

NIH-Wide Strategic Plan

Fiscal Years 2016-2020



Turning Discovery Into Health





To the American People,

As the United States' biomedical research agency, the National Institutes of Health (NIH) has been the driving force behind many decades of advances that have improved health of people in every corner of America and the world. The vast majority of NIH's funds go to support scientists at universities, research institutions, and small businesses in all 50 states, with their many discoveries serving to fuel the U.S. biomedical industry and keep our Nation globally competitive.

Yet, much remains to be done. The coming years are certain to pose new challenges for human health and offer new opportunities for scientific exploration. NIH will address this rapidly changing landscape by pursuing, with greater vigor than ever, our mission of seeking fundamental knowledge about the nature and behavior of living systems and applying that knowledge to enhance health, lengthen life, and reduce illness and disability.

In this research strategic plan for Fiscal Years 2016-2020, prepared at the [request of Congress](#), we share a framework that places NIH's enduring mission in the context of tomorrow's challenges and opportunities. Working with our many partners in the public and private sectors, NIH will use this framework as we strive to turn scientific discoveries into better health, while upholding our responsibility to be wise stewards of the resources provided to us by the American people.

This research strategic plan is designed to harmonize decision making across the Agency. It will complement, but not replace, the strategic plans of the individual Institutes, Centers, and Program Offices, because these organizations have their own strategic plans that align with their Congressionally mandated missions. Moreover, the plan is not meant to catalogue all of the many things NIH has done or will do in the future. Rather, we have selected examples to provide the reader with clear illustrations of the points being made.

Your support of NIH's mission is vital to our success. Every dollar that our Nation invests in NIH is an investment in options for a healthier, more productive life for you—and for future generations.

With sincere appreciation,

A handwritten signature in black ink, appearing to read "Francis S. Collins".

Francis S. Collins, M.D., Ph.D.
Director, National Institutes of Health

Table of Contents

OVERVIEW.....	3
Mission and Goals.....	4
Organization	4
Research Landscape	5
The Vision and The Challenge.....	7
NIH’S STRATEGY	9
Objective 1: Advance Opportunities in Biomedical Research.....	9
Fundamental Science.....	12
Treatments and Cures	16
Health Promotion and Disease Prevention	23
Objective 2: Foster Innovation by Setting NIH Priorities	28
Objective 3: Enhance Scientific Stewardship	33
Objective 4: Excel as a Federal Science Agency by Managing for Results	42
A Few Bold Predictions for America’s Future	45

NIH-Wide Strategic Plan Framework

Overview

- Mission of NIH
- Unique moment of opportunity in biomedical research
- Current NIH-supported research landscape
- Constraints confronting the community in the face of lost purchasing power

Advance Opportunities in Biomedical Research

Fundamental Science

- Foundation for progress
- Consequences often unpredictable
- Technology leaps catalyze advances
- Data science increases impact/efficiency

Health Promotion/Disease Prevention

- Importance of studying healthy individuals
- Advances in early diagnosis/detection
- Evidence-based reduction of health disparities

Treatments/Cures

- Opportunities based on molecular knowledge
- Breakdown of traditional disease boundaries
- Breakthroughs need partnerships, often come from unexpected directions
- Advances in clinical methods stimulate progress

Set Priorities

- Incorporate disease burden as important, but not sole factor
- Foster scientific opportunity; remain nimble
- Advance opportunities presented by rare diseases
- Consider value of permanently eradicating a pandemic risk

Enhance Stewardship

- Recruit/retain outstanding research workforce
- Enhance workforce diversity
- Encourage innovation
- Optimize approaches to inform funding decisions
- Enhance impact through partnerships
- Ensure rigor and reproducibility
- Reduce administrative burden

Excel as a Federal Science Agency by Managing for Results

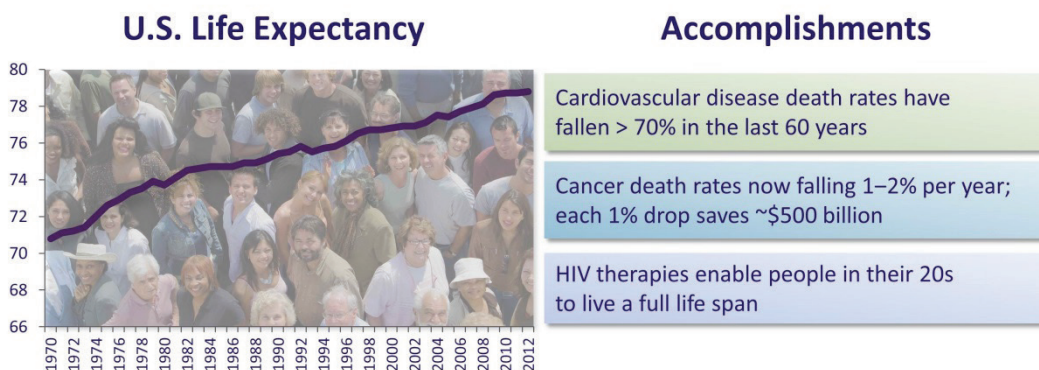
OVERVIEW

The [National Institutes of Health \(NIH\)](#) is the United States' premier agency for biomedical research, which spans the broad spectrum of basic, translational, clinical, behavioral and social sciences research dealing with many aspects of biology and almost every human disease and disability.

Begun in 1887 as a one-room laboratory on Staten Island, NY, the agency was officially designated "NIH" by Congress in 1930. Since then, NIH has grown to be the world's largest source of medical research funding, and the [driving force behind decades of advances](#) that have expanded fundamental scientific knowledge and improved health.

To date, 148 NIH-supported researchers have received [Nobel Prizes](#) for their groundbreaking achievements. These, along with other NIH-funded research advances, are behind many of the gains that our nation has enjoyed in public health.

Biomedical Research's Impact on U.S. Health



A baby born in the United States today can expect to live to nearly age 79—about three decades longer than one born in 1900. Such [progress](#) is made possible by NIH's support of many different types of research focused on a wide range of diseases and conditions. [Health improvements](#) fueled by NIH-funded research include significant declines in the U.S. death rates from heart disease, stroke, diabetes, and cancer, as well as the transformation of HIV/AIDS from a swiftly fatal disease to a manageable, chronic condition with a near-normal life expectancy.

Mission and Goals

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

To carry out this mission, NIH's goals are: to foster fundamental creative discoveries, innovative research strategies, and their applications as a basis for ultimately protecting and improving health; to develop, maintain, and renew scientific human and physical resources that will ensure the nation's capability to prevent disease; to expand the knowledge base in medical science and associated sciences in order to enhance the nation's economic well-being and ensure a continued high return on the public investment in research; and to exemplify and promote the highest level of scientific integrity, public accountability, and social responsibility in the conduct of science.

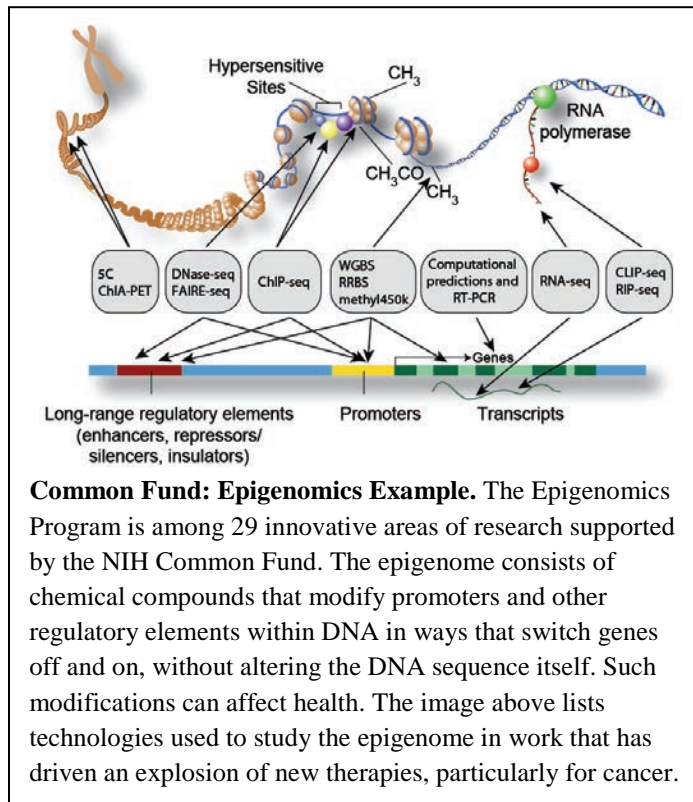
Organization

NIH is an operating division of the [Department of Health and Human Services \(HHS\)](#), responsible for helping the Department realize its [strategic goal of advancing scientific knowledge and innovation](#).

To accomplish this, NIH consists of [27 Institutes and Centers \(ICs\)](#), along with Program Offices, which collectively are referred to as ICOs. These ICOs have [individual strategic plans](#) and specific research agendas, which are aligned with the legislative mandates that are often related to specific diseases or body systems. To support these missions, most of NIH's ICOs receive a specific appropriation from Congress, and support research and research training through extramural funding awarded to universities, academic health centers, and other research institutions. Most also conduct research and research training in their own intramural laboratories, the majority of which are located on the NIH's main campus in Bethesda, MD.

In Fiscal Year (FY) 2014, NIH reviewed more than 51,000 research project grant (RPG) applications and awarded approximately 10,000 new and competing RPGs to institutions/organizations to support specific projects performed by designated investigators in areas representing their research interests and competencies. The average duration of an NIH grant award is about 4 years; funding the out years of a multi-year award is predicated on submission of an acceptable annual progress report. The total number of active grants in FY 2014 was more than 47,000.

Research Landscape



Extramural. NIH currently devotes approximately 84% of its budget to grants and contracts supporting more than 300,000 members of the research workforce, including 35,000 principal investigators, in the extramural biomedical and behavioral/social sciences research communities. NIH funds researchers at all career stages who are located at many kinds of institutions, organizations, and small businesses in all 50 states.

Decisions about NIH grant awards are informed by a highly competitive, two-stage peer-review process that involves initial evaluation by more

than 18,000 reviewers from the scientific community, and second-level review by members of the ICO's national advisory councils, who take into account of the ICO's research program priorities. Ultimately, ICO Directors are responsible for approving funding.

Because a broad research portfolio is critical for carrying out NIH's mission, the agency's portfolio of grants and contracts covers the full range of biomedical, behavioral, and social sciences research, from basic to applied. In addition to research supported by individual ICOs, the [NIH Common Fund](#), within the NIH Office of the Director, funds cross-cutting, trans-NIH scientific programs that are high impact, transformative, and managed against defined milestones. This fund, which currently supports 29 innovative programs, acts as a "venture capital" space, providing the NIH Director with a strategic and nimble approach to address key roadblocks in biomedical research and capitalize on emerging opportunities.

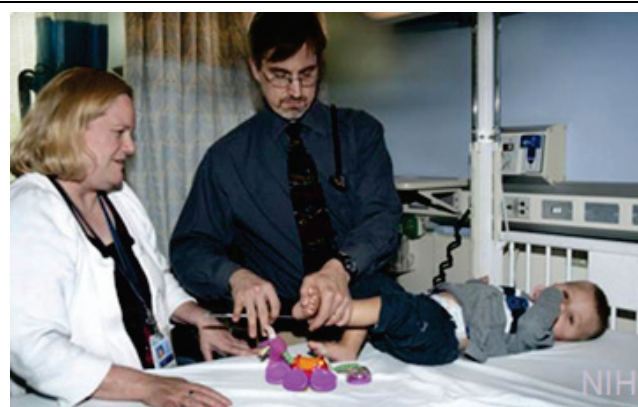


Intramural. Approximately 11% of NIH’s budget supports about 7,000 researchers at NIH intramural research facilities. Scientists in the NIH Intramural Research Program include approximately 1,000 principal investigators, 1,500 staff clinicians and staff scientists, and 4,500 trainees.

The Intramural Research Program facilitates high-impact science in a variety of important

ways. For example, the program serves as a test bed for unique approaches to difficult research challenges, with the resulting solutions often being adopted by the extramural scientific community.

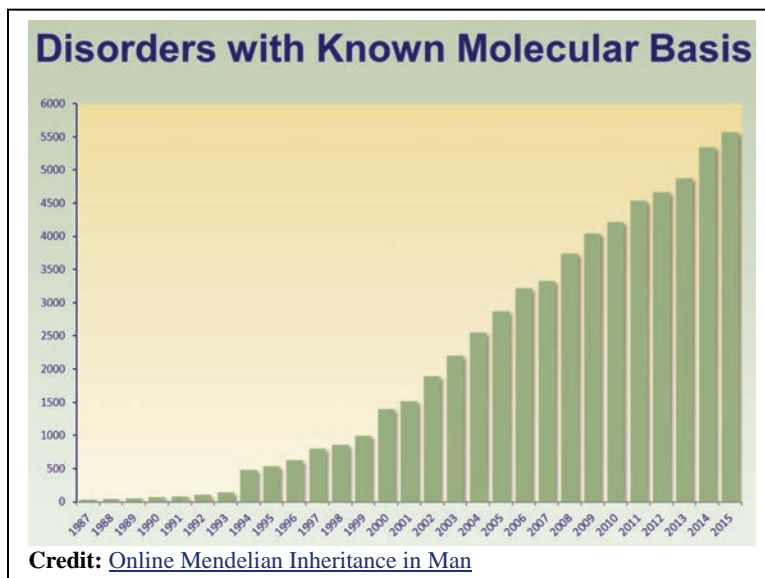
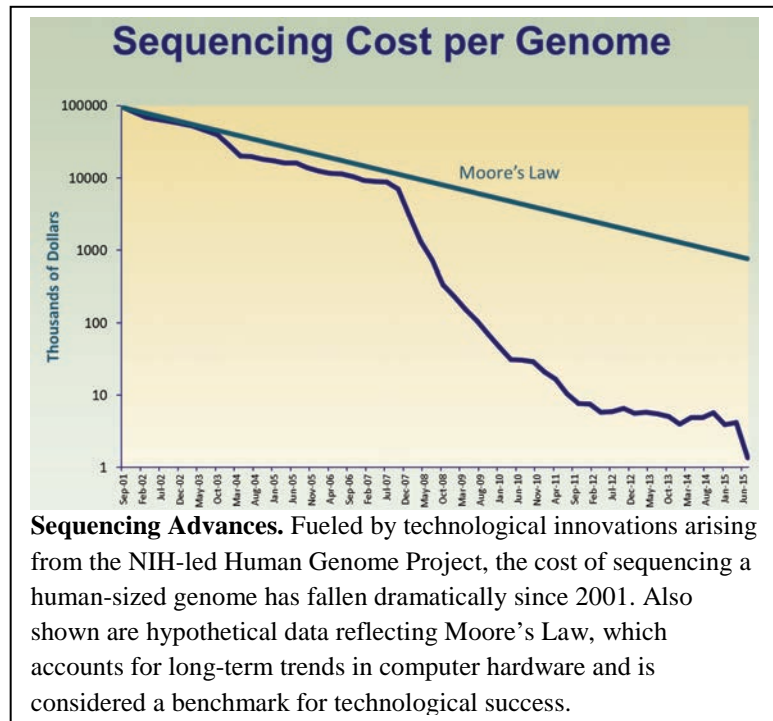
The program is also home to the [NIH Clinical Center](#), the world’s largest hospital dedicated to clinical research. Among the many ways in which the Clinical Center promotes translational research is its ability to link patient care directly to basic research discoveries, and its pioneering programs for the study of undiagnosed diseases and rare diseases and conditions.



Helping People With Undiagnosed Diseases. An estimated 25 million to 30 million Americans suffer from rare disorders that can be very difficult to diagnose. Building on the success of the NIH Clinical Center’s [Undiagnosed Diseases Program](#), NIH has established a nationwide [Undiagnosed Diseases Network](#) to promote use of genomic data in disease diagnosis and enlist the help of basic researchers in elucidating disease mechanisms in order that treatments can be developed.

The Vision and The Challenge

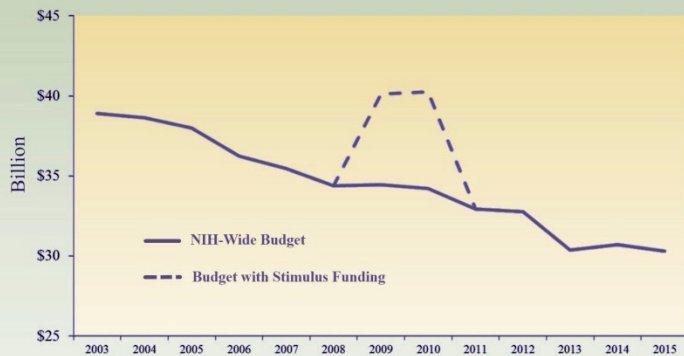
Our nation and the world stand at a unique moment of opportunity in biomedical research. Understanding of basic biological mechanisms is growing exponentially, generating vast troves of data and propelling biomedicine into the “Big Data” sphere. Incredible technological advances, including innovations in DNA sequencing, imaging, bioinformatics, and high-throughput screening of potential therapies, are also driving discovery. Fueled by these advances, our approach to biomedical research has changed in revolutionary new ways that span scientific disciplines and take a far more cross-cutting, integrative view of biology and human health.



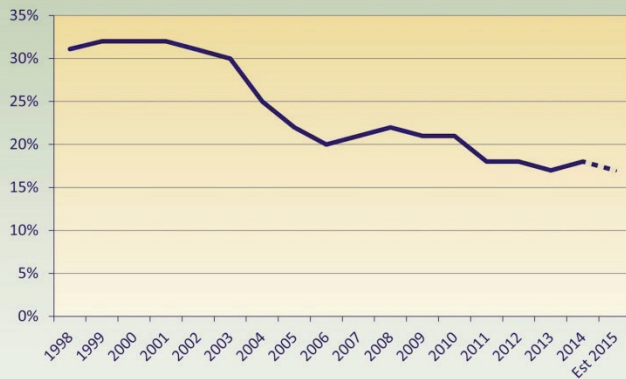
For example, in recent years, more cost-effective DNA sequencing technologies have opened the door to studying the molecular causes of disease, with exciting implications for expanding fundamental understanding, accelerating therapeutic development, and improving disease prevention and health promotion. Much can be learned about the specific biological mechanisms involved

in health and disease by using genomic technologies to identify genes that influence the risk of developing a wide range of conditions, both rare and common.

NIH Research Purchasing Power FY 2003-2015



NIH Grant Application Success Rates FY 1998 – 2015



Clearly, NIH needs to capitalize upon this moment of extraordinary opportunity to continue—and to accelerate—its efforts to realize its vision of turning scientific discoveries into improved health. Yet the agency faces a variety of constraints and challenges.

For example, NIH funding has not kept pace with inflation, and the agency has lost approximately 22% of its research purchasing power since 2003. This has resulted in a situation in which many innovative research ideas cannot be funded; NIH currently funds about 1 in 6 grant applications, compared to its historical funding rate of 1 in 3.

A strengthened and sustained commitment to NIH-supported research is critical because delays in scientific progress can have a dire

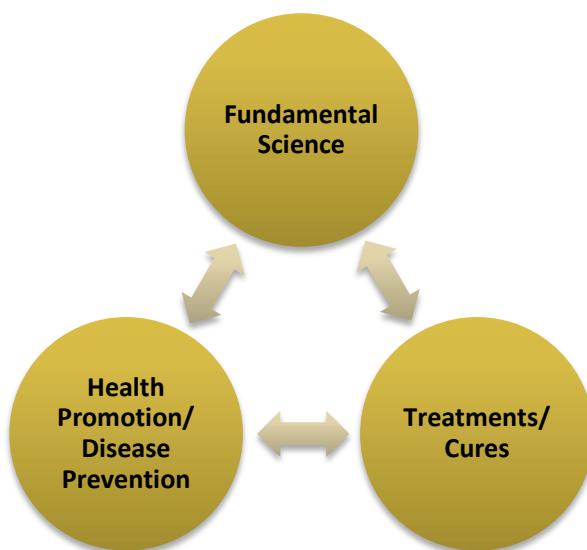
impact on the health of individuals and the communities in which they live, as well as our nation’s overall public health and wellbeing. Investments in NIH research also make a strong positive contribution to the U.S. economy, playing an essential role in our nation’s ability to retain its world-leading biomedical workforce and to remain competitive in an increasingly global business environment. Without predictable funding, it is becoming increasingly more difficult to attract much-needed new talent to the U.S. biomedical research workforce, particularly physician-scientists who have other stable and satisfying career options.

NIH'S STRATEGY

To establish a framework for carrying out its mission and optimize return on public investment, NIH's strategy will focus on four essential, interdependent objectives. These objectives are: advance opportunities in biomedical research, foster innovation by setting NIH priorities, enhance scientific stewardship, and excel as a federal science agency by managing for results.

Objective 1: Advance Opportunities in Biomedical Research

Over the next 5 years, NIH will capitalize upon a broad range of cross-cutting opportunities to move biomedical research forward in three highly important, interdependent areas: exploration of fundamental science, discovery of treatments and cures, and advancement of health promotion and disease prevention. These activities will be catalyzed by new approaches, strongly supported by NIH, that are aimed at speeding discovery across the biomedical research enterprise. This includes efforts to promote increased data sharing, to enhance the ability of scientists to pursue interdisciplinary studies, and to enable new types of partnerships.



NIH encourages and, in many cases, collaborates with researchers from both the private and public sectors, including other HHS divisions, science agencies, philanthropic foundations, academia, and industry, to advance its mission of improving human health. Among the federal science agencies that NIH often coordinates and works closely with are the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), the Agency for Healthcare Research and Quality (AHRQ), the HHS Office of the Assistant Secretary for Preparedness and Response (ASPR), the National Science Foundation (NSF), the Department of Energy (DOE), and the Defense Advanced Research Projects Agency (DARPA).

NIH's Frequent Federal Partners

U.S. Department of Health and Human Services	Mission	Select Collaborations with NIH
 Agency for Healthcare Research and Quality	Produces evidence to make health care safer, higher quality, more accessible, equitable, affordable. Partners with others to ensure such evidence is understood and used.	U.S. Preventive Services Task Force (USPSTF)
 Centers for Disease Control and Prevention	Works to protect Americans from health, safety, security threats. Conducts science and provides health information to protect against such threats.	SEARCH for Diabetes in Youth
 Centers for Medicare and Medicaid Services	Administers Medicare, Medicaid, the Children's Health Insurance Program (CHIP), and parts of the Affordable Care Act (ACA).	Data sharing between CMS and NCI's SEER (Surveillance, Epidemiology, and End Results) Program, NIDDK's U.S. Renal Data System, and NHLBI's Research Cohorts
 Food and Drug Administration	Protects public health by ensuring safety, efficacy, and security of drugs, biological products, medical devices, food, cosmetics, and radiation-emitting products. Helps speed innovations to make medical products safer, more affordable, and effective.	Accelerating Medicines Partnership®
 Health Resources and Services Administration	Works to improve health and achieve equity through access to quality services, a skilled health workforce, and innovative programs.	Maternal and Child Health Research Network Programs
 Indian Health Service	Raises the physical, mental, social, and spiritual health of American Indians and Alaska Natives to the highest level.	Native American Research Center for Health (NARCH) , (also with AHRQ, HRSA)
 <small>ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE</small> Office of the Assistant Secretary for Preparedness and Response	Leads the country in preparing for, responding to, and recovering from the adverse health effects of emergencies and disasters by supporting our communities' ability to withstand adversity, strengthening our health and response systems, and enhancing national health security.	Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) , (also with CDC, FDA, VA, DoD, USDA, Homeland Security, USDA)
 <small>Substance Abuse and Mental Health Services Administration</small> Substance Abuse and Mental Health Services Administration	Reduces the impact of substance abuse and mental illness on America's communities.	Patient-Reported Outcomes Measurement Information System® (PROMIS®) , (also with CDC, CMS, FDA)

NIH's Frequent Federal Partners

Other Federal Agencies	Mission	Select Collaborations with NIH
 Department of Defense	Provides the military forces needed to deter war and to protect the security of our country.	Federal Interagency Traumatic Brain Injury Research (FITBIR) database, (also with VA)
 Defense Advanced Research Project Agency	Makes pivotal investments in breakthrough technologies for national security.	Tissue Chip for Drug Screening , (also with FDA)
 Department of Energy	Ensures America's security and prosperity by addressing its energy, environmental, and nuclear challenges through transformative science and technology solutions.	Structural biology with linear accelerator beam lines
 Department of Veterans Affairs	Fulfills President Lincoln's promise "to care for him who shall have borne the battle, and for his widow, and his orphan," by serving and honoring the men and women who are America's Veterans.	Interagency Pain Research Coordinating Committee (IPRCC) , (also with AHRQ, CDC, DoD, FDA)
 Environmental Protection Agency	Protects human health and the environment.	Toxicology Testing in the 21st Century (Tox21) , (also with FDA)
 National Science Foundation	Promotes the progress of science to advance the national health, prosperity, and welfare; to secure the national defense, and for other purposes.	BRAIN Initiative[®] , (also with DARPA)
 Department of Agriculture	Provides leadership on food, agriculture, natural resources, rural development, nutrition, and related issues based on sound public policy, the best available science, and effective management.	National Collaborative on Childhood Obesity Research

Fundamental Science

To achieve its mission, NIH must support the many types of fundamental scientific inquiry that are so essential to the progress of biomedicine. Fundamental science includes [basic biological research](#) that generates the knowledge of how living systems work at the molecular, cellular, and organismal level.

Such knowledge is the foundation for translational and clinical studies that, over time, can lead to major medical advances. Because the private biopharmaceutical sector [funds only a limited amount of basic research](#), NIH-supported research serves as the world's leading source of foundational knowledge of relevance to both the public and private sectors of biomedicine.

History shows that major biomedical advances frequently spring from unexpected sources. As anyone familiar with the story of penicillin's discovery knows, it is impossible to predict exactly what a basic researcher may uncover and what positive health benefits may eventually arise from such fundamental discoveries.

Furthermore, no one can foresee what threads of foundational knowledge will be woven together to produce a new breakthrough, which could open up entirely new fields or pave the way for new technology that will enable researchers to tackle questions once beyond the reach of biomedical science. Most of the examples cited in this section are those in which a basic science discovery has led to a significant clinical advance—an advance that could not have been foreseen at the time of the original basic research. One dramatic example is the story of how fundamental advances in cell biology led to development of a class of drugs widely used to lower the risk of cardiovascular disease. In the early 1970s, NIH-supported basic researchers

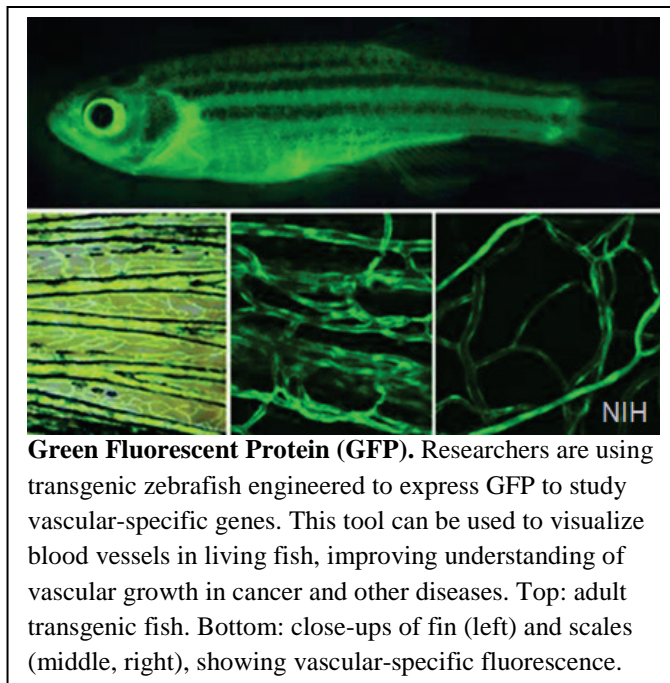


Credit: University of Texas Southwestern Medical School at Dallas
Cholesterol Pioneers. The basic science discoveries of Michael Brown and Joseph Goldstein paved the way for development of statin drugs for lowering cholesterol.

Joseph Goldstein and Michael Brown studied families with very high cholesterol levels and discovered that cells have low-density lipoprotein (LDL) receptors that remove cholesterol from the blood. That Nobel Prize-winning work, coupled with the NIH-funded [Framingham Heart Study's](#) landmark 1961 finding that high blood cholesterol is a major cardiovascular disease risk factor, set the stage for the first cholesterol-lowering statin drug in 1987.

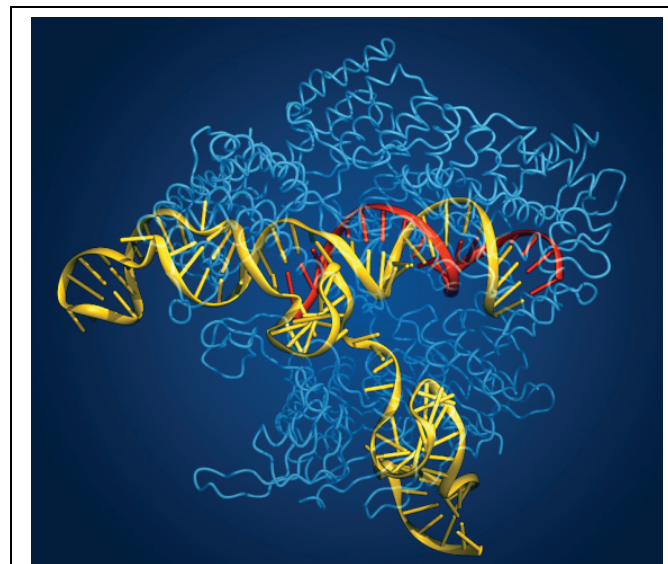
Likewise, NIH-funded basic research was instrumental in the development of

zidovudine (AZT), the first anti-retroviral drug approved for treating the human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS). The drug was developed in the early 1960s to treat cancer, but failed to show efficacy. It faded from view until 1985, when others thought of using AZT as an AIDS drug because of its ability to inhibit reverse transcriptase, an enzyme that HIV uses to replicate. Reverse transcriptase was discovered by basic virology research several years before AIDS was identified. In 1975, NIH grantees David Baltimore and Howard Temin shared a Nobel Prize in Physiology or Medicine for that work.



Green Fluorescent Protein (GFP). Researchers are using transgenic zebrafish engineered to express GFP to study vascular-specific genes. This tool can be used to visualize blood vessels in living fish, improving understanding of vascular growth in cancer and other diseases. Top: adult transgenic fish. Bottom: close-ups of fin (left) and scales (middle, right), showing vascular-specific fluorescence.

Basic innovation is also essential for the advancement of fundamental science because new technologies and methods can open whole new areas of scientific inquiry. In a tale of discovery

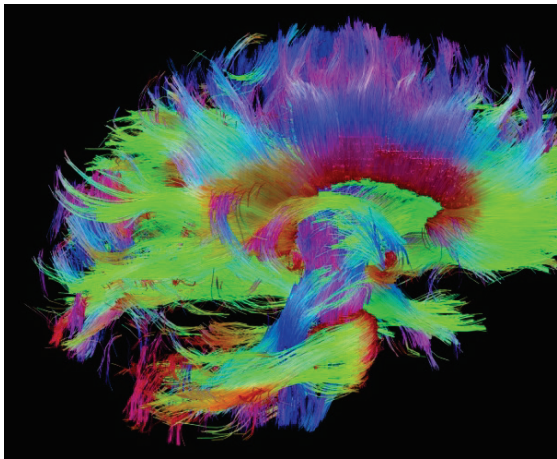


Credit: Bang Wong/Broad Institute of Harvard and MIT
Gene-Editing Technologies. Crystal structure of the new CRISPR/Cas9 system, which enables DNA to be edited with unprecedented precision. Researchers use RNA guides called CRISPRs (red) to steer the Cas9 gene-editing enzyme (light blue) to a specific site on a DNA strand (yellow) that they wish to modify. New mouse models of disease and next-generation antibiotics are among the things this customizable system is being used to create.

spanning more than three decades and culminating in the 2008 Nobel Prize in Chemistry, NIH grantees Martin Chalfie, Osamu Shimomura, and Roger Tsien discovered a green fluorescent protein (GFP) in jellyfish and went on to develop GFP into a key tool for observing biological processes that were previously invisible to researchers.

More recently, researchers have developed revolutionary customizable, gene-editing tools, such as CRISPR/Cas9. These technologies are enabling efforts to study genes in specific, targeted ways, often in real time.

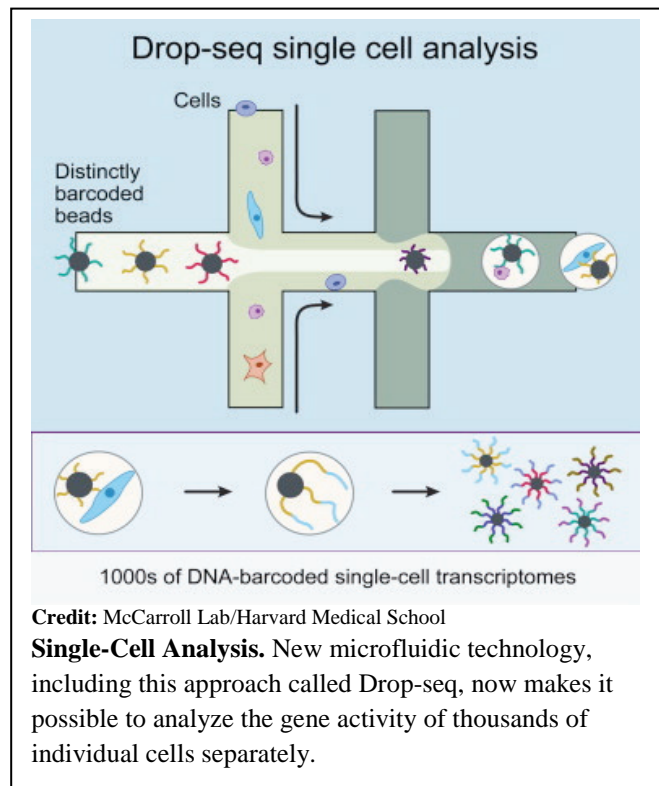
On the other hand, new scientific challenges can inspire the creation of new technologies. Compelling recent



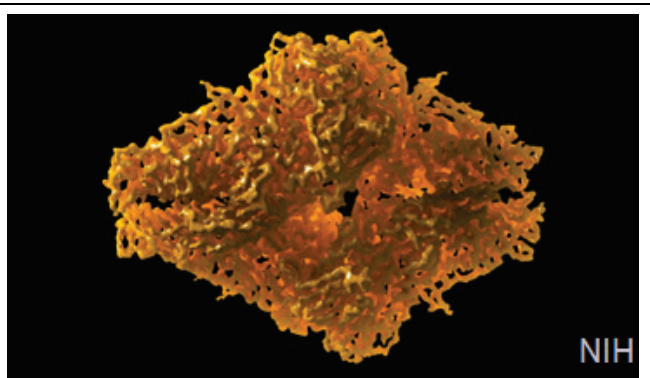
Credit: Laboratory of Neuro Imaging and Martinos Center for Biomedical Imaging/Massachusetts General Hospital
The Human Connectome Project. Wiring diagram of a healthy human brain produced by tracking the movement of water molecules through nerve fibers by diffusion tensor magnetic resonance imaging. This is an example of work being done by the Human Connectome Project.

examples of this innovative force in action include NIH’s Human Connectome Project and the multi-agency Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) Initiative, in which NIH plays a leadership role. With more than 100 billion cells and 100 trillion connections, the human brain remains one of science’s most daunting frontiers and one of medicine’s greatest challenges. To revolutionize understanding of how the brain enables the body to record, process, utilize, store, and retrieve vast quantities of information, BRAIN is supporting development of entirely new technologies, including some with the potential to benefit many other areas of biomedical research, such as single-cell analysis methods.

Engineers, computer scientists, nanotechnologists, physicians, and neuroscientists will use these and other leading-edge technologies to work together to achieve BRAIN’s goal of measuring real-time cognition, emotion, perception, and behavior at the scale of complex neural networks in living organisms—all at the speed of thought. A bold plan for the BRAIN initiative, extending over a 12-year period, was recently put forward by an expert working group of neuroscientists, and serves as the current blueprint for this project. Ultimately, the foundation of understanding developed by the BRAIN Initiative® will help reveal the underlying pathology in a vast array of brain disorders and provide new therapeutic avenues to treat, cure, and prevent neurological and psychiatric conditions, such as Alzheimer’s disease, autism, schizophrenia, depression, epilepsy, and addiction.

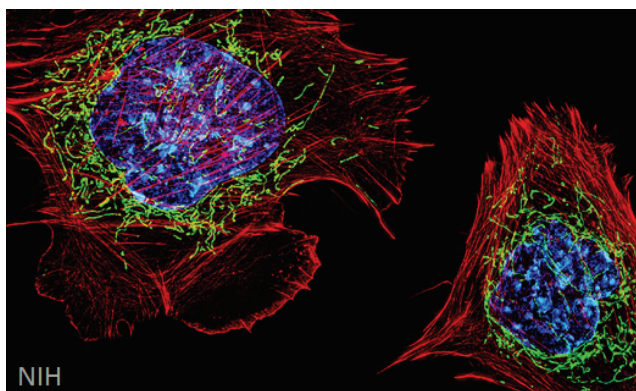


Indeed, the impact of technologies inspired by a specific discovery-driven initiative can extend far beyond the life of the initiative, catalyzing avenues of basic research never imagined at the outset. For example, the goal of sequencing the human genome yielded the technologies now driving many diverse “omic” areas of basic research. That includes microbiomics, in which next-generation DNA sequencing is being used to explore the complex communities of microbes that live on and in the human body and how they interact with human cells to influence health and disease.



New Tools for Structural Biology. Cryo-electron microscopy (cryo-EM) image showing the structure of a metabolic enzyme called beta-galactosidase in near-atomic detail. This imaging technology provides a new path for solving molecular puzzles that may revolutionize many areas of biomedical research and drug development.

Other frontiers in fundamental science include: molecular immunology, which is using RNA seq and other transcriptome analysis tools to characterize in unprecedented detail how immune cell repertoires vary in health and disease; structural biology, which is undergoing a major leap forward in defining three-dimensional submicroscopic structures because of the development of cryo-electron microscopy (cryo-EM); and cell biology, which is benefiting from novel approaches to light microscopy that have pushed resolution below the diffraction limit. In addition, the development of innovative “tissue- and organ-on-a-chip” systems is helping to bridge the gap between fundamental and translational science, providing new models of



New Tools for Cell Biology. Super-resolution imaging of fibroblasts, one of the most common cells in mammalian connective tissue. Scientists used these mouse fibroblasts to test the power of a new technique called structured illumination microscopy (SIM). Clearly visible in this image are the cell’s nuclear DNA (blue), mitochondria (green), and cellular skeleton (red).

complex pathology for understanding basic mechanisms of disease.

Fundamental science also includes basic behavioral and social science research that generates knowledge of how living systems interact with and are influenced by experiences at the individual, family, social, organizational, and environmental levels. NIH-supported research on the neurobiological and learning mechanisms of goal-directed versus habitual behaviors provide important insights on how unhealthy habitual behaviors can be brought under greater control and how

behavior change can be maintained. The study of stress responses and stress resilience offers potential approaches to help individuals better adapt to negative life events. Understanding decision-making processes, especially under various emotional and cognitive states, also sheds new light on how medical decisions, both by provider and patient, are made and can be improved. NIH-supported basic behavioral and social science research serves as the foundation for the development of innovative approaches to improve health via changes in behavior and the environment.

[Data science](#) also holds tremendous potential, not only for enhancing the efficiency of the conduct of science, but also for increasing the impact of fundamental science, along with many other areas of biomedical research. To this end, NIH will serve as a focal point for catalyzing this historic research opportunity, continuing to leverage its roles as an influential convener and major funding agency to encourage rapid, open sharing of data and greater harmonization of scientific efforts. NIH will also maintain and expand its support of research aimed at addressing new computational challenges in accessing, managing, analyzing, integrating, and mining the huge amounts of data, often referred to as “Big Data,” being generated by biomedical scientists. One hope is that advances in bioinformatics and computational biology will lead to basic researchers conducting more experiments via computer simulation (*in silico*), with the ensuing results being used to generate and test novel hypotheses that will be rapidly shared with the broad research community.

From FY 2016-2020, NIH will support a broad, balanced portfolio of basic research across a wide range of scientific disciplines, a portfolio that will be complemented by vigorous support of innovations in technology and data science. By maintaining and strengthening its already impressive foundation of fundamental science, biomedical research will be poised to identify and capitalize upon potential opportunities for revolutionary breakthroughs with the potential for preventing, treating, and curing disease.

Treatments and Cures

To achieve its mission, NIH is strongly committed to supporting the process of turning advances in fundamental scientific knowledge into treatments and cures. When integrated with existing knowledge about cells, systems, and organisms, insights generated by this innovative work will provide a new conceptual framework for therapeutic development that is based on a deeper understanding of biological systems and how, depending upon context, these complex mechanisms interact to influence health and disease.

This process begins with basic research discoveries in biology, disease, or behavior that serve to further understanding of the basis of a disease and to identify potential therapeutic targets. Cell or tissue samples, animal models, and/or computer simulations are then used to design and

test candidate approaches for diagnostics, devices, treatments, and/or cures. If the candidate approaches prove to be safe and effective in this pre-clinical testing, the experimental treatments and/or cures are then moved into human clinical trials, where they are tested for safety and efficacy. It must be emphasized that advances in these areas are closely interconnected and often do not progress in a linear manner. In fact, sometimes the process even circles back on itself in a “virtuous cycle,” with applied research informing new ideas in basic research.

The randomized trial is the gold standard by which clinical researchers determine the safety and/or effectiveness of interventions that are thought to have potential to improve human health. NIH, which currently devotes approximately 10% of its budget to supporting clinical trials, has a distinguished history of funding landmark trials that have led to a wide spectrum of interventions. Such interventions have included coronary bypass surgery, treatments for breast cancer, lifestyle improvements to prevent diabetes, approaches for lowering blood pressure, screening methods for lung cancer, hormone replacement therapy in postmenopausal women, and anti-retroviral drugs in people with, or at high risk for, HIV infection. In recent years, NIH developed an increasing interest in fostering approaches to enhance the speed and efficiency with which trials are conducted, as well as to learn more about the role of “pragmatic trials,” which are trials of direct interest to patients and clinicians.

Traditionally, diseases have been researched and treated within an organ-based framework, e.g., diseases of the heart, the eye, the gastrointestinal tract, and so forth. Today, thanks to fundamental research, researchers have learned that many apparently different diseases have commonalities at the molecular level. These molecular similarities have led us to think in new ways about the roots of disease and open the door to identifying therapies that work across different organ systems and disease states. These shifts in thinking have profound implications for the future of scientific research and, ultimately, for the future of medicine. Tools and technologies that offer opportunities to screen rapidly for similarities among seemingly disparate diseases, as well as seemingly disparate drugs, are providing opportunities to repurpose existing drugs for use in conditions other than those for which they were originally developed. For example, thanks to an innovative public-private partnership, an experimental drug originally developed to fight cancer is now being tested for [Alzheimer’s disease \(AD\) in human clinical trials](#). The compound, called saracatinib, is particularly exciting because it acts through a different mechanism than other AD experimental therapies.

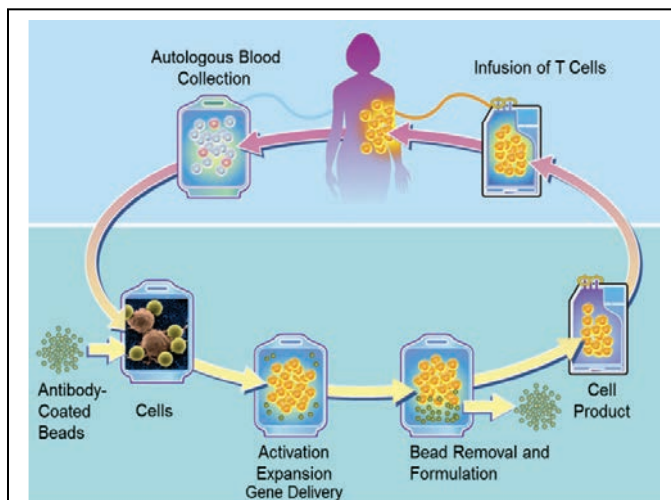
As important as this new emphasis on cross-cutting molecular mechanisms may be, there remains much that can be learned by studying the rare or unique. Especially for rare diseases caused by mutations in a single gene, the identification of a specific molecular defect through DNA sequencing can point directly to possible treatment strategies. Still, even in such cases, the

road from discovery to treatment may be long, as evidenced by the two decades between discovery of the gene for cystic fibrosis (CF) and FDA approval of the first drug that directly affects a CF-causing molecular defect. For more common disorders, finding rare individuals carrying a genetic protective factor can provide critical clues to new therapeutic strategies. For example, a search for genes involved in cholesterol metabolism turned up a few healthy individuals with a rare gene variant that leads to very low levels of cholesterol and a very low incidence of cardiovascular disease. Further studies showed this gene variant reduces production of a protein called PCSK9, setting off a race among pharmaceutical firms to develop a new class of drugs that lower cholesterol by blocking this protein. Many experts think there are more such drug targets out there waiting to be discovered through molecular characterization and stratification of common diseases and disease risk factors; NIH is assembling the right research teams and resources to find such targets.

Progress toward treatment and cures is certainly not limited to high-throughput screening and DNA sequencing. Consider the example of cancer immunotherapy. In the early 1970s, basic research, spearheaded in large part by NIH-funded scientists, led to the development of methods to splice fragments of DNA together, giving birth to the field of biotechnology. When merged with fundamental advances in molecular immunology, this set of technologies made it possible to begin pursuing ideas for cancer immunotherapy—a radical new approach that involves enlisting a patient’s own immune system in the fight against cancer. In one promising strategy, T cells are collected from patients and engineered to produce special surface proteins, called chimeric antigen receptors. This work has already saved the lives of children with acute

lymphoblastic leukemia and adults with chronic lymphocytic leukemia and refractory multiple myeloma.

Like the previous examples of statin and HIV drugs, it must be emphasized that cancer immunotherapy owes its success to decades of NIH-funded fundamental science. In fact, a recent [analysis](#) of a cancer immunotherapy approach pioneered by NIH grantee James Allison, who is a 2015 Lasker Award winner, documented the contributions of 7,067 scientists over more than a century, with many working on basic research with no clear connection to cancer.



Credit: Carl June/University of Pennsylvania

Cancer Immunotherapy. The approach illustrated above, called chimeric antigen receptor (CAR) therapy, involves genetically engineering a key part of the immune system (T cells) to recognize specific proteins, or antigens, on tumor cells and attack them.

Scientific innovation is also central to the quest to find new ways of combating the growing threat of antibiotic-resistant bacteria, which each year infect more than 2 million Americans and kill at least 23,000. For example, an ingenious microfluidic system that can trap and sort single cells has enhanced efforts to mine one of nature’s richest sources of potential antibiotics: dirt. Certain microorganisms that naturally live in soil produce antibiotic-like compounds that are highly toxic to other microbes. Thanks to their improved ability to “dig through dirt,” NIH-funded researchers recently uncovered a new class of antibiotic drugs with the power not only to kill a wide range of infection-causing bacteria, but to kill them in a way that may reduce the problem of antibiotic resistance.

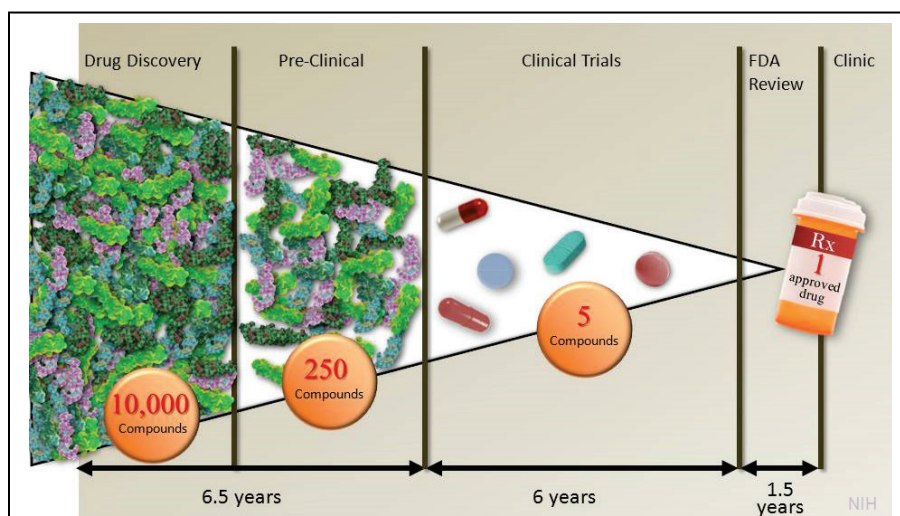


Credit: Slava Epstein/Northeastern University

Digging for New Antibiotics. Innovative microfluidic chip system being used to search dirt for new sources of antibiotics. Besides discovering a powerful new antibiotic called teixobactin, researchers have isolated more than 25 potential new drugs, including an anti-cancer agent and a compound that targets tuberculosis-causing bacteria.

Discovery of potential therapeutic targets and candidate therapies are essential first steps in the development of new treatments and cures, but they are far from the only steps. The transition of scientific discoveries to human clinical trials has become increasingly costly and

time consuming, with a great number of candidate therapies failing to cross what has been dubbed the “[Valley of Death](#).” NIH-funded research will play an increasingly important role in identifying hurdles in this process, as well as generating approaches for accelerating the development and testing of potential treatments and cures.



The Translational Timeline. Development of a new therapeutic is a long, costly, and risky endeavor. Currently, a novel drug, device, or other medical intervention takes about 14 years and \$2 billion to develop, with a failure rate exceeding 95%.



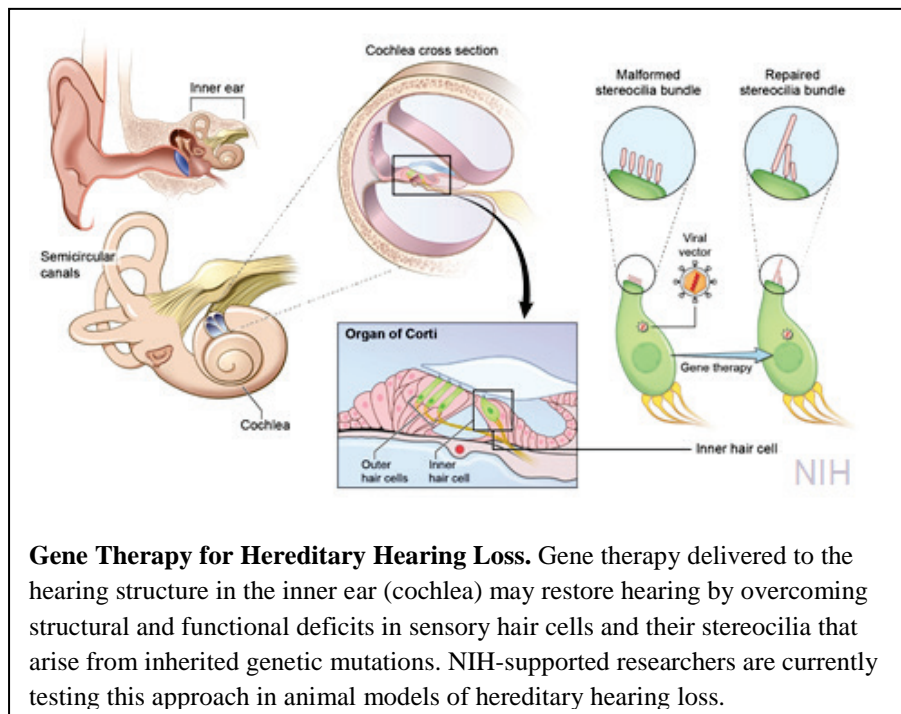
Also, as part of its effort to push research beyond a strictly organ-based view of health and disease, NIH will encourage efforts to study the interactions of various diseases and conditions. The aim is to gain a better understanding of the cumulative and synergistic impacts that multiple chronic conditions and comorbidities can exert upon the human body, thereby informing efforts to develop therapeutic and preventive approaches for these complex challenges. Among the many comorbidities in need of additional research is pain. On behalf of HHS,

NIH has established the [Interagency Pain Research Coordinating Committee](#), which has generated a [National Pain Strategy](#) and facilitated collaborations aimed at advancing fundamental understanding of pain and improving pain-related treatment.

To speed the movement of discoveries from the lab to the clinic, NIH will also accelerate and expand upon its efforts to encourage development of more precise, individualized ways of managing and preventing disease. Known collectively as [precision medicine](#), these emerging approaches for preventing, diagnosing, and treating disease take into account individual variability in genes, environment, and lifestyle. While individualized, molecularly based strategies are in use for some conditions, including cancer, HIV/AIDS, and hepatitis C, more research is needed to realize precision medicine’s promise for all conditions. Among the frontiers in this area is pharmacogenomics, which studies how an individual’s genetic makeup (or the genetic makeup of a tumor) affects response to drugs. The goal of such research is to enable health-care providers to prescribe the right drug at the right dose at the right time for each patient. One example of pharmacogenomics is the [National Cancer Institute \(NCI\)-Molecular Analysis for Therapy Choice \(NCI-MATCH\) clinical trial](#), which will build a foundation for the oncology component of the multi-agency [Precision Medicine Initiative® \(PMI\)](#), in

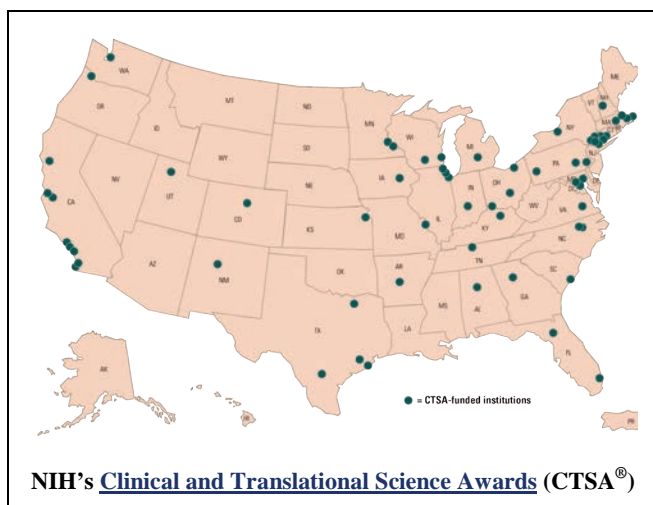


which NIH has a lead role. In this trial, involving up to 3,000 patients with different types of advanced solid tumors and lymphomas, researchers will analyze a patient’s tumor for “actionable” genetic abnormalities and use that information to select molecularly targeted drug(s) most likely to work for that particular patient.



Other innovative approaches with precise therapeutic potential include gene therapies, including approaches aimed at correcting vision and hearing loss; cell-based therapies; and gene editing systems. In a recent proof-of-concept study, NIH-funded researchers paired the latter two technologies to develop a potential cure for sickle cell disease, a painful, life-threatening disorder caused by mutations in the beta globin gene. To accomplish this, the researchers generated induced pluripotent stem cells (iPSCs) derived from the white blood cells of people with sickle cell disease; used CRISPR/Cas9 gene editing to replace the mutant gene; and then converted the iPSCs into normal red blood cells. If the technology proves safe and effective in additional pre-clinical and clinical tests, gene-corrected red blood cells could be generated from individuals with sickle cell disease and used for transfusions, reducing need for donor blood and providing hope for an eventual cure.

Along with advances in basic and translational research, advances in clinical research are essential to NIH’s efforts to catalyze the development of treatments and cures. To move clinical science forward, NIH will seek to foster and reward innovations in the design, execution, and management of clinical studies.



One of the primary ways in which NIH will encourage innovation in the clinical research enterprise is through its support of the [Clinical and Translational Science Awards program](#), which is a national network of institutions engaged in developing and testing new approaches for clinical research and training. To promote the effective research use of clinical data, NIH will engage in efforts to create and implement health data standards in electronic health records and health

information exchange systems. The agency will also back the development of alternative clinical trial designs that permit flexibility, while maintaining the utmost priority of patient safety. NIH will also work closely with its sister HHS agencies, including FDA, AHRQ, and CDC, to improve clinical research methodologies in a variety of important areas, such as identifying new approaches for [combating antibiotic-resistant bacteria](#) and [timely reporting of clinical trial results](#). These and other steps will increase the rate at which clinical research findings inform current areas of scientific inquiry and stimulate entirely new avenues for biomedical research, which could in turn spark ideas for further treatment and prevention strategies.

Despite the many exciting scientific opportunities for speeding the development of treatments and cures, significant challenges remain. Over the next 5 years, NIH will support research aimed at addressing a wide range of obstacles that lie at various points throughout the therapeutic development process. NIH will strive to forge new connections across research disciplines to advance understanding of molecular mechanisms and discovery of treatments and cures for a wide range of illnesses. Systems-based and interdisciplinary approaches are vital to making progress toward treatments tailored to individual patients. To improve the efficiency, relevance, and accuracy of preclinical research, NIH will catalyze powerful innovations, including molecule cross-coupling methods that will open a vast new frontier of “chemical space” and human 3D organoid technologies that will be better than animal models. Through its National Center for Advancing Translational Sciences, NIH will continue to support efforts to transform and accelerate the translational process, using science to find new ways to bridge the gaps and get more treatments to more patients more quickly. NIH will also work to speed and streamline clinical trials by encouraging the use of molecular knowledge to select the individuals most likely to respond to experimental therapies, and promoting respect for research volunteers through steps such as the updating of the [Common Rule protections](#) for human subjects research.

Health Promotion and Disease Prevention

Along with basic research and research aimed at developing treatments and cures, NIH supports research to promote health; to prevent diseases, disorders, conditions, or injuries; and to detect and/or prevent progression of asymptomatic disease. This broad and deep research portfolio encompasses studies of biology, behavior,

environment, and health-related policies. Among the many advances in this area are identification and assessment of risk and protective factors; screening and identification of at-risk individuals/groups, (e.g., human papilloma virus testing for cervical cancer screening); development and evaluation of risk-reduction strategies; and translation, implementation, and dissemination of preventive interventions, (e.g., Sudden Infant Death Syndrome campaign).

While NIH supports its own distinct and robust research portfolio, it collaborates with CDC, AHRQ, the Health Resources and Services Administration (HRSA), and other HHS agencies



Ebola Vaccine Research. The U.S. and Liberian governments are partnering with several pharmaceutical firms and other organizations to test effectiveness of several vaccine candidates.

involved in complementary activities related to health promotion and disease prevention, including efforts in dissemination and implementation. Recent collaboration between CDC and NIH on surveillance and initiation of clinical trials of [candidate vaccines against Ebola](#) virus disease in West Africa is one noteworthy example. Likewise, NIH, in collaboration with other HHS agencies, is playing a key role in the implementation and dissemination of the [HHS Secretary's new multi-pronged, evidence-based initiative](#) to combat the use of opioid drugs.



Environmental influences on Child Health Outcomes (ECHO)

Focus Areas

- Upper and lower airway
- Obesity
- Pre-, peri-, and post-natal outcomes
- Neurodevelopment



This NIH-funded initiative will bring together multiple existing research cohorts to investigate environmental and genetic influences on pediatric health. Data collection will include demographics, descriptors of early health and development, genetic background, a broad range of environmental factors, and other outcomes reported by patients and caregivers. A significant additional element will be an IDeA States Pediatric Clinical Trials Network.

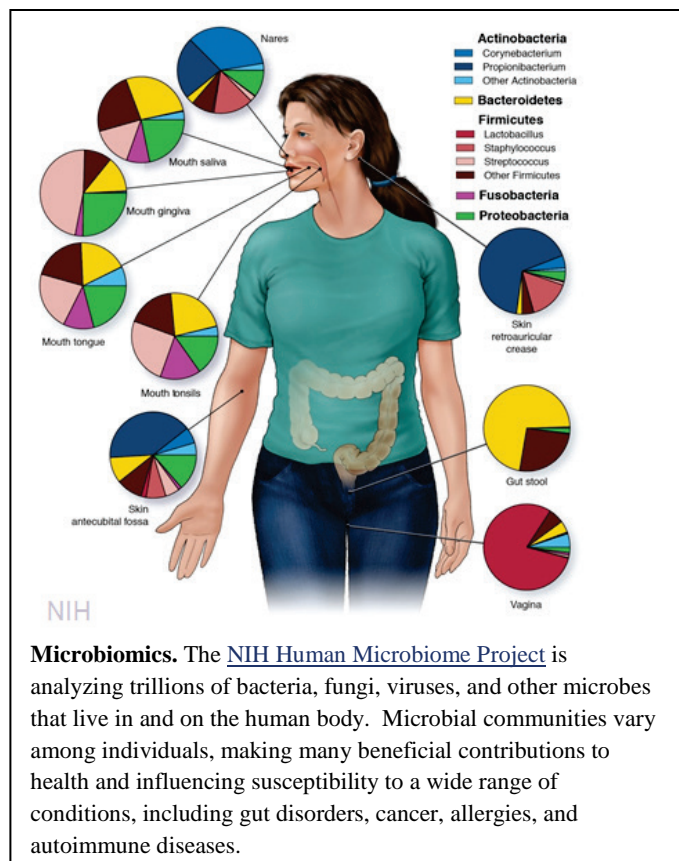
Over the next 5 years, NIH's health promotion and disease prevention efforts will place particular emphasis on research in several key areas: studying healthy individuals across the lifespan; applying technological advances in early detection, diagnosis, and prevention; and utilizing evidence-based interventions to reduce health disparities.

NIH will promote research on healthy development and aging, as well as on understanding disease susceptibility and prevention across the life span. A lifetime

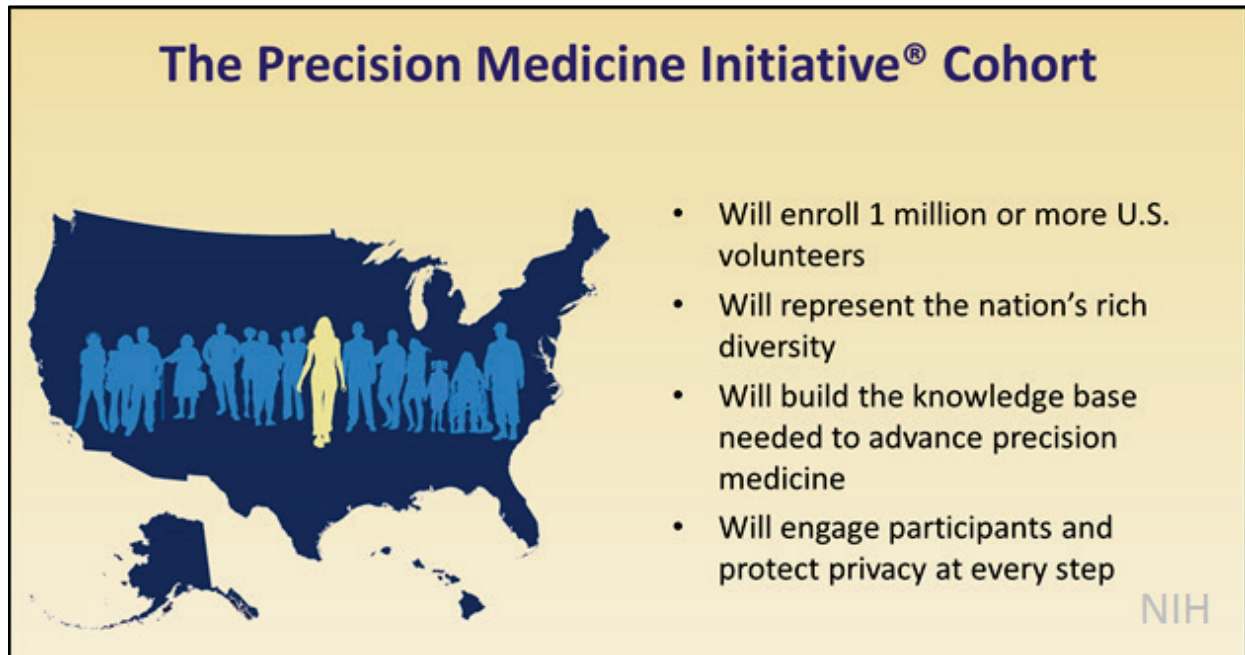
of benefits will result from efforts to establish healthy behaviors early in life and to identify and prevent the mechanistic antecedents to chronic conditions that begin during pre-, peri-, or post-natal periods of development. One example of this is NIH's new [Environmental influences on Child Health Outcomes \(ECHO\) initiative](#). To understand how things can go wrong in the human body, it is essential to understand how things work when everything goes right. For example, studies of normal embryonic development have informed efforts to understand, prevent, and treat birth defects caused by genetic and a broad range of environmental factors.

In another example of research aimed at health promotion and disease prevention, NIH will expand efforts to track the composition of microbial communities over the course of an individual's life. Such action is motivated, in part, by the explosion in understanding of the role played by the microflora in the development of the immune system.

To make similar advances in other areas, NIH will continue to support research into the basic mechanisms of development and aging in healthy individuals. This will



include intensifying studies of “resilience”—that is, to understand why some individuals’ bodies age more slowly and/or are better able to resist disease risks posed by particular genetic, lifestyle, and/or environmental factors. NIH will also strive to develop tools to enhance measurement of physical, social and environmental exposures, as well as to assess the impacts of such exposures on development, health, and longevity. In addition, NIH-funded research will explore why people make unhealthy or risky choices, generating valuable information for devising risk reduction and/or early intervention strategies.

The graphic features a dark blue silhouette of the United States map. Inside the map, there is a group of stylized human figures in various colors (red, green, blue, yellow, purple) representing diversity. To the right of the map, there is a list of four bullet points. The NIH logo is in the bottom right corner of the graphic.

The Precision Medicine Initiative® Cohort

- Will enroll 1 million or more U.S. volunteers
- Will represent the nation’s rich diversity
- Will build the knowledge base needed to advance precision medicine
- Will engage participants and protect privacy at every step

NIH

Technological innovations will also be instrumental for research aimed at making advances in the early detection, diagnosis, and prevention of disease. At the forefront of this effort will be the NIH-led [PMI cohort](#). Taking advantage of emerging biomedical tools and technologies, such as availability of electronic health records, DNA sequencing, and exposure monitoring, PMI’s longitudinal research cohort of 1 million or more U.S. volunteers will establish a base of scientific knowledge that can be used to develop prevention and screening strategies tailored to individuals at the most opportune times across the course of their lives.

PMI will also take advantage of the latest methods and approaches in data science, including advances in large-scale databases, computational tools, and -omics methodologies to characterize individuals. In addition, PMI will offer researchers the ability to test whether mobile technologies are useful in adapting preventive strategies to individuals’ needs and preferences, enhancing delivery of interventions, and improving monitoring of compliance and outcomes. PMI will [pioneer efforts to merge, integrate, and analyze data](#) from a wide variety of sources with implications for prevention, including basic biological data, health status



mHealth. Capitalizing upon advances in mobile health (mHealth) technologies, the PMI research cohort will use smart phones, along with other mHealth devices and applications, to correlate activity, physiologic measures, and environmental exposures with health outcomes. mHealth will also give PMI participants ready access to data and information to improve their own health.

information from electronic health records, individual data on environmental exposures, geospatial data on community environmental exposures, and so on.

NIH will also build upon ongoing efforts to develop better methods for screening, assessing, and identifying those at risk for onset or progression of asymptomatic diseases/disorders. One notable success in the realm of prevention of a common, chronic disease is the [NIH-led Diabetes Prevention Program \(DPP\) trial](#), which involved overweight or obese U.S. adults

with prediabetes. DPP researchers found that exercise and dietary changes leading to modest weight loss (5%-7% of body weight) could prevent or delay development of type 2 diabetes. Furthermore, the prevention program was shown to be effective in both men and women and all racial/ethnic groups studied, including those disproportionately burdened by obesity.

Also needed are molecular, cellular, and imaging technologies that provide greater power to identify diseases and conditions in early, more readily treatable states before they progress to symptomatic or metastatic disease. To further facilitate early diagnosis and detection, NIH will encourage the development of point-of-care technologies that lead to less costly, more rapid results, and improved patient outcomes.

NIH will also cultivate efforts to provide clinicians and researchers with access to efficient, precise, and valid patient-reported measures of health and well-being. For example, NIH currently supports the [Patient-Reported Outcome Measurement Information System® \(PROMIS®\)](#), which is using measurement science to create a state-of-the-art assessment system for self-reported health.

Vaccines—one of biomedicine’s most powerful tools for preventing and eradicating disease—also are heavily reliant upon NIH-funded research and innovation. Over the next 5 years, NIH will take advantage of its intramural [Vaccine Research Center](#), along with its network of [Vaccine and Treatment Evaluation Units](#) located across the nation, to support the full spectrum of vaccine development from early discovery to clinical evaluation for a wide variety of infectious diseases.

Particular emphasis will also be placed upon innovative approaches, such as a universal influenza vaccine and other DNA-based vaccines, to improve protection and optimize production.

NIH also will promote health and encourage disease prevention by facilitating collaboration across biomedical, behavioral and social sciences, as well as disciplines not traditionally considered to involve health, such as architecture, transportation, and urban planning. Although many behaviors that increase disease risk have been

identified, more effective approaches to promoting behavior change are still needed. Basic, behavioral, and social sciences research can inform new strategies for preventing distinct conditions caused by high-risk behaviors that share an underlying basis. One example is the wide range of cancers and other diseases associated with use of various forms of tobacco.

Importantly, NIH will continue to pursue research aimed at developing evidence-based interventions to reduce health disparities. Such efforts will address the importance of understanding social determinants of health, disease, and disability; disproportionate disease risk; and opportunities for progress in prevention. For instance, an [NIH-supported study](#) of women who received housing vouchers that enabled them to move from high-poverty to low-poverty neighborhoods found that such women were less likely to be obese or have diabetes than similar controls. NIH-funded research will also evaluate methods to disseminate evidence-based interventions to promote health and prevent disease—with particular emphasis on comorbid conditions—in a variety of community health and clinical settings, as well as identify barriers to adoption of such interventions. Understanding mechanisms that lead to disparities in health outcomes by race/ethnicity and socioeconomic status will require multi-disciplinary collaboration of population, clinical, and basic scientists. An NIH-wide assessment of current minority health and health disparities research using standardized coding will inform the development of a strategic plan to guide this emerging scientific area.

Health promotion and disease prevention clearly represent a critical facet of the NIH mission and its aim of improving the health of whole populations. It is imperative that NIH act upon opportunities to advance this vital area, which is complementary to the discovery of treatments and is integral to the entire biomedical research continuum.

NIH Universal Flu Vaccine

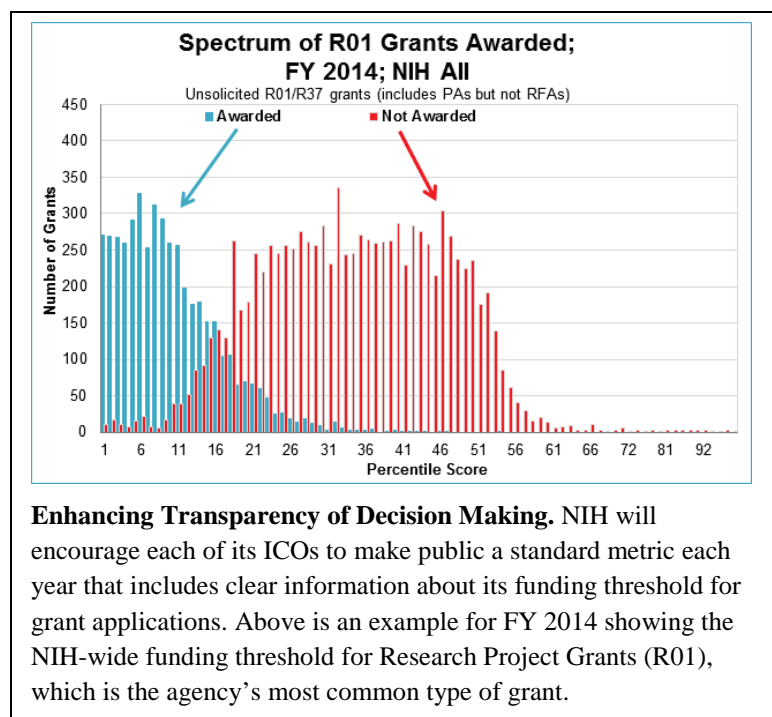
- Up to **50,000** U.S. deaths associated with flu annually
- **\$87 billion** in economic costs
- Protection currently involves getting a flu shot **every year**
- Vaccine manufacture takes **6 months**; requires predicting this year's flu strain before production

Thanks to improved understanding of an influenza surface protein called hemagglutinin A (HA), vaccine researchers are targeting a part of HA that remains relatively constant among different strains of the flu virus.

Objective 2: Foster Innovation by Setting NIH Priorities

In order for NIH to achieve its mission, it must serve as an effective and efficient steward of public resources. To advance these efforts over the next 5 years, NIH will focus intensely on prioritization. The process of setting NIH's research priorities must balance the opportunities presented by the best science, public health needs, and the unique ability of NIH to address challenges in human health that would otherwise go unmet. These priorities, which will require NIH's constant review and adjustment, must be flexible and based on the best science of the moment; formulas and fixed percentages are inconsistent with NIH's efforts to carry out its mission in an effective and efficient manner that is driven scientifically.

NIH has long relied upon a multifaceted approach for funding decisions that involves peer review by scientific experts to determine scientific merit of a research proposal, review for program priority by a second set of scientific experts and thought leaders from the lay public serving on ICO national advisory councils, individual ICO strategic plans, and, ultimately, the scientific expertise of ICO Directors, informed by their staff. NIH will continue and strengthen its commitment to a transparent, evidence-based process that encompasses these action-oriented principles: enhance the nimbleness needed to meet public health needs and capitalize upon scientific opportunity, using new portfolio analysis tools; incorporate burden of disease as an important, but not sole, factor; take advantage of opportunities presented by rare diseases to advance research; and consider the value of permanently eradicating a disease.



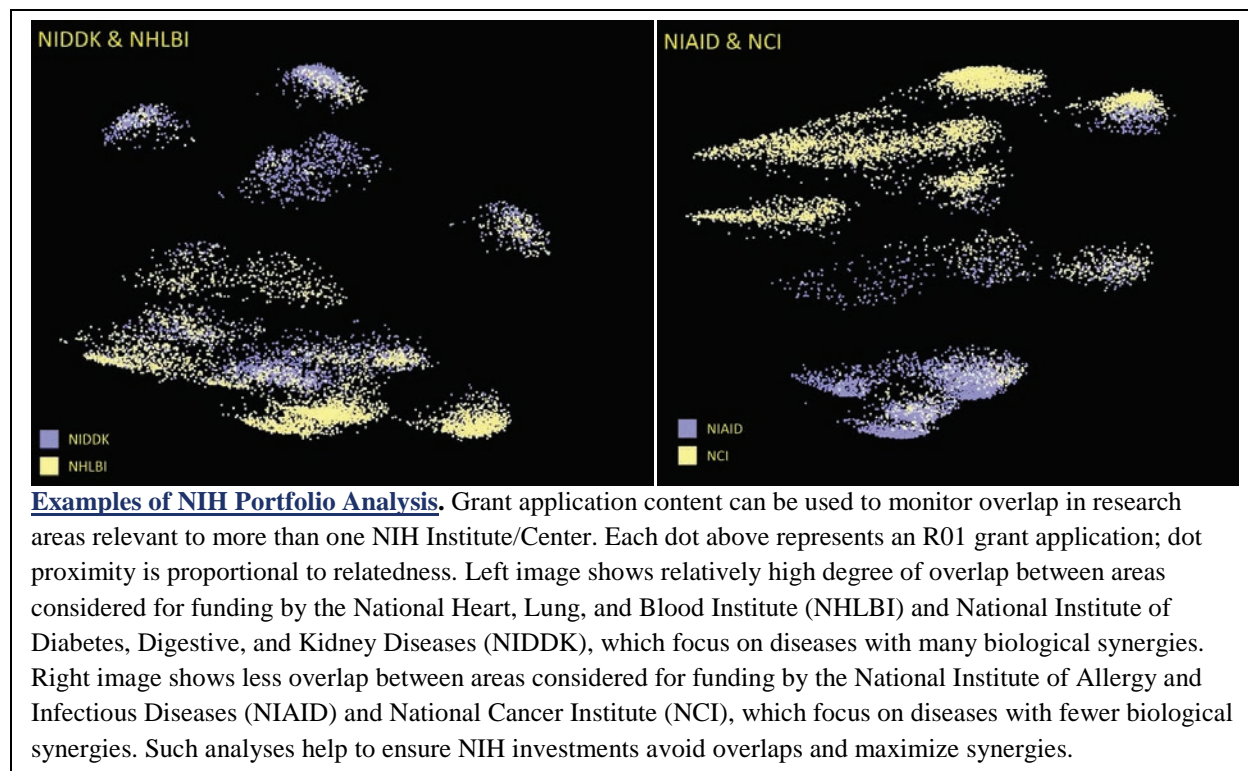
Going forward, NIH will take additional steps to enhance the transparency of its decision process by making public a standard metric for funding each year. NIH will also harmonize approaches to decision making by ensuring ICOs set their individual paylines—the funding cutoff point for grant applications based solely upon peer-review scores—to provide maximum flexibility for use of the select pay option. Select pay refers to funds set aside to support grant applications that, based upon scores from peer

review, do not fall within the payline, but that fill an important research gap and/or are of particular programmatic relevance to an ICO's scientific and health priorities. Final decisions on

the use of select pay are made by the NIH ICO Directors following discussions with their Advisory Councils and appropriate ICO staff.

Enhance Nimbleness. NIH and all of its ICOs will nurture the nimbleness necessary to shift resources in response to unexpected scientific breakthroughs, to capitalize on scientific opportunities on the horizon, and to address emerging public health needs. Advancing human health requires taking advantage of scientific opportunities as they arise. It is important to recognize that different scientific fields mature at different rates, and the same amount of funding in two fields can lead to very different scientific returns.

To help inform these decisions, NIH will explore the strengths and weakness of different types of grant programs, along with other funding mechanisms, to identify optimal approaches. Among the nimble approaches currently at NIH's disposal are Other Transaction Authority, which enables support of high-risk, milestone-driven research supported through the NIH Common Fund and various ICOs; [fast-track review](#) of Small Business Innovation Research and Small Business Technology Transfer awards, in which Phase I and Phase II grant applications are reviewed together, reducing funding gaps between phases; and various scientific challenge prizes, which include competitions to encourage development of novel methods for [analyzing individual cells](#); point-of-care diagnostics for [antibiotic-resistant infections](#); and [new products or services to harness the power of Big Data](#) to improve health. Of course, it requires more than investment to drive biomedical progress—scientific opportunities also need to be present. To enhance surveillance of the scientific landscape, NIH will utilize a network of internal and

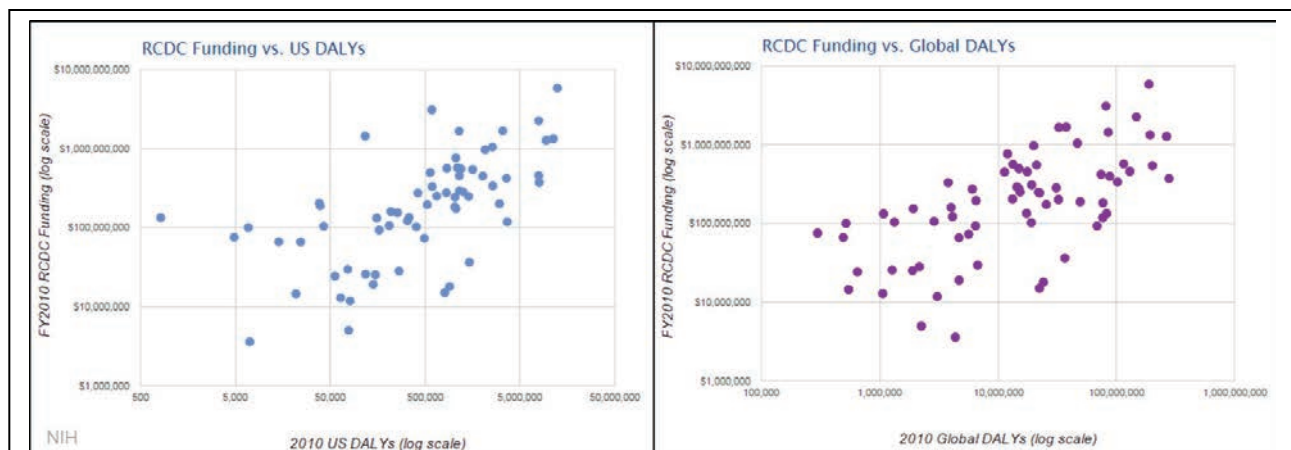


external expertise, and will continue to develop, improve, and use new tools for portfolio analysis to identify scientific opportunities, high-performing areas of research, and areas of potential overlap among ICOs. To further empower its ability to monitor highly active or emergent areas of public health concern and scientific opportunity, NIH will train staff in the effective analysis of social media trends and other nontraditional sources of information.

A recent example of how NIH's rapidly responsive flexibility has served to address an urgent public health crisis is its pivotal role in the development and accelerated clinical testing of a [vaccine against the deadly Ebola virus](#). Likewise, NIH's nimbleness in the face of unexpected scientific breakthroughs has enabled it to take a leadership role in the [BRAIN Initiative](#)[®], which has the ambitious goal of producing the first dynamic picture of the human brain, showing how individual cells and complex circuits interact in both time and space.

Consider Burden of Disease. The relative burden that various diseases place upon human health and wellbeing will serve as a crucial, but not the only, consideration in aligning NIH's research priorities with public health needs. To this end, NIH will work with its many partners, including CDC, to strengthen the collection of high quality, comparable data on the burden of disease and will integrate analyses of such data into its priority setting process.

It must be emphasized that there currently are multiple types and sources of disease burden data, and these data vary depending on whether researchers measure death or disability, direct or indirect economic costs, and domestic or global populations. However, none of these measures incorporates the cost of conducting basic research, which is essential for finding interventions. Another important variable is the degree to which subjective judgments factor into the process, making it extremely difficult to compare all diseases and conditions with a



Disability Adjusted Life Years Compared to NIH Spending. Understanding the burden of disease is a vital consideration for setting NIH's research funding priorities. These graphs show how NIH's FY 2010 funding levels for a variety of diseases and conditions (RCDC) related to U.S. and global disability-adjusted life years (DALYs)—a measure that quantifies the number of healthy years of life lost due to morbidity or premature mortality caused by disease. Such data can help NIH monitor the public health landscape for unmet needs and emerging challenges.

single measurement. Additional caveats regarding the use of current disease burden datasets to establish research priorities include the lack of patient-derived assessments and inconsistent accounting of the burden on caregivers. Finally, it is imperative to keep in mind that current burden of disease does not necessarily predict future burden of disease.

Advance Research Opportunities Presented by Rare Diseases. If NIH had used burden of disease as the sole determinant for setting its priorities over the past century, rare disease research, in all likelihood, would have been seriously neglected. While any given rare disease affects a relatively low number of people, such conditions represent a significant health problem when they are considered together, affecting some 25 million Americans collectively.

In recent years, FDA approvals of “[orphan drugs](#)” to treat diseases and disorders affecting fewer than 200,000 people in the United States have been increasing. However, effective treatments are lacking for many rare diseases, constituting an important public health need that NIH research still needs to address. Besides helping individuals affected by rare diseases, such research can provide insights that spill over into other, more common diseases and greatly enhance understanding of healthy physiology. For example, studies of the molecular mechanisms involved in a very rare premature aging condition called progeria have revealed [valuable insights into the normal aging process](#).

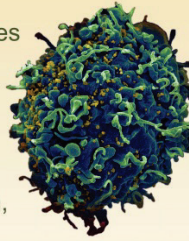
NIH is uniquely situated to tackle the challenges, as well as capitalize on the opportunities, presented by rare diseases over the next 5 years. In contrast to the typical situation in private industry, public funding enables researchers to pursue scientific questions, such as those posed by rare diseases, on the basis of opportunity, not just perceived market value.

Consider the Value of Permanently Eradicating a Disease. Achieving the complete cure or eradication of any disease is one of the ultimate goals of medical research. While each year brings NIH-funded science closer to improved treatments for any number of diseases and conditions, the ability to completely remove the threat of a single disease from the face of the Earth is a rare opportunity. Just think of the monumental effort it took to eradicate smallpox and how, even after decades of intense vaccination campaigns, the world is just now on the verge of eliminating polio.

Biomedical research stands at another such pivotal moment today: [the very real possibility of entirely eliminating HIV/AIDS](#). Decades of robust investment in HIV/AIDS research has resulted in extraordinary improvement in the health of infected individuals, and NIH now plans to support the best science to eliminate HIV/AIDS as a public health threat domestically and globally. While the traditional, non-statutory 10% set aside for HIV/AIDS research, overseen by the Office of AIDS Research, was an appropriate response to the crisis more than two decades ago, NIH no longer sees the value in this formula-driven approach. That does not mean taking

HIV/AIDS Research Priorities

- Reduce incidence, including vaccines
- Safer, easier-to-use therapies
- Work toward a cure
- HIV-associated comorbidities, co-infections
- Cross-cutting areas: Basic research, health disparities, training



Over the course of the next 3-5 years, NIH-supported HIV/AIDS research will center on the scientific opportunities that are most likely to contribute to: ending the AIDS pandemic, developing a cure for HIV/AIDS, taking care of people who are already infected, and achieving an AIDS-free generation.

the foot off the accelerator, however. To seize this unique moment, NIH will [prioritize its research efforts](#) to end the worldwide scourge of HIV/AIDS and usher in the first AIDS-free generation in more than half a century.

Not only does this research strategy hold out the hope of eliminating the death and suffering caused by this worldwide epidemic, it makes good economic sense: every new case of HIV diagnosed in the United States (currently, about 50,000

per year) translates into a lifetime cost of approximately \$350,000 for treatment with antiretroviral drugs. Getting to zero new cases of HIV/AIDS would save our nation an estimated \$17.5 billion annually.

As NIH takes these and other factors into account in setting biomedical research priorities, it is imperative that the agency be judicious and transparent in decisions about investing the monies entrusted to it by the American public. Going forward, NIH will consider using the previously described HIV/AIDS research prioritization process as a potential model approach for shaping its research focus in other scientific areas. Through concerted efforts to improve and refine key priority-setting activities, the agency is committed to increasing the already high rate of return that NIH-supported research delivers to the nation in the form of scientific advances and improved human health.

Objective 3: Enhance Scientific Stewardship

To achieve its mission and maintain its role as the world’s premier biomedical research agency, NIH must support the best scientific ideas and brightest scientific minds while, at the same time, earning and maintaining public trust. NIH’s role as a steward of public resources also requires not only supporting innovative research, but also fostering innovation across the entire research enterprise by enhancing individual and collective scientific stewardship. NIH must live up to the commitment that every dollar is being spent in a way that maximizes long term public benefit. Over the next 5 years, NIH will take several significant steps to strengthen and sustain its most valuable resource—the scientific workforce—and to strive for the highest level of scientific integrity, public accountability, and social responsibility in the conduct of science.

Recruit and Retain an Outstanding Biomedical Research Workforce. To ensure that the nation cultivates a thriving and talented next generation of scientists, NIH will seek ways to [strengthen the biomedical research work force](#). Such efforts will include improving the outlook and opportunities for new and early stage investigators through policies and grant mechanisms that are designed to support investigators at the outset of their careers. NIH will continue to take steps to enable exceptional early career scientists to flourish independently by bypassing the traditional postdoctoral training period, to bridge the gap from early- to mid-career investigator, and to normalize grant success rates between early stage investigators and more experienced investigators. For example, within the next 4 years, NIH will be evaluating its Early Independence Awards program to gauge its success in fostering independent and productive research careers.

Another way in which NIH will aim to ensure that all of America develops and maintains an outstanding biomedical research workforce is through its [Institutional Development Award \(IDeA\) program](#). By broadening the geographic distribution of NIH funding for biomedical research, the IDeA program fosters health-related research and enhances the competitiveness of researchers at institutions located in states in which the aggregate success rate for grant applications to NIH has historically been low. Such activities also benefit unique populations—such as rural and medically underserved communities—in Puerto Rico and the 23 states that are currently part of the IDeA program.

NIH will also continually evaluate the effectiveness of its scientific training programs and efforts. For example, it will identify and target specific areas of biomedical research in which workforce training should be tailored to meet growing needs, including revitalizing physician-scientist training, fostering recruitment to expand the data science workforce, and promoting the cross-training of basic scientists, clinical scientists, and physician-scientists to facilitate the development of inter- and cross-disciplinary research teams and to stimulate translational research. Furthermore, NIH will promote innovative training programs to prepare trainees for

the wide spectrum of career options that will be available in tomorrow's biomedical research workforce. For example, the recently established [Broadening Experiences in Scientific Training \(BEST\)](#) program will enhance training for graduate students and postdoctoral scholars to prepare them for careers outside of conventional academic research. Ultimately, a stable, predictable funding stream is needed to attract and retain new talent for the research workforce.



[Enhancing the Diversity of the NIH-Funded Workforce Program.](#)

Through this national collaborative, the Diversity Program Consortium, in partnership with NIH, will develop, implement, and evaluate innovative approaches to research training and mentoring. The goal is to engage individuals from diverse backgrounds and help them prepare for and succeed in biomedical research careers.

Enhance Workforce Diversity. NIH strongly believes that diversity in the biomedical research workforce is critical to producing new scientific discoveries. From NIH's vantage point, racial and ethnic diversity is paramount. It is also important to pursue diversity in other areas, including sex and gender, socioeconomic status, geographic location, and disability status.

In an effort to understand why the biomedical workforce does not reflect the diversity of the Nation, NIH sponsored a [landmark study](#) that demonstrated a disparity in R01 funding to African-American/Black applicants. Importantly, NIH has launched a broad range of efforts to redress this untenable situation, including a thorough analysis of potential biases in peer review and experiments in anonymized review. Under the leadership of its first [Chief Officer for Scientific Workforce Diversity](#), NIH will work to implement the [recommendations](#) of the Advisory Committee to the Director's Working Group on Diversity in the Biomedical Research Workforce. This comprehensive strategy aims to enhance scientific workforce diversity, engaging partners from academia and industry to achieve diversity at all stages of biomedical research career trajectory.

Examples of [new NIH programs that are part of this strategy](#) are the BUilding Infrastructure Leading to Diversity (BUILD) initiative, which has the long-term goal of catalyzing cultural changes at academic institutions so that talented students from groups historically

underrepresented in biomedical research are well-prepared to enter research careers, and the NIH National Research Mentoring Network (NRMN), which will facilitate the development of robust mentoring relationships by pairing scientific leaders with early career scientists from underrepresented groups across the nation. A unique attribute of these programs is that they are being run as a “trial” with a data-coordinating center, collecting common measures across all programs. In this manner, NIH will be able to identify subsets of “best practices” and then swiftly apply them across the network. These best practices will also be used to inform enhancement of other programs that are designed to enhance diversity of the biomedical research workforce.

Ensure Rigor and Reproducibility. As a global leader of biomedical research, NIH has a responsibility for maintaining and bolstering the public’s confidence in research results. To uphold this responsibility, NIH will take the lead in promoting [new approaches](#) toward enhancing the rigor of experimental design, analysis, and reporting. These efforts are not aimed at rare instances of research misconduct or willful deception, which require separate oversight mechanisms, but are intended to improve the biomedical research community’s overall culture and training to encourage best practices for rigorous scientific methods.

NIH recently initiated several activities aimed to encourage transparency and [reproducibility of research results](#). Over the next 5 years, NIH will build upon these activities, which include: discussing ways to improve rigor and reproducibility with science journal editors; establishing principles and guidelines for reporting preclinical research; emphasizing the importance of studying sex differences and incorporating sex as a variable in preclinical research; developing training modules and curriculum for the next generation of scientists on approaches to enhance

Clinical Trials Data Sharing

- Provide a way for patients and the public to find trials of interest to them
- Inform future research, improve study design, enhance the evidence base, and prevent duplication of unsafe or unsuccessful trials
- Fulfill an ethical responsibility to people who volunteer to participate in research
- Affirm public trust in clinical research



NIH has a responsibility to share clinical trials data while safeguarding the interests of researchers and research participants. HHS has proposed regulations to implement reporting requirements for clinical trials subject to Title VIII of the Food and Drug Administration Amendments Act of 2007. NIH also has proposed a policy to promote transparency for all NIH-funded clinical trials.

reproducibility of their research; ensuring compliance with policies for open access to the published literature and data sharing; and continuing to [expand the studies included in the NIH-supported ClinicalTrials.gov](#) results database to improve dissemination of clinical trial results. Moving forward, NIH will continue to develop and promote other innovative initiatives to promote scientific rigor across the entire biomedical research enterprise.

Reduce Administrative Burden. NIH is committed to streamlining its reporting

processes to reduce the administrative burden on its grantees as much as possible, while maintaining the agency's necessary oversight role. These actions have been informed by recommendations from a 2015 report from an ad hoc committee of The National Academies of Sciences, Engineering, and Medicine, "[Optimizing the Nation's Investment in Academic Research: A New Regulatory Framework for the 21st Century, Part 1](#)"; and a 2012 report from the National Research Council's Committee on Research Universities, "[Research Universities and the Future of America: Ten Breakthrough Actions Vital to Our Nation's Prosperity and Security](#)." NIH has already made changes to many steps throughout the grant award process to optimize the system as much as possible, but there is no easy, one-size-fits-all solution. Over the next 5 years, NIH will continue to evaluate opportunities to streamline and automate this process to allow scientists to focus their attention first and foremost on their research.

Optimize Approaches to Inform Funding Decisions. At NIH, the crucial, initial assessment of a grant application's scientific merit is conducted through the agency's highly respected peer review system. Still, there is always room for further optimization. During FY 2016-2020, NIH will step up efforts to make its peer review and post-grant award system even stronger by: enhancing diversity and fairness; optimizing the process for promoting interdisciplinary and team science; and voicing an expectation that all NIH grantees serve on NIH peer-review study sections when asked, thus ensuring that every researcher "gives back" to the scientific enterprise as a whole.

NIH leadership will also encourage sharing of best practices in portfolio analysis and strategic planning among ICOs. Individual ICOs play a key role in funding decisions through their Program Officers, who field grant applicants' inquiries and manage specialized portfolios of grants; their National Advisory Councils, which provide a second level of review for scientific merit; and their Directors, who have the ultimate authority over funding decisions. To help inform these decisions, NIH will continue to explore the efficacy of different funding approaches—comparing mechanisms to ascertain if their strengths and weaknesses and analyzing whether there is an optimal threshold of funding for research groups via RPG mechanisms.

Since it is virtually impossible to predict where the next great breakthrough will emerge, NIH places a heavy emphasis on maintaining a diverse and broad portfolio. However, NIH currently uses the number of projects that it supports as the key metric in assessing program breadth. Emergent data suggest that on average, there are optimal levels of funding for research groups, beyond which, there is only minimal increase in return. NIH must therefore decide if portfolio breadth would be best achieved through an increase in the number of investigators that it supports as opposed to the number of projects it supports. Over the next 5-year period, pilot programs will be put in place to test this important question.

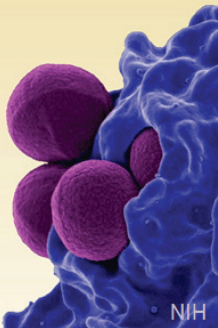
Encourage Innovation. As part of its responsibility to be a wise steward of the resources provided by the American public, NIH will catalyze innovative research through novel funding mechanisms, groundbreaking initiatives, and creative policy approaches. One major way in which NIH will accomplish this is by promoting high-risk, high-reward research through intensely competitive programs that fund individual investigators with the most promising cross-cutting research or ideas. Such programs include the [NIH Common Fund’s New Innovator, Pioneer, and Transformative Research Awards](#), the [National Institute of General Medical Sciences’ Maximizing Investigators’ Research Award](#), the [National Cancer Institute’s Outstanding Investigator Award](#), the [National Institute on Drug Abuse’s Avenir Awards](#), and the [National Institute of Environmental Health Sciences’ Method to Extend Research in Time Awards](#). There is growing evidence that such approaches are working, with a [2012 independent review of Pioneer awards](#) concluding that these awards resulted in higher impact and more innovative research relative to the traditional R01 award.

NIH will also support innovative short-term initiatives that take advantage of emerging technologies to focus resources on specific high-impact, trans-NIH basic research questions, such as those posed by the BRAIN Initiative® and various Common Fund initiatives. On the translational and clinical front, NIH will encourage innovative clinical trial design and data-sharing activities through collaborative efforts with the FDA and other stakeholders. In addition, NIH will continue to facilitate communication and coordination among clinical researchers about new trial designs and best practices, whether at the level of policies for funded researchers, interdisciplinary working groups, or clinical trial networks.

Enhance Impact through Partnerships. To increase the reach of NIH-funded research, NIH will leverage its resources by partnering with other organizations in the public and private sectors. Not only do such partnerships enable NIH to make maximum use of finite resources, they can lead to sector-spanning synergies that result in creative new ways of fulfilling NIH’s mission. This will include building on current efforts within NIH to capitalize upon trans-disciplinary knowledge, as well as fostering mechanisms to establish new collaborations. As part of this activity, NIH will work closely with FDA, CDC, AHRQ, HRSA, SAMHSA, and other HHS and federal agencies that will provide the necessary knowledge and expertise to

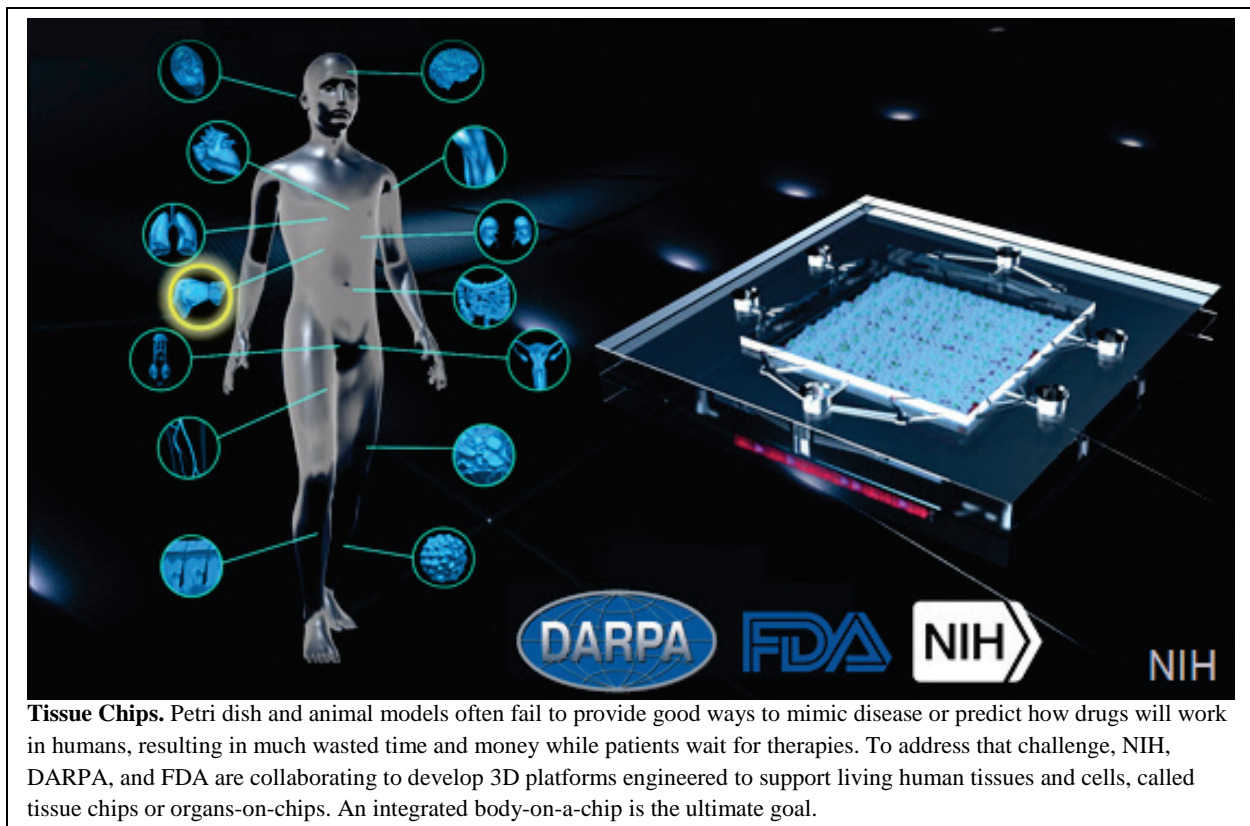
Antimicrobial Resistance Point-of-Care Diagnostics

- Urgent need for rapid tests for resistant bacterial infections
- Such tests would guide antibiotic selection, use
- \$20 million prize to encourage test development



One goal of the cross-agency National Strategy for Combating Antibiotic-Resistant Bacteria is to advance the development and use of rapid diagnostics for highly resistant bacterial infections. In addition to supporting multiple research projects aimed at enhancing diagnostics, NIH plans to offer a challenge award of up to \$20 million to the first group(s) to develop a rapid, point-of-care test that can be easily used by health care professionals in real-world settings.

help translate NIH research findings into new drugs, technologies, and evidence-based practices for improving health. For example, NIH recently partnered with other federal agencies to develop the [National Strategy for Combating Antibiotic-Resistant Bacteria](#). Also, NIH's National Institute of Allergy and Infectious Diseases leads an interagency workgroup on developing therapeutics and vaccines against the emerging global public health threat posed by the [Middle East Respiratory Syndrome Coronavirus \(MERS-CoV\)](#). Other federal agencies represented include CDC, FDA, Department of Defense, and Biomedical Advanced Research and Development Authority.



Other outstanding examples of cross-agency collaboration are the [Tissue Chip for Drug Screening program](#), in which NIH, FDA, and DARPA are collaborating to develop 3D human tissue chips that mimic human physiology. On another highly innovative front, the [Interagency Artificial Pancreas Working Group](#), in which the National Institute of Diabetes and Digestive and Kidney Diseases, the National Institute of Biomedical Imaging and Bioengineering, and the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development are working with FDA, patient advocates, and industry toward development of an artificial pancreas, which could be the most revolutionary advance in diabetes care since the discovery of insulin.

Patients, disease advocacy organizations, and community members at the local, state, and federal levels also are playing an increasingly significant role in spurring advances in biomedical

research. Consequently, NIH will embrace these and other members of the public as active partners in the research enterprise, with the aim of generating more effective—and more relevant—research outcomes. This will include seeking input from diverse volunteers at all stages of the research process, from study design to data collection and analysis. The PMI cohort will be among the NIH-led efforts pioneering this highly interactive, proactive participation model. Besides forging partnerships with individuals, NIH’s new model for research will underscore the importance of reaching out to previously underrepresented groups, consulting with communities, providing equal access to research studies and results, protecting patient privacy, and conducting research in an ethical and responsible manner.

Another important area of partnership that NIH will seek to encourage over the next 5 years is cultivating public-private partnerships with health-related industries, including small businesses, venture capital companies, biotech companies, and large pharmaceutical companies. Such efforts, exemplified by the [Accelerating Medicines Partnership](#), will bring

	Alzheimer's Disease	Type 2 Diabetes	Autoimmune Diseases
			
	Alzheimer's Disease	Type 2 Diabetes	Autoimmune Diseases
Industry members	   	    	     
Government members	 		 
Non-profit members	 GEOFFREY BEENE  	 	 Alliance for Lupus Research     

Accelerating Medicines Partnership®. This bold public-private partnership seeks to transform discovery and validation of therapeutic targets and biomarkers for complex diseases by integrating cutting-edge molecular profiling and big data analytical approaches. AMP currently has pilot programs for Alzheimer’s disease, type 2 diabetes, and the autoimmune diseases rheumatoid arthritis and lupus.

together the expertise and resources necessary to address the gap in the development pipeline between scientific discovery and the commercial marketplace, with the goal of turning breakthrough basic science discoveries into useful drugs and other biomedical products more quickly. Helping to facilitate NIH's public-private partnerships is the [Foundation for the National Institutes of Health \(FNIH\)](#), which Congress established in 1990 as an independent non-profit charged with supporting NIH's mission. For example, FNIH manages [The Biomarkers Consortium](#), which brings together industry, patient advocacy organizations, academia, and government agencies and institutes to develop and support research aimed at qualifying promising biological markers for use in diagnosing disease, predicting therapeutic response, or improving clinical practice. Current members include NIH, FDA, the Pharmaceutical Research and Manufacturers of America (PhRMA), the Centers for Medicare & Medicaid Services (CMS), and the Biotechnology Industry Organization (BIO), along with more than 30 companies and not-for-profit organizations.

NIH, in collaboration with AHRQ and other HHS agencies, will also seek to strengthen its existing ties to and forge new partnerships with clinicians and professional societies. Physicians, nurses, and other healthcare professionals, both individually and collectively, are essential for the design and implementation of NIH-supported research studies, the timely dissemination and implementation of evidence-based practices into healthcare, and the education of fellow clinicians, patients, and the general public about evidence-based interventions and treatments.

In addition to partnerships within the United States, NIH has a responsibility to reach out to partners that are integral to its efforts to address global health challenges and improve the health of all humankind. Such actions are not only consistent with our nation's scientific and humanitarian values, but are frequently in our own best interest because infectious diseases do not respect national boundaries. Forging such partnerships involves negotiating international collaborations with non-governmental organizations, private industry, and governments of other nations. These partnerships may serve to promote biomedical science, for example, by sharing samples and data, or by building research capacity, such as is being done in the [Human Heredity and Health in Africa \(H3Africa\)](#) initiative and



H3Africa. Zambian Deputy Minister of Health Chitalu Chilufya (middle, blue suit) welcomed members of the H3Africa Consortium to Livingstone, Zambia, for their sixth meeting on May 9, 2015. Also present were representatives of NIH and the Wellcome Trust.

the [Medical Education Partnership Initiative](#) in sub-Saharan Africa. Other globally oriented partnerships promote the implementation of research results, such as NIH's milestone-driven projects with the [Bill & Melinda Gates Foundation](#) to reduce premature births, improve maternal and infant nutrition, develop models to accelerate drug discovery for tuberculosis, design vaccines against HIV and other infectious diseases, and devise affordable point-of-care diagnostic technologies.

Engage in Proactive Risk Management Practices. To meet the evolving needs of an ever-changing and increasingly challenging biomedical research environment, NIH's risk management abilities will continue to grow and mature over the next 5 years. Using standardized approaches, NIH must systematically assess its administrative processes, operational procedures, and scientific programs, for potential risks that could lead to failure. The identified risks must be prioritized and then proactively addressed by applying appropriate human and monetary resources to minimize, monitor, and control the potential impact of these risks to the NIH mission.

Over the next 5 years, NIH will pursue these and many forward-looking measures to reinvigorate our role as a visionary, yet careful, steward of the resources entrusted to us by the American people. Such actions will ensure that the U.S. biomedical research enterprise remains firmly on the pathway to a bright and sustainable future.

Objective 4: Excel as a Federal Science Agency by Managing for Results

As a public science agency, NIH is obligated to use transparent, scientific approaches in its decision making. Ultimately, NIH is accountable to the American people, who have every right to expect all of their government agencies not only to perform, but also to excel. To fulfill this responsibility in a thoughtful manner that goes beyond one-size-fits-all solutions, NIH will build upon its strong tradition of excellence by managing for results in the following ways:

Develop the “Science of Science.” NIH will take greater leadership in developing and validating the methodologies that are needed to evaluate scientific investments. For example, new approaches to portfolio analyses have been devised that allow for a rapid assessment of potential overlap and gaps.

Over the next 5 years the portfolio of each ICO will be compared to one another as well as those agencies and foundations for which grant portfolio data is available. NIH has also promoted more robust bibliometric measures through development of [disambiguation tools](#) and a [normalized citation metric](#) termed the Relative Citation Ratio (RCR). In addition, the agency is considering outside bibliometric approaches, such as those developed by the [Eigenfactor® Project](#). However, more tools are clearly required to help NIH better assess what value each grant in its portfolio provides and to test whether the mechanisms that it is employing for supporting investigators is optimal. For example, several recent [studies](#) have suggested that there is a limit to the value added in providing more and more funding to a single laboratory.

Balance Outputs with Outcomes. By their nature, outputs are easier to measure and have a shorter lag time between the onset of the activity and the “result.” In contrast, outcomes, which should have some effect on the external environment, are much harder to measure, in part, because the lag time between the activity and the “result” is longer and often unpredictable. Further, because outputs are easier to measure, organizations often use them without full consideration of the perverse incentives they may be creating.

Much of NIH’s investment is made through its grant portfolio. In an attempt to evaluate the “success” of a grant, a wide range of scientific outputs can now be assembled, each with its own inherent flaws. Nevertheless, the use of bibliometrics that account for variations in publication and citation practices among different scientific disciplines can provide a preliminary indication of a program’s “value.” The number of patents and/or investigational new drug (IND) applications filed can also be a surrogate for program worth, but again, these take time, and by themselves are not necessarily predictors of outcomes that may take much longer to realize. For example, who would have assigned a very high value to early research on thermophilic microorganisms in the late 1960s that ultimately led to the discovery of Taq

polymerase and the development of the polymerase chain reaction (PCR) technique that fueled the biotech revolution?

For evaluation of NIH-supported training, a standard approach is to count the number of trainees in tenure-track or tenured positions at universities around the world. This is a relatively facile measure in the era of social media. But this has led to a systematic undervaluation of trainees who have gone on to important careers in industry, policy development, intellectual property adjudication, or teaching, to list a few. NIH has recently made providing postdocs and graduate students with a broad exposure to [career options](#) as a critical part of a successful training program, and will now align its stated goals with the measures used to assess the programs that undergird the efforts.

Improving the health of the nation and the world is the ultimate outcome that NIH aims to achieve. And over the last several decades, it is clear that NIH-supported research has had a major positive [impact on human health](#). Major prizes, such as the Laskers and Nobels, are also an indication of how the world views major advances in science, and NIH has been responsible for supporting the work of a very [large number](#) of those honored with such prizes over the last few decades. But within the 5-year horizon contemplated for this Strategic Plan, it would be difficult to chart a course toward widespread population benefit from NIH investments in research—the timelines are just too long.

Conduct Workforce Analyses. In general, workforce analysis has proven to be challenging for many fields, but NIH has created a [static representation of the Ph.D. workforce](#) and is currently working on a dynamic model that can be used in concert with all relevant stakeholders (universities, research institutes, industry, the federal government, policy think tanks, and the K-community college educational system) to better predict the number of Ph.Ds. and postdoctoral fellows that would be optimal for NIH to support. Particularly vexing is the continued decline of physician-scientists. A recent snapshot has been generated of the M.D., M.D.-Ph.D. census, but more work must be done to design interventions that will increase the number of these invaluable members of the workforce. While NIH has engaged in many research partnerships, it will also formulate and evaluate new approaches to engaging physician-scientists through inclusion of professional organizations, academic health center leadership, and, of course, the trainees themselves.

Continuous Review of Peer Review. There are many other elements of peer review that demand continuous evaluation. As science becomes more interdisciplinary in nature, new approaches to review need to be tested and validated, including asynchronous, electronic reviews and two- or three-stage “editorial board” models. In addition, the cost/benefit ratio of each must be evaluated. NIH will also continue to seek measures to compare the “performance” of each study section.

Evaluate Steps to Enhance Rigor and Reproducibility. NIH, in partnership with fellow science agencies, journal publishers, professional societies, universities, foundations, and a number of other stakeholder groups, has launched a series of initiatives to enhance the rigor and reproducibility of the conduct of science and reporting of scientific results. Each of these initiatives will be evaluated over the next 5 years for beneficial effects, as well as for any unanticipated, negative consequences.

Reduce Administrative Burden. There are a wide range of administrative burdens placed upon NIH's stakeholders, and several recent studies have enumerated many of these. In approaching this issue, NIH first must classify each burden with regard to origin—some are mandated in law; others are rooted in policy; and still others can be traced to historic custom. NIH's goal over the next 5 years will be to reduce or, wherever possible, eliminate those burdens that arise from custom and/or policy. NIH will also work with Congress to ascertain which of the burdens arising from laws can be modified to provide some relief.

Track Effectiveness of Risk Management in Decision Making. Winston Churchill once said: "Never let a good crisis go to waste." When unexpected issues arise, it is important to do a formal analysis of not only what events occurred, but also why they occurred. In this manner, NIH's risk management system can be continuously adapted to include new elements that had not previously been considered or even anticipated.

A Few Bold Predictions for America's Future

Despite the risks associated with making short-term predictions, it behooves NIH to lay out ambitious outcome objectives for the next 5 years. Below are just a few of the outcomes that NIH will strive to deliver for the benefit of the American people and all humankind. This list of potential advances should be taken as “stretch goals” that can only be achieved by stable funding support and intense scientific effort. These are definitely aspirational goals, rather than guaranteed outcomes. This list also is not exhaustive; it is entirely possible that the greatest research achievements by 2020 will come from directions no one can currently anticipate. Finally, it is likely not all of these goals will be attained by 2020, but they are offered in hope that this kind of bold visioning can inspire the rapidly moving field of biomedical research to aim even higher.

- Many thousands of cancer patients will experience enhanced survival from application of precision medicine.
- A candidate vaccine that induces a broad antibody-binding response to multiple strains of the influenza virus will be in clinical trials—a critical step towards a universal flu vaccine.
- NIH-supported research will develop effective, tailored behavioral and social interventions to promote health and prevent illness in populations that experience health disparities.
- Application of pharmacogenomics in real-world clinical settings will lead to improved outcomes in the use of several drugs.
- A pivotal efficacy trial of a novel HIV vaccine, expected to begin in the Republic of South African in 2016, will confer at least 50% protection against the acquisition of HIV.
- NIH-supported clinical trials will show that at least a half-dozen interventions thought to be clinically beneficial actually have no value.
- Radical new methods for structural biology will revolutionize drug screening and optimization.
- NIH-supported research will directly contribute to FDA-approved therapies for at least a dozen rare diseases.
- Application of certain mobile health (mHealth) technologies will provide rigorous evidence for their use in enhancing health promotion and disease prevention.
- A wearable biosensor for monitoring blood-alcohol levels in real time will be developed and show efficacy for preventing alcohol-related injury and disease.
- Technologies to reverse paralysis and restore some normal functions will be available to spinal cord injury patients.
- Vaccines against respiratory syncytial virus will be field test for efficacy, promising a solution for this leading cause of childhood pneumonias.
- Research on the artificial pancreas will lead to advanced trials showing significantly better management of diabetes, without dangers of hypoglycemia.
- NIH will be known as the model agency for applying the scientific method to itself—for learning and implementing in a rigorous way, how best to support biomedical research.

Many NIH Success Stories – And More to Come



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