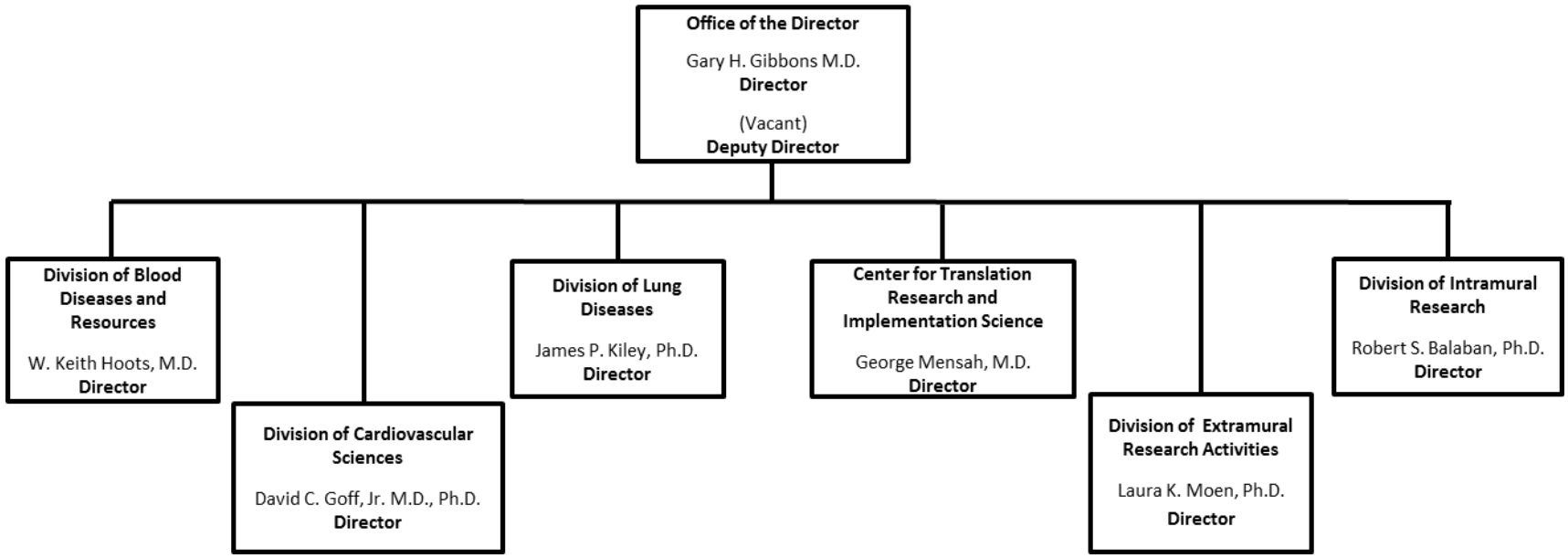
DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Heart, Lung, and Blood Institute (NHLBI)

NATIONAL INSTITUTES OF HEALTH
National Heart, Lung, and Blood, Institute



NATIONAL INSTITUTES OF HEALTH

National Heart, Lung, and Blood Institute

For carrying out section 301 and title IV of the PHS Act with respect to cardiovascular, lung, and blood diseases, and blood and blood products, ~~$2,237,268,000~~$3,112,032,000.

NATIONAL INSTITUTES OF HEALTH
National Heart, Lung, and Blood Institute

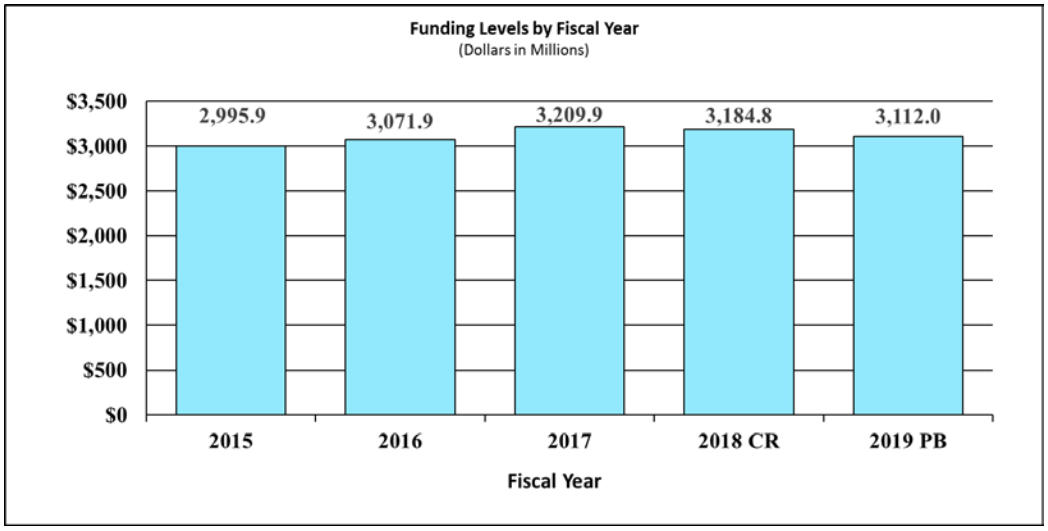
Amounts Available for Obligation[1]
(Dollars in Thousands)

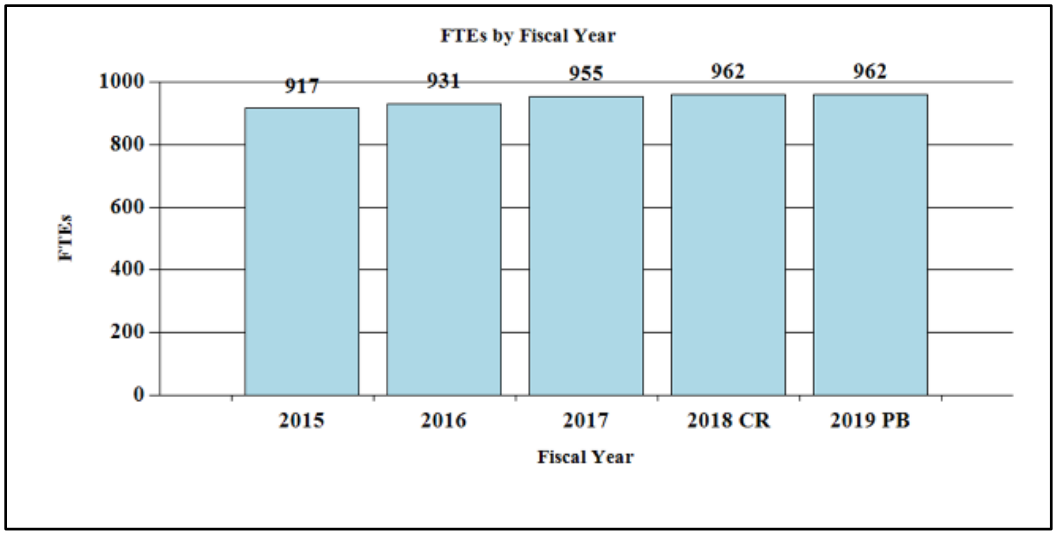
Source of Funding	FY 2017 Final	FY 2018 Annualized CR	FY 2019 President's Budget
Appropriation	$3,206,589	$3,206,589	$3,112,032
Mandatory Appropriation: (non-add)			
Type 1 Diabetes	*(0)*	*(0)*	*(0)*
Other Mandatory financing	*(0)*	*(0)*	*(0)*
Rescission	0	-21,776	0
Sequestration	0	0	0
Secretary's Transfer	-7,152	0	0
Subtotal, adjusted appropriation	$3,199,437	$3,184,813	$3,112,032
OAR HIV/AIDS Transfers	10,492	0	0
Subtotal, adjusted budget authority	$3,209,929	$3,184,813	$3,112,032
Unobligated balance, start of year	0	0	0
Unobligated balance, end of year	0	0	0
Subtotal, adjusted budget authority	$3,209,929	$3,184,813	$3,112,032
Unobligated balance lapsing	-86	0	0
Total obligations	$3,209,843	$3,184,813	$3,112,032

[1] Excludes the following amounts for reimbursable activities carried out by this account:
FY 2017 - $17,559 FY 2018 - $17,904 FY 2019 - $15,603

Fiscal Year 2019 Budget Graphs

History of Budget Authority and FTEs:





NATIONAL INSTITUTES OF HEALTH
National Heart, Lung, and Blood Institute

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2018 Amount Authorized	FY 2018 Annualized CR	2019 Amount Authorized	FY 2019 President's Budget
Research and Investigation	Section 301	42§241	Indefinite	$3,184,813,054	Indefinite	$3,112,032,000
National Heart, Lung, and Blood Institute	Section 401(a)	42§281	Indefinite		Indefinite	
Total, Budget Authority				$3,184,813,054		$3,112,032,000

NATIONAL INSTITUTES OF HEALTH
National Heart, Lung, and Blood Institute

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
2009	$2,924,942,000	$3,025,500,000	$3,006,344,000	$3,015,689,000
Rescission				$0
2010	$3,050,356,000	$3,123,403,000	$3,066,827,000	$3,096,916,000
Rescission				$0
2011	$3,187,516,000		$3,182,524,000	$3,096,916,000
Rescission				$27,192,768
2012	$3,147,992,000	$3,147,992,000	$3,036,189,000	$3,084,851,000
Rescission				$5,830,368
2013	$3,076,067,000		$3,085,390,000	$3,079,020,632
Rescission				$6,158,041
Sequestration				($154,545,663)
2014	$3,098,508,000		$3,077,916,000	$2,988,605,000
Rescission				$0
2015	$2,987,685,000			$2,997,870,000
Rescission				$0
2016	$3,071,906,000	$3,035,062,000	$3,135,519,000	$3,115,538,000
Rescission				$0
2017[1]	$3,113,533,000	$3,190,474,000	$3,242,685,000	$3,206,589,000
Rescission				$0
2018	$2,534,803,000	$3,256,521,000	$3,322,774,000	$3,206,589,000
Rescission				$21,775,946
2019	$3,112,032,000			

[1] Budget Estimate to Congress includes mandatory financing.

Justification of Budget Request

National Heart, Lung, and Blood Institute

Authorizing Legislation: Section 301 and title IV of the Public Health Service Act, as amended.
Budget Authority (BA):

	FY 2017 Actual	FY 2018 Annualized CR*	FY 2019 President's Budget	FY 2019 +/- FY 2018
BA	$3,209,929,000	$3,184,813,000	$3,112,032,000	-$72,781,000
FTE	955	962	962	0

*this amount is rounded.

Program funds are allocated as follows: Competitive Grants/Cooperative Agreements; Contracts; Direct Federal/Intramural and Other.

Director's Overview

The National Heart, Lung, and Blood Institute (NHLBI) will continue its strong tradition of supporting research to better understand the basic biology of the heart, lungs, blood, and sleep – and to prevent and treat the disorders that occur when these organs and systems break down.

Public health outcomes that once seemed impossible are now within reach. In FY 2019, NHLBI will leverage emerging scientific opportunities to improve health and longevity for the millions of Americans suffering from heart, lung, blood, and sleep disorders.

The Institute will explore gene editing technologies to accelerate the development of new cures for sickle cell disease. NHLBI's growing precision medicine efforts will mine genomic data and other information about disease pathways to inform the development of more personalized treatments. Working in partnership with the Food and Drug Administration (FDA), NHLBI will continue to advance the field of regenerative medicine. Moreover, by engaging with diverse communities, the Institute will improve the adoption of evidence-based interventions and reduce the impact of treatable health problems such as obesity. These efforts will be coupled to programs to nurture a diverse, talented generation of researchers to meet tomorrow's public health challenges head on.

Investing in Basic Research to Understand Health and Disease
NHLBI's support of fundamental discovery science continues to make essential contributions to our understanding of normal biology and mechanisms of disease, and to the development of new approaches to prevent, diagnose, and treat heart, lung, blood, and sleep disorders.

For example, basic research has helped reveal how stem cells build the lung's complex architecture during development, and how stem-like cells remaining in the adult lung might be used to repair a damaged lung. In an NHLBI-funded study, researchers used prior knowledge about genes and molecules involved in lung development to provide visual signatures for unique

lung cell types.[1] They found two distinct populations of cells, MANC and AMP, that had distinct responses to injury. MANC cells promoted the growth and regeneration of functional lung tissue; whereas AMP cells promoted the creation of fibrous connective tissue, a harmful response and a known contributor to chronic lung diseases like idiopathic pulmonary fibrosis. This discovery may pave the way for new therapeutic approaches that tap into developmental pathways to promote recovery of healthy lung tissue and inhibit formation of scar tissue.

The Power of Data to Personalize Medicine

The NHLBI Trans-Omics for Precision Medicine program (TOPMed) has genomic data from about 120,000 diverse individuals enrolled in more than 60 NHLBI-funded studies. These data will be analyzed along with data on medical history, socioeconomic status, lifestyle and environmental factors, imaging, and biomarkers – with the goal of discovering new disease pathways and developing more personalized interventions. The TOPMed dataset was one of three selected for inclusion in a pilot launch of the NIH Data Commons, a new public-private partnership that NIH will use to bring research findings into a cloud-computing environment with state-of-the-art data management and analysis tools to enhance data sharing, collaboration, and innovation.

The Institute also recently provided early, open access to the complete primary dataset from the Systolic Blood Pressure Intervention Trial (SPRINT). This NHLBI-funded trial found that intensive blood pressure treatment can reduce heart attacks, strokes, and death in high-risk adults over 50 years of age. The SPRINT Data Analysis Challenge, conducted in partnership with the New England Journal of Medicine, invited researchers to propose and explore new scientific questions based on the trial's primary data.[2] The Challenge attracted global participations, with approximately 16,000 followers on social media, 200 competing teams, and three final winners who presented at a national conference. The winning team developed a tool that enables clinicians to quickly assess whether intensive blood pressure management is appropriate for a specific patient.

Understanding Population Differences to Reduce Health Disparities

Fueled by progress in preventing and treating cardiovascular diseases (CVD), the Nation has experienced substantial declines in CVD death rates over the past 35 years. Yet many groups, defined by gender, race, ethnicity, age, socioeconomic status, and geography, continue to experience a high risk of CVD and poor outcomes. A recent study found high CVD mortality rates throughout the U.S. heartland, from southeastern Oklahoma to eastern Kentucky.[3] Having such regional data can help inform efforts to reduce CVD mortality in high-burden communities.

For example, researchers with NHLBI's Strong Heart Study are partnering with educators to implement a CVD prevention program in ten medically underserved Montana towns. In rural North Carolina, researchers are studying the use of mobile health technology to improve CVD education and prevention efforts.[4] A new NHLBI initiative, DECIPHeR, will solicit and

[1] Zepp, JA et al. Cell, 2017. https://www.ncbi.nlm.nih.gov/pubmed/28886382
[2] https://challenge.nejm.org/pages/home
[3] Roth, GA et al. JAMA, 2017. https://www.ncbi.nlm.nih.gov/pubmed/28510678
[4] See 5R01HL120702-04 and 5R01HL120690-04 at https://projectreporter.nih.gov

coordinate further studies of this kind, to explore how evidence-based interventions can be adapted to the needs, resources, and sociocultural norms of diverse communities across the U.S.

Nurturing a Diverse and Talented Biomedical Workforce
NHLBI is committed to developing, sustaining, and strengthening a robust biomedical workforce that reflects the Nation's diversity and breadth of talent.

NHLBI is finding other innovative ways to increase support for early-stage investigators. In FY 2017, a new program[5] issued its first awards to support 39 emerging and outstanding investigators who are conducting high-risk, high-reward research. NHLBI also offers short-term bridge awards to promising scientists so that they can stay productive and have time to compete for longer-term funding. The Institute is committed to bringing more physicians into the research workforce, and a new program launched in FY 2018 – Stimulating Access to Research in Residency – will help train more clinician-scientists. These and other ongoing NHLBI programs align with NIH's Next Generation Researchers Initiative.

Advancing Stem Cell Science for Safe and Effective Regenerative Medicine
NHLBI has taken a lead role in managing the Regenerative Medicine Innovation Project (RMIP) under the 21st Century Cures Act.[6] The Act authorized NIH, in coordination with FDA, to invest $30 million in clinical research with adult stem cells over four years, beginning in FY 2017. Working closely with FDA, a trans-NIH Regenerative Medicine working group led by NHLBI solicited research proposals from the regenerative medicine community, leading to eight projects that cover a broad spectrum of science and new technologies, and have the potential to advance understanding and treatment of common diseases – including diabetes, anemia, corneal and other eye diseases, and chronic skin ulcers – as well as rare diseases, including idiopathic pulmonary fibrosis, inherited skin diseases, and sickle cell disease. NIH will continue to work with FDA to engage the research community and to solicit new applications under the RMIP to bring the use of adult stem cells safely into clinical practice.

Program Descriptions and Accomplishments

Cardiovascular Diseases
This program supports research to advance understanding, prevention, and treatment of pediatric and adult cardiovascular diseases (CVD), including heart attack, heart failure, stroke, and congenital heart disease. Additionally, the program supports the development of innovative technologies for early detection and intervention in patients with CVD.

Although CVD is often considered a disease of aging, the program's comprehensive portfolio is aimed at keeping the heart healthy across the entire lifespan. This approach recognizes that risk factors for CVD, such as unhealthy behaviors (e.g., smoking) or an unhealthy environment (e.g., second-hand smoke), can start in childhood and persist long after. Researchers with NHLBI's Coronary Artery Risk Development in Young Adults (CARDIA) Study have found that a risk

[5] https://grants.nih.gov/grants/guide/rfa-files/RFA-HL-16-024.html
[6] https://www.nih.gov/research-training/medical-research-initiatives/rmi

calculator based on lifestyle measures can be used to estimate cardiovascular risk 25 years out, and may be a useful tool in CVD prevention efforts targeting young people.[7]

In addition to prevention efforts, NHLBI is investing in new ways to treat CVD. For example, NHLBI-funded researchers have learned that inflammation plays an important role in CVD, and have identified specific inflammatory pathways as targets for therapy. Since the 1970s, NHLBI has supported basic research on a secreted protein called Interleukin-1 (IL-1) and its role in atherosclerosis, a disease that involves inflammation within arteries and is a significant underlying cause of cardiovascular events such as heart attack and stroke.

This 40-year investment into research on IL-1 is paying off in the form of new therapies being tested in clinical trials. An industry-sponsored study published in 2017 showed that Canakinumab, a drug that targets inflammation, reduced the risk of heart attacks, strokes, and death by 15 percent among people who had survived a prior heart attack.[8] A current NHLBI-funded study, the Cardiovascular Inflammation Reduction Trial (CIRT), is testing methotrexate, a less expensive anti-inflammatory drug, to determine if it reduces heart attacks, strokes, or death in people who have multiple coronary blockages or have experienced a prior heart attack.[9]

Another line of research points to a potential new therapeutic approach for patients with heart failure. The adult human heart has little regenerative capacity under normal conditions, but NHLBI-funded researchers have found new evidence that the failing heart has the capacity to repair itself. In a study on mice with heart failure, they found that by interrupting a signaling pathway that normally represses survival genes in heart muscle cells, they were able to improve heart function in the mice.[10]

[7] Gooding, HC et al. JAMA Intern Med, 2017. https://www.ncbi.nlm.nih.gov/pubmed/28715555
[8] Ridker, PM et al. NEJM, 2017. https://www.ncbi.nlm.nih.gov/pubmed/28845751
[9] https://projectreporter.nih.gov/project_info_description.cfm?aid=9266464
[10] Leach, JP et al. Nature, 2017. https://www.ncbi.nlm.nih.gov/pubmed/28976966

Program Portrait: Addressing HIV-related Comorbidities

The human immunodeficiency virus (HIV) epidemic is evolving. Once a death sentence, HIV infection has become a chronic, manageable disease thanks to antiretroviral therapies (ART). People with HIV are living longer, healthier lives, but as they age, they also face unique susceptibilities to age-related cardiovascular disease (CVD). For example, people with HIV have a two to ten-fold greater risk of venous thromboembolism (a blood clot in a vein) and an approximately two-fold greater risk of heart attack compared to people without HIV.[11] By 2030, it is estimated that 78 percent of HIV-positive individuals will be diagnosed with some form of CVD.[12]

NHLBI has been at the forefront of efforts to address CVD among people with HIV. For example, in FY 2014, in collaboration with the National Institute of Allergy and Infectious Diseases, NHLBI began funding the Randomized Trial to Prevent Vascular Events in HIV (REPRIEVE) study. This is the first large-scale clinical trial to test whether a daily dose of lipid-lowering medication (pitavastatin) can reduce the risk of heart disease among HIV-infected individuals.[13]

In addition to CVD, researchers are learning that there is an exceptionally high prevalence of chronic lung diseases and sleep disorders among older people with HIV, as well as blood disorders that may occur as a complication of ART. Thus, while preventing and curing HIV infection remains a high priority, researchers from different disciplines are also mobilizing to understand and reduce the impact of these comorbidities. To facilitate this effort, two established population studies that NIH has funded for several decades will now be followed and analyzed as a combined cohort. The Multicenter AIDS Cohort Study (MACS) started in 1984, and includes more than 2,000 men; the Women's Interagency HIV Study (WIHS) started in 1994, and includes more than 2,300 women. Both studies include HIV-positive and HIV-negative participants. If appropriations allow, awards to support this combined cohort study will be issued in FY 2019, with NHLBI acting as the primary steward in close collaboration with 11 co-funding Institutes.

Lung Diseases

This program conducts and supports research that expands our understanding of lung biology and how lung diseases start and progress, as well as basic and clinical studies that lead to new and improved ways to diagnose, treat, and prevent lung diseases. Research areas include asthma, chronic obstructive pulmonary disease (COPD), cystic fibrosis, sleep-disordered breathing, pulmonary fibrosis, lymphangioleiomyomatosis (LAM), pulmonary complications of AIDS and tuberculosis, pediatric lung diseases, and more.

Among these diseases, COPD takes the greatest toll in terms of sheer numbers, affecting 16 million Americans and causing more deaths each year than any other disease but CVD or cancer. To confront this national health problem, NHLBI collaborated with Federal agencies, patients, caregivers, health care providers, non-profit organizations, and others to develop a COPD National Action Plan.[14] Finalized and released in May 2017, the plan is organized around five goals: To empower the COPD community to recognize and reduce the burden of COPD; to improve the diagnosis, prevention, treatment, and management of COPD; to collect, analyze, report, and disseminate COPD-related public health data; to increase and sustain research related to COPD; and to translate national policy, educational, and program recommendations into research and public health care actions. Since the release of the plan, NHLBI's Division of Lung Diseases has continued to work closely with other Federal agencies, medical and scientific

[11] Funderburg, NT et al. Thrombosis Research, 2014. https://www.ncbi.nlm.nih.gov/pubmed/24759134
[12] Smit, M et.al. Lancet Infectious Diseases 2015. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4528076/
[13] https://clinicaltrials.gov/ct2/show/NCT02344290
[14] https://www.nhlbi.nih.gov/health-pro/resources/lung/copd-national-action-plan

organizations, and patient advocacy groups to ensure that the collaboration so important to the plan's development continues and drives the plan's implementation.

At the same time, guided by the plan and the Institute's Strategic Vision, NHLBI continues to support research to better understand COPD and develop more effective interventions against it. For example, NHLBI's Subpopulations and Intermediate Outcome Measures in COPD (SPIROMICS) study is looking at genetic, clinical, biological, and other data including lung imaging, to help understand risk factors for COPD and poor outcomes from the disease.

Data from the Centers for Disease Control and Prevention show that women are more likely to die from COPD than men,[15] and new research shows that genetic factors may play a role in this. In one study, researchers analyzed genetic data from more than 10,000 current and former smokers with COPD and found that variations in a fetal lung development gene, *CELSR1*, were associated with COPD in women, but not men.[16] Identification of further sex-specific risk factors and pathways may enable new interventions to reduce death and disability from COPD in women.

Genetic and disease pathway information is also helping researchers develop more precisely tailored interventions for severe asthma. Prior NHLBI-funded research has demonstrated that symptoms and long-term outcomes of severe asthma can differ significantly from patient to patient, which has led to the identification of several clinical asthma subtypes.[17] Building from this information, NHLBI is supporting a new Precision Interventions for Severe and Exacerbation Prone Asthma (PrecISE) Network, in which targeted interventions will be guided by biomarkers specific to different asthma subtypes. Moreover, PrecISE will use a sequential, adaptive trial design allowing researchers to continuously analyze data as it is collected, to add new biomarkers for distinct asthma types, and to adjust the trial interventions as needed.[18]

Translational and clinical research programs, such as the Centers for Advanced Diagnostics and Experimental Therapeutics in Lung Diseases (CADET), are helping translate new knowledge about disease mechanisms into new therapies. As researchers learn more about the inflammatory pathways involved in lung diseases, treatments are moving beyond steroids into a first wave of new therapeutics that target inflammation, such as compounds that target FBXO3, a protein known to promote inflammation. Other potential therapies under development are focusing on breaking apart mucus to improve airflow.[19]

Researchers are also beginning to understand how cellular aging contributes to the risk and progression of idiopathic pulmonary fibrosis (IPF). A recent NHLBI-supported study showed that aging cells, without the capacity to produce new lung tissue, are increased in the lungs of patients with IPF and contribute to disease progression in a mouse model of IPF.[20] Selective

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[15] http://www.lung.org/lung-health-and-diseases/lung-disease-lookup/copd/learn-about-copd/how-serious-is-copd.html
[16] Hardin, M et.al. Am J Respir Cell Mol Biol, 2017. https://www.ncbi.nlm.nih.gov/pubmed/27854507/
[17] http://www.severeasthma.org/home.html
[18] https://grants.nih.gov/grants/guide/rfa-files/RFA-HL-17-010.html
[19] Livraghi-Betrico, A et al. Mucosal Immunol 2017. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5250616/
[20] Schafer, MJ et al. Nat Communications 2017. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5331226/

elimination of these aged cells improved lung health in the IPF mouse models. Other NHLBI-funded studies are revealing how the age-related shortening of telomeres, the caps on the ends of chromosomes, is associated with IPF and may be a useful diagnostic tool.[21]

Program Portrait: Supporting Women's Health During and After Pregnancy

For reproductive-age women, health complications during pregnancy are a serious concern, particularly for women giving birth to their first child. To better understand and predict the health risks facing first-time mothers, the Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-to-Be (nuMoM2b) is examining the risk factors associated with adverse pregnancy outcomes in a cohort of more than 10,000 women of geographically and ethnically diverse backgrounds. Past studies provided evidence to support a link between the risk of cardiovascular disease and certain pregnancy complications, including gestational hypertension and preeclampsia – which is marked by hypertension and elevated protein in urine. However, these studies lacked sufficient cohort sizes and often did not include measurements of biological markers. NHLBI is collaborating with the National Institute of Child Health and Human Development (NICHD) to fund extended analyses of the nuMoM2b cohort, specifically examining the links between pregnancy, sleep health, and cardiovascular outcomes.

In 2011, NHLBI and NICHD began the nuMoM2b Sleep-Disordered Breathing Study, which has found that pregnant women with obstructive sleep apnea (interrupted breathing during sleep) have an increased risk of hypertensive disorders and diabetes during pregnancy. In 2018, NHLBI and NICHD will build on this finding and launch a phase III clinical trial to determine whether treatment of sleep apnea reduces the risk of gestational hypertension, diabetes, and pre-eclampsia. NHLBI also has launched the nuMoM2b Heart Health Study to assess how sleep-disordered breathing contributes to risk of cardiovascular disease and other adverse outcomes *after* pregnancy, which may lead to targeted screening and intervention protocols.

Blood Diseases

This program supports research on the causes, prevention, and treatment of non-cancerous blood diseases including anemias, such as sickle cell disease and thalassemia; venous thromboembolism; malaria; and hemophilia. The program also assumes major responsibility in ensuring the adequacy and safety of the Nation's blood supply and in supporting scientific advances in stem cell biology, and new gene and cell-based therapies to repair and regenerate human tissues.

In recent years, there has been encouraging progress in understanding the intricate machinery and behavior of diverse cell types in the blood, which is yielding promising drug targets for blood disorders. For example, recent studies highlight the importance of autophagy; this is a naturally occurring process that helps cells stay healthy by recycling or destroying non-functional proteins and other cell components that can become toxic. In one recent NHLBI-funded study, researchers used patient-derived cells to screen for potential drugs to treat a rare blood disorder, Diamond-Blackfan anemia (DBA), which affects the ability of bone marrow to produce red blood cells. By testing more than 1,200 small molecules on cells from DBA patients, the researchers found one molecule that enhanced the production of red blood cells by stimulating autophagy.[22] This study could serve as a model for future large-scale genetic and chemical screens to identify potential drug therapies for a variety of blood disorders.

[21] Newton, CA et al. JHLT, 2017. https://www.ncbi.nlm.nih.gov/pubmed/28262440
[22] Doulatov, S et al. Science Trans Med 2017. https://www.ncbi.nlm.nih.gov/pubmed/28179501

Another recent study found that autophagy also may be involved in helping preserve the regenerative capacity of blood-forming cells, called hematopoietic stem cells, as they age.[23] The potential to modulate autophagy and thus improve the functional lifespan of these stem cells could lead to new approaches for stabilizing a patient's blood supply without relying entirely on blood donation and transfusion.

Other new research shows that certain types of hematopoietic stem cells can be generated in an unexpected place – the lungs. While bone marrow is known to be the body's major source of hematopoietic stem cells, NHLBI-funded researchers recently found that the lungs contain stem cells that can produce some types of immune cells, as well as platelets, the cells that accumulate to create blood clots and stop bleeding.[24] Further study of hematopoietic stem cells in the lungs could reveal pathways and signals for platelet production distinct from those in bone marrow, and thus lead to new strategies to treat platelet deficiency, which is common in people with cancer and certain viral infections, including HIV.

NHLBI researchers also are working to bring more effective treatments to patients with hemophilia, a blood-clotting disorder that causes a risk of severe bleeding, even from relatively minor wounds. The current standard treatment, developed in part through NHLBI-funded research, is replacement therapy – in which clotting factors (Factors VIII or IX) are infused into the patient's bloodstream. However, in some patients, factor replacement therapy triggers an immune response that limits it effectiveness. Thus, new alternative therapies, including gene and cell therapy techniques, are being developed and tested. For example, an NHLBI-funded clinical trial is testing the safety and efficacy of gene therapy in men with hemophilia B.[25] Early promising results show that close to half of the men who received the normal factor IX gene were able to stop their regular replacement therapy.[26] NHLBI also is supporting new research centers that will focus on strategies for preventing or eliminating the immune response to factor replacement therapy.[27]

The blood disease program also is playing a lead role in working with investigators across the country to accelerate cures for sickle cell disease and thalassemias as part of the NIH Sickle Cell Cures Initiative, which is expected to deliver new therapies to patients within five years.

[23] Ho, TT et al. Nature 2017. https://www.ncbi.nlm.nih.gov/pubmed/28241143
[24] Lefrançais, M et al. Nature 2017. https://www.ncbi.nlm.nih.gov/pubmed/28329764
[25] https://clinicaltrials.gov/ct2/show/study/NCT00979238
[26] Nathwani, AC et al. NEJM 2014. https://www.ncbi.nlm.nih.gov/pubmed/25409372
[27] https://grants.nih.gov/grants/guide/rfa-files/RFA-HL-18-014.html

Program Portrait: Sickle Cell Cures Initiative

As many as 100,000 people nationwide, most of them African American, have sickle cell disease (SCD), in which red blood cells take on a sickle shape and can block the flow of blood to the body, leading to frequent pain. Although a bone marrow transplant can cure the disease for young patients who have an immunologically matched donor, this treatment is not an option for many patients.

However, thanks to NHLBI-funded research, a cure that works for all SCD patients is within sight. SCD is caused by a mutation in hemoglobin—the protein that carries oxygen in red blood cells. Building on a foundation of basic research on hemoglobin, coupled with exciting recent advances in gene editing technology, researchers are now able to correct for this mutation in laboratory studies. NIH and NHLBI are leveraging these advances to launch a Sickle Cell Cures Initiative that will mobilize researchers to develop and deliver new therapies to patients within the next five years.

The framework for the Sickle Cell Cures initiative is based in part on an NHLBI workshop held in March 2017, "Accelerating Cures in Hemoglobinopathies," which brought together top researchers and industry leaders. The initiative will include establishing a consortium of professionals and patients to accelerate promising new gene- and cell-based therapies. To save costs and maximize gains from existing resources, the initiative will coordinate ongoing NHLBI-funded clinical trials and support the manufacture of new cell-based therapies through NHLBI's Production Assistance for Cellular Therapies (PACT) program.

Intramural Research

The Intramural Research Program provides a unique environment for conducting innovative basic and clinical research at laboratories on the NIH campus, including studies at the NIH Clinical Center, often conducted in partnership with local hospitals. The program provides opportunities for scientists and trainees to work together towards a better understanding of molecular, cellular, and organ physiology, and ultimately the treatment of human diseases.

The NHLBI intramural program is leading the world's most cutting-edge research and clinical trials on sickle cell disease (SCD), a rare blood disorder caused by a genetic mutation. While certain medications can reduce pain and hospitalizations from SCD, and a bone marrow transplant can effectively cure the disease for some patients, there is currently no cure that works for everyone. Because bone marrow typically must come from an immunologically matched relative, this treatment is not a viable option for most patients. To make such transplants more widely applicable, intramural researchers have developed a new protocol and are now testing it in a clinical trial; known as a haploidentical transplantation, it involves obtaining bone marrow from a parent, child, or sibling of the patient who is a partial immunological match.[28]

Researchers are also working to develop gene- and cell-based therapies that are effective and safe for all patients. Recognizing that bone marrow stem cells produce all types of blood cells for the life of the patient, one strategy involves genetic approaches to replace or repair bone marrow stem cells. By using the patient's own bone marrow stem cells, researchers can replace a faulty hemoglobin gene or edit the misspelled gene and transplant the corrected cells back into the patient, without the risk of immune rejection. This remarkable progress, the diligence and creativity of NHLBI intramural researchers, and the heroic contributions of patients with SCD, were featured in the *First in Human* documentary series about research at that NIH Clinical Center.

[28] Bauer, DE et al. Blood Cells, Molecules and Diseases 2017. https://www.ncbi.nlm.nih.gov/pubmed/28893518

Intramural researchers are also leading the way in developing imaging techniques to monitor sub-cellular structures and processes, in animals and humans. Using high-speed microcopy to capture real-time imaging of artery perfusion and permeability in mouse blood vessels, one team found that pressure changes within arteries are transmitted to and absorbed by the endothelial basement membrane, which may protect endothelial cells from mechanical forces caused by changes in blood pressure.[29]

Research Management and Support (RMS)

RMS activities include administrative and technical functions that support and enhance the effectiveness of the Institute's research investments. This includes providing administrative, budgetary, logistical, and scientific support in the review, award, and monitoring of research grants and clinical trials, training awards, and research and development contracts. RMS functions also encompass strategic planning, trans-NHLBI and NIH coordination, evaluation of the Institute's programs, regulatory compliance, international coordination, interactions with other Federal agencies and Congress, and dissemination of research findings to the public.

[29] Lucotte, BM et al. PNAS 2017. https://www.ncbi.nlm.nih.gov/pubmed/28373558

NATIONAL INSTITUTES OF HEALTH
National Heart, Lung, and Blood Institute

Detail of Full-Time Equivalent Employment (FTE)

OFFICE/DIVISION	FY 2017 Final			FY 2018 Annualized CR			FY 2019 President's Budget		
	Civilian	Military	Total	Civilian	Military	Total	Civilian	Military	Total
Center for Translation Research and Implementation Science									
Direct:	15	3	18	18	3	21	18	3	21
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	15	3	18	18	3	21	18	3	21
Division of Blood and Resources									
Direct:	33	-	33	31	-	31	31	-	31
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	33	-	33	31	-	31	31	-	31
Division of Cardiovascular Sciences									
Direct:	124	1	125	120	2	122	120	2	122
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	124	1	125	120	2	122	120	2	122
Division of Extramural Research Activities									
Direct:	92	-	92	91	-	91	91	-	91
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	92	-	92	91	-	91	91	-	91
Division of Intramural Research									
Direct:	446	8	454	446	12	458	446	12	458
Reimbursable:	38	1	39	38	1	39	38	1	39
Total:	484	9	493	484	13	497	484	13	497
Division of Lung Diseases									
Direct:	31	-	31	33	-	33	33	-	33
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	31	-	31	33	-	33	33	-	33
Office of the Director									
Direct:	135	4	139	142	1	143	142	1	143
Reimbursable:	23	1	24	23	1	24	23	1	24
Total:	158	5	163	165	2	167	165	2	167
Total	937	18	955	942	20	962	942	20	962
Includes FTEs whose payroll obligations are supported by the NIH Common Fund.									
FTEs supported by funds from Cooperative Research and Development Agreements.	0	0	0	0	0	0	0	0	0

FISCAL YEAR	Average GS Grade
2015	12.5
2016	12.5
2017	12.6
2018	12.6
2019	12.6

NATIONAL INSTITUTES OF HEALTH
National Heart, Lung, and Blood Institute

Detail of Positions[1]

GRADE	FY 2017 Final	FY 2018 Annualized CR	FY 2019 President's Budget
Total, ES Positions	2	2	2
Total, ES Salary	357,923	364,902	368,047
GM/GS-15	92	92	92
GM/GS-14	158	158	158
GM/GS-13	194	194	194
GS-12	75	78	78
GS-11	54	54	54
GS-10	0	0	0
GS-9	44	44	44
GS-8	9	9	9
GS-7	9	9	9
GS-6	3	3	3
GS-5	0	0	0
GS-4	7	7	7
GS-3	3	3	3
GS-2	1	1	1
GS-1	1	1	1
Subtotal	650	653	653
Grades established by Act of July 1, 1944 (42 U.S.C. 207)	0	0	0
Assistant Surgeon General	2	2	2
Director Grade	6	6	6
Senior Grade	6	7	7
Full Grade	3	4	4
Senior Assistant Grade	1	1	1
Assistant Grade	0	0	0
Subtotal	18	20	20
Ungraded	329	329	329
Total permanent positions	662	685	685
Total positions, end of year	959	996	996
Total full-time equivalent (FTE) employment, end of year	955	962	962
Average ES salary	178,962	182,451	184,024
Average GM/GS grade	12.6	12.6	12.6
Average GM/GS salary	110,769	112,929	113,903

[1] Includes FTEs whose payroll obligations are supported by the NIH Common Fund.