructures. Increasing coordination and engagement throughout the agency and managing risk while fostering innovation are critical to the stewardship of the nation's biomedical and behavioral research ecosystem. Over the next 5 years, NIH will implement strategies to excel as a federal science agency dedicated to protecting and improving public health.

NIH will continue implementing its *Optimize NIH* efforts, which were established as part of the *Reimagine HHS* effort to improve performance across the Department's divisions. Through the *Optimize NIH* initiative, the agency is focusing on administrative areas that could be made more efficient and effective if managed centrally, or better harmonized across ICs and OD offices. Using a combination of process mapping, surveys, and focus groups, the agency will carefully evaluate which approach or combination of approaches would yield the greatest improvements in each area. NIH's optimization efforts are guided in a data-driven and scientific manner, using teams led

by NIH experts in administrative operations with full engagement by employees.

Examples of functional areas that have already seen substantial improvement through *Optimize NIH* include management of federal advisory committees, employee ethics requirements, and *Freedom of Information Act (FOIA)* requests. NIH has adopted a unified system to standardize and streamline management of FOIA requests across the agency and has launched a public-facing portal, FOIAXpress, to improve the FOIA requestor experience. The launch of this portal increased information request processing speed by 83 percent, decreased the backlog by 11 percent, and offered solutions that can be leveraged across HHS. The lessons learned through the optimization of initial functional areas will inform NIH's approach to other business practice enhancements, such as information technology security, acquisitions, appointment of employees via a specialized hiring mechanism, travel management, and property management.

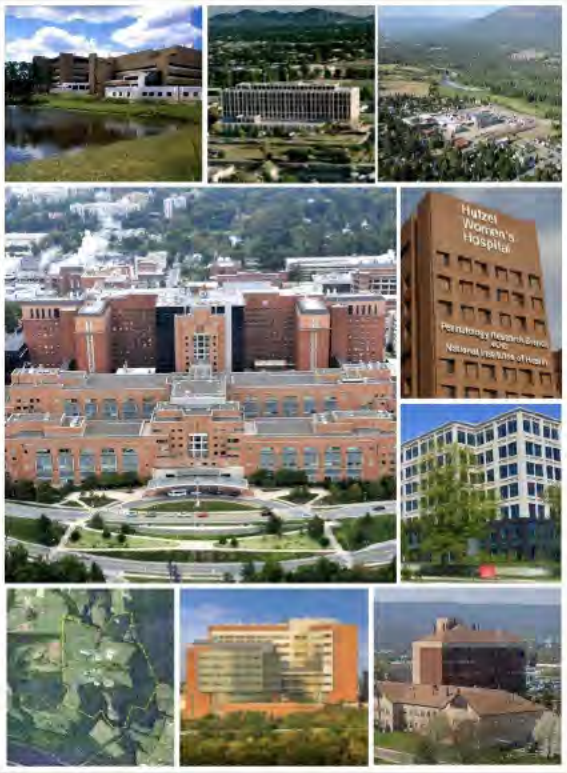
Optimize NIH will also continue to establish best practices for evaluating employee workload to improve the management of resources, inform hiring decisions, and reduce workload inequities. Workload harmonization across ICs and OD offices is already underway for scientific review, grants management, and program management, with additional areas identified for future improvement. NIH will also continue to harmonize and align each IC's strategic plan with a common template derived from the *NIH-Wide Strategic Plan*. Taken together, *Optimize NIH* projects will improve organizational effectiveness and performance and maximize the investment made by American taxpayers.

In alignment with the *Reimagine HHS* and *Optimize NIH* initiatives and in response to NIH community feedback, the NIH OD launched the OD Strategic Engagement Agenda to foster a unified and coordinated OD, which engages seamlessly with the ICs to advance the mission of the agency. This data- and participant-driven initiative will solicit and incorporate employee input through listening tours, working groups, and an online ideation campaign to improve communication and functionality within the OD through coordination and engagement with the ICs. By working toward these goals and improving on the use of OD operating principles of transparency, accountability, strategy, coordination, and decisionmaking, NIH will increase the efficiency and effectiveness of collaboration across NIH.

Meeting the goal of increased efficiency and effectiveness of operations across the agency requires the systematic assessment and management of risk in NIH's administrative and scientific programs, processes, and procedures. NIH is committed to integrating an ERM framework into its organizational culture to help prevent surprises, avoid operational failures, and allow quicker recovery when the unexpected happens. For example, NIH evaluated the extramural grant program using a fraud risk framework to identify vulnerabilities and develop mitigation strategies, including a staff fraud awareness and training program, to reduce the risk

Figure 28. NIH Campuses

Aerial views and photos of various building on NIH campuses showing a portfolio of biomedical research, administrative, and infrastructure-supporting facilities. From left to right and top to bottom: Research Triangle Park, North Carolina; Phoenix Epidemiology and Clinical Research Branch, Phoenix, Arizona; Rocky Mountain Laboratories, Hamilton, Montana; NIH Main Campus, Bethesda, Maryland; Pregnancy and Perinatology Branch, Detroit, Michigan; National Cancer Institute at Shady Grove, Rockville, Maryland; NIH Animal Center, Poolesville, Maryland; Bayview Campus, Baltimore, Maryland; and Frederick National Laboratory for Cancer Research, Frederick, Maryland.



Credit: Office of Research Facilities Development and Operations, NIH.

of fraud in the NIH extramural program and protect public funds. By conducting risk assessments and leveraging data collected within the ERM framework, NIH will improve information sharing and leadership decisionmaking and will prioritize corrective actions for identified risks. Incorporating ERM practices into daily operations also supports NIH in taking risks intelligently and prudently to achieve desired mission outcomes and enhances the agency's transparency and accountability to the public.

Underpinning NIH efforts to optimize its administrative and scientific operations are efforts to advance the agency's physical and technological infrastructures. For example, many of the agency's research and supporting facilities were constructed more than 50 years ago and require significant operating and maintenance costs, repairs, and upgrades to remain competitive in a global research environment. As resources become available, NIH will make strategic investments in building, expanding, and modernizing infrastructure on all its campuses.

It is critical that NIH provide, maintain, and operate its physical infrastructure—buildings and facilities capable of fulfilling and responding to the complex, collaborative, and changing nature of biomedical and behavioral science (Figure 28). The conduct of scientific discovery is enabled through safe and reliable facilities that can be adapted to support research on existing and emerging public health challenges, such as Alzheimer's disease and viral pandemics. NIH will closely link its strategic research goals to the availability, suitability, and capability of existing facilities and will plan, program, and budget for redeveloped and new facilities using planning and space utilization principles consistent with recognized business practices and the National Academies of Sciences, Engineering, and Medicine recommendations.[166] This integration of strategic research and infrastructure planning will enhance the oversight, prioritization, and delivery of facilities to meet the changing scientific needs over time.

CROSSCUTTING T

Many scientific challenges and opportunities are not unique to any one Objective in this Strategic Plan. To emphasize this, NIH has identified five key Crosscutting Themes that span all aspects of NIH's Strategy.

Improving Minority Health and Reducing Health Disparities

Underserved groups—including Black, Latinx, and Indigenous and Native American persons, Asian Americans and Pacific Islanders, and other persons of color; members of religious minorities; lesbian, gay, bisexual, transgender, and queer (LGBTQ+) persons; persons with disabilities; persons who live in rural areas; or persons otherwise adversely affected by persistent poverty or inequality—have distinct health needs and often experience disparities in health outcomes. NIH maintains that racial and ethnic minorities, rural residents, people with low incomes, SGM, and other populations experiencing health disparities should be included in all relevant research, such that there is sufficient representation of each population to conduct relevant analyses. Inclusivity in research generates more broadly applicable information and improves scientific understanding of the health and well-being of specific population groups.

To promote health equity, NIH remains committed to supporting a robust program of research examining how biological, behavioral, environmental, sociocultural, and other factors interact with and shape individuals' health trajectories across the lifespan. The science of minority health and health disparities is founded on the principle that the social construct of individual race and ethnicity and socioeconomic status influence behavior, biology, and health outcomes in many defined and undefined ways. These individual factors interact with structural social determinants that may promote cumulative adversity that leads to worsened health outcomes through biological mechanisms.

Racism and discrimination are increasingly recognized as contributing to poorer health outcomes for

racial and ethnic minorities and other disproportionately affected populations. There is also a growing societal recognition that racism and discrimination extend beyond the behavior of individuals and are embedded in social, institutional, organizational, and governmental structures, processes, procedures, and practices that limit opportunities and resources to segments of the population.[167] NIH understands that health research needs to routinely incorporate constructs and measurement of structural racism or discrimination across multiple domains and levels of influence if minority health is to be optimized, health equity achieved, and health disparities eliminated.[168]

Understanding why underrepresented groups experience specific health outcomes is at the core of minority health science. It is essential to identify contributing factors to minority health conditions independent of whether a health disparity exists or is identified. Minority health research is the scientific investigation of distinctive health characteristics and attributes of minority racial and/or ethnic groups that are usually underrepresented in biomedical research to understand health outcomes in these populations and develop interventions to reduce disparities in health outcomes The *NIH Minority Health and Health Disparities Strategic Plan*[169] sets the direction and goals for NIH research in this area. Several NIH ICs and OD offices have core missions to address the health of underserved and underrepresented populations and to ensure they are adequately included in all NIH research. In addition, NIH-wide strategic plans identify efforts specific to the needs of underrepresented populations to develop synergy and facilitate collaborations across NIH.[170,171,172]

Promoting the recruitment, retention, and advancement of scientists from underserved groups will also have a significant influence on workforce development and will provide opportunities for individual scientists to achieve their full potential, thereby improving research on minority health and reducing health disparities.

Women's Health

Enhancing Women's Health

Women's health is a wide-ranging topic that goes beyond reproductive health to address a broader spectrum of diseases and conditions experienced by women throughout their lifespan. To advance science for the health of women, the *Trans-NIH Strategic Plan for Women's Health Research*[173] established NIH priorities across the research continuum and emphasized the importance of interdisciplinary partnerships. The NIH policy on *Sex as a Biological Variable,*[174] along with the expanded *NIH Inclusion Policy*[175] that requires investigators to report Phase III clinical trial results by sex or gender, race, and ethnicity to *ClinicalTrials.gov,*[176] will build foundational knowledge, accelerate translational research, and ultimately enable women to receive evidence-based interventions specific to their needs.

Promoting the recruitment, retention, and advancement of women scientists will also have a significant influence on workforce development, as well as provide opportunities for individual scientists to achieve their full potential, thereby improving research on the health of women.

Public Health Challenges Across the Lifespan

Addressing Public Health Challenges Across the Lifespan

NIH supports biomedical and behavioral research applicable to the full spectrum of public health challenges and needs, such as acute and chronic diseases, persistent and emerging infectious diseases, cancers, substance use disorders, disordered eating, Alzheimer's disease and related dementias, the health impacts of environmental exposures, and many more.[177] NIH research must address the prevention, treatment, and management of public health challenges; meet new challenges with fundamental research; and be ready to mobilize cutting-edge science in emergent situations.

Many public health challenges affect people of various ages and populations differently. To promote health across the lifespan, NIH efforts include targeted studies of specific age groups; studies of diseases that are unique to, or more common in, certain age groups; longitudinal cohort studies that follow the health outcomes of groups of individuals over long periods of time (including across generations); and studies that examine how early exposures, adversity, and positive experiences affect later health outcomes. The critical issue of maternal mortality and morbidity in the U.S. is one example of a public health challenge that requires multifaceted approaches at different points in the lifespan. Risks include not only complications at the time of pregnancy, birth, and

postpartum, but also cumulative and intergenerational impacts and exposures.

In addition to these programmatic approaches, NIH policies set the expectation that all supported studies will be designed to include children and older adults unless there is a scientific or ethical reason to exclude them. This policy ensures that the scientific findings for a given disease or condition are applicable to all those affected.[178]

Collaborative Science

Promoting Collaborative Science

Complex public health challenges and scientific questions require collaborative, team-driven research involving experts working together across multiple scientific fields, resulting in innovations that exceed the capacity of a single laboratory or discipline. NIH promotes opportunities that bring together scientists and clinicians and recognizes patients and research participants as partners and collaborators to generate outcomes that address the public health challenges that communities face. NIH partners with a wide array of other federal agencies, and domestic and international organizations in the public and private sectors to leverage their respective expertise and translate NIH research findings into new therapies, technologies, and evidence-based practices for improving health. For example, efforts to accelerate COVID-19 diagnostics, therapeutic interventions, and vaccine development are being conducted alongside sister agencies within HHS and representatives from academic, nonprofit, and commercial organizations.[179]

Scientific progress also benefits from collaboration across NIH ICs and OD offices. These NIH collaborations occur at every level of NIH operation, resulting in innovative scientific programs that address a wide range of health conditions. For example, the Pediatric Research Consortium brings together staff from across NIH to discuss issues in pediatric research for a range of health conditions. NIH also cultivates strategic partnerships across HHS to strengthen the public health ecosystem. For example, NIH plays a key role in the Department-wide implementation and dissemination of the HHS Secretary's evidence-based initiative to combat opioid use disorder.

Data Science

Leveraging Data Science for Biomedical Discovery

An immense amount of data is generated throughout the research enterprise, from fundamental experiments using cells and model organisms to human clinical studies and community-level epidemiological research. The exponential growth of data has resulted from the development of advanced biomedical technologies and computational processing unavailable a decade ago, including advanced AI and virtual reality technologies. These transformative changes require innovative approaches and business practices to address opportunities and challenges in data science. Storing, managing, standardizing, analyzing, sharing, and disseminating vast amounts of data are therefore critical priorities for NIH.

The *NIH Strategic Plan for Data Science*[180] provides a roadmap for modernizing and integrating the NIHfunded biomedical data ecosystem, which comprises the universe of data infrastructure, resources, tools, and workforce. Combining existing strengths with new strategic partnerships, NIH works to ensure that data resources are guided by the FAIR principles (Figure 21).[181,182] Implementing the *NIH Strategic Plan for Data Science* will enhance the scientific community's ability to address new challenges, maximize the value of data generated, and accelerate discoveries that lead to better health outcomes. Woven into this plan is NIH's commitment to rapid, open sharing of data and greater harmonization of data science efforts across research domains, while respecting participant privacy, security of sensitive data, and Tribal sovereignty with respect to data.

Bold Predictions

In the previous iteration of the *NIH-Wide Strategic Plan*, NIH set out 14 ambitious goals, or "Bold Predictions," for the next 5 years. These short-term predictions were considered aspirational goals for biomedical and behavioral research that were potentially within reach, but by no means guaranteed outcomes. The 14 Bold Predictions were not an exhaustive list of all of the potential avenues of success for NIH but were designed to illustrate some of the potential achievements in a wide range of research fields that might be possible under NIH's stewardship. NIH has made significant progress on all 14 Bold Predictions, with four being fully realized within the ambitious 5-year timeframe. Despite the risks associated with making short-term predictions, it is important that NIH continue to place high hopes on the ability for NIH-supported research to push the boundaries of innovation faster than ever before. Below are some of the outcomes that NIH will strive to deliver over the next 5 years.

1. The *All of Us* Research Program will reach its goal of 1 million diverse participants and will have gathered the most diverse collection of data (e.g., deep phenotypic, -omic, EHR, digital health technology) on 1 million or more participants of any research resource in the world.
2. The regular use of genomic information will have transitioned from boutique to mainstream in all clinical settings, making genomic testing as routine as complete blood counts.
3. Human studies on type 1 diabetes will assess the long-term survival and function of encapsulated human islets, as well as their efficacy in preventing or delaying the onset of complications and increasing overall survival.
4. Incorporating novel genomics findings from clinical studies on congenital heart disease will help researchers move toward precision therapy and personalized counseling, leading to improved outcomes and longevity for affected children and adults.
5. The high burden of heart disease in communities of color and rural areas will be reduced, especially for major outcomes, such as maternal morbidity and mortality, hypertension, and heart failure.
6. A gene therapy for muscular dystrophy will restore the function of the mutated gene and improve patient outcomes.
7. Gene-based therapies for SCD will be evaluated and refined in large-scale clinical trials, offering a cure to the approximately 100,000 people in the U.S. and 20 million globally who suffer severe pain and premature death from this condition.
8. First-in-human clinical trials will demonstrate the efficacy of iPSC-derived products.
9. Engineered biological cells and scaffolds will be successfully used to repair and replace tissue damaged by chronic wounds or such disorders as osteoarthritis.
10. Insight will be gained into the ultimate ability to regenerate human limbs, using emerging technologies to activate the body's own growth pathways and processes.
11. Research on new approaches to cervical cancer screening will lead to the development of self-sampling for women, with the potential to substantially reduce the incidence and mortality of this disease.
12. At least one novel, non-hormonal pharmacologic treatment for endometriosis will be identified and moved to clinical trials.
13. The number of maternal deaths per year in the U.S. will be significantly decreased, particularly among Black and American Indian or Alaska Native women, by implementing results of research studies focusing on links between social determinants and biological risk factors.
14. Following PRGLAC Task Force findings that almost no data exist on medications in pregnant and lactating women, label changes will be facilitated by results of clinical trials for at least three therapeutics specific to (1) pregnant women and lactating women and (2) children.
15. NIH-wide research will lead to new implementation strategies for pre-exposure prophylaxis that will significantly reduce the number of new HIV infections and to new longacting therapies to improve viral load suppression among people with HIV to levels that prevent transmission.

Bold Predictions (continued)

16. At least one candidate universal influenza vaccine against groups 1 and 2 with 75 percent efficacy will be submitted to the FDA for consideration.
17. NIH-supported researchers will develop a universal coronavirus vaccine.
18. By actively engaging with underserved populations to reduce disparities for COVID-19, researchers will prevent and curb the spread of COVID-19 and save lives.
19. AI will reveal molecular signatures associated with the return to health after an acute illness (e.g., COVID-19).
20. Biomarkers will guide the choice of the most effective therapy for each individual rheumatoid arthritis patient.
21. NIH-supported research will lead to the development of a clinically actionable biomarker for precision psychiatry, using neuroimaging and/or additional physiological and psychological biomarkers.
22. Comprehensive atlases of cell types in the mouse and human brain will provide a deeper understanding of the circuits underlying behavior and a foundation for understanding the circuits affected in complex human brain disorders, including depression.
23. Invasive and noninvasive human brain recording and stimulation technologies will enable new paradigms for interventions in movement disorders and neuropsychiatric diseases, as well as the development of brain-machine interfaces for sensory and motor neural prostheses.
24. Preventive approaches targeting vascular risk factors will reduce the risk for dementia and promote healthy brain aging.
25. At least one promising lifestyle intervention to prevent Alzheimer's disease and related dementias will be rigorously demonstrated in the next 5 years.
26. The role of cellular senescence in aging and disease will be clarified and translated into interventions to improve health.
27. Infant survival will be optimized by synthesizing milk that captures all of the components and properties of human milk, even individualizing it to the characteristics of the infant's mother.
28. NIH research will discover how technology exposure and media use affect developmental trajectories, health and educational outcomes, and parent–child interactions in childhood in the post-COVID-19 era.
29. NIH research will lead to optimized treatment for infants with Neonatal Opioid Withdrawal Syndrome.
30. NIH research will identify one promising intervention to mitigate risks of altered brain development trajectories produced by exposure to alcohol and other drugs among adolescents.
31. Increasing evidence of the effectiveness of nonpharmacologic treatments for pain will transform the way pain is managed and decrease the need for opioids and other medications.
32. Effective screening based on a person's genetics, environmental exposures, and sociobehavioral factors will significantly decrease the 9 million lives lost each year to global air pollution by identifying those who are most vulnerable for early intervention.
33. NIH and NASA will spearhead the development of a space-based platform that will monitor species diversity and predict geographic areas of climate concern.
34. The number of NIH R01 awards that support principal investigators from underrepresented racial and ethnic groups will be increased by 50 percent, and the racial funding disparities gap for NIH R01 grants will be eliminated by fiscal year 2025.
35. New forms of scientific communications, such as preprints, will accelerate clinical research and shorten the evidence-to-practice cycle.

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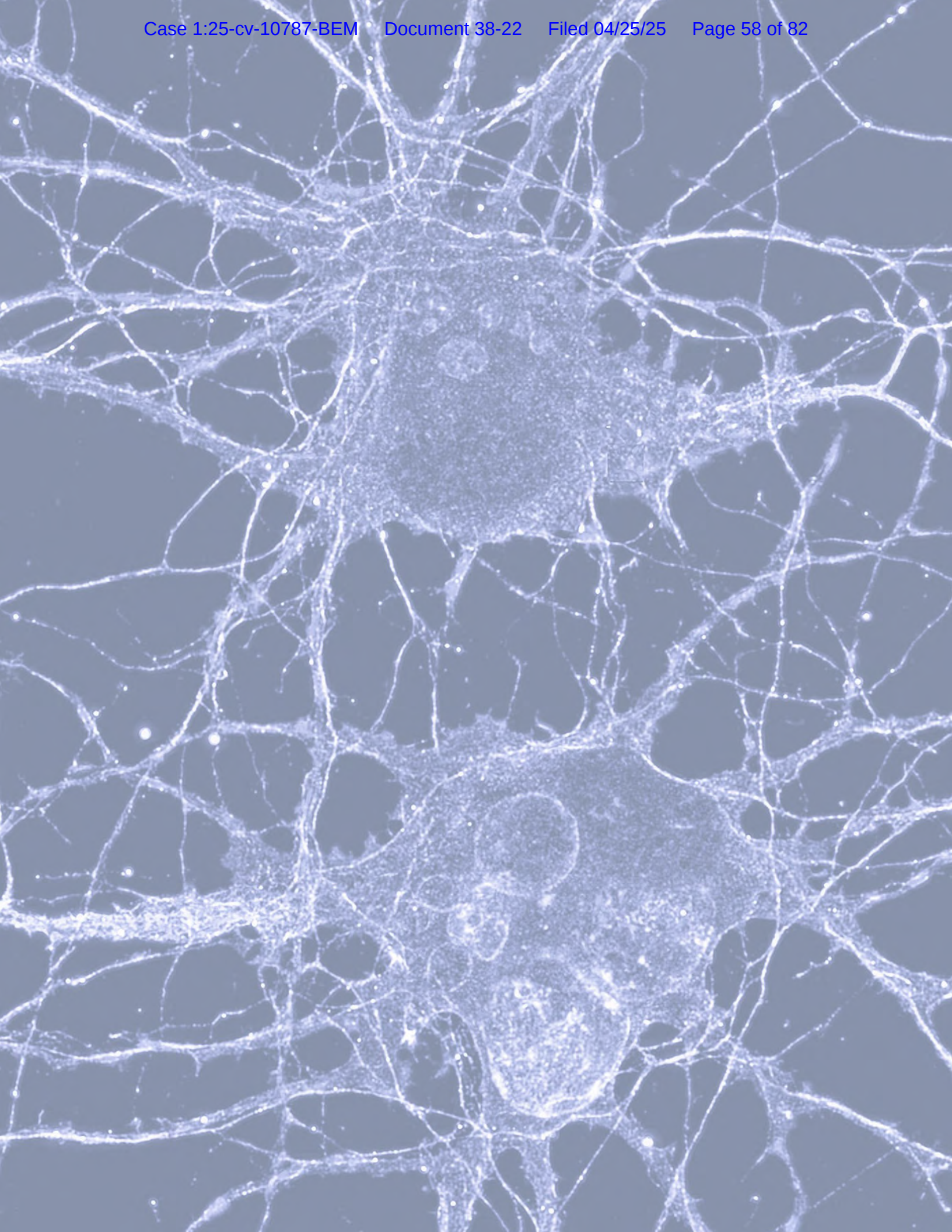


Appendix I: NIH Statutory Authority

Begun as a one-room Laboratory of Hygiene in 1887 (renamed the Hygienic Library in 1891), the National Institutes of Health (NIH) today is one of the world's foremost medical research centers. An agency of the U.S. Department of Health and Human Services, NIH is the federal focal point for health research. The Statutory Authority granted to NIH generally appears in Title IV of the *Public Health Service (PHS) Act*, 42 U.S.C. 281 et seq. This authority has a long history with many revisions and additions granted by new legislation over the years. Below are several highlights from the legislative history of NIH.

The Ransdell Act, P.L. 71–251

On May 26, 1930, the *Ransdell Act* reorganized, expanded, and redesignated the Hygienic Laboratory of the Public Health Service as the National Institute of Health (NIH), authorizing $750,000 for construction of two buildings for NIH and creating a system of fellowships.

The Public Health Service Act, P.L. 78–410

On July 1, 1944, the *PHS Act* (P.L. 78—410) consolidated and revised existing public health legislation, dividing the PHS into the Office of the Surgeon General, the Bureau of Medical Services, the Bureau of State Services, and NIH. The *PHS Act* gave NIH the legislative basis for its postwar program, with general authority to conduct and support research into the diseases and impairments of man, authorized research projects and fellowships, and made the National Cancer Institute a division of NIH.

The National Heart Act of 1948, P.L. 80–655

On June 16, 1948, the *National Heart Act of 1948* amended the *PHS Act* and authorized the National Heart Institute and changed the name of the National Institute of Health to National Institutes of Health.

The Public Health Improvement Act, P.L. 106–505

On November 13, 2000, the *Public Health Improvement Act* amended the *PHS Act* and provided new authorities to NIH and other PHS agencies and placed ongoing activities or programs in statute.

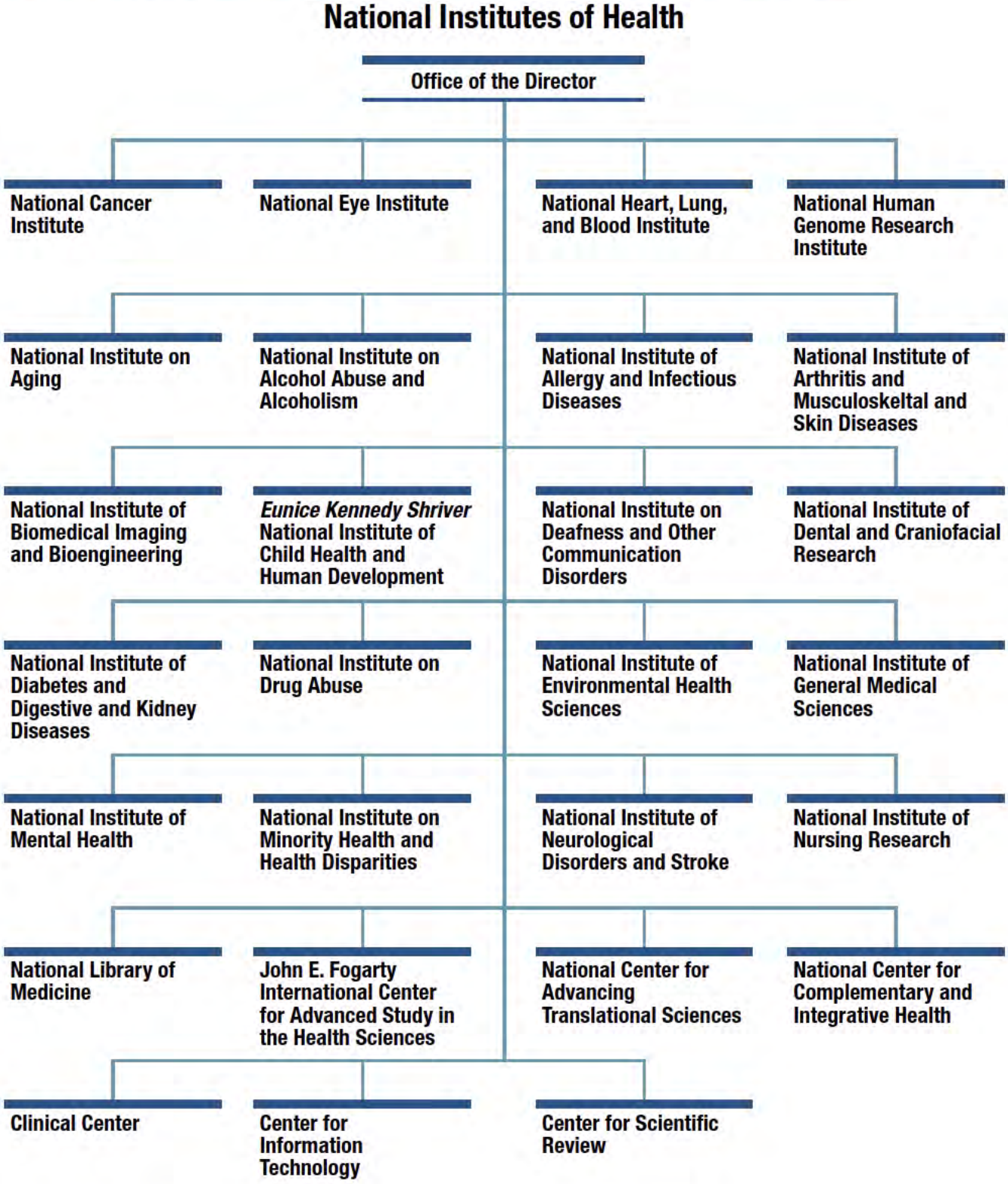
The National Institutes of Health Reform Act of 2006, P.L. 109–482

On January 15, 2007, the *NIH Reform Act of 2006* affirmed the importance of NIH and its vital role in advancing biomedical research to improve the health of the nation. The law reinforced how NIH's 27 Institutes and Centers, along with various other NIH components, work together on the nation's largest medical research enterprise. Among its provisions, the *NIH Reform Act* revised Title IV of the *PHS Act* to create the Division of Program Coordination, Planning, and Strategic Initiatives, to be supported by a Common Fund.

The 21st Century Cures Act, P.L. 114–255

On December 13, 2016, the *21st Century Cures Act* provided NIH with critical tools and resources to advance biomedical research across the spectrum, from foundational basic research studies to advanced clinical trials of promising new therapies. The Cures Act provided NIH with important new authorities that could be employed to hasten its mission to improve the health of Americans.

Appendix II: NIH Organizational Chart



Appendix III: Strategic Planning Process

The National Institutes of Health (NIH)-Wide Strategic Plan outlines NIH's research priorities and how these priorities align with the agency's mission and goals in an evolving research landscape. It represents one facet of NIH's stewardship of federal dollars and contributes to maintaining transparency and accountability to its many stakeholders.

Biomedical and behavioral science is progressing rapidly. To keep pace and capitalize on scientific advances while addressing evolving public health needs, NIH updates the NIH-Wide Strategic Plan every 5 years. The NIH-Wide Strategic Plan is a living document, with each iteration building off the foundation of the previous plan and aligning with the agency's near-, mid-, and long-range goals. This latest iteration of the NIH-Wide Strategic Plan, covering fiscal years 2021–2025, retains many of the core elements of the NIH-Wide Strategic Plan for fiscal years 2016–2020. However, the Strategic Plan has been revised, updated, and expanded in response to the many discoveries and changes in the field made during the past 5 years. As part of this process, the Framework around which the Strategic Plan is organized has also been revised.

In September 2019, NIH began updating the NIH-Wide Strategic Plan to cover fiscal years 2021–2025. The goal was to follow a process that was transparent, focused on science and good stewardship of research, guided by evidence, and informed by NIH's many stakeholders.

The strategic planning process entailed four phases: (1) pre-planning, (2) gathering internal input and development of the Strategic Plan framework, (3) gathering input from external stakeholders, and (4) drafting and publishing the Strategic Plan. The following are key activities undertaken during these four phases.

Pre-Planning

The NIH Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI) within the Office of the Director (OD), coordinated the development of the NIH-Wide Strategic Plan for fiscal years 2021–2025. At the initiation of this process, DPCPSI developed a timeline for the strategic planning process and established an internal NIH-Wide Strategic Plan Working Group, composed of staff from each Institute and Center (IC) and OD Office, representing the range of NIH's activities and research portfolio. The first Working Group meeting was held at the end of September 2019.

Gathering Internal Input and Development of the Strategic Plan Framework

From October to December 2019, the Working Group met biweekly to develop the Framework for the Strategic Plan, which outlines, at a high level, NIH's priorities for biomedical and behavioral research that will be addressed over the next five years. The Framework of the NIH-Wide Strategic Plan for fiscal years 2016-2020 was used as a starting point, and the Framework for the new Strategic Plan evolved over several meetings. The proposed framework was reviewed by the IC Directors at the end of October, the Advisory Committee to the NIH Director in December, and the DPCPSI Council of Councils in January 2020. The final Framework was approved by NIH Leadership.

In parallel with development of the Framework, ICs and OD Offices were asked to provide information on biomedical and behavioral research advances that have been made under the NIH-Wide Strategic Plan for fiscal years 2016–2020 and proposed activities that will be conducted during the next 5 years. The Working Group reviewed the content provided and, through an iterative process of voting and deliberation, proposed for NIH Leadership's approval the top NIH-wide accomplishments and priorities for each section of the Framework.

Gathering Input from External Stakeholders

NIH recognizes that input from external stakeholders—including members of the scientific and health care communities, professional societies, advocacy organizations, industry, other federal agencies, and

the general public—provides valuable insight to be considered during its strategic planning process.

To solicit comments on the proposed Framework from external stakeholders, the Working Group developed a Request for Information (RFI) in the NIH Guide (NOT-OD-20-064[1]) and the *Federal Register* (FRN 2020-02919[2]), which was advertised broadly. Comments were accepted online from February 12, 2020, to April 1, 2020. NIH received 160 responses to the RFI from external stakeholders. In addition, NIH hosted two webinars on March 9 and 16, 2020, to provide the opportunity for stakeholders to ask questions on the Strategic Plan development process and comment on the Framework. A summary of RFI responses, the webinar slides, and transcript, will be made available on the NIH-Wide Strategic plan webpage.[3]

Drafting and Publishing the Strategic Plan

In January 2020, the Working Group began drafting the Strategic Plan based on the Framework and the prioritized content approved by NIH Leadership. As it became available from the RFI and webinars, the Working Group reviewed public feedback on the Framework and adjusted the draft Strategic Plan in response to this input.

Finalizing and Publishing the Strategic Plan

The draft Strategic Plan was finalized through an iterative review process with NIH Leadership. Beginning in July 2020, the draft Strategic Plan was reviewed by IC and OD Office Directors, and subsequently by the NIH Director and Deputy Director. It was then reviewed by the DPCPSI Council of Councils and the Advisory Committee to the NIH Director. Following final review and approval by the NIH Director and Deputy Director, and subsequent sign off by the U.S. Department of Health and Human Services, the final version of the NIH-Wide Strategic Plan for fiscal years 2021–2025 was posted publicly on NIH's website and widely disseminated to NIH stakeholders.

Endnotes

1 https://grants.nih.gov/grants/guide/notice-files/NOT-OD-20-064.html
2 https://www.federalregister.gov/documents/2020/02/13/2020-02919/request-for-information-rfi-inviting-comments-and-suggestions-on-a-framework-for-the-nih-wide
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Appendix IV: NIH Common Fund Strategic Plan Report

About the NIH Common Fund

The National Institutes of Health (NIH) Common Fund[1] programs represent time-limited, strategic investments in biomedical and behavioral research (collectively referred to as *biomedical research* in the remainder of this appendix) designed to achieve high-impact goals and catalyze discovery. Approximately 30 multidisciplinary scientific programs are supported by the NIH Common Fund, spanning NIH's mission and addressing challenges and opportunities that are of high priority for NIH as a whole. These bold scientific programs often accelerate emerging science, enhance the biomedical research workforce, remove research roadblocks, or support high-risk, high-reward science. NIH Common Fund programs frequently produce resources—such as datasets, tools, technologies, or methods—that are designed to spur subsequent biomedical advances often not possible otherwise. The work supported by the NIH Common Fund is inherently risky, but this risk is embraced because of the potential for transformative impact in advancing science and, ultimately, improving human health.

The origins of the NIH Common Fund lie in the NIH Roadmap for Medical Research, which was launched in 2004. The *NIH Reform Act of 2006* created the NIH Common Fund as a source of support for these transformative, NIH-wide programs within the NIH Office of the Director (OD). This established a novel approach to support crosscutting, NIH-wide programs in areas of emerging scientific opportunities, rising public health challenges, and knowledge gaps that deserved special emphasis or would otherwise benefit from strategic planning and coordination. The Act also mandated an emphasis on goals and milestones in NIH Common Fund programs and directed NIH to encourage participation by early-career researchers.

The Office of Strategic Coordination (OSC) within the NIH Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI) is responsible for managing the NIH Common Fund. OSC coordinates teams across NIH who collectively plan, implement, and oversee each program to ensure broad impact. Individual awards supported through the NIH Common Fund are administered in partnership with NIH Institutes and Centers (ICs).

About the NIH Common Fund Strategic Plan Report

The *Public Health Service Act* requires, as part of the NIH-Wide Strategic Plan, that the NIH Director submit a report to Congress containing a strategic plan for funding research "that represents important areas of emerging scientific opportunities, rising public health challenges, or knowledge gaps that deserve special emphasis and would benefit from conducting or supporting additional research that involves collaboration between two or more national research institutes or national centers, or would otherwise benefit from strategic coordination and planning" through the NIH Common Fund (42 U.S.C. §282a(c)(1)(C); 282(b)(7)(A)(i)).

NIH Common Fund Program Lifecycle

The congressional mandate to support goal- and milestone-driven programs underlies a critical feature of NIH Common Fund programs: Each program establishes high-impact goals that are expected to be achieved within a maximum of 10 years. This program enables new needs or opportunities to be supported as they emerge. The NIH Common Fund supports research programs that transcend the scientific boundaries of the individual ICs, are synergistic with current IC-funded research, and would benefit from limited-term NIH Common Fund investment. These programs are identified through a strategic planning process that includes input from many stakeholders who first identify broad scientific areas that are priorities for NIH as a whole and subsequently establish a focused strategy for scientific initiatives that will catalyze progress within that area. This process ensures that the programs provide maximum utility to the

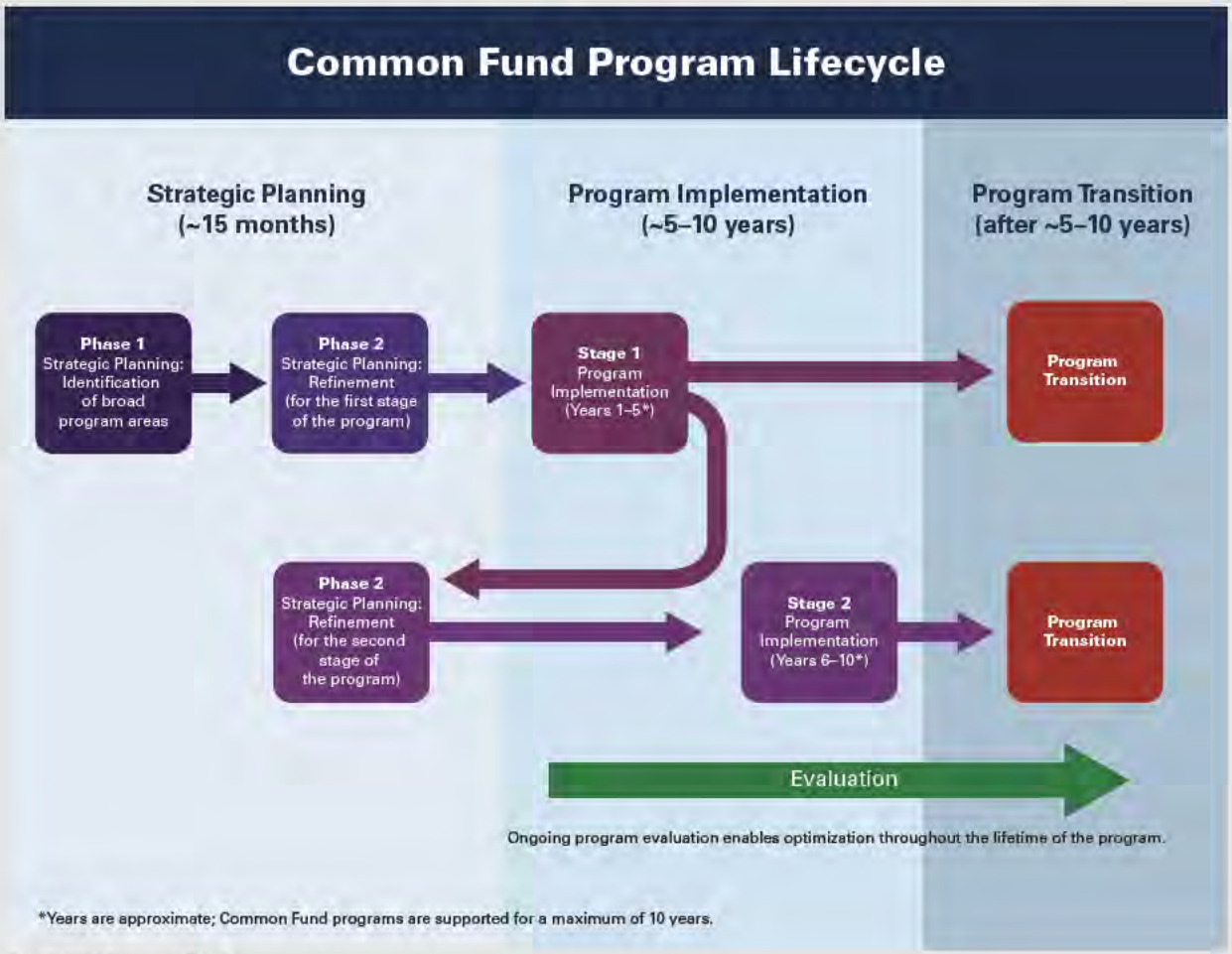
broad biomedical community and that they address major roadblocks to research progress. At the completion of each program, the tools, technologies, and data produced by the program are taken up and used by the community at large, and the infrastructure that the NIH Common Fund has built transitions to other sources of support. The lifecycle of a NIH Common Fund program is shown in Figure 29.

NIH Common Fund strategic planning is a two-phase process. Phase 1 of strategic planning identifies broad areas that are high priorities for NIH and for which transformational progress can be envisioned. Phase 2 of strategic planning involves analysis of the scientific landscape within a given field to identify the specific challenges and opportunities for progress. Programmatic goals are established, with a series of funding initiatives collectively designed to achieve those goals. The strategic planning process is described in more detail in the next section, "NIH Common Fund Strategic Planning Process."

Following strategic planning and selection of new program areas, research projects addressing goals and milestones identified during the planning process are supported through a variety of funding mechanisms. Awards are often implemented as partnerships among the many scientific investigators supported by a program and expert NIH staff, collaboratively working together to achieve defined goals. NIH Common Fund programs are actively managed to ensure that the output of each program is maximally useful to the broader scientific community. Assessment of the utility of the program to the community is emphasized and is achieved through a variety of evaluative processes.

Figure 29. Lifecycle of NIH Common Fund Programs

"Common Fund Program Lifecycle": Infographic. Note that not all programs follow this exact timeline.



Credit: NIH Common Fund.

Evaluation is an ongoing activity throughout the lifecycle of the program and includes both formal and informal evaluative activities. Informal evaluation involves convening grantees and NIH-wide teams to review progress, discuss new challenges, and develop strategies to adapt as part of routine program management. It also involves gathering input from external consultants and using their input, together with internal analysis, to help guide the implementation of the program. Formal evaluations involve the development of baseline data for new programs and the development of multiple metrics of outcomes. The utility of data, resources, technologies, and other program outputs is assessed through surveys, expert opinion, and the analysis of bibliometric data, such as citation analyses. Challenges and opportunities to strengthen each program are considered continuously, but this assessment is also done systematically for every program on an annual basis. This management process ensures that the programs stay on track toward their stated goals while also allowing adjustments to ensure that the impact of each program is maximized.

Another ongoing activity for the NIH Common Fund is the support of infrastructure designed to maximize the accessibility and utility of NIH Common Fund datasets and digital resources. To this end, the NIH Common Fund Data Ecosystem (CFDE)[2] is working to ensure all NIH Common Fund datasets are findable, accessible, interoperable, and reusable (FAIR), providing training for users to operate on data in a cloud environment and ensuring that NIH Common Fund data continue to be available after individual programs are completed. For more information on the CFDE, see Figure 30.

The final stage of NIH Common Fund support involves the transition of mature programs to other sources of support or use within the scientific community.

Although represented as sequential activities, the management of each program has an iterative nature. Plans for implementation and transition are considered early in the lifecycle but may be adapted in response to the science. Similarly, scientific progress may demand changes in the strategic plan, as new opportunities or challenges are identified. Nevertheless, early consideration of implementation and transition ensures that program goals and milestones are established to meet the needs identified during strategic planning and to provide a sustainable model for continued use by the scientific community when NIH Common Fund support for a program has ended.

Figure 30. NIH Common Fund Data Ecosystem

NIH Common Fund programs are intended to provide resources that accelerate discovery across many different biomedical research fields. Often these resources include large datasets and associated digital tools needed to mine and analyze the data. To maximize impact, these datasets and tools must be leveraged by researchers from different disciplines, using varying expertise in bioinformatics and large-scale data analysis. Additionally, these datasets must be usable together across interoperable platforms. However, current approaches to data storage, management, and analysis mean that data are often not findable, accessible, interoperable, and reusable (FAIR).

To address this challenge, the NIH Common Fund is supporting the NIH Common Fund Data Ecosystem (CFDE), an ongoing investment in data management infrastructure that will support past, current, and future NIH Common Fund datasets.

The CFDE includes several integrated efforts:

- **CFDE Coordinating Center**—The Coordinating Center will manage and organize CFDE activities, engage with participating NIH Common Fund programs, connect with user communities, support training, develop tools and standards, and provide technical expertise.
- **Participating NIH Common Fund Data Coordinating Centers**—These Centers will work with the CFDE Coordinating Center to understand its program's unique requirements for data storage and analysis, adopt/adapt guidelines and best practices, share resources and tools, establish and enable use cases for cross-data analyses, and provide training.
- **Leveraging NIH-wide cloud service provider partnerships**—Using the Science and Technology Research Infrastructure for Discovery, Experimentation, and Sustainability (STRIDES) will ensure that data are onboarded to the cloud in a consistent manner and provide favorable pricing for cloud data storage and use.

Ultimately, the CFDE is intended to amplify the impact of many NIH Common Fund programs by enabling researchers to interrogate multiple disparate datasets and thereby make new kinds of scientific discoveries that were not possible before.

NIH Common Fund Strategic Planning Process

Strategic planning for the NIH Common Fund involves the identification of NIH-wide challenges and opportunities that meet NIH Common Fund program criteria[3] (Figure 31). It is designed to be flexible from year to year to adapt to emerging opportunities, the changing needs of the scientific community, and the availability of funds. Broad topics identified in Phase 1 are refined into well-defined programs and initiatives in Phase 2.

Figure 31. NIH Common Fund Program Criteria

Transformative: **Programs must have high potential to dramatically affect biomedical research.**

Catalytic: **Programs must achieve a defined set of high-impact goals within a defined period of time.**

Synergistic: **Outcomes must synergistically promote and advance individual missions of ICs to benefit health.**

Crosscutting: **Program areas must cut across missions of multiple ICs, be relevant to multiple diseases or conditions, and require a coordinated approach across NIH.**

Unique: **Programs must be something no other entity is likely or able to do.**

Phase 1 identifies broad scientific needs and opportunities, focusing on the greatest challenges to research discovery and translation, as well as on the most promising emerging opportunities to catalyze research across a variety of scientific disciplines and disease conditions. Although specific Phase 1 activities vary, ideas may be gathered through meetings with external scientific experts, solicitation of ideas from ICs, discussions with NIH Leadership and Advisory Committees, and engagement with the broader scientific community.

To effectively evaluate the responsiveness of the proposed idea to NIH Common Fund criteria, as well as the potential impact of the program, the following questions are typically posed:

- What is the greatest opportunity in biomedical research today? How can this opportunity be realized?
- Why is now the right time for this idea (i.e., why is this idea timely)?
- What would be the goals of the program, and what initiatives or activities are envisioned to achieve these goals?

Generally, Phase 1 strategic planning activities generate many more ideas than can be supported. Ideas are prioritized by the NIH Director, with input from the OSC, DPCPSI, and Principal Deputy Directors. IC Directors may also provide input to the NIH Director on prioritization of concepts. A small subset of prioritized ideas then moves into Phase 2 planning.

Phase 2 refines the prioritized set of broad ideas identified in Phase 1 into specific, well-defined initiatives. An NIH-wide Working Group representing a broad range of interested scientific communities is formed to continue the planning process and, if the program is approved, lead program implementation. Phase 2 strategic planning also occurs before decisions are made to provide a second stage of support for existing programs. OSC assesses the progress of NIH Common Fund programs at the end of the first stage of funding to determine whether a second stage of funding (up to a limit of 10 years total) is necessary to reap maximum benefit from the program. The Phase 2 refinement process includes analysis of NIH and external scientific research portfolios (Figure 32), solicitation of input from subject-matter experts, and input from IC Directors.

During Phase 2 planning, the DPCPSI Council of Councils (CoC)[4] provides input about whether the proposed idea addresses the NIH Common Fund criteria and, if so, whether the proposed program initiatives are likely to achieve the program goals and produce the highest possible impact. When the concept for a potential new program is cleared by the CoC, the Working Group develops a program proposal that clearly describes scientific needs, gaps, and opportunities; goals and milestones of the proposed program; description of program management; and a budget for all years of the program. Program proposals are presented to the NIH Director for a final decision about program approval.

Figure 32. Portfolio Analysis: Focusing Scope and Identifying Opportunities

Portfolio analysis occurs during Phase 2 of the strategic planning process. It is a vital part of strategic planning that provides critical information concerning ongoing efforts in areas being considered as potential NIH Common Fund programs. Portfolio analysis helps identify specific areas where strategic investment by the NIH Common Fund could support unique and potentially transformative research.

The Somatic Cell Genome Editing (SCGE) program, launched in fiscal year 2018, included a robust portfolio analysis during the planning process to identify specific activities in support of the program's overall goal to advance therapeutic use of precision genome editing approaches to treat or cure numerous diseases caused by genetic mutations. With the discovery of CRISPR and similar tools that can precisely change genetic sequences, this field experienced an explosion of interest. However, remaining gaps in research investment were holding back the translation of genome editing approaches into the clinic, especially for rare or uncommon diseases. Information on private-sector and other government agency investment was provided by consultation with experts, complementing the SCGE portfolio analysis that assessed NIH investment in genome editing tools and technologies in fiscal year 2016. This analysis identified critical gap areas, including gene editing reporter systems and in vitro models for testing efficacy and safety. Additionally, the analysis demonstrated a pressing need to develop new genome editing tools that were less likely to produce adverse or off-target effects. Furthermore, the analysis revealed that current investment in genome editing delivery vehicles was highly focused on a single viral vector (adeno-associated virus, or AAV) with inherent limitations. Other delivery systems—such as nanoparticles, alternative viruses, ribonucleoprotein complexes, and exosomes—were largely overlooked, despite representing potentially transformative approaches to overcoming limitations associated with AAVs.

The results of this portfolio analysis, combined with expert input, identified areas of scientific opportunity that became the basis of the SCGE program initiatives. These initiatives include (1) developing animal models for testing genome editing tools; (2) generating assays and models to test the efficacy and safety of genome editing tools; (3) improving genome editing delivery systems—including a wide range of delivery systems beyond AAVs—to target specific cells and tissues; (4) expanding the number and types of genome editing complexes; and (5) distributing the knowledge and resources developed through this program to the scientific community.

A follow-up analysis conducted in 2020 confirmed that the SCGE program is stimulating research in gap areas identified in the baseline portfolio analysis. This analysis showed that the SCGE program is filling an important niche by supporting research on exploring the use of exosomes, nanoparticles, and ribonucleoproteins as delivery vehicles. The analysis also revealed that the SCGE program is developing genome editing tools that target a wide range of tissues and organs, including one organ system (the gastrointestinal tract) that is not targeted by any other NIH-supported genome editing projects, as well as other several tissues or organs for which SCGE projects are the only ones using non-AAV delivery systems for targeted delivery.

Strategic Planning Activities Since 2015

Prior to the passage of the *21st Century Cures Act*,[5] the NIH Common Fund developed a biennial strategic planning report. With the passage of this Act, the NIH Common Fund Strategic Planning Report is now included within the NIH-Wide Strategic Plan. Described here are the strategic planning activities that have taken place since the last NIH Common Fund Strategic Planning Report in 2015.[6]

Strategic Planning 2015–2016

In 2015, OSC held the "Innovate to Accelerate" 2-day strategic planning workshop that brought together more than 20 innovative thinkers representing diverse areas of expertise to brainstorm ideas for potential new NIH Common Fund programs beginning in fiscal year 2018 or later. Following the workshop, all ideas that emerged from the workshop were posted in an online discussion forum, where an additional cohort of approximately 300 selected scientific experts were invited to view ideas, provide comments and suggestions, and submit one original idea for inclusion in the online discussion. All ideas and associated discussions were considered along with ideas submitted by IC Directors.

From these activities, two ideas were prioritized for further planning and ultimately were launched in fiscal year 2018:

- Human BioMolecular Atlas Program (HuBMAP)[7] (Figure 33)—The planning process that led to the HuBMAP program identified understanding human physiology and disease at the level of individual cells as a challenge that we now have the technologies to address. Because the cell is the fundamental unit of the human body, an understanding of normal and disease processes at this level is anticipated to lead to more specific and effective therapies. In recent years, technologies that enable the analysis of single

Figure 33. Human BioMolecular Atlas Program

The Human BioMolecular Atlas Program is a collaborative effort to develop an open and global platform to map healthy cells in the human body.

Credit: NIH Common Fund.

cells within the context of the tissues have made the goals of HuBMAP feasible. However, this challenge is enormous, given that the human body has approximately 37 trillion cells. HuBMAP is developing an open and global platform to map healthy cells in the human body, coordinating with other international efforts. Capitalizing in part upon the foundation laid by the NIH Common Fund's Single-Cell Analysis Program,[8] HuBMAP is building the framework needed to construct cell atlases, tools, and resources to understand the function of and relationship among all the cells in the human body. This understanding is expected to lead to new insights into human health, growth, development, aging, and disease.

- Transformative High Resolution Cryo-Electron Microscopy (CryoEM)[9]—Improvements in cryoEM technologies and new computational methods to analyze the associated data have created a transformative opportunity in structural biology. With these new methods, investigators can analyze protein structures more easily than ever before, providing the basis for smart drug design and fundamental biological insights. However, the high cost of required equipment and limited workforce proficient in this technology represent a substantial challenge. The CryoEM program addresses this challenge. It is broadening access to high-resolution cryoEM for biomedical researchers by creating national service centers and cultivating a skilled cryoEM workforce by developing and implementing cryoEM training materials. By expanding access and training for cryoEM, this program aims to enable research and accelerate development of drugs and vaccines to combat many diseases and conditions.

In addition to launching new programs, several existing NIH Common Fund programs underwent planning for a second stage of support that began in fiscal year 2018. These programs are described below:

- Illuminating the Druggable Genome (IDG)[10] (Figure 34)—Most drugs target proteins within four families: G protein–coupled receptors, nuclear receptors, ion channels, and protein kinases. However, only a small number of proteins within each of these families are well studied, and these proteins typically are present in many cells throughout the body. Therefore, drugs that target these proteins may cause widespread adverse effects in cells and tissues that are not affected by disease. However, the lesser known members of these protein families may be present in fewer tissues and thus have potential as specific drug targets leading to fewer side effects. Technological advances in genomics, protein characterization, and computational methods provide an opportunity to identify and study large numbers of unknown proteins. IDG originally launched a pilot stage in fiscal year 2014 to compile data about the uncharacterized proteins within the four protein classes that are most frequently targeted by drugs. In the second stage, implementation, IDG is capitalizing on the information gathered and technologies developed in the pilot to further elucidate the

Figure 34. Illuminating the Druggable Genome Program

The goal of the Illuminating the Druggable Genome program is to compile data about the uncharacterized proteins within the four protein classes that are most frequently targeted by drugs.

Credit: NIH Common Fund.

function of uncharacterized proteins within three key families: G protein–coupled receptors, ion channels, and protein kinases. IDG is also expanding the informatics tools developed in the pilot stage and disseminating the IDG-generated resources to the biomedical research community.

- Metabolomics[11]—Chemical reactions in the body produce small molecules, called metabolites, that can provide important information about diet, environmental exposures, and drug metabolism. The study of all of the metabolites in a given sample, or metabolomics, therefore provides a powerful tool for researchers and clinicians to understand an individual's current physiological state and possibly to develop personalized diagnoses and treatment approaches. The NIH Common Fund's Metabolomics program was established to support broader use of metabolomic analysis in basic research and in the clinic. The first stage of the Metabolomics program contributed to wider use of metabolomic approaches in the biomedical research community and enhanced researchers' ability to conduct metabolic analyses. In the second stage, the Metabolomics program aims to enhance metabolomics data sharing; develop novel tools to facilitate data analysis; and generate standards, guidelines, and resources to enable metabolomics research.

- Undiagnosed Diseases Network (UDN)[12] (Figure 35)—Rare diseases collectively affect approximately 25 million Americans,[13] many of whom face a long and frustrating process to arrive at a diagnosis. The NIH Intramural Research Program launched the Undiagnosed Diseases Program (UDP) in 2008 with the goal of diagnosing, understanding, and treating rare disorders. This program leveraged revolutionary genomic sequencing technologies to aid in the diagnosis of rare diseases and developed a robust interdisciplinary approach to disease diagnosis that proved successful. However, the overwhelming patient need far exceeded the capacity of the UDP. In 2013, the NIH Common Fund launched UDN with the goal of expanding the proven approach of UDP to academic health centers across the county, working through challenges associated with implementing this approach in different clinical and economic models. UDN promotes the use of genomic data in disease diagnosis and engages basic researchers to uncover underlying disease mechanisms so that treatments can be identified. UDN accepted 601 participants undiagnosed by traditional medical practices in the first 20 months of operation. Of those who completed their UDN evaluation during this time, 35 percent were given a diagnosis. Many of these diagnoses were rare genetic diseases, including 31 previously unknown syndromes. In the second stage, UDN is focusing on forming a sustainable national resource to diagnose both rare and new diseases, advancing laboratory and clinical research, enhancing global coordination and collaboration among laboratory and clinical researchers, and sharing resulting data and approaches throughout the scientific and clinical communities.

Figure 35. Undiagnosed Diseases Network

The Undiagnosed Diseases Network is a research study to improve the level of diagnosis of rare and undiagnosed conditions.

Credit: NIH Common Fund.

Strategic Planning 2016–2017

Anticipated budget limitations led to a scaled-down strategic planning process in 2016–2017, focused on two existing NIH Common Fund programs requesting a second stage of support in fiscal year 2019:

- Diversity Program Consortium (DPC): Enhancing the Diversity of the NIH-Funded Workforce[14] (Figure 36)—In 2012, The Advisory Committee to the NIH Director Working Group on Diversity in the Biomedical Research Workforce issued a report[15] acknowledging NIH's longstanding recognition that diversity in the biomedical research workforce is critical to ensuring the most creative minds have the opportunity to contribute to our research and health goals. However, despite ongoing investment by NIH and others to increase the number of scientists from underrepresented groups, unacceptable disparities in the biomedical workforce remain. The DPC was established to develop, implement, assess, and disseminate innovative and effective training and mentoring approaches to enhance the participation and persistence of individuals from underrepresented backgrounds

in biomedical research careers so that future programs may be more effective at recruiting and retaining a diverse workforce. Launched with planning grants in 2013, the first stage of the program had three initiatives: (1) Building Infrastructure Leading to Diversity (BUILD), which is developing approaches to determine the most effective ways to engage and retain students from diverse backgrounds in biomedical research and to prepare students to become future contributors to the NIH-funded research enterprise; (2) the National Research Mentoring Network, a national network of mentors and mentees providing mentorship, professional development, training, networking, and resources; and (3) the Coordination and Evaluation Center, which is coordinating and evaluating DPC activities. In the second stage of the program, two additional initiatives are being supported. The Sponsored Programs Administration Development program aims to increase the productivity of sponsored programs offices (or similar entities) at academic institutions to enhance biomedical research and research training. The DPC Dissemination and Translation Awards (DPC DaTA) supports non-DPC institutions to employ DPC methods to evaluate the effectiveness of a biomedical research training, mentoring, or research capacity-building intervention.

Figure 36. Diversity Program Consortium

The Diversity Program Consortium was established to develop, implement, assess, and disseminate innovative and effective training and mentoring approaches to enhance the participation and persistence of individuals from underrepresented backgrounds in biomedical research careers so that future programs may be more effective at recruiting and retaining a diverse workforce.

Credit: NIH Common Fund.

- Extracellular RNA Communication (ERC)[16]—Once thought to exist only inside cells, RNA is now known to travel outside cells and play a role in communication among cells throughout the body. When the ERC program was launched in 2013, researchers understood that RNA was exported from cells, but fundamental questions about the function of these extracellular RNAs (exRNAs), how exRNAs are targeted to deliver messages to other cells, and how exRNAs are regulated had yet to be fully explored. Additionally, a lack of standards, protocols, and data infrastructure was a significant roadblock that hindered research progress and prevented comparison of experiments between different laboratories. The ERC program aimed to enable researchers to tackle fundamental questions about exRNAs in a coordinated way, thereby establishing new biological paradigms and accelerating development of exRNAs as potential therapeutics or in diagnostics. The first stage of this program catalogued exRNA molecules found in human biofluids from more than 2,000 healthy donors; established data standards, created a data portal, and developed novel tools and reagents; and identified potential exRNA biomarkers for nearly 30 diseases. In the second stage of the program, ERC is focusing on tool and technology development addressing major roadblocks to understanding exRNAs, including better understanding of the larger complexes, like extracellular vesicles that carry exRNAs through the body.

Strategic Planning 2017–2018

In 2017, NIH leadership identified two timely, high-priority research areas suitable for NIH Common Fund support. Due to the pressing public health needs that these programs are intended to address, both programs were planned and launched on an accelerated timeline.

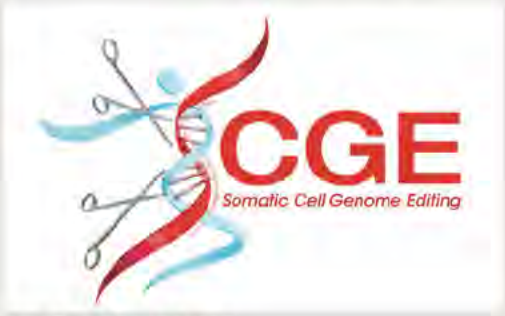
- Acute to Chronic Pain Signatures (A2CPS)[17]—As part of NIH's response to the growing opioid crisis, the A2CPS program aims to further our understanding of the transition from acute to chronic pain. Acute pain following injury resolves in many patients, but for a large number of people, the pain becomes chronic, even after the injury itself has healed. This transition is poorly understood and therefore prevention or treatment is difficult. The A2CPS program is addressing this challenge

by developing a set of objective biomarkers (i.e., a "signature") to predict susceptibility for transitioning to chronic pain after an acute pain event. The A2CPS program enhances the objectives of the NIH Helping to End Addiction Long-term℠ (HEAL) Initiative,[18] a transagency effort to speed scientific solutions to end the opioid public health crisis. A2CPS will benefit the HEAL℠ research priority to enhance pain management. Building upon previous efforts by the NIH Pain Consortium and others, this program was well positioned to rapidly launch in advance of HEAL℠ but is now fully coordinated with HEAL℠ initiatives. It began a planning stage in fiscal year 2019, scaling up to implementation in fiscal year 2020.

- Somatic Cell Genome Editing (SCGE)[19] (Figure 37)—The development of tools and approaches to precisely change genomic sequences, including CRISPR, have raised the possibility of a fundamentally new approach to treat an enormous number of genetic diseases. Capitalizing on the rapidly expanding field of precision genome editing tools, planning for the SCGE program identified several critical areas in need of strategic investment to accelerate development of new genome editing–based therapies. Significant ongoing investments were advancing this nascent field but were largely focused on ex vivo genome editing approaches, in which cells are edited outside of the body and then reintroduced; in vivo approaches involving editing cells within the body were lagging behind, despite applicability to a larger number of diseases. Additionally, a significant technological challenge was targeting the editing machinery to the appropriate cells and avoiding off-target effects. Building upon these opportunities and challenges, the SCGE program aims to improve the efficacy and specificity of gene editing approaches to help reduce the burden of common and rare diseases caused by genetic changes. SCGE is developing tools to perform and assess effective and safe genome editing in nonreproductive (i.e., somatic) cells of the body, including approaches to ensure genome editing tools are delivered specifically to the targeted cell type within the body. By sharing these resources with the entire research community, SCGE aims to reduce the time and cost required to develop new therapies. An accelerated planning process that brought together thought leaders from academia, industry, and government allowed this program to be quickly launched in fiscal year 2018.

Figure 37. Somatic Cell Genome Editing Program

The Somatic Cell Genome Editing program is working to improve the efficacy and specificity of gene editing approaches to help reduce the burden of common and rare diseases caused by genetic changes.



Credit: NIH Common Fund.

Additionally, discussions between NIH leadership and IC Directors revealed enthusiasm for developing high-priority initiatives that extend from existing NIH Common Fund programs and leverage previous investments. Within the CryoEM program, a new effort was developed to increase access to cryo-electron tomography, a related technology that enables improved imaging of molecules within intact cells and tissues in 3-D. Additional efforts to address the opioid public health crisis were supported through an expansion of the Stimulating Peripheral Activity to Relieve Conditions (SPARC)[20] program, launching a new initiative to generate anatomical and functional data from neural circuits mediating visceral pain.

Strategic Planning 2018–2019

To plan for new NIH Common Fund programs for potential launch in fiscal year 2021 or later, OSC hosted a series of web-based workshops[21] with editors from a diverse array of biomedical and behavioral research journals. The objective of these workshops was to learn about new scientific trends, emerging areas of research, and crosscutting challenges that may contribute to planning for new NIH Common Fund programs. Journal editors, with the exposure to and assessment of new scientific advances, are in a good position to understand the current scientific landscape. One prominent theme articulated in these

workshops was the emerging opportunities presented by integration of artificial intelligence (AI) and machine learning approaches into biomedical research. Independently, in recognition of the opportunity and challenges posed by AI in biomedicine, NIH organized a workshop in July 2018, Harnessing Artificial Intelligence and Machine Learning to Advance Biomedical Research.[22] These initial discussions contributed to additional planning activities and, ultimately, a new NIH Common Fund program in AI (see the next section, "Strategic Planning 2019–2020," for more details).

In addition to input gathered through the journal editor workshops, OSC also solicited ideas from IC Directors. From this process, three ideas emerged that are now being pursued as potential NIH Common Fund programs.

- **Harnessing Data Science for Health Discovery and Innovation in Africa**[23]—This program will leverage data science technologies and prior NIH investments to develop solutions to Africa's most pressing public health problems through a robust ecosystem of new partners from academic, government, and private sectors. Extensive mobile phone coverage in Africa provides an opportunity to rapidly advance health care delivery systems through mobile health applications, point-of-care technologies, and self-management systems. Additionally, this program leverages and builds upon substantial investment in African research and research training by NIH ICs, the NIH Common Fund, and other organizations. For example, the Data Science in Africa program will build on and translate the resources and expertise developed through the Human Heredity and Health in Africa[24] program into products and policies impacting health in Africa and around the world. The program aims to promote sustainability of the African health research enterprise by encouraging robust partnerships with African governmental, private, and academic partners and will also consider ethical, legal, and social issues for data science research and its applications to public health in Africa. This program was approved by the NIH Director and is anticipated to launch in fiscal year 2021.
- **Faculty Institutional Recruitment for Sustainable Transformation (FIRST)**[25]—Despite ongoing investment in programs designed to enhance the diversity of the biomedical workforce, underrepresentation of some racial and ethnic groups, particularly at the faculty level, remains a persistent challenge. Many previous efforts have focused on individuals; however, substantial evidence suggests that targeting institutional culture change is needed to achieve the desired results. Early success of the NIH Distinguished Scholars Program[26] and other cohort-based recruitment programs indicates that recruitment of a critical mass of investigators committed to diversity and inclusion may foster the institutional changes needed to create meaningful changes in diversity at the faculty level. The FIRST program aims to create cultures of inclusive excellence at NIH-funded institutions, establishing and maintaining scientific environments that can cultivate and benefit from a full range of talent. It will establish a faculty cohort model for hiring, mentoring, and professional development; integrated, institution-wide approaches to address bias, faculty equity, mentoring, and work-life issues; and a coordination and evaluation center to conduct independent evaluations of program impacts. This program was approved by the NIH Director and is anticipated to launch in fiscal year 2021.
- **Nutrition for Precision Health, powered by the NIH *All of Us* Research Program**—Current dietary recommendations are often confusing, sometimes contradictory, and generally do not consider individual differences. Rapidly advancing technologies—including high-throughput *-omics* (e.g., genomics, epigenomics, proteomics, metabolomics) and AI—combined with the growing emphasis on personalized medicine approaches present an opportunity to develop more precise and dynamic nutritional recommendations. The program, still in development, would aim to understand individual responses to diet, enabling tailored dietary recommendations to be provided by physicians and the development of tools to allow individuals to make more informed decisions about healthy food choices. This program is anticipated to launch in fiscal year 2021.

Strategic Planning 2019–2020

To plan for new NIH Common Fund programs to begin in fiscal year 2022 or beyond, OSC used an online crowdsourcing platform to solicit ideas from

the NIH community for bold investments that could become future NIH Common Fund programs. The community was also encouraged to provide constructive comments on ideas submitted by others, so that each idea could benefit from the collective expertise of the NIH community. In addition to gathering ideas through the crowdsourcing site, IC Directors were also invited to submit ideas.

From this process, one idea focused on exploring transposable elements and somatic mosaicism was selected for further development. This potential program, Somatic Mosaicism and Retrotranspositions (SMaRt), would investigate genetic elements that make up approximately half of the human genome and which, in some cases, have the ability to move within the genome and thereby create genetically distinct cells within a single individual. This mobility can result in genomic damage and disease, but the extent to which this process happens and how it is regulated is largely unknown. If approved, the SMaRT program would aim to deliver new paradigms concerning the regulation of these elements and how their transposition contributes to normal biology and disease. Pending approval, this program is anticipated to launch in fiscal year 2022.

In addition to the strategic planning process above, several other NIH-wide efforts contributed to development of new NIH Common Fund programs. At the NIH Leadership Forum, NIH leadership and IC Directors identified cellular senescence as a high-priority research area. Cellular senescence refers to a highly stable state of cell cycle arrest in which cells stop dividing, often in response to various stressors, such as aging and inflammation. A better understanding of the mechanisms of cellular senescence and how this process affects tissue and organ function may lead to new approaches for addressing the deleterious effects of aging and of numerous diseases and conditions. If approved, this program is planned to launch in fiscal year 2022.

Finally, the Advisory Committee to the NIH Director Working Group on Artificial Intelligence provided NIH-wide recommendations[27] on how NIH could leverage and promote AI to advance research across many biomedical topics and have positive effects across diverse fields. Several of these recommendations formed the basis for a new potential NIH Common Fund program, Artificial Intelligence for BiomedicaL Excellence (AIBLE).[28] This program aims to generate new biomedically relevant datasets amenable to machine learning analysis at scale. This program is anticipated to launch in fiscal year 2021. For more details, see Figure 38.

Figure 38. Artificial Intelligence for BiomedicaL Excellence Program

Following a 2018 NIH workshop on artificial intelligence (AI) and machine learning in biomedical research, the NIH Director formed the Advisory Committee to the NIH Director (ACD) Working Group on Artificial Intelligence. This group was charged with determining opportunities for NIH-wide efforts in AI and ways these efforts could cross biomedical topics to positively affect diverse fields, identifying ways for NIH to build connections between the data science and biomedical research communities, defining approaches to cross-training computer scientists and biomedical researchers, and identifying ethical consideration for biomedical research and AI.

This working group delivered its final recommendations in December 2019. Several of these recommendations fit well with the criteria for NIH Common Fund programs, whereas other recommendations were within the mandate of the NIH's Office of Data Science Strategy. An NIH-wide working group convened and conducted planning activities to determine how an NIH Common Fund program could effectively address the relevant recommendations, leading to development of the Artificial Intelligence for BiomedicaL Excellence (AIBLE) program. The overall goal of this program is to generate new biomedically relevant datasets amenable to machine learning analysis at scale, achieved through the following initiatives:

- Support data design centers to generate rubrics of amenability to machine learning approaches that allow the evaluation of datasets and plans to generate datasets, create infrastructure to disseminate tools, and host and promote datasets.
- Develop software and firmware tools to accelerate AI readiness.
- Enhance existing data generation efforts to improve AI readiness.
- Generate gold-standard, multimodal human datasets that adhere to the rubrics established by the program.
- Use the rubrics to evaluate and update select existing public biomedical research data.

Because this potential program leveraged the carefully developed recommendations from the ACD working group, it is anticipated to launch on an accelerated timeline in fiscal year 2021.

Strategic Planning 2020–2021

OSC is currently beginning a new round of strategic planning in 2020. Still in the early stages of development, this round of strategic planning is intended to leverage existing community-generated white papers (i.e., assessments of scientific opportunities and needs in a given scientific area). By reviewing these thoughtful analyses from many scientific societies or other groups, NIH may obtain well-considered input that reflects consensus views and that may reveal overlapping challenges and opportunities affecting multiple communities. Potential program concepts will also be solicited from the IC Directors and may arise from discussions involving NIH leadership, Advisory Councils, or other entities providing input to NIH.

Planning for Transition from NIH Common Fund Support

NIH Common Fund programs are designed to achieve a set of high-impact goals within a defined time frame. At the conclusion of each program, deliverables will either stimulate IC-funded research or will transition to support by ICs or other entities that find the resources generated by the program useful.

Transition plans are considered early in the lifecycle of an NIH Common Fund program, and these plans are reconsidered throughout the lifecycle to ensure the transition accommodates the changing needs of both the program and the external scientific community. A detailed description of the NIH Common Fund's Human Microbiome Project[29] transition is provided as an example in Figure 39.

Figure 39. Transition of the Human Microbiome Project

The Human Microbiome Project (HMP), supported by the NIH Common Fund from 2007 to 2016, developed numerous research resources to enable the study of the microbial communities that live in and on the human body and the roles these communities play in health and disease. The first stage of HMP developed DNA sequence datasets and computational tools for characterizing the microbiome in healthy adults and in people with microbiome-associated diseases. The second stage of HMP created integrated datasets of multiple biological properties from both the microbiome and the host over time in people with specific microbiome-associated diseases.

HMP was an extremely successful program. Some of its major accomplishments include sequencing approximately 3,000 reference bacterial genomes isolated from the human body; generating a comprehensive profile of the healthy human microbiome; developing integrated datasets of metagenomic, transcript, protein, and metabolite profiles from microbiome and host in multiple human cohorts; developing software and online resources to enable studies of the microbiome; and publication of more than 700 scientific papers.

HMP helped catalyze the nascent field of microbiome research, laying the foundation for continued NIH investment through the Institutes and Centers (ICs) after the program ended. NIH investment in microbiome research outside of HMP has increased more than 40-fold since the inception of HMP and now spans more than 20 ICs. The Trans-NIH Microbiome Working Group was established in 2012 to provide a forum for coordinating NIH research activities related to the human microbiome. Ongoing access to critical HMP resources, including datasets and digital tools, will be accomplished through the Common Fund Data Ecosystem (CFDE). Inclusion of these resources within the CFDE ensures that the biomedical research community continues to benefit from HMP and that investment in HMP is leveraged for maximum possible impact.

The NIH Common Fund Budget

The NIH Common Fund budget for fiscal years 2018–2021 is shown in Table 1. Although NIH Common Fund programs are planned in advance, the specific activities funded in each program depend on the budget made available through annual appropriations. As programs end, funds are freed to support new programs and planned expansions of ongoing programs.

Table 1: The NIH Common Fund Budget, Fiscal Years 2018–2021

	Fiscal Year 2018 Actual	Fiscal Year 2019 Actual	Fiscal Year 2020 Actual	Fiscal Year 2021 President's Budget Request[a]
NIH Common Fund (dollars in millions)	$600.7	$619.2	$639.1	$596.5
NIH Common Fund Percentage of NIH Labor/U.S. Department of Health and Human Services Funding[b]	1.62%	1.59%	1.54%	1.54%

[a] Includes March 17, 2020, budget amendment of $439.584 million for the National Institute of Allergy and Infectious Diseases.
[b] Excludes mandatory funding for the Type 1 Diabetes Research program and funding appropriated through the Interior, Environment, and Related Agencies Appropriations Act for the National Institute of Environmental Health Sciences Superfund Research Program. Includes program evaluation financing resources.

The *Public Health Service Act* requires that the NIH Common Fund Strategic Plan Report include an estimate of amounts needed for (i) maximizing the potential of the Common Fund research under 42 U.S.C. 282(b)(7)(A)(i); (ii) to be sufficient only for continuing to fund research activities previously identified by the Division of Program Coordination, Planning, and Strategic Initiatives; and (iii) to be necessary to fund research described in 42 U.S.C. 282(b)(7)(A)(i) that (1) is in addition to the research activities described in clause (ii) and (2) for which there is the most substantial need. See 42 U.S.C. 282a(c)(1)(C).

Budgets for ongoing NIH Common Fund programs are planned in advance to maximize the potential of all programs. Therefore, the amounts described in (i) and (ii) are the same and are equal to the total budget for all NIH Common Fund programs. In addition to the amount for ongoing NIH Common Fund programs, funds are available for new initiatives each year. These new initiatives are identified by the strategic planning principles outlined in this report, thus ensuring they address research areas of substantial need. Within each of the programmatic areas identified through strategic planning, the NIH peer review process also identifies specific research proposals addressing areas of substantial need. Therefore, the amounts described in (iii) are equal to the amount reserved for new NIH Common Fund initiatives.

Each year, as part of the President's Budget Request, the NIH Common Fund describes both the amounts estimated for each ongoing program (i and ii) and the amounts budgeted for new initiatives (iii). Table 2 shows the estimates presented in the Fiscal Year 2021 President's Budget Request; prior years' Requests can be found at https://commonfund.nih.gov/about/budgetrequests.

Table 2: NIH Common Fund President's Budget Request, Fiscal Year 2021

NIH Common Fund Program (Dollars in Thousands)	Fiscal Year 2019 Final	Fiscal Year 2020 Enacted	Fiscal Year 2021 President's Budget Request
4D Nucleome	27,997	28,860	27,485
Acute to Chronic Pain Signatures	2,094	16,636	14,648
Big Data to Knowledge (BD2K)	2,605	0	0
Enhancing the Diversity of the NIH-Funded Workforce	52,656	53,713	47,401
Extracellular RNA Communication	6,728	5,846	10,497
Gabriella Miller Kids First Pediatric Research	13,482	13,000	13,000
Genotype-Tissue Expression (GTEx) Resources	772	0	0
Global Health	15,569	11,565	9,261
Glycoscience	19,435	13,362	5,191
Health Care Systems Research Collaboratory	1,988	1,750	1,694
High-Risk Research	206,110	193,100	186,001
NIH Director's Pioneer Award	*45,446*	*54,265*	*51,293*
NIH Director's New Innovator Award Program	*102,692*	*77,815*	*79,795*
Transformative Research Award	*35,149*	*38,402*	*34,659*
NIH Director's Early Independence Award Program	*22,823*	*22,618*	*20,255*
Human BioMolecular Atlas Project (HuBMAP)	15,005	27,031	31,040
Illuminating the Druggable Genome	12,970	13,390	12,971
Knockout Mouse Phenotyping Program	13,757	11,000	0
Library of Integrated Network-Based Cellular Signatures (LINCS)	9,946	87	0
Metabolomics	12,403	12,401	12,000
Molecular Transducers of Physical Activity	44,744	46,126	42,609
New Models of Data Stewardship	199	0	0
NIH Center for Regenerative Medicine (NCRM)	7,597	5,700	0
Protein Capture	1,334	0	0
Science of Behavior Change	12,674	222	0
Somatic Cell Genome Editing	33,324	38,937	44,232
S.P.A.R.C. - Stimulating Peripheral Activity to Relieve Conditions	51,559	47,268	41,883
Strengthening the Biomedical Research Workforce	56	0	0
Transformative High Resolution Cryo-Electron Microscopy (CryoEM)	14,895	51,800	36,290
Undiagnosed Diseases Network	29,207	24,401	21,683
Strategic Planning, Evaluation, and Infrastructure	10,061	22,917	21,129
Subtotal NIH Common Fund	619,166	639,111	579,017
New Initiatives in NIH Common Fund	0	0	17,450
Total NIH Common Fund	**619,166**	**639,111**	**596,467**

Endnotes

1 https://commonfund.nih.gov.
2 https://commonfund.nih.gov/dataecosystem.
3 https://commonfund.nih.gov/sites/default/files/Initiatives_6-28-11.pdf.
4 https://dpcpsi.nih.gov/council.
5 https://www.congress.gov/114/plaws/publ255/PLAW-114publ255.pdf.
6 https://commonfund.nih.gov/sites/default/files/2015%20Common%20Fund%20Strategic%20Planning%20Report_final%20-%20508.pdf.
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14 https://commonfund.nih.gov/diversity.
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25 https://commonfund.nih.gov/first.
26 https://diversity.nih.gov/programs-partnerships/dsp.
27 https://acd.od.nih.gov/documents/presentations/12132019AI.pdf.
28 https://dpcpsi.nih.gov/sites/default/files/CoC_May_2020_1.05PM_Concept_Clearance_AIBLE_Brennan_508.pdf.
29 https://commonfund.nih.gov/hmp.

Appendix V: Acronyms

3-D	three-dimensional
A2CPS	Acute to Chronic Pain Signatures
ABCD	Adolescent Brain Cognitive Development
ACTIV	Accelerating COVID-19 Therapeutic Interventions and Vaccines
AFREhealth	African Forum for Research and Education in Health
AHRQ	Agency for Healthcare Research and Quality
AI	artificial intelligence
AIBLE	Artificial Intelligence for BiomedicaL Excellence
AMD	age-related macular degeneration
AMP	Accelerating Medicines Partnership
AMP-AD	AMP-Alzheimer's Disease
AMP-PD	AMP-Parkinson's Disease
AMP-RA/Lupus	AMP-Rheumatoid Arthritis/Lupus
AMP-T2D	AMP-Type 2 Diabetes
ASSIST	Application Submission System & Interface for Submission Tracking
BIRCWH	Building Interdisciplinary Research Careers in Women's Health
BRAIN	Brain Research through Advancing Innovative Neurotechnologies®
BUILD	Building Infrastructure Leading to Diversity
CAR	chimeric antigen receptor
CC	NIH Clinical Center
CDC	Centers for Disease Control and Prevention
CFDE	Common Fund Data Ecosystem
CIT	Center for Information Technology
ClinGen	Clinical Genome
CoC	Council of Councils
CORD-19	COVID-19 Open Research Dataset
COVID-19	coronavirus disease 2019
cryoEM	cryo-electron microscopy
CSR	Center for Scientific Review
CTSA	Clinical and Translational Science Awards
DASH	Data and Biospecimen Hub
DoD	U.S. Department of Defense
DPC	Diversity Program Consortium
DPC DaTA	DPC Dissemination and Translation Awards
DPCPSI	Division of Program Coordination, Planning, and Strategic Initiatives
DR2	Disaster Research Response
DRC	Democratic Republic of the Congo
ECHO	Environmental influences on Child Health Outcomes
ENCODE	ENCyclopedia of DNA Elements
ERC	extracellular RNA communication
ERM	Enterprise Risk Management
EVD	Ebola virus disease
exRNA	extracellular RNA
FAIR	findable, accessible, interoperable, and reusable
FDA	U.S. Food and Drug Administration
FIC	Fogarty International Center
FIRST	Faculty Institutional Recruitment for Sustainable Transformation
FOIA	Freedom of Information Act
GACD	Global Alliance for Chronic Diseases
GBD	Global Burden of Disease
H3Africa	Human Heredity and Health in Africa Consortium

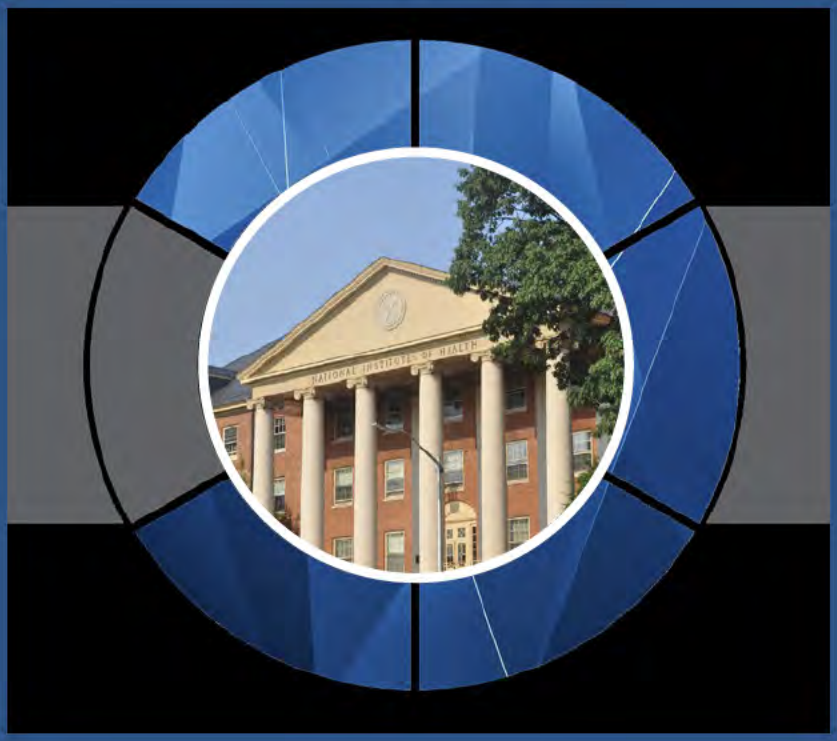
HEAL	Helping to End Addiction Long-term℠
HHS	U.S. Department of Health and Human Services
HMP	Human Microbiome Project
HRSA	Health Resources and Services Administration
HuBMAP	Human BioMolecular Atlas Program
IC	Institute and Center
IDeA	Institutional Development Award
IDG	Illuminating the Druggable Genome
IMPROVE	Implementing a Maternal health and PRegnancy Outcomes Vision for Everyone
INCLUDE	INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndromE
IPRCC	Interagency Pain Research Coordinating Committee
iPSC	induced pluripotent stem cell
ISS-NL	International Space Station U.S. National Laboratory
MOSAIC	Maximizing Opportunities for Scientific and Academic Independent Careers
MoTrPAC	Molecular Transducers of Physical Activity Consortium
NARI	Native American Research Internship
NASA	National Aeronautics and Space Administration
NCATS	National Center for Advancing Translational Sciences
NCCIH	National Center for Complementary and Integrative Health
NCD	noncommunicable diseases
NCI	National Cancer Institute
NEI	National Eye Institute
NGRI	Next Generation Researchers Initiative
NHGRI	National Human Genome Research Institute
NHLBI	National Heart, Lung, and Blood Institute
NIA	National Institute on Aging
NIAAA	National Institute on Alcohol Abuse and Alcoholism
NIAID	National Institute of Allergy and Infectious Diseases
NIAMS	National Institute of Arthritis and Musculoskeletal and Skin Diseases
NIBIB	National Institute of Biomedical Imaging and Bioengineering
NICHD	*Eunice Kennedy Shriver* National Institute of Child Health and Human Development
NIDA	National Institute on Drug Abuse
NIDCD	National Institute on Deafness and Other Communication Disorders
NIDCR	National Institute of Dental and Craniofacial Research
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
NIEHS	National Institute of Environmental Health Sciences
NIGMS	National Institute of General Medical Sciences
NIH	National Institutes of Health
NIH RePORTER	NIH *Research Portfolio Online Reporting Tools Expenditures and Results*
NIMH	National Institute of Mental Health
NIMHD	National Institute on Minority Health and Health Disparities
NINDS	National Institute of Neurological Disorders and Stroke
NINR	National Institute of Nursing Research
NLM	National Library of Medicine
OD	NIH Office of the Director
OSC	Office of Strategic Coordination
PALM	Pamoja Tulinde Maisha
PATH	Population Assessment of Tobacco and Health

PHS	Public Health Service
PMC	PubMed Central
PPP	public–private partnership
PRGLAC	Pregnant Women and Lactating Women
RCDC	Research, Condition, and Disease Classification
RCMI	Research Centers in Minority Institutions
RFI	Request for Information
SAMHSA	Substance Abuse and Mental Health Services Administration
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SCAP	Single Cell Analysis Program
SCD	sickle cell disease
SCDIC	Sickle Cell Disease Implementation Consortium
SCGE	Somatic Cell Genome Editing
SEER	Surveillance, Epidemiology, and End Results
SGM	sexual and gender minority
SIG	Shared Instrumentation Grant
SMaRt	Somatic Mosaicism and Retrotranspositions
SPARC	Stimulating Peripheral Activity to Relieve Conditions
SPRINT	Systolic Blood Pressure Intervention Trial
SSC	Symptom Science Center
STRIDES	Science and Technology Research Infrastructure for Discovery, Experimentation, and Sustainability
TRSP	Tobacco Regulatory Science Program
UDN	Undiagnosed Diseases Network
UDP	Undiagnosed Diseases Program
VA	U.S. Department of Veterans Affairs

Acknowledgments

The *NIH-Wide Strategic Plan for Fiscal Years 2021–2025* is the product of many contributors. The NIH Director would like to thank the following stakeholders, committees, and staff for their time and effort in helping to develop this Strategic Plan.

- We would like to thank the **NIH-Wide Strategic Working Group,** whose enthusiasm, knowledge, and commitment made this document possible: Elizabeth Baden, Julie Frost Bellgowan, Michelle Bennett, Laura Berkson, David Bochner, Laura Brockway-Lunardi, Thomas Calder, Cindy Caughman, Mindy Chai, Stephanie Clipper, Laura Cole, Christine Cooper, Stephanie Courchesne-Schlink, Jessica Creery, Ned Culhane, Hope Cummings, Charles Dearolf, Clarence Dukes, Deborah Duran, Yvette Edghill Spano, Nicole Garbarini, Taylor Gilliland, Shefa Gordon, John Grason, Rebecca Hong, Cristina Kapustij, Edmund Keane, Mary Beth Kester, David Kosub, Ira Kukic, Erica Landis, Charlene Le Fauve, Issel Anne Lim, Ryan Mahon, Rebecca Meseroll, Wynn Meyer, Lara Miller, Kathryn Morris, Kate Nagy, Patty Newman, Sheila Newton, Rosanna Ng, Samia Noursi, Eileen Oni, Wilma Peterman Cross, Kamilah Rashid, Reaya Reuss, Sarah Rhodes, David Saeger, Leigh Samsel, Claire Schulkey, Paul Scott, Ching-Yi Shieh, Kelly Singel, Tyrone Spady, Erin Spaniol, Meredith Stein, Daniel Stimson, Nathaniel Stinson, Denise Stredrick, Rachel Sturke, Meredith D. Temple-O'Connor, Kimberly Thigpen Tart, Leslie Thompson, Valerie Virta, Marina Volkov, Julie Wallace, Elizabeth Walsh, Bridget Williams-Simmons, Nora Wong.
- In addition, we thank those across NIH who took the time to review the Framework and draft Strategic Plan and provide content. This includes **Institute, Center,** and **OD Office Directors** and **staff**.
- We would like to thank the **NIH Advisory Committee to the Director** and the **NIH Division of Program Coordination, Planning, and Strategic Initiatives Council of Councils** for their insightful feedback on the Framework and draft Strategic Plan.
- Finally, we are enormously appreciative of the robust input into the strategic planning process from **stakeholder communities,** including members of the scientific and health care communities, professional societies, advocacy organizations, industry, other federal agencies, and the general public. We look forward to your continued involvement as NIH works to implement the vision outlined here.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