# New genetic risk factor for inflammation identified in African American women

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African Americans have higher blood levels of a protein associated with increased heart-disease risk than European Americans, despite higher "good" HDL cholesterol and lower "bad" triglyceride levels. This contradictory observation now may be explained, in part, by a genetic variant identified in the first large-scale, genome-wide association study of this protein involving 12,000 African American and Hispanic American women.

Lead researcher Alexander Reiner, M.D., an epidemiologist at Fred Hutchinson Cancer Research Center, and colleagues describe their findings online ahead of the Sept. 7 print issue of the American Journal of Human Genetics.

Specifically, the researchers looked for genetic signposts associated with elevated levels of C-reactive protein, or CRP – a marker of inflammation that is linked with increased risk of heart disease, diabetes and some cancers.

"Most previous studies examining the genetic determinants of elevated CRP have focused on tens of thousands of white individuals of European descent," said Reiner, a member of the Hutchinson Center's Public Health Sciences Division. "Since minorities – African Americans and Hispanic Americans in particular – tend to have higher CRP levels than other U.S. racial and ethnic groups, it's important to understand whether genetic factors might contribute to these differences."

Reiner and colleagues identified several genetic factors linked to CRP that are relatively specific to African Americans. They found a variation in TREM2, a family of genes on chromosome 6p21 that are expressed in white blood cells and appear to be important for regulating the degree of inflammation generated when white blood cells respond to infection or tissue injury.

"TREM genes were recognized relatively recently to be involved in inflammation and autoimmune disorders. Our finding adds further support to the importance of this gene family in generating and regulating inflammatory responses," said Reiner, who is also a professor of epidemiology at the University of Washington School of Public Health.

They also discovered that approximately 20 previously identified genetic factors associated with elevated CRP in whites are also shared among African Americans and Hispanic Americans – genes that involve pathways related to innate immunity as well as metabolism of fat and sugar.

Identifying the genetic variants that regulate CRP levels may help researchers settle a point of scientific controversy: whether chronic, low-grade inflammation causes cardiovascular disease or whether it is just a reaction to the disease process of atherosclerosis, also known as hardening of the arteries.

"This finding may allow us to study whether CRP is a direct cause of heart disease or merely an early warning sign," Reiner said. "Moreover, understanding the genes that regulate the inflammatory response in humans could lead to the development of new anti-inflammatory drugs for treatment of an assortment of chronic diseases ranging from diabetes to cancer."

In addition to genetics, environmental factors that are known to contribute to elevated CRP and low-grade, chronic inflammation include obesity, cigarette smoking and estrogen therapy.

While low-grade inflammation may contribute to increased risk of cardiovascular disease and other health disparities among African Americans and Hispanic Americans, prior studies suggest the correlation between CRP and obesity does not appear to completely explain higher CRP levels among people of African descent.

For the study, Reiner and colleagues scanned the genomes of 8,280 African American and 3,548 Hispanic American, postmenopausal participants in the Women's Health Initiative to look for variations in DNA – called single-nucleotide polymorphisms, or SNPs – that were associated with elevated CRP. The Hutchinson Center houses the Clinical Coordinating Center of the WHI, one of the largest U.S. prevention studies of its kind involving more than 161,000 women nationwide.

"This pool of genotyping data offers unique and exciting opportunities to search for genetic factors that influence disease risks in the two largest minority populations in the United States: African Americans and Hispanics," said senior author Hua Tang, Ph.D., an associate professor of genetics and statistics at Stanford University. These groups suffer disproportionate burdens of heart disease, certain types of cancer and other illnesses but are under-represented in many ongoing genetic-association studies. "Our ultimate goal is to design better disease prevention, diagnostic and therapeutic strategies so that all people can benefit from advancements in genomics medicine," Tang said.

**More information:** Genome-wide association and population genetic analysis of C-reactive protein in African American and Hispanic American women: the Women's Health Initiative SNP Health

Association, *American Journal of Human Genetics*.