

# UPDATES FROM US HEALTH AGENCIES

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Recent activity in government and non-government agencies may affect readers of *Ethnicity & Disease* and other healthcare professionals working with ethnic minority and under-served populations. Below are some current items of interest.

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## FROM THE NATIONAL INSTITUTES OF HEALTH (NIH)

### International Effort Finds New Genetic Variants Associated with Lipid Levels, Risk for Coronary Artery Disease

Environmental and genetic factors influence a person's lipid levels, which are important risk factors for coronary artery disease (CAD). While there is some understanding of the environmental contribution, the role of genetics has been less defined. Now, in an international collaboration supported primarily by NIH, scientists have discovered more than 25 genetic variants in 18 genes connected to cholesterol and lipid levels. Seven of the 18 genes previously had not been connected to these levels, while the 11 others confirm previous discoveries.

The purpose of the study was to identify comprehensively genetic variants that influence lipid levels and to examine the relationships between these genetic variants and risk of CAD. To identify genetic variants that play a role in lipid levels, researchers turned to a relatively new approach, known as a genome-wide association study (GWAS). The GWAS strategy enables researchers to survey the entire human genome, not just the genetic variants in a few genes. Typically, GWAS studies have been carried out in samples where all individ-

uals are examined with the same gene chip, an experimental device that allows investigators to measure more than 100,000 genetic variants in a single experiment. But in this study, investigators developed and employed new statistical methods that allowed them to combine data across different gene chips and thus examine much larger numbers of participants.

Scientists estimate that the genetic contribution to lipid levels is approximately 30%–40%; the genetic variants uncovered in the new study are responsible for approximately 5%–8% of that contribution, the scientists note, which means there is more work to be done.

To determine if the genetic variants associated with lipid levels also influence risk of heart disease, the researchers compared their results with results from the Wellcome Trust Case Control Consortium's recent genome-wide association study of CAD involving 15,000 British individuals. They found that all gene variants associated with increased low-density lipoprotein levels also were more prevalent among people with CAD. People with the gene variant for high triglyceride levels also had an increased risk for CAD, although the relationship was not as strong. No relationship was found between high-density lipoprotein and CAD.

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## FROM THE NATIONAL HEART, LUNG, AND BLOOD INSTITUTE (NHLBI)

### Diuretics Most Effective Blood Pressure Medication for People with Metabolic Syndrome

New research shows that in people with high blood pressure as part of metabolic syndrome, a cluster of conditions that increases the risk for heart disease, diuretics offer greater protection against cardiovascular disease, including heart failure, and are at least as effective for lowering blood pressure as newer, more expensive medications. The

findings run counter to current medical practices that favor angiotensin-converting enzyme (ACE) inhibitors,  $\alpha$ -blockers, and calcium-channel blockers for treatment of high blood pressure in those with metabolic syndrome. In addition, the results provide important new evidence supporting the use of diuretics for initial blood pres-

sure-lowering therapy in Black patients with metabolic syndrome.

The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) is the largest study to compare a diuretic (chlorthalidone) with three newer classes of medications to treat high blood pressure: a calcium-channel blocker (amlodipine besylate), an  $\alpha$ -blocker (doxazosin mesylate), and an ACE inhi-

tor (lisinopril). Each drug was used to start treatment, and other medications could be added if necessary to control blood pressure. The study originally reported in 2002 that diuretics were the most beneficial of the drug classes studied for treating high blood pressure and for protecting against adverse cardiovascular outcomes.

This latest analysis shows that even among men and women

with metabolic syndrome, and for both Black and non-Black participants, the less costly diuretics consistently control blood pressure and are equally beneficial in preventing heart attack and coronary heart disease death. They are also more beneficial than newer medications in preventing one or more other

forms of cardiovascular disease, including heart failure and stroke.

In both Black and non-Black study participants with metabolic syndrome, the diuretic-based treatment was more protective against heart failure and also against overall cardiovascular disease (coronary heart disease,

stroke, heart failure, or peripheral arterial disease combined) when compared with the ACE inhibitor and  $\alpha$ -blocker. Compared with the calcium-channel blocker, the diuretic was more protective against heart failure.

When compared with those taking diuretics, Black participants with metabolic syndrome

who received ACE inhibitors had poorer blood pressure control and a 24% greater risk of overall cardiovascular disease, including a 19% greater risk of coronary heart disease, a 37% greater risk of stroke, and a 49% greater risk of heart failure. They also had a 70% greater risk of kidney failure.

## FROM THE NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES (NIAID)

### Scientists Identify New Cellular Receptor for HIV

A cellular protein that helps guide immune cells to the gut has been newly identified as a target of HIV when the virus begins its assault on the body's immune system, according to researchers from NIAID. "The identification of this new receptor opens up new avenues of investigation that may help further elucidate the complex mechanisms of the pathogenesis of HIV infection," said NIAID Director Anthony S. Fauci, MD.

Several other immune cell receptors bind to HIV. Most important among these, the CD4 molecule, identified as an HIV receptor in 1984, functions as the principal receptor for HIV. The CCR5 and CXCR4 molecules, discovered in 1996, serve as co-receptors that HIV uses to enter its target cells. In the new study, NIAID scientists identified a cell adhesion molecule known as integrin alpha 4 beta 7 as another

potentially important receptor for HIV.

Early in the course of HIV infection, the virus rapidly invades and replicates in gut-associated lymphoid tissue (GALT), the immune cells of the gut. Once seeded with HIV, the gut is rapidly depleted of CD4+ T cells, the main target of HIV, triggering the process that ultimately leads to AIDS.

"In the very early days of infection, it is in the GALT where most of the damage caused by HIV occurs," says

Elena Martinelli, PhD, a lead author of the paper and a fellow in Dr. Fauci's laboratory. "The gut is where the virus really takes hold. We found that integrin alpha 4 beta 7, whose natural function is to direct T cells to the GALT, is also a receptor for HIV. It is very unlikely that this is a coincidence."

For more information on HIV/AIDS, see <http://www3.niaid.nih.gov/healthscience/healthtopics/HIVAIDS/overview.htm>.