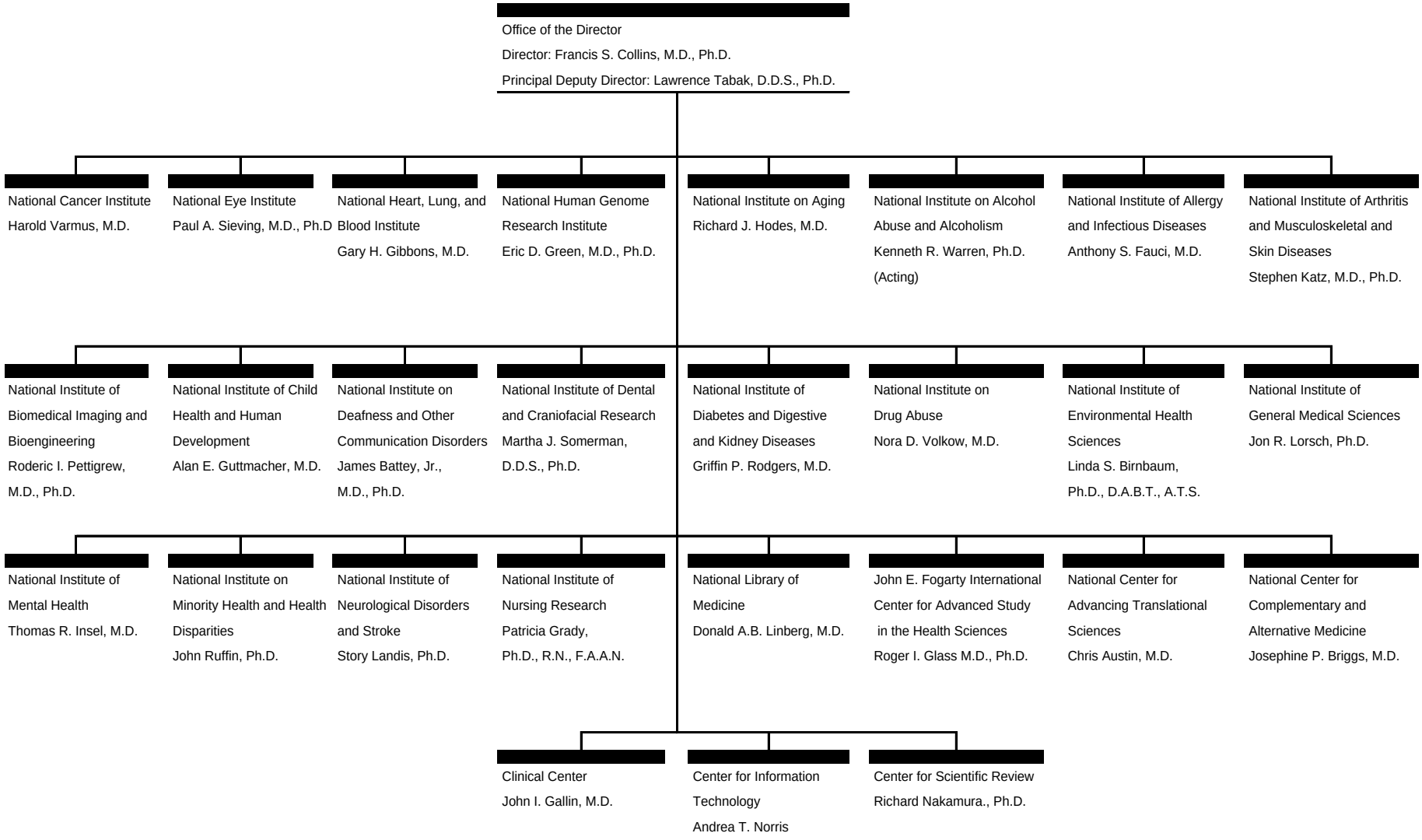
Department of Health and Human Services
National Institutes of Health

Executive Summary

National Institutes of Health



FY 2015 Budget Request
National Institutes of Health

Introduction and Mission

The mission of the National Institutes of Health (NIH) is to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability. In pursuit of this mission, NIH conducts or supports research designed to understand the basic biology of human health and disease; apply this understanding towards designing new approaches for preventing, diagnosing, and treating disease and disability; and ensure that these new approaches are available to all.

As the Nation's medical research agency and the largest source of funding for biomedical and behavioral research in the world, NIH plays a unique role in turning basic scientific discovery into improved health. A significant and enduring investment by NIH in basic research today assures the breakthroughs in the health care of tomorrow. This robust research enterprise depends upon NIH's ability to recruit and retain the Nation's brightest minds into successful scientific careers. With continued support, NIH contributes significantly to the economic engine that drives American competitiveness in science and technology and will realize a Nation in which all Americans enjoy long healthy lives.

National Institutes of Health
FY 2015 Congressional Justification

All Purpose Table
(Dollars in Thousands)

	FY 2013 Actual[1]	FY 2014 Enacted	FY 2015 President's Budget	FY 2015 Request +/- FY 2014 Enacted
Labor/HHS Discretionary Budget Authority	**$28,926,041**	**$29,926,104**	**$30,126,104**	**$200,000**
Interior Budget Authority	74,871	77,349	77,349	0
Total Discretionary Budget Authority	**$29,000,912**	**$30,003,453**	**$30,203,453**	**$200,000**
Mandatory Type 1 Diabetes Research	142,350	139,200	150,000	10,800
Total Budget Authority	$29,143,262	$30,142,653	$30,353,453	$210,800
NIH Program Level [2]	**$29,151,462**	**$30,150,853**	**$30,361,653**	**$210,800**
Number of Competing RPGs	*8,234*	*8,997*	*9,326*	*329*
Total Number of RPGs	*34,840*	*34,213*	*34,197*	*(16)*
FTEs	*18,234*	*18,234*	*18,234*	*0*

[1] Includes effect of sequestration and transfers.

[2] Includes NLM Program Evaluation of $8.20 million in FY 2013, FY 2014 and FY 2015.

FY 2015 Budget Request
National Institutes of Health

OVERVIEW OF BUDGET REQUEST

Total Budget Request
(Dollars in Millions)

	FY 2014 Enacted	FY 2015 President's Budget
Total Program Level [1]	$30,151	$30,362
Change from FY 2014 Enacted: Dollars	--	$211
Change from FY 2014 Enacted: Percent	--	0.7%

[1] Includes Labor/HHS Budget Authority, Interior Superfund Appropriation, Type 1 Diabetes mandatory funds, and NLM Program Evaluation.

The National Institutes of Health (NIH) requests a total program level of $30.362 billion for fiscal year (FY) 2015, $211 million above the FY 2014 level. This funding will enable NIH to sustain the pursuit of fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability. Investment in NIH provides the Nation with a unique resource–a scientific agency devoted to the creation of a knowledge base needed to conquer the most devastating human diseases and disabilities. The promise of NIH is that someday all people will be able to lead long and healthy lives.

In striving to fulfill this promise, the 27 Institutes and Centers that comprise NIH work together with the NIH Office of the Director to support the science needed to develop new ways to prevent, diagnose, and treat the diseases and disorders that cause the greatest burdens to society. For example, in large part due to advances supported by NIH, deaths from heart disease have fallen by more than 60 percent since 1970[1]. In addition to focusing on those diseases with the greatest burden, NIH also conducts research on rare and neglected conditions that would otherwise go unaddressed. For many suffering from these conditions, NIH is their only hope. And knowledge gained about rare diseases often has important implications for more common conditions as well. For example, in 2012, NIH scientists identified a genetic mutation that causes cold temperatures to trigger an allergic reaction–a condition called cold urticaria. In addition to informing efforts to find a cure for this rare condition, this finding provided important information on how the immune system functions.

[1] *Calculated from Health, United States, 2011: with Special Feature on Socioeconomic Status and Health,* http://www.cdc.gov/nchs/data/hus/hus11.pdf

NIH research results not only help generate new approaches to diagnose and treat known diseases, but also help to address emerging threats. In the mid-1980s, a diagnosis of AIDS was considered a death sentence. Yet, in large part because of what was already known through basic research on the immune system and retroviruses, not only was the cause of AIDS quickly identified, but effective strategies toward its prevention and treatment were being pursued in short order. The result has been that in 30 years' time we have moved from contemplating a decrease in world population due to AIDS to designing approaches to end the epidemic.

Science moves at an unpredictable pace and not all areas of inquiry progress in the same way. In establishing funding priorities, NIH must maintain strong, diverse investments in basic science; the development of effective diagnostics, treatments, and preventive measures for both common and rare diseases; and the need to sustain a vital and cutting-edge workforce and scientific infrastructure. This approach allows NIH to capitalize on scientific opportunities as they emerge, as well as maintaining the flexibility to respond to urgent public health needs.

In addition to the base Budget request, the FY 2015 President's Budget contains a proposed Opportunity, Growth, and Security Initiative to support the President's priorities to grow the economy and create opportunities. This Initiative includes $970 million to restore NIH to the level proposed in the FY 2014 President's Budget ($31.3 billion). These funds, which would be used to increase the number of new grants and provide additional resources for signature biomedical research activities, are described in the Overall Appropriations section under Narrative by Activity.

In FY 2015, NIH will focus on the following priority themes:

1. Today's Basic Science for Tomorrow's Breakthroughs
2. Precision Medicine
3. Big Opportunities in Big Data
4. Nurturing Talent and Innovation

By pursuing these priorities, NIH will drive the engine of discovery, innovation, and improved health. NIH is uniquely poised to pursue the priorities because of our public responsibility, resources, or willingness to pursue areas and diseases which others are not.

Theme 1: Today's Basic Science for Tomorrow's Breakthroughs

NIH is the largest funder of basic biomedical research in the world. By funding basic research, NIH provides the foundational knowledge of the mechanisms of biology and behavior that are necessary to understand the causes of disease onset and progression, identify risk factors and biological markers that allow for better diagnostics, and develop new cures and preventive treatments. Often, this foundational knowledge is built in small increments that eventually lead to major breakthroughs, but it also provides the necessary groundwork for tackling newly emerging infectious diseases or complex chronic diseases that are rapidly increasing in burden. Therefore, support of a broad basic research portfolio is essential in fulfilling NIH's mission of addressing the public health challenges of both today and the future.

Basic research results advance not only knowledge of a specific disease or condition but also build the tools that will help advance understanding in many other areas. For example, several NIH-supported researchers have developed and are refining a new technology called CRISPR (clustered regularly interspaced short palindromic repeats), which enables scientists to target genes for deletion, addition, activation, or suppression with such specificity that it amounts to performing their own genetic microsurgery. Using this system, researchers have altered DNA in human cells, rats, mice, zebrafish, bacteria, fruit flies, yeast, nematodes, and crops. This method arose from basic research in an area unrelated to gene editing, and its wide-ranging applicability makes the technology potentially valuable for numerous purposes, including treatment of genetic diseases.

NIH also supports key collaborations in basic research. The Knockout Mouse Phenotyping Program (KOMP2), supported by NIH in cooperation with the European Union, Wellcome Trust, Canada, and the Texas Enterprise fund, is systematically producing mice that have specific traits that are useful as models for understanding how genes work and how they are related to diseases. The Library of Integrated Network-based Cellular Signatures (LINCS), created by NIH-funded researchers, is providing a blueprint of how the basic parts of cells, including genes, proteins and other molecules, work together and are maintained not only in health but also in how they respond to disease. The Genotype Tissue Expression (GTEx) Program is illuminating how genes work in different tissues and in different people; and the 1000 Genomes project is supporting the development of cost-effective and high-throughput genome sequencing methods for protein coding regions of the genome to help enhance our understanding of how proteins are made. The results of the Human Genome Project revealed that the protein-coding portions of DNA account for only about 1.5 percent of the genetic material found in humans, while the purpose of the other 98.5 percent remained unknown. To unravel this mystery, NIH initiated the Encyclopedia of DNA Elements (ENCODE) project to identify all functional elements of the human genome sequence, including those that act through the production of protein and RNA, as well as regulatory elements that control gene activity of cells. Through this herculean effort, researchers have now linked more than 80 percent of the human genome sequence to a specific biological function, and mapped more than 4 million regulatory regions where proteins specifically interact with the DNA–representing a major advance in the emerging science of "epigenomics." This information is freely available online in a resource that can be accessed by all researchers to use in further studies.

Numerous other basic research projects funded by NIH are producing findings that are increasing our understanding of disease processes or new ways of treating diseases or conditions. For example, researchers funded by NIH's National Institute of General Medical Sciences (NIGMS) have achieved major advances in understanding the process of protein production from RNA by providing the means to visualize the molecular machinery that initiates this process. The National Eye Institute (NEI) has funded research that has identified small fragments of proteins in the cornea that fight infections and have the potential to be manufactured as a new class of low-cost, non-toxic antibiotics. Researchers funded by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) are generating significant data to help understand the role of the immune system in skeletal muscle regeneration after injury. These are only a few examples of the knowledge, tools, and resources being developed through NIH's funding of basic research.

The BRAIN Initiative[SM]

The complexity of the human brain was once thought to be beyond understanding–the brain comprises nearly 100 billion cells that make an astounding 100 trillion connections. Current state-of-the-art imaging can provide mostly a static picture of brain activity, and electrodes can control and record electrical activity from single and small groups of neurons in specific locations, but a leap in scientific understanding and technological capability is needed in order to map entire brain circuits. Leveraging investments and diverse expertise from private foundations, industry, and other government agencies, the goal of the BRAIN (Brain Research through Advancing Innovative Neurotechnologies) Initiative is to accelerate the development and application of next-generation tools to construct dynamic pictures of the brain that reveal how millions of brain cells and complex neural circuits interact in real time to produce the extraordinarily complex array of human behaviors.

The FY 2015 Budget includes $100 million for the BRAIN Initiative, an increase of $60 million over FY 2014, to ramp up activities in the second year. This bold multi-agency initiative requires ideas from the best scientists and engineers across many diverse disciplines and sectors. The BRAIN Initiative will build on the rapidly growing scientific foundation of neuroscience, genetics, physics, engineering, informatics, nanoscience, chemistry, mathematics, and technological advances of the past few decades to catalyze an interdisciplinary effort of unprecedented scope. Recent NIH-funded breakthroughs illustrate the transformative potential of technology to understand the brain's intricate architecture and complex functions:

- Imaging the brain: the Human Connectome Project has driven the development of increasingly sophisticated imaging tools, providing the first ever systematic map of the wiring diagram of nerve cells within the living human brain.
- Measuring brain activity: large-scale, multielectrode arrays are now being used in live animals to record from thousands of neurons simultaneously across different brain areas.
- Precision manipulation of brain activity: using optogenetic methods, scientists were able to switch depression-related behavior on and off in mice with flashes of an LED light, uncovering new insights into mechanisms of depression.
- Tracing the brain's connections: a ground-breaking technology called CLARITY takes a fully intact, opaque brain and transforms it into a clear, gel-based brain, allowing unprecedented 3-D visualization of molecular, cellular, and neuro-anatomic structure.

NIH has established a high-level working group of 18 external advisors, including three ex-officio members from the federal partner agencies, to define the goals of the BRAIN Initiative for NIH and develop a rigorous plan for achieving its scientific vision, including timetables, milestones, and cost estimates. The advisory group delivered an interim report detailing high-priority areas for FY 2014 funding in September of 2013, and will complete a final report with comprehensive recommendations in Summer 2014.

In accordance with recommendations issued by the working group, NIH's $40 million investment in the BRAIN Initiative in FY 2014 will focus on expanding and enhancing the arsenal of tools and technologies for unlocking the mysteries of the brain. The first wave of funding opportunities under the BRAIN Initiative were released on December 17: two focus on

developing methods for classifying and accessing diverse cells and circuits of the brain; three focus on developing and optimizing technologies for recording and modulating collections of cells that function together as a circuit; and one supports the formation of interdisciplinary teams of scientists to develop the next generation of non-invasive imaging technologies for human research.

Ultimately, application of the tools and technologies developed under the Brain Initiative will provide critical insight into brain circuitry and activity. This foundation of knowledge will help reveal the underlying pathophysiology in numerous brain disorders and may provide new therapeutic avenues to treat, cure, and even prevent neurological and psychiatric conditions, such as Alzheimer's disease, autism, epilepsy, schizophrenia, depression, chronic pain, addiction, post-traumatic stress disorder, and traumatic brain injury.

The Microbiome – New Insights into the Invisible Ecosystem in and on the Human Body and its Role in Health

The human body is host to trillions of microbes – outnumbering the body's cells by 10 to 1. Some of these bacteria, fungi, and viruses cause disease, but many are necessary for human health. To characterize these microbes and understand their influence on human health, the Human Microbiome Project (HMP) was launched by NIH in 2007. The first phase of the HMP, in volving the sequencing of microbial reference genomes from five areas of the body – the digestive tract, mouth, skin, nose and vagina – determined that more than 10,000 microbial species occupy the human body and that the microbiome provides more genes that contribute to human survival than the human genome itself (8 million vs. 22,000). A deeper understanding of the microbiome has led to numerous insights on how microbes keep us healthy and make us sick:

- The gut microbiome affects nutrition. NIH-funded researchers found that an acute form of malnutrition called kwashiorkor, which is common in the African nation of Malawi, is likely caused by both inadequate caloric intake and an improper balance of microbes in the gut. Even though all the kids in the study had a poor diet, the gut microbiome of healthy kids differed dramatically from those with kwashiorkor. The researchers concluded that children carrying the "bad" kwashiorkor gut microbes could not make the most efficient use of the Malawian diet, and thus ended up with malnutrition.

- The link between red meat consumption and heart disease may be influenced by how well gut microbes can break down carnitine, a compound found in red meat. The NIH-supported study showed that the gut microbes of meat eaters were more efficient at breaking down carnitine than those in non-meat eaters. In mice, the carnitine break-down product appeared to promote atherosclerosis, or clogging of the arteries. Therefore, a diet high in carnitine-containing red meat may shift our gut microbe composition to those that like carnitine, potentially making meat eaters even more susceptible to atherosclerosis.

- Gut microbes may also play significant roles in the development of immune system disorders. Type 1 diabetes is an autoimmune disease in which the body's own immune system attacks and destroys insulin-producing beta cells in the pancreas. NIH-funded researchers have reported that certain gut microbes protect against Type 1 diabetes in mice, essentially by blunting the immune system attack that causes Type 1 diabetes. The gut microbiome has been also been linked to arthritis. In a recent NIH-funded study, investigators found that 75% of people with new-onset, untreated rheumatoid arthritis had the bacterium *Prevotella copri* in their intestinal microbiome. When the team administered the bacteria to healthy mice, they developed more severe symptoms than the mice that had not received the bacteria, providing evidence for its potential harmful role in the development of rheumatoid arthritis.

Ongoing HMP projects are continuing to reveal the critical roles these diverse organisms play in a host of diseases and conditions, with specific projects focusing on obesity, asthma, kidney disease, Crohn's disease, ulcerative colitis, esophageal cancer, psoriasis, dermatitis, dental caries, periodontal disease, and a number of childhood disorders, such as pediatric abdominal pain, intestinal inflammation, and a severe condition in premature infants in which the intestine actually dies. Additionally, NIH-funded investigators are studying how the infant gut microbiome becomes established and what effect environmental changes, such as diet and antibiotic exposure, may have on "normal" gut microbiome early in life. The long-term objective of the HMP is to identify opportunities to improve human health through monitoring or manipulation of the human microbiome. The HMP investment by the Common Fund has stimulated microbiome research throughout NIH, and support by Institutes and Centers will exceed $30 million in FY 2015.

Theme 2: Precision Medicine

In addition to funding a diverse and robust portfolio in basic research, NIH also supports research focused on improving disease prevention, diagnosis and treatment. The primary goal of NIH translational and clinical research is to improve public health interventions and to provide the best available care for those who need it. Precision medicine refers to the tailoring of treatments to the individual characteristics of each patient. To do so, NIH seeks to understand human variability and identify individuals who differ in the susceptibility to a particular disease, in the trajectory of those diseases if they develop, or in response to a specific treatment. In this way, specific preventive or therapeutic interventions can be tailored–avoiding needless treatment and expense for those who will not benefit. Understanding the characteristics that make an individual more susceptible to a disease or disorder or identifying predictive markers for response to a particular treatment will also improve screening and allow for better implementation of interventions in any number of healthcare and community settings.

NIH undertakes the challenges of precision medicine through myriad strategies. A key cornerstone has been creating the infrastructure to enable such research. To do so, NIH partners with a multitude of public and private entities within public health to pursue varied approaches. For example, NIH's National Center for Advancing Translational Sciences (NCATS) works with the pharmaceutical industry, academia, and the U.S. Food and Drug Administration (FDA) to look for new uses of drugs that have been found to be safe in humans. And an exciting new venture between NIH and ten biopharmaceutical companies and several non-profit organizations aims to transform the current model for developing new diagnostics and treatments by working together to identify and validate biological targets of disease. Focusing first on pilot projects in the areas of Alzheimer's disease, type 2 diabetes, and the autoimmune disorders of rheumatoid arthritis and lupus, the ultimate goal of the Accelerating Medicines Partnership is to increase the number of new diagnostics and therapies for patients and to reduce the time and cost of their development.

The field of medicine is rapidly advancing, and these advances are leading to increased precision in the diagnosis and treatment of individuals. Along this path, recent NIH advances include using a revolutionary brain-computer interface to enable a patient who had been paralyzed for nearly 15 years to be able to control a robot arm to retrieve and drink from a thermos of coffee. An NIH-supported study on peanut allergy demonstrated that sublingual immunotherapy (SLIT), in which a small amount of the substance that causes the allergic reaction is placed under the tongue, successfully reduced an allergic reaction in 70 percent of participants in a randomized, controlled trial. And a recent study has shown that bariatric surgery can help control type 2 diabetes more effectively than intensive medical therapy alone (lifestyle counseling, weight management programs, frequent home glucose monitoring, and the use of diabetes medications), and can reduce the need for medications to lower glucose, harmful lipids, and blood pressure.

Tissue on a chip

The current drug development pipeline has significant bottlenecks, and the movement of basic research into clinical use is slower than desired. Animal models have been the gold standard for testing the safety and efficacy of new therapeutic compounds. However, more than 30 percent of medications have generally failed in human trials because they are determined to be toxic,

despite promising and expensive studies in animal models. To help streamline therapeutic development, NIH along with its partners, the Defense Advanced Research Projects Agency (DARPA) and FDA, embarked in 2012 on a bold, technology-driven initiative to improve the process for predicting whether drugs will be safe in humans. This tissue-on-a-chip research initiative is aimed at developing 3-D human tissue chips that accurately model the structure and function of human organs, such as the lung, liver, and heart.

NIH and DARPA have complementary but distinct goals for this collaboration. While DARPA's initiative focuses on engineering aspects, the NIH initiative focuses on how well these new technologies mimic the biology and pathophysiology of human organ systems. Led by NCATS, 15 NIH Institutes and Centers are assisting in the coordination of this cross-cutting trans-NIH program, and to date, 19 grants have been awarded. Research teams have begun to develop 3-D cellular microsystems that recreate the genomic diversity, disease complexity, and drug responses of approximately 10 different human organ systems, including the heart, lung, and nervous system. Additionally, NIH-funded researchers are exploring the potential of stem and progenitor cells to be reprogrammed into multiple cell types, which could be used as a source of cells to populate tissue chips. Currently, investigators are making great strides both in the reliable differentiation and maturation of induced pluripotent stem (iPS) cells into the desired cell types and in combining those cells into cellular microsystems. NIH and DARPA investigators are also beginning to integrate individual tissues (e.g., heart, lung, or nervous system) onto miniaturized platforms that combine 2-4 systems together. The goal of the project is to have a commercially viable prototype chip available at the end of the five-year award period (2017). Although a high-risk endeavor, the development of genetically diverse tissues-on-a-chip will allow assessment of personalized responses to drugs prior to clinical trials, a technological advance that will make clinical trials safer, cheaper, and more effective.

New Common Fund DARPA-like Program

The Common Fund request for FY 2015 includes $30 million for a new DARPA-like program that would utilize Other Transaction Authority (OTA) to support high risk, goal-driven activities that aim to achieve rapid technology development. One project under consideration, Bioelectronic Medicines, would seek to establish methods to stimulate the peripheral, autonomic, and enteric nervous systems and thereby control the function of physiologic systems. This could lead to proof of concept for an entirely new class of neural control devices that have the potential to precisely treat a wide variety of diseases and conditions.

Universal Influenza Vaccine

On average, more than 30,000 people in the United States die each year from seasonal influenza infections. Some of the currently circulating avian strains (H5N1 and H7N9) have also sporadically infected humans and could have pandemic potential if they were to evolve the ability for sustained human-to-human transmission. Given how rapidly influenza surface proteins evolve, new vaccines must be developed annually to protect against seasonal influenza, and as needed, to help protect against newly emerging pandemic influenza strains. Current vaccine strategies are directed to those portions of the influenza virus that change season to season. To better protect against seasonal influenza and influenza strains with pandemic potential, researchers are on the path to develop a "universal" influenza vaccine that would

induce a potent immune response to the common elements of the influenza virus that undergo very few changes from season to season, and from strain to strain. A universal influenza vaccine has the potential to protect against multiple influenza strains over several years, and potentially reduce the need for yearly vaccinations.

NIH is funding research to support the development of such a vaccine. For instance, the National Institute of Allergy and Infectious Diseases' Vaccine Research Center (VRC) is conducting studies to better understand the immune response to influenza infections and vaccine candidates, and is exploring different vaccine delivery platforms and strategies for generating broadly-neutralizing antibodies. The VRC also has supported several early-stage clinical trials of candidate universal influenza vaccines. NIAID is also funding a variety of extramural projects focused on the development of a universal influenza vaccine and on the development of immunological agents that will increase a vaccine's effectiveness when administered.

The Promise of Induced Pluripotent Stem Cells

Induced pluripotent stem cells (iPSCs) are revolutionizing the study of disease. iPSCs are derived from mature cells, typically from a patient's skin or blood, which researchers can reprogram back to an immature state. These cells can then be programmed into a wide variety of cell types, including liver cells, neurons, cardiac cells, and blood cells. Once they have been reprogrammed into different cell types, iPSCs can be used to understand the molecular pathways in biological development and human disease. The ability to manipulate these cells to answer critical scientific questions is a vital part of NIH's goal for this research investment. For example, disease-specific iPSCs have already been developed from patients with a variety of conditions, such as Alzheimer's, Long QT syndrome, Timothy Syndrome, schizophrenia, and Fragile X syndrome. These cells will be useful models for better understanding the cellular abnormalities in these disorders. NIH-supported consortia have built repositories of iPSC cells from patients with various conditions that are being used in a wide range of research.

Building on these advances in developing disease-specific stem cells, a group of NIH-funded scientists has discovered how to use human iPSCs to form groups of cells that mimic the three-dimensional organization and other specific features of the human forebrain. These 3-D cultures may provide more physiologically relevant systems to assess aberrant developmental processes relevant to a wide variety of brain disorders.

NIH is also investing in the use of iPSCs for drug development research. In Parkinson's disease research, for example, NIH-supported scientists collected skin cells from patients with genetically inherited forms of the disease and reprogrammed the cells into nerve cells that resembled those that die as a result of the disease. When the scientists tested various potential drug treatments to address the defects in the cells, they found that the cells' responses to treatments depended on the type of Parkinson's that each patient had. This use of iPSCs could help determine which patients might respond best to a particular treatment in clinical trials.

iPSCs are also being used as tools for drug screening for treatments for diseases such as amyotrophic lateral sclerosis (ALS, or Lou Gehrig's disease). ALS is an ultimately fatal disease characterized by the progressive loss of motor neurons in the spinal cord. An ideal treatment for this disease would be a drug that stabilizes human motor neurons against cell death. With NIH funding, research teams have generated iPSCs from individuals with inherited and sporadic forms of ALS and reprogrammed the cells into neurons. Researchers are now using these neurons to test potential drug candidates for their ability to reverse the ALS effects.

Another step along the pathway to human treatments with iPSCs is testing in animal models. After the first successful use of iPSCs to treat sickle cell anemia in mouse models, researchers have been working toward this goal for other diseases. In promising NIH-funded research, animal models of Duchenne muscular dystrophy showed improved muscle function after a transplant of muscle progenitor cells that were derived from iPSCs.

Moving forward, the use of iPSC technology will continue to advance the study of disease mechanisms as well as to facilitate development and optimization of treatments for patients. NIH remains committed to supporting this research through extramural research grants to institutions throughout the country and NIH intramural research programs, such as the Center for Regenerative Medicine, with the ultimate goal of using iPSCs to develop specific cells and tissues for human cell-based therapy. The clinical promise of iPSCs is generating interest worldwide, and the first clinical trial of a product developed using iPSCs—a potential therapy for age-related macular degeneration—is poised to begin soon in Japan, Additional NIH investment in this area will enable research leading to new treatments to be tested in clinical trials.

Preventing Suicide in the Military

Historically, the suicide rate among Army personnel has been lower than that for a demographically comparable civilian population. In 2004, however, the suicide rate among soldiers began rising, reaching a new record level several years in a row including 2012. This serious issue was the impetus behind the development of the Army Study to Assess Risk and Resilience in Service members (Army STARRS), the largest study of suicide and mental health among military personnel ever undertaken. A collaboration between the Department of Army, NIH's National Institute of Mental Health (NIMH), and several academic partners, this project is designed to identify, as rapidly as possible, risk and protective factors that will help the Army develop effective strategies to reduce rising suicide rates, and to address associated mental health problems among soldiers. Army STARRS's five components examine historical administrative data collected by the Army and Department of Defense as well as current data collected from soldiers in all phases of Army service. This research will help inform our understanding of suicide in the overall population, leading to more effective prevention and treatment for service members and civilians alike.

Now in its fifth year, Army STARRS is well on its way to achieving its initial goals. As of December 2013, seventy-six Army installations have been involved in the study, and more than 112,000 soldiers have volunteered to participate across all study components. All soldiers who participate are asked to complete a comprehensive survey. A subgroup of those soldiers, nearly half, also were administered a battery of neurocognitive tests. In addition, more than 43,000 soldiers voluntarily donated blood samples for biomarker analysis. The majority of study components have completed participant enrollment and have transitioned to the analysis stage. The first series of data papers were recently accepted for publication. The research team has been briefing Army senior leadership multiple times per year and is now actively engaged with the Army organizations responsible for suicide prevention in order to facilitate the translation of study findings into practical applications.

Theme 3: Big Opportunities in Big Data

With advancing technological and computational capabilities, biomedical researchers are generating a vast amount of data at an unprecedented pace. These large and complex datasets–often referred to as "Big Data"–are generated from an array of devices such as genomic sequencing machines and other high-speed technologies, novel imaging strategies, electronic health records (EHRs), and smart phone applications that monitor patient health. Sharing Big Data readily and responsibly is a critical step in translating new discoveries into clinical applications, and these efforts are consistent with wider Administration efforts to increase access to federally funded research results. However, real challenges arise when scientists try to visualize, manipulate, or mine these complex datasets. The computational foundation required for maintaining, securing, and processing large-scale datasets typically goes far beyond the capabilities of individual investigators. Additionally, a well-trained workforce with requisite skills to manage, analyze, store, and preserve complex scientific data is essential to realize the full value of Big Data.

Cross-cutting NIH Efforts

In 2012, NIH established an overarching initiative–termed Big Data to Knowledge (BD2K)–to accelerate the pace of discovery through the use of biomedical Big Data, to be led by the new NIH Associate Director for Data Science, Dr. Philip Bourne. By the end of this decade, the goal of BD2K is to enable a quantum leap in the ability of the biomedical research enterprise to maximize the value of the growing volume and complexity of biomedical data. To achieve this goal, BD2K will support four programmatic efforts:

- Facilitation of broad use and sharing of large, complex biomedical datasets through the development of policies, resources and standards;
- Development and dissemination of new analytical methods and software;
- Enhanced training of data scientists, computer engineers, and bioinformaticians; and
- Establishment of Centers of Excellence to develop generalizable approaches that address important problems in biomedical analytics, computational biology, and medical informatics.

Plans are already in motion to support these programs. The first funding opportunity announcement for the Big Data Centers of Excellence was released recently, and NIH has committed $24 million annually over four years to support the initial grants for this part of the BD2K program. BD2K also issued a Request for Information (RFI) for public input on developing a biomedical Data Catalogue that would enable researchers to easily find, share, and cite biomedical research data. An RFI to gather public input on the training and education needs to support the BD2K initiative was also issued. The input from the RFIs will be used to facilitate focused and actionable discussion during a number of workshops in the BD2K programmatic areas of interest. The workshops will be available to the public via webcast. In FY 2015, the total NIH investment in BD2K is estimated at $88 million, or roughly double the FY 2014 level.

In addition, through the NIH InfrastructurePlus Initiative, also established in 2012, an adaptive environment will be created at NIH that will facilitate the optimal use of Big Data in order to sustain world-class biomedical research, including enhancement of the NIH high-performance computational environment; implementation of agile and cost-effective approaches to storing and hosting highly complex and heterogeneous datasets; and continued development of an information rich environment of systems, applications, and tools. The InfrastructurePlus Initiative will be led by the NIH Chief Information Officer.

National Database for Autism Research (NDAR)

Big Data opportunities are being created to address some of our most disabling diseases and conditions. Here is just one example. Prompted by the need to accelerate progress in autism spectrum disorders (ASD) research, NIH created the National Database for Autism Research (NDAR). NDAR is a research data repository that holds genetic, phenotypic, clinical, and medical imaging data from participants in ASD-research studies. It also functions as a scientific community platform, defining the standard tools and policies to integrate the computational resources developed by scientific research institutions, private foundations, and other Federal and state agencies supporting ASD research. All data within NDAR use the same structure to

enable comparison and analysis by other qualified researchers. This secondary data analysis provides scientists with the tools to validate research results and to conduct studies using data from multiple sources to create larger sample populations.

Through strong partnerships with private organizations, such as Autism Speaks and the Simons Foundation, NDAR has incorporated data from more than 60,000 de-identified research participants into the database. Most public and private funders of ASD research have now made data sharing with NDAR an integral part of funding new research projects. At NIH, 80 percent of newly awarded human-subject grants related to ASD have an expectation for data sharing with NDAR; by 2015, virtually all NIH-funded human-subjects ASD research is expected to include these terms. This community-wide data-sharing initiative supported by NIH will make great strides in facilitating collaboration between scientists, enabling rigorous comparison of results between research studies, and preventing unnecessary duplication of experiments.

Like NDAR, multiple Big Data platforms will accelerate the translation of data bytes to bedside applications that advance the detection, diagnosis, and treatment of disease. With proper investments and coordination with other government agencies and private sector stakeholders, the infrastructure and workforce challenges can be overcome to realize the full potential of the data revolution.

Combating the Challenge of Alzheimer's Disease

Alzheimer's disease (AD), the most common form of dementia, affects between 4 and 5.1 million Americans each year, slowly destroying brain regions that are critical for memory, reasoning, and even the most basic daily living skills. A recent report from NIH's Health and Retirement Study estimated the cost of caring for persons over age 70 with dementia in the U.S. was between $159 billion and $215 billion in 2010. By 2040, these costs are projected to increase dramatically to nearly a trillion dollars per year. NIH, with the National Institute on Aging (NIA) taking the lead, supports a number of studies aimed at enabling us to better understand, diagnose, prevent, and treat AD. Some of the latest advances in AD research include the following:

- For the first time, a genetically engineered animal model exhibits the full array of AD-associated brain changes, further supporting the idea that increases in a molecule known as beta-amyloid causes the disease. Improved animal models are key to advancing understanding of this complex disease and testing promising interventions. For example, NIH-funded scientists are exploring an innovative technique to help repair Alzheimer's-damaged brain cells. In a mouse model of AD, they were able to trigger supporting cells of the brain, called glial cells, to regenerate into healthy, functional neurons.

In separate studies, research teams supported by NIH, including NIA intramural investigators, have reported that rare variations in the TREM2 and the PLD3 genes can double or even triple an individual's risk for developing Alzheimer's disease. TREM2 is a gene involved in inflammation and the immune response, and PLD3 appears to influence levels of toxic beta-amyloid in the brain, thought to be a main contributor to the disease process. These discoveries provide potential treatment targets for AD and important clues in understanding the disease NIH's long-term planning efforts are one component of HHS's National Plan to Address Alzheimer's Disease. As the lead agency in implementing Goal #1 of the National Plan, Prevent and Effectively Treat Alzheimer's Disease by 2025, NIH adopted milestones to guide and track the implementation of recommendations articulated in the May 2012 Alzheimer's Disease Research Summit. NIH's efforts to track research progress will be greatly facilitated by the launch of the International Alzheimer's Disease Research Portfolio (IADRP), a new, publicly available Big Data database that captures current Alzheimer's disease research investments and resources. The IADRP will enable public and private funders to coordinate research planning, leverage resources, avoid duplication, and identify promising areas of growth.

NIH continues to invest in a broad spectrum of basic discovery and translational research activities critical to the development of disease-modifying strategies to combat Alzheimer's disease, and the total funding level for FY 2015 across NIH is estimated at $566 million. In response to the President's Alzheimer's Initiative, NIH established the AD Genetics Data Warehouse–a collaborative effort between geneticists and the National Human Genome Research Institute (NHGRI) Large-Scale sequencing program to identify further genetic risk and protective factors. Now in its third phase, scientists supported by the Alzheimer's Disease Neuroimaging Initiative (ADNI) have gathered and analyzed thousands of human brain scans, genetic profiles, and biomarkers and are continually refining ways of detecting AD at the earliest stage possible. More than 35 NIH-funded clinical trials are under way, and more than 40 compounds are being tested as potential preventive and therapeutic interventions for Alzheimer's and cognitive decline. With NIH support, the U.S Department of Veterans Affairs and participating centers in 15 states are broadly implementing the Resources for Enhancing Alzheimer's Caregiver Health (REACH), the first intensive caregiver support intervention to be proven effective in ethnically diverse populations.

Theme 4: Nurturing Talent and Innovation

A diverse, well-trained, and highly creative workforce is critical to the success of biomedical research and is essential for the development of new scientific insights and the translation of these insights into improved health for all. NIH has dedicated training grants and fellowships for graduate students and postdoctoral researchers to ensure that it maintains such a workforce into the foreseeable future.

Recognizing that the behavioral and biomedical research enterprise has grown in size and complexity in the past decade, and that the NIH budget is not likely to grow significantly in the next few years, a working group of the Advisory Committee to the Director (ACD) was charged with examining the future of the biomedical research workforce in the United States.

The ACD found that although the vast majority of people holding biomedical PhDs are productively employed, the proportion of PhDs that move into tenure-track or tenured faculty positions represents a minority of the trainee outcomes. An increasing number of trainees now conduct research in non-academic venues such as government or private sector, or are in research-related areas, such as teaching or research policy.

NIH has been working to implement many of the ACD's recommendations. In FY 2013 the NIH Common Fund initiated the Strengthening the Biomedical Research Workforce Program, which aims to support innovative training approaches that will expand knowledge and skills beyond those required for academic-based scientific careers. The goal of this program is to better prepare pre-doctoral students and postdoctoral scientists for the breadth of careers in the biomedical research workforce, and to establish an awardee network to develop, share, evaluate, and disseminate best practices within the entire training community. The Common Fund issued ten Broadening Experiences in Science Training (BEST) DP7 awards to institutions across the country in September. The BEST Funding Opportunity Announcement was re-issued in FY 2014 with the aim of funding an additional group of awards. In addition, NIH announced plans to encourage the adoption of individual development plans for all trainees and report on those plans in grant progress reports (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-13-093.html).

In order to develop NIH's ability to assess the performance of its training activities, the ACD recommended that NIH improve its means of identifying and tracking more comprehensively all graduate students and postdoctoral researchers supported by NIH. Doing so will provide a sound basis for assessing workforce needs and planning future training activities. NIH's efforts to improve the tracking and analysis of training activities include automating training tables in reporting documents and establishing structured data collection programs like SciENcv (Science Experts Network *curriculum vitae*), which is a data platform that allows each researcher to record all research activity and current biographical information at a single site. SciENcv was piloted in FY 2013 (http://nexus.od.nih.gov/all/2013/11/20/test-drive-sciencv/) and its implementation will be expanded in FY 2014. These initiatives will offer comprehensive career outcomes data, will better inform prospective graduate students and postdoctoral researchers about potential careers in biomedical research, and will ease the reporting burden associated with managing training programs and reporting on career outcomes.

Increasing Diversity

Achieving diversity in the NIH-funded biomedical research workforce is critical to the full realization of our national research goals and is in the best interest of our country. Yet, despite longstanding efforts from the NIH and other entities across the biomedical and behavioral research landscape to increase the number of scientists from underrepresented groups, diversity in biomedicine still falls far short of mirroring that of the U.S. population. Further, an NIH-commissioned study revealed a disturbing shortfall in success rates for research grant (R01) applications between White applicants and Black applicants. In response to the unacceptable status quo, the NIH Director charged the ACD to provide concrete recommendations on ways to improve the recruitment and retention of individuals who are underrepresented in the NIH-funded biomedical workforce.

Delivered in June 2012,[1] the ACD's recommendations covered four general areas to encourage workforce diversity: 1) enhanced mentoring/career preparation and retention; 2) increased support for comparatively under-resourced institutions with track records for producing and supporting scientists from underrepresented groups; 3) improved research on peer review and piloting intervention testing; and 4) better data collection and evaluation. These recommendations form the backbone of NIH's Biomedical Research Workforce Diversity Initiative, a multi-pronged approach to foster and promote diversity in the biomedical research workforce.

The centerpiece of the initiative is the Common Fund's Enhancing the Diversity in the NIH-Funded Workforce Program. This Program consists of three highly integrated initiatives through which awardees will collectively develop, implement, and test novel ways of engaging, training, and mentoring young scientists and will disseminate successful approaches across the nation for large-scale impact.

The Building Infrastructure Leading to Diversity (BUILD) initiative is a set of experimental training awards designed to learn how to attract students from diverse backgrounds into the training pipeline and to encourage their persistence to become future NIH-supported researchers. BUILD is designed to provide relatively under-resourced institutions with the opportunity to develop novel approaches to training and mentoring their students, many of whom are from disadvantaged backgrounds and/or backgrounds that are nationally underrepresented in biomedical research. Through the BUILD initiative, eligible institutions will design and implement new models of research training that emphasize attainment of hallmarks of success in addition to scientific competencies and progression to further scientific training, such as ability to network effectively, creativity/innovative thinking, writing/effective communication, and leadership. The initiative will provide awards to approximately 10 institutions across the country; transformative impact will occur via nationwide dissemination of effective approaches developed through BUILD. A Funding Opportunity Announcement for BUILD awards was published in December 2013.

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[1] *For more information, see http://acd.od.nih.gov/dbr.htm.*

- The National Research Mentoring Network (NRMN) will create a single nation-wide network of mentors and mentees that will connect students, postdoctoral fellows, and faculty to experienced mentors; develop novel mentoring strategies; establish standards for good mentorship; provide training opportunities for mentors; and provide networking and professional opportunities for mentees (see Funding Opportunity Announcement for NRMN).
- The Coordinating and Evaluation Center (CEC) within the Diversity program will work across all components of the consortium to determine what works and for whom. CEC will coordinate activities of the consortium as a whole, work with BUILD and NRMN awardees to establish hallmarks of success at all career stages, coordinate evaluation of BUILD and NRMN activities, and disseminate successful approaches to the biomedical research and training community (see Funding Opportunity Announcement for CEC).

Beyond the Common Fund Program, the NIH will ensure that diversity is a core consideration of NIH governance by recruiting a Chief Officer for Scientific Workforce Diversity and creating an NIH Steering Committee Working Group on Diversity. These entities will:

- Conduct evaluation studies related to the review and funding of grants, to establish hallmarks of success at all career stages, to understand potential bias, and test various bias and diversity awareness training programs for NIH staff to determine the most effective approaches; and
- In collaboration with the Workforce initiative described above, develop better means of tracking all trainees and enhance data collection capabilities with respect to data on Hispanic sub-populations, individuals with disabilities, socioeconomic status, and education.

Supporting Early-Career Investigators

NIH recognizes that there is a pool of talented junior scientists who have the intellect, scientific creativity, drive, and maturity to flourish independently without the need for traditional postdoctoral training. Reducing the amount of time these scientists spend in training provides them with the opportunity to start highly innovative research programs as early in their careers as possible. It also allows host institutions to invigorate their scientific communities by integrating the fresh perspectives brought by the junior investigators.

Two awards NIH uses to support early-career investigators are the NIH Director's Early Independence Award and the NIH Pathway to Independence Award. The Early Independence Award provides a way for some exceptional early-career investigators to skip postdoctoral training altogether and to begin independent research directly after completing their terminal degree, while the NIH Pathway to Independence Award is designed to facilitate a timely transition from a mentored postdoctoral research position to a stable research position with independent support at an earlier career stage than is currently the norm.

Cultivating Innovation

The past few decades have brought tremendous scientific advances that can greatly benefit medical research. While this unprecedented period of progress will hopefully continue into the foreseeable future, human health and well-being would benefit from accelerating the current pace of discovery. One way to achieve this goal is to support scientists of exceptional creativity who propose highly innovative approaches to major contemporary challenges in biomedical research. By bringing their unique perspectives and abilities to bear on key research questions, these visionary scientists may develop seminal theories or technologies that will propel fields forward and speed the translation of research into improved health.

To address this need, NIH has created three complementary programs—the NIH Director's Pioneer Award, New Innovator Award, and Transformative Research Award. Recipients of these awards are responsible for some of the most exciting new scientific breakthroughs. For example, Dr. Peng Yin and Dr. William Shih, both awardees of the New Innovator Award, created "DNA bricks," which are three-dimensional structures of synthetic DNA strands that may help develop targeted drug-delivery mechanisms. Another significant breakthrough was led by Dr. Karl Deisseroth, recipient of the Pioneer Award in 2005 and the Transformative Research Award in 2012. Dr. Deisseroth has developed a new brain-imaging technology, called CLARITY (highlighted above), that allows researchers to study a fully intact brain from both the global and microscopic perspectives.

Peer Review Innovation

Since 2007, NIH has been making substantial efforts to reduce the cost of peer review by the use of electronic meetings, non-refundable airline tickets, use of NIH conference space instead of hotels, and elimination of refreshments. That is estimated to have reduced peer review costs by $13 million per year in FY 2013 compared to FY 2007. For FY 2015, NIH will strive to achieve further savings by increasing the proportion of virtual peer review meetings to 15 percent, aiming to save an additional $2 million. As part of these efforts, NIH will monitor, assess, and report on if and how increased virtual panels broaden the reviewer community.

Conclusion

Investment in NIH is an investment in the overall health, economic strength, and global wellbeing of the country. NIH research has led to countless improvements in public health and safety, from a new treatment for cystic fibrosis to an awareness campaign that resulted in a dramatic decrease in the number of infants lost to Sudden Infant Death Syndrome to a new vaccine to prevent cervical cancer. NIH has been the economic engine driving the creation of thousands of research and development jobs. Scientists supported by NIH are at the forefront of breakthrough discoveries in all areas of biomedicine and are engaged in innovative biotechnology endeavors that will advance diagnosis and treatment for countless diseases, improving the health of all Americans while also driving the biotechnology sector. As a world leader in biomedical research, NIH is also a force for scientific diplomacy. In a world brought together through technology, NIH-funded scientists collaborate with colleagues across the globe to examine diseases that threaten health in all parts of the world. Working together to facilitate

research progress, train the next generation of biomedical researchers, and promote biosecurity, NIH strives to create a safer, healthier, more secure world.

The benefits of NIH investments are substantial, and in order for NIH to succeed in addressing the public health challenges of today and tomorrow, it must be strategic in how it deploys its resources. This requires planning and assessment of its research portfolio; as well, it must balance capitalizing on scientific opportunity and combating current public health threats, with creating the knowledge base to move quickly when new threats and opportunities appear.

In recognition of the important role that biomedical science plays in innovation and economic growth, many countries around the world have significantly increased their investment in biomedical science. Between 1999 and 2009, Asia's share (including China, India, Japan, Malaysia, Singapore, South Korea, Taiwan, and Thailand) of worldwide R&D expenditures grew from 24 percent to 32 percent, while U.S. R&D expenditures declined from 38 percent to 31 percent.[2] While the U.S. currently leads the world in R&D spending, China's increasing investment in R&D is projected to close the gap and surpass the U.S. in total R&D spending by about 2022.[3] The European Commission has also recently urged its member nations to increase their investment in research substantially, recommending budgets of €80 billion ($108 billion) in 2014–2020, a 40-percent increase over the previous seven-year period.[4] As the largest funder of biomedical research in the world, NIH must continue its efforts to train, develop, and sustain a diverse, productive workforce for continued leadership in biomedical innovation.

[2] *Leadership in Decline, United for Medical Research, 2012* http://www.unitedformedicalresearch.com/wp-content/uploads/2012/07/Leadership-in-Decline-Assessing-US-International-Competitiveness-in-Biomedical-Research.pdf

[3] *2014 Global R&D Funding Forecast, 2013* http://www.battelle.org/docs/tpp/2014_global_rd_funding_forecast.pdf?sfvrsn=4

[4] http://ec.europa.eu/programmes/horizon2020/en/what-horizon-2020

Impact of Budget Level on Performance
(Dollars in Millions, except where noted)

Programs and Measures	FY 2014 Enacted [3,4]	FY 2015 PB	FY 2015 +/- FY 2014
Research Project Grants	$16,077.332	$16,196.847	0.7%
Competing Average Cost (in thousands)	$474.181	$443.096	-6.6%
Number of Competing Awards (whole number)	8,997	9,326	3.7%
Estimated Competing RPG Success Rate (absolute rate)	17.3%	17.4%	0.1%
Research Centers	$2,713.055	$2,722.834	0.4%
Other Research	$1,824.798	$1,867.979	2.4%
Training	$752.877	$767.132	1.9%
Research & Development Contracts	$2,990.346	$3,030.746	1.4%
Intramural Research	$3,395.910	$3,435.324	1.2%
Research Management and Support	$1,528.653	$1,544.027	1.0%
Common Fund (non-add)	*$533.039*	*$583.039*	*9.4%*
Buildings & Facilities Appropriation	$128.663	$128.663	0.0%
Other Mechanisms[1]	$666.068	$668.101	0.3%
Total, Program Level[2]	**$30,150.853**	**$30,361.653**	0.7%

[1] Includes Office of the Director-Other, building repair & improvement (R&I) funds allocated for the NCI-Frederick facility, Superfund Research activities funded from the Interior appropriation, and National Library of Medicine (NLM) Program Evaluation.

[2] Includes discretionary budget authority received from Labor/HHS appropriations (ICs) and the Interior appropriation (Superfund). Also includes mandatory budget authority derived from the Special type 1 Diabetes account, and NLM Program Evaluation.

[3] FY 2014 figures are shown on a comparable basis to FY 2015, reflecting the NCBI and PA proposal.

[4] The amounts in the FY 2014 column take into account funding reallocations, and therefore may not add to the total budget authority reflected herein.

FY 2015 Budget Request
National Institutes of Health

Overview of Performance

The National Institutes of Health (NIH) mission is to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability. Investments in basic biomedical and behavioral research make it possible to understand the causes of disease onset and progression, design preventive interventions, develop better diagnostics, and discover new treatments and cures. Realizing the benefits of fundamental biomedical discoveries depends on the translation of that knowledge into the development of new diagnostics, therapeutics, and preventive measures to improve health. Investments in translational research are leading to the identification of new targets and pathways for the development of new therapeutics.

The FY 2015 NIH Budget Request reflects the agency's longstanding commitment to invest strategically using performance-based analysis, as emphasized in the GPRA Modernization Act of 2010 (P.L. 111-352). Through the continuous evaluation and strategic management of its research portfolio, NIH focuses on funding research that shows the greatest promise for improving the overall health of the American people. In addition, NIH continually seeks to identify and address high-priority scientific opportunities and emerging public health needs. By managing its research portfolio to support key research priorities, NIH ensures the most effective use of funds to achieve the greatest impact on the health and welfare of the Nation. In particular, NIH's strong peer-review process, site visits, performance monitoring, program evaluation and performance-based contracting enable the agency to ensure that its investments generate results for the American people.

NIH strives to achieve transparency and accountability by regularly reporting results, achievements, and the impact of its activities. To increase transparency and promote effective use of resources, NIH began reporting the amount of indirect costs paid per grant on its Research Portfolio Online Reporting Tools website (NIH RePORT) in October 2013. The agency supports a wide spectrum of biomedical and behavioral research and engages in a full range of activities that enable research, its management, and the communication of research results. Because of this diversity and complexity, NIH uses a set of performance measures that is representative of its activities and is useful for tracking progress in achieving performance priorities. This representative approach has helped NIH to share progress of its performance priorities with HHS, the rest of the Executive Branch, the Congress, and the public.

The NIH performance measures reflect the agency's overall goals to advance basic biomedical and behavioral science, support translational research, and enhance the development of human capital and strengthen the scientific workforce. The measures also support the goals and objectives of the HHS Strategic Plan 2014-2018. In particular, NIH substantially contributes to the HHS Strategic Goal 2–Advance Scientific Knowledge and Innovation. For example, in FY 2015, in support of Objective A (Accelerate the process of scientific discovery to improve

health) under Goal 2, NIH will support research with the goals of: (1) making freely available to researchers the results of 400 high-throughput biological assays, screened against a library of 300,000 unique compounds, that are expected to provide a scientific resource that will accelerate the discovery of protein functions that control critical processes such as development, aging, and disease; and (2) identifying and characterizing two molecular pathways of potential clinical significance that may serve as the basis for discovering new medications for preventing and treating asthma exacerbations. Moreover, in support of Objective D (Increase our understanding of what works in public health and human services practice) under Goal 2, NIH will support research to identify three effective system interventions generating the implementation, sustainability, and ongoing improvement of research-tested interventions across healthcare systems.

Performance Management

Performance management at NIH is an integrated and collaborative process to ensure that the agency is achieving its mission to conduct and support research to improve public health. At the agency level, the NIH Director sets priorities, monitors performance, and reviews results across the 27 Institutes and Centers (ICs) and the Office of the Director (OD). The OD is the central office responsible for setting policy for NIH, and for planning, managing, and coordinating the programs and activities of all NIH components. The NIH Director provides leadership to the ICs and helps identify needs and opportunities, especially for efforts that involve multiple ICs. Each IC and OD office carries out priority setting, performance monitoring, progress reviews, and makes adjustments based on progress achieved in their respective areas of science. In addition to the performance management processes that occur for the NIH research program, there are equivalent processes for administrative management functions.

The NIH performance framework includes: (1) priority setting with input from key stakeholders; (2) implementation and management of activities that support priorities; (3) monitoring and assessment of progress, and identification of successes and challenges; (4) oversight by IC leadership and OD office directors in assessing overall progress toward priorities and identification of best practices, appropriate next steps, and corrective actions (as needed); (5) incorporation of regular feedback from IC and OD office leadership to enhance activities; (6) regular reviews of priorities, progress, and outcomes by the NIH Director and IC Directors; and (7) regular review of performance and priorities by external expert review groups including grant peer-review groups, Advisory Councils, and ad hoc working groups.

Qualitative and quantitative information is used to monitor progress and help to identify successes as well as obstacles in achieving short and long term goals. Supporting high-performing research is a process of adapting to new developments or newly identified barriers, or shifting resources to pursue promising unanticipated results that may provide critical new information. Moreover, the impact of research may not be immediately known and may depend on additional development or on advances in other fields. Despite these challenges, NIH leadership is able to manage performance effectively by using the best available information to assess progress toward achieving priorities and making appropriate adjustments.

Research is an inherently collaborative endeavor, and partnerships are crucial to achieving scientific research outcomes. The role of the extramural research community (the scientists at universities and hospitals across the country and around the world) as NIH's partner in research is well known. However, of increasing importance are partnerships with private companies, not-for-profit institutions, non-governmental organizations, other Federal agencies, and state and international entities. Joint research and training activities and other exchanges with such groups increase the leverage of NIH resources and support vibrant partnerships to help NIH achieve its mission. Moreover, such partnerships facilitate valuable information feedback loops that identify emerging needs, suggest important new research questions, and otherwise inform priority setting. Partnerships also provide access to populations that are essential to advancing knowledge.

All scientific research carried out through NIH support is subjected to a rigorous and consistently applied review process. For example, the Extramural Research Program, which includes the largest category of NIH-funded research, utilizes two levels of peer review. The first level consists of chartered scientific review groups composed of outside experts in particular scientific disciplines. The second level is the National Advisory Councils of the ICs. For the Intramural Research Program, the progress of individual scientists and their laboratories is evaluated once every four years by Boards of Scientific Counselors composed of external experts. These reviews enable ongoing assessments of all intramural labs and the accomplishments of the scientists who contribute to them. It is through this well-honed system of peer review that NIH maintains its focus on supporting research of the highest possible quality.

The NIH approach to performance management is undergirded by the NIH Governance Structure. That structure includes the NIH Steering Committee[5] and five standing Working Groups[6]. Ad hoc working groups are established, as needed, to address emerging issues. The premise of the structure is that shared governance, which depends on the active participation of the IC Directors with the NIH Director, will foster the collaborative identification of corporate issues and a transparent decision-making process. With active participation by the IC Directors in NIH-wide governance, NIH can maximize its perspective and expertise in the development and oversight of policies common to NIH and its ICs. Through the governance process, corporate decisions are made; these may be long-term and strategic (e.g., facilities planning, budget strategy, research policy direction) or short-term and tactical (e.g., stipend levels, resource allocations and compliance oversight). This process does not include issues related to the setting of scientific priorities, which is reserved for meetings of all IC Directors. The NIH Director meets with the IC Directors on a bi-weekly basis, and scientific initiatives are discussed as well as major management issues that affect the agency. In addition, scientists—from within and outside the agency—are invited to present on new or emerging research opportunities. The NIH Director stays informed of priorities through regular meetings with IC and OD Office Directors. Similarly, the IC Directors monitor performance through regular meetings with the Division Directors and Scientific/Clinical Directors in their respective ICs.

[5] *The NIH Steering Committee is composed of the NIH Director, Deputy Director (ex-officio), the Directors of NCI, NHLBI, and NIAID, as well as a balance of Directors from the smaller and medium-sized institutes.*

[6] *The five standing working groups are: Extramural Activities, Intramural, Information Technology, Facilities, and Management and Budget.*

Based on these reviews, leadership and their staff take appropriate actions to support research activities. For example, the reviews may lead to the development of new award programs for early-career researchers, the development of new funding announcements for promising research areas, or new collaborations across NIH and/or with other Federal and non-Federal partners. The NIH Director and senior leadership receive regular updates on the progress of the priorities, provide feedback, and incorporate the latest information into the NIH's overall planning and management efforts. This constant feedback loop enables NIH to make critical adjustments periodically to align activities and target resources in support of its research priorities.

FY 2015 Budget by HHS Strategic Goal
National Institutes of Health
(Dollars in Millions)

HHS Strategic Goals	FY 2013 Actual	FY 2014 Enacted	FY 2015 President's Budget
1.Strengthen Health Care	**$745**	**$1,003**	**$1,612**
1.A Make coverage more secure for those who have insurance and extend affordable coverage to the uninsured			
1.B Improve health care quality and patient safety			
1.C Emphasize primary & preventative care linked with community	745	1,003	1,612
1.D Reduce growth of healthcare costs while promoting high-value, effective care			
1.E Ensure access to quality, culturally competent care for vulnerable populations			
1.F Promote the adoption and meaningful use of health information technology			
2. Advance Scientific Knowledge and Innovation	**$27,021**	**$27,811**	**$26,834**
2.A Accelerate the process of scientific discovery to improve patient care	27,021	27,811	26,834
2.B Foster innovation at HHS to create shared solutions			
2.C Invest in the regulatory sciences to improve food & medical product safety			
2.D Increase our understanding of what works in public health and human service services			
3. Advance the Health, Safety and Well-Being of the American People			
3.A Promote the safety, well-being, resilience, and healthy development of children and youth			
3.B Promote economic & social well-being for individuals, families and communities			
3.C Improve the accessibility and quality of supportive services for people with disabilities and older adults			
3.D Promote prevention and wellness			
3.E Reduce the occurrence of infectious diseases			
3.F Protect Americans' health and safety during emergencies, and foster resilience in response to emergencies			
4. Increase Efficiency, Transparency and Accountability of HHS Programs	**$1,000**	**$1,011**	**$1,581**
4.A Ensure program integrity and responsible stewardship of resources	1,000	1,011	1,581
4.B Fight fraud and work to eliminate improper payments			
4.C Use HHS data to improve American health and well-being of the American people			
4.D Improve HHS environmental, energy, and economic performance to promote sustainability			
5. Strengthen the Nation's Health and Human Service Infrastructure and Workforce	**$386**	**$327**	**$335**
5.A Invest in HHS workforce to meet America's health and human service needs today & tomorrow	386	327	335
5. B Ensure that the Nation's health care workforce meets increased demands			
5.C Enhance the ability of the public health workforce to improve health at home and abroad			
5.D Strengthen the Nation's human service workforce			
5.E Improve national, state & local surveillance and epidemiology capacity			
TOTAL, Program Level	**$29,151**	**$30,151**	**$30,362**

NATIONAL INSTITUTES OF HEALTH
FY 2015 Congressional Justification
Budget Mechanism - Total

(Dollars in Thousands)

MECHANISM	FY 2013 Actual [2]		FY 2014 Enacted [2,3]		FY 2015 President's Budget		FY 2015 +/- FY 2014	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	25,140	$11,119,346	23,632	$10,959,764	23,236	$11,198,737	-396	$238,973
Administrative Supplements	*(1,315)*	248,370	*(1,215)*	154,272	*(1,204)*	149,179	*(-11)*	-5,093
Competing:								
Renewal	1,766	904,567	2,006	1,280,732	1,960	956,371	-46	-324,361
New	6,419	2,525,738	6,950	2,977,247	7,322	3,167,151	372	189,904
Supplements	49	8,926	41	8,231	44	8,788	3	557
Subtotal, Competing	8,234	$3,439,230	8,997	$4,266,210	9,326	$4,132,310	329	-$133,900
Subtotal, RPGs	33,374	$14,806,946	32,629	$15,380,246	32,562	$15,480,226	-67	$99,980
SBIR/STTR	1,466	638,517	1,584	697,086	1,635	716,621	51	19,535
Research Project Grants	34,840	$15,445,463	34,213	$16,077,332	34,197	$16,196,847	-16	$119,515
Research Centers:								
Specialized/Comprehensive	1,177	$1,994,721	1,128	$1,960,307	1,149	$1,962,737	21	$2,430
Clinical Research	58	370,187	58	407,107	58	402,021	0	-5,086
Biotechnology	89	156,159	88	157,710	90	170,682	2	12,972
Comparative Medicine	52	132,623	52	132,864	52	132,327	0	-537
Research Centers in Minority Institutions	21	55,055	21	55,067	21	55,067	0	0
Research Centers	1,397	$2,708,745	1,347	$2,713,055	1,370	$2,722,834	23	$9,779
Other Research:								
Research Careers	3,677	$614,651	3,715	$625,157	3,710	$626,778	-5	$1,621
Cancer Education	96	34,466	96	35,500	96	36,561	0	1,061
Cooperative Clinical Research	431	434,870	492	456,827	492	463,979	0	7,152
Biomedical Research Support	122	69,214	88	64,588	88	64,432	0	-156
Minority Biomedical Research Support	310	104,656	313	104,927	316	105,146	3	219
Other	1,748	525,628	1,778	537,799	1,804	571,083	26	33,284
Other Research	6,384	$1,783,484	6,482	$1,824,798	6,506	$1,867,979	24	$43,181
Total Research Grants	42,621	$19,937,692	42,042	$20,615,185	42,073	$20,787,660	31	$172,475
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	3,071	$132,034	3,126	$138,879	3,195	$141,865	69	$2,986
Institutional Awards	12,468	601,489	12,481	613,998	12,520	625,267	39	11,269
Total Research Training	15,539	$733,524	15,607	$752,877	15,715	$767,132	108	$14,255
Research & Develop. Contracts	2,339	$2,895,302	2,210	$2,990,346	2,186	$3,030,746	-24	$40,400
(SBIR/STTR) (non-add) [1]	*(120)*	*(59,137)*	*(127)*	*(64,982)*	*(127)*	*(70,995)*	*(0)*	*(6,013)*
Intramural Research	7,126	$3,282,734	7,137	$3,395,910	7,137	$3,435,324	0	$39,414
Res. Management & Support	5,580	1,485,463	5,697	1,528,653	5,697	1,544,027	0	15,374
Res. Management & Support (SBIR Admin) (non-add) [1]	*(2)*	*(3,185)*	*(10)*	*(6,084)*	*(10)*	*(5,934)*	*0*	*(-150)*
Office of the Director								
OD - Other		607,663		572,519		574,552		2,033
OD Common Fund (non-add) [1, 4]		*(513,476)*		*(533,039)*		*(583,039)*		*(50,000)*
ORIP/SEPA (non-add) [1, 4]		*(289,376)*		*(294,195)*		*(294,195)*		*(0)*
OD Appropriation (non-add) [1,4]		*(1,410,515)*		*(1,399,753)*		*(1,451,786)*		*(52,033)*
Buildings and Facilities[5]		126,013		136,341		136,663		322
Appropriation [1]		*(118,109)*		*(128,663)*		*(128,663)*		0
Type 1 Diabetes[6]		-142,350		-139,200		-150,000		-10,800
Subtotal, Labor/HHS Budget Authority		**$28,926,041**		**$29,926,104**		**$30,126,104**		**$200,000**
Interior Appropriation for Superfund Res.		74,871		77,349		77,349		0
Total, NIH Discretionary B.A.		**$29,000,912**		**$30,003,453**		**$30,203,453**		**$200,000**
Type 1 Diabetes		142,350		139,200		150,000		10,800
Total, NIH Budget Authority		**$29,143,262**		**$30,142,653**		**$30,353,453**		**$210,800**
NLM Program Evaluation		8,200		8,200		8,200		0
Total, Program Level		**$29,151,462**		**$30,150,853**		**$30,361,653**		**$210,800**

[1] All items in italics and brackets are non-add.

[2] FY 2013 and FY 2014 figures are shown on a comparable basis to FY 2015, reflecting the NCBI and PA proposal.

[3] The amounts in the FY 2014 column take into account funding reallocations, and therefore may not add to the total budget authority reflected herein.

[4] Number of grants and dollar amounts for the Common Fund, ORIP and SEPA components of OD are distributed by mechanism and are noted here as a non-add. The Office of the Director - Appropriations also is noted as a non-add since these funds are accounted for under OD-Other.

[5] Includes B&F appropriation plus building repair and improvement (R&I) dollars appropriated to NCI for the Frederick MD facility.

[6] Number of grants and dollars for mandatory Type I Diabetes are distributed by mechanism above; therefore, Type I Diabetes amount is deducted to provide subtotals only for the Labor/ HHS Budget Authority.