

An anatomical illustration of the human heart and lungs. The heart is shown in a cross-section, revealing its four chambers and internal structures. The lungs are depicted in a reddish-pink color, with a network of blue and red blood vessels branching out from the heart. The entire scene is set against a dark blue background with white ribcage outlines. A white rectangular box is positioned in the upper left quadrant, containing the text 'The National Heart, Lung, and Blood Institute' and a vertical line. To the right of this box, the website address 'www.nhlbi.nih.gov/' is written in a light blue font. In the bottom left corner, the 'Scientia' logo is visible, consisting of a circular icon of dots followed by the word 'Scientia' in white.

**The National Heart, Lung,  
and Blood Institute**

[www.nhlbi.nih.gov/](http://www.nhlbi.nih.gov/)



National Heart, Lung,  
and Blood Institute

## THE NATIONAL HEART, LUNG, AND BLOOD INSTITUTE



The National Heart, Lung, and Blood Institute (NHLBI) is one of 27 Centers, Institutes, and Offices within the National Institutes of Health (NIH). It was established originally as the National Heart Institute in 1948 with a mission to support research and research training in the prevention, detection, and treatment of diseases of the heart and blood vessels. In 1972, the National Heart Institute was renamed the NHLBI and given a mandate to expand its mission to include lung and blood diseases. Since that time, NHLBI has further expanded its activities to include research on sleep disorders. In all of these areas, the NHLBI maintains a strategic desire to understand and promote health and resilience, stimulate discoveries in the causes of disease, enable the translation of discoveries from basic research into clinical practice, and foster training and mentoring of emerging scientists and physicians.

In this exclusive interview, we have had the opportunity to speak with four representatives of the NHLBI. Dr George A. Mensah, MD, FACC, is Director of the Center for Translation Research and Implementation Science, Dr James Kiley, PhD, is Director of the Division of Lung Diseases, Dr W. Keith Hoots, MD, is Director of the Division of Blood Diseases and Resources, and Dr David Goff, MD, PhD, is the Director of the Division of Cardiovascular Sciences. Together, these four division directors discuss the NHLBI's commitment to tackling heart, lung and blood diseases, which include many of the leading causes of death worldwide. Here, they share some of the NHLBI's achievements, and discuss the challenges that lie ahead for these fields of research.

**‘The conditions that fall within NHLBI’s research portfolio include some of the most common diseases and risk factors as well as some of the leading causes of death in men and women in the United States and worldwide.’**



**Please describe some of the most common conditions that fall under the categories of heart, lung and blood diseases, and give us an idea of their prevalence and severity.**

**Dr George A. Mensah:** The conditions that fall within NHLBI's research portfolio include some of the most common diseases and risk factors as well as some of the leading causes of death in men and women in the United States and worldwide. For example, diseases of the heart such as heart attack, sudden cardiac arrest, heart failure, hypertension, and atrial fibrillation, remain the number one cause of death in the United States. An estimated 85.6 million American adults (more than one in three) have at least one or more of these heart diseases. High blood pressure alone affects more than 80 million American adults. Diseases of the lung such as asthma, emphysema, and chronic obstructive pulmonary disease (COPD) also cause substantial death and disability and remain the third leading cause of death in the United States and accounted for nearly 150,000 deaths in 2014 alone. Some of the common blood diseases addressed by NHLBI include sickle cell disease, chronic anaemias, thalassemia, haemophilia, and other bleeding disorders.

**NHLBI plays a huge role in supporting COPD research in the US – what causes this condition and why is it so common in western countries?**

**Dr James Kiley:** Cigarette smoking is the major culprit for COPD. While smoking rates have declined in the US, there are currently up to 100 million adults that are smokers or ex-smokers. Second hand smoke remains an issue as smoking is not universally banned in public places. Although more data is needed, there is some evidence that other environmental and occupational exposures, such as airborne particulates, can increase COPD prevalence. Genetic factors also play a role. One genetic condition, alpha-1-antitrypsin deficiency, is known to lead to COPD. Additional genetic factors, which we are still learning about, also contribute to a predisposition to COPD, particularly when they are combined with a history of smoking. The role of non-optimal lung development during the early stages of life is currently under investigation as a possible predisposing factor to COPD. Finally, COPD is a disease commonly found in older individuals, and we are still trying to understand what role aging may play in the disease course.

**Despite the ubiquity of asthma worldwide, current drugs primarily work by dampening inflammation in the lungs, rather than also treating the structural problems, or remodelling, present in the lung tissue of asthma patients. What promising projects is the NHLBI currently involved with to address this deficit?**

**Dr James Kiley:** The question raises a larger question of whether the inflammation observed in patients with asthma results in



remodelling or remodelling occurs as a ‘primary process’ independent of inflammation. Inflammation is likely the precursor of remodelling, and, therefore, managing the inflammation is expected to prevent remodelling. Evidence is accumulating, in pre-clinical models, that downstream effects of inflammation can include activation of cell signalling pathways that affect the integrity of the airway epithelium and vasculature as well as resulting in proliferation of smooth muscle cells and mucus cell hypertrophy and mucus hypersecretion. It’s also been shown (in preclinical models) that several targeted therapeutics currently being evaluated for the treatment of asthma, can abrogate some of the downstream pathophysiology associated with inflammation. Thus, it’s vital that we continue to probe the pathophysiologic consequences of inflammation as well as the molecular and cellular effects, in addition to clinical outcomes, of therapeutic interventions. In this way, we can increase

our understanding of the entire therapeutic range of a particular intervention, and, through comprehensive patient phenotyping, tailor therapy to the appropriate patient strata. It is also possible that rather than remodelling, there are structural differences in the airways of people who develop asthma and the inflammation that is characteristic of asthma makes the anatomic changes manifest. NHLBI has numerous supported research activities to understand what occurs in patients with severe disease and the relative contributions of inflammation and other biologic processes to asthma.

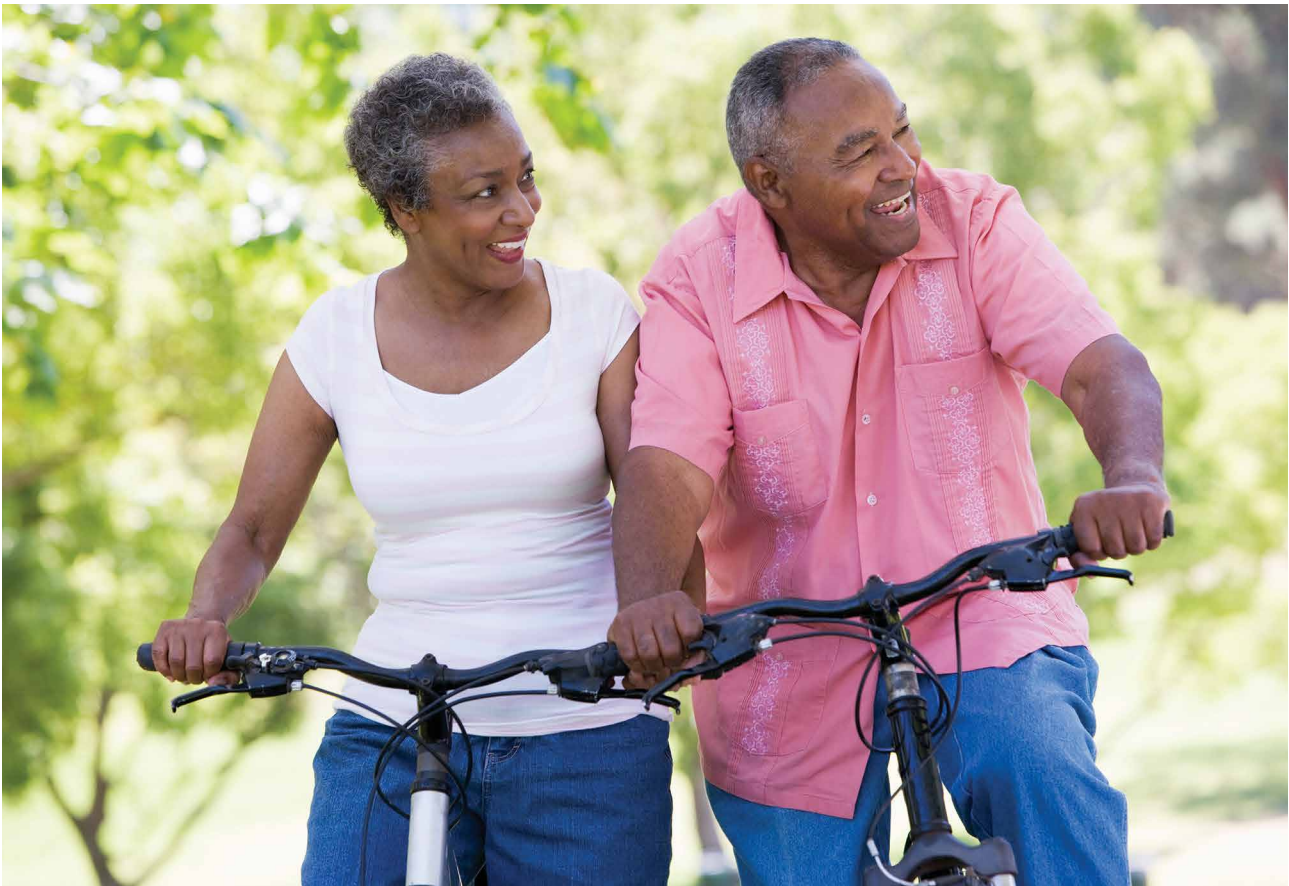
**What do you believe are the biggest challenges facing lung research in the US?**

**Dr James Kiley:** Personalised or precision medicine is a huge challenge to address in lung research, whether it is at the point of primary prevention (or maintaining ‘resilience’ or lung health) or management of existing lung disease. Most of the diseases we study are ‘complex diseases’ and the interplay between multiple etiologic factors (including genetics or inter-individual variability) and time presents a challenge to understand the best approach for each patient throughout the lifespan. The major challenges to address in lung research include identifying better ‘markers’ of health and disease throughout development, and across the lifespan to enable the development of disease-modifying interventions and primary prevention strategies. We also need to leverage the vast amounts of existing data and the potential for future data collection to its maximum advantage.

One major challenge for moving theory into practice is developing better models of lung diseases. This means better models of human cells and tissues that we can manipulate in the lab as well as better animal models that really recapitulate the important aspects of the human disease. Without these models, it is difficult to understand on a molecular and cellular level what is going wrong in disease and it is also difficult to pre-clinically test possible therapeutics. With the recent advances in stem cell technologies and CRISPR gene editing, these challenges might be met in the next several years. The areas of regeneration, precision medicine, implementation, and primary prevention of lung diseases are major challenges, but offer great promise for new strategies to advance lung biology and disease research.

**Another huge area of NHLBI’s focus is Sickle Cell Disease. In the 1970s, the average life expectancy in the US was 14 years for people living with the disease, and this has now risen to about 40 to 60 years. What has been the NHLBI’s role in improving the outcomes of individuals with this genetic condition?**

**Dr W. Keith Hoots:** The NHLBI has a long history of working to improve the outcomes for individuals with Sickle Cell Disease. And given that the life expectancy for people living with SCD has increased, NHLBI has begun to fund research focused on the care of adolescents and adults. Adolescents and adults with SCD experience difficulties in accessing high quality longitudinal medical care from qualified providers and are unable to benefit from evidence-based therapies that may reduce morbidity and mortality during the third and fourth decades of life. NHLBI recently funded the Sickle Cell Disease Implementation Consortium (SCDIC), which is currently supporting eight regional centres to undertake the analyses of barriers to care in defined geographical areas (urban, suburban, and rural) as well as develop interventions to remedy these barriers and allow access to health



care. In addition, the project will create implementation protocols that compare novel strategies to improve care with standard management. NHLBI has funded eight geographic areas, and has committed \$33,000,000 over a six-year period to this [program](#).

NHLBI has also been funding STRIDE, a multi-centred [study](#) to investigate the safety and feasibility of performing stem cell transplantation in subject with sickle cell disease over the age of 18. Previously the vast majority of stem cell transplants have been performed in children. However, many adults suffer from a chronic disease burden of pain, renal, cardiac, pulmonary and neurological disease. The STRIDE study will conduct HLA-identical transplantation in 60 adult subjects, and compare the clinical course to 60 adults with SCD who do not have HLA-identical donors. This study, which is just starting, has the potential to change the natural history of SCD in older subjects, in whom the effects of current therapeutic efforts have been minimal.

Finally, NHLBI is currently funding a major program to promote innovative basic and translational research in the hemoglobinopathies. The Excellence in

Hemoglobinopathies Research Awards (EHRA) funded eight groups of investigators to develop multidisciplinary projects that will lead to new therapeutic and diagnostic modalities for SCD and thalassemia. The funded projects include new therapeutics to elevate the foetal haemoglobin level (the most powerful known modifier of the severity of SCD); new therapeutics for sickle cell pain; novel modulators of inflammation; and treatments for SCD-associated kidney disease.

**Although prevalence is low in the US, Sickle Cell Disease and other blood disorders such as thalassemia are far more common in sub-Saharan Africa and in Southeast Asia. Does NHLBI collaborate with other countries so that the benefits of research conducted in the US are extended to helping people in developing countries?**

**Dr W. Keith Hoots:** The worldwide burden of SCD is rising. Between 2010 and 2050, it is expected that about 14.2 million affected babies will be born worldwide. More than 75% of SCD births occur in sub-Saharan Africa. In sharp contrast to children with SCD in the US, 50–80% of affected Africans now die before the age of five years, often as a

consequence of limited health resources and infrastructure. While high regional disease prevalence would be expected to facilitate epidemiologic, translational, and clinical research, most sub-Saharan African nations lack the means and capacity required to pursue such investigations. Two related Funding Opportunity Announcements (FOAs) were published by the NHLBI in January, 2016 and responsive applications were reviewed in July of 2016. The first award will support the development of a Sub-Saharan African (SSA) [Collaborative Consortium](#), which will engage in capacity building activities and develop an infrastructure upon which a future SCD in Sub-Saharan Africa Research Network can be built. The second award will support an African based Data Coordinating Center (DCC) that will work closely with the Collaborative Consortium.

The NHLBI also funded a Sickle Cell Disease Ontology Workshop that was convened in Cape Town South Africa in February 2016. The meeting's objective was to develop and standardise a sickle cell disease specific ontology appropriate to the African region. The intent was to harmonise definitions of phenotypes, diagnostics, therapeutics, quality of life, as well as disease modifiers and stage. This standardisation will expedite



future African SCD research. Thirty-seven experts participated, and the workshop proceedings and results were published in [Applied and Translational Genomics](#) in March, 2016.

**As a new division director, coming in as NHLBI embarks in the implementation of its new strategic plan, what are your scientific priorities to have the biggest impact on the Nation's health?**

**Dr David Goff:** It is an exciting time to join the leadership team at NHLBI. As a new division director, one of my top priorities will be to listen to smart scientists inside and outside of NHLBI to help identify new strategic initiatives that hold the greatest promise for making progress. While I have much to learn in that process, several areas of focus are already clear.

Research on the preservation of heart health in childhood through early adulthood holds great promise for improving the Nation's health. Most of our children are born with ideal, or nearly ideal, heart health, but far too many of our children find that health frittered away by early adulthood, by which time, far too many Americans smoke cigarettes, eat an unhealthy diet, and are inactive. The consequences include obesity, high blood pressure, high cholesterol, diabetes, and preventable heart disease. Discovering how to preserve the heart health most of our children are born with could lead to the elimination of epidemic heart disease. We should also not lose sight of the great advances our scientists are making understanding the causes of birth defects that affect the heart. Heart defects are among the most common birth defects in the US. Research on the causes, prevention, and treatment of birth defects will make a big difference for these families!

Heart diseases, and many other health problems, occur much more

often among the poor than among the wealthy. The identification of programs and policies that work to address these inequities could make major contributions to our Nation's health. NHLBI-funded research is already making progress in this effort. For example, Dr Lisa Cooper and her colleagues have identified ways to improve treatment and control of high blood pressure in a low-income population in Baltimore. Discovering effective ways to promote heart health equity and eliminate heart health disparities would help reduce the life expectancy gaps between wealthier and poorer Americans.

The revolution in omic technologies offers unprecedented opportunities for gaining insights into the biological continuum from the genotype to the expressed phenotype. Interrogation of the different omic domains including the genome, epigenome, transcriptome, proteome, metabolome, and microbiome can now help us understand the functional consequences of an individual's interaction with the environment and subsequently also help identify the molecular determinants that (a) predispose some to adverse heart health or (b) confer protection in others. More importantly, by generating functional information at a much more granular level than possible before, omics can help identify subtle biological changes that are predictive of future clinical manifestation of a disease (dilated cardiomyopathy as an example). Such information can also help distinguish between similarly appearing but different disease conditions facilitating the tailoring of treatment strategies.

Research on how to improve the implementation and dissemination of proven prevention and treatment strategies into clinical and public health practice is needed. We know much of what we should do to improve heart health and prevent heart disease. We need to learn how to do a better job of accomplishing those goals. For example, we have known for many years that smoking is harmful, and smoking cessation

is beneficial. We need more effective smoking cessation programs and more effective ways for delivery of those programs to people addicted to tobacco products. Likewise, we need better ways of preventing and controlling high blood pressure and cholesterol.

**Can you please offer some insight on what the future may hold for cardiovascular disease research in the US, and the challenges you may meet?**

**Dr David Goff:** The past 50 years have seen tremendous progress in research on heart health and heart disease. Due to this research death rates from heart diseases have declined by about two-thirds in the US. Put another way, if we had the same death rates from heart disease today that we had in the mid-1960s, three times as many Americans would die each year of heart disease. We've come a long way, yet heart disease remains our leading cause of death. While much work remains to be done, it may now be reasonable to consider the elimination of heart disease. At one point, elimination of small pox seemed impossible. I believe we can eliminate most forms of heart disease through continued research and implementation of that knowledge. Our biggest challenge may well be complacency bred from decades of uninterrupted progress. Recent evidence that the decline in heart disease death rates has ended should serve as a wake-up call to redouble our efforts to support research and to implement what we already know.

The high cost of technology-intensive research represents another challenge. The cost of cutting edge research has increased more rapidly than other parts of our economy, putting strain on funding agencies and research institutions.

At the more basic research end of the scientific spectrum, a number of technological developments are poised to make an impact on health. The development of induced pluripotent stem cells and their differentiation to cardiomyocytes is poised to impact cardiovascular research in a number of ways, from enabling drug discovery to disease modelling to cell therapy and tissue engineering of blood vessels and cardiac patches. Genome editing with CRISPR/Cas 9 also has enormous potential, raising the possibility that monogenic diseases could one day be treated by gene correction, although many challenges remain to be



overcome. Nanotechnology offers a range of options for imaging disease processes and for targeted delivery of therapeutics such as siRNA, for example to modulate inflammatory processes. The challenge will be to move these technologies towards translation into clinically useful entities.

Finally, assuring a strong supply of talented and well-prepared scientists is an ongoing challenge. Twenty-first century science is so complex that the educational process has become demanding in terms of both time and financial resources. To become a competitive scientist often means putting other life decisions, such as starting a family, on hold until education is completed, educational loans are paid off, and careers are established. We need to address this issue in the very near future to avoid losing to other career options many of the bright young people, especially those from under-represented populations, who could discover new treatments or cures for heart disease.

Despite these challenges, I remain very optimistic about the opportunities we face to substantially reduce, and perhaps even eliminate, epidemic heart disease this century. Accomplishing this goal will require a redoubling of our efforts to train new scientists, support critical research, and translate knowledge into heart health through clinical and public health practice.

**Finally, Dr Mensah, would you like to share your thoughts on the future of all heart, lung and blood research, and the biggest challenges you expect to encounter?**

**Dr George A. Mensah:** In addition to the challenges mentioned specifically for heart, lung, and blood diseases and sleep disorders, we also have the overarching challenge of

translating research discoveries into routine clinical and public health practice in order to maximise the return on NHLBI's research investments. This additional challenge falls under the rubric of dissemination and implementation gaps. For example, although we have very compelling research evidence of the safety and efficacy of interventions for high blood pressure and numerous guidelines for the prevention, treatment, and control of this important condition, only about half of Americans with high blood pressure have it under control. In fact, in African American men, fewer than half of those with hypertension have it under treatment and control at a time when successful blood pressure control in African Americans has been demonstrated in clinical trials and routine clinical practices. For example, in the Kaiser Permanente Southern California health system, control of high blood pressure was achieved in more than 80% of African Americans and baseline racial and ethnic disparities in blood pressure control were eliminated. The primary drivers of successful high blood pressure control are now better understood and include important systems-level changes such as those instituted in the Kaiser Permanente study. The NHLBI remains committed to advancing research that seeks to understand the strategies needed to ensure rapid adoption and sustained use of proven effective interventions so that, as a nation, we can successfully turn research discoveries into health.



[www.nhlbi.nih.gov/](http://www.nhlbi.nih.gov/)