

Genes Associated with C-Reactive Protein Levels Differ by Race and Ancestry

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S Lowry

C-reactive protein (CRP), a widely used marker of systemic inflammation, is a risk factor for cardiovascular disease, and is associated with obesity and other metabolic conditions. CRP expression is influenced by several genes, but exactly which genes are associated with CRP levels may vary somewhat by race and ancestry. Serum levels of CRP are higher in African Americans and Hispanic Americans than in European Americans. Several CRP-associated genes have been identified in populations of European and Asian ancestry, but it is unclear whether these same genes influence serum CRP levels in other populations.

Dr. Alex Reiner and colleagues in the Public Health Sciences Division collaborated to identify new genetic variants associated with CRP levels in Hispanic American and African American women. They also aimed to assess whether CRP levels in these populations are associated with those variant genes that have previously been identified in European and Asian populations.

This study was the first large genome-wide association study (GWAS) of CRP to include subjects of Hispanic and African descent. The study included 8,220 African American and 3,548 Hispanic American postmenopausal women who were enrolled in the Women's Health Initiative when they were between the ages of 50-79. Loci which were previously identified in European and Asian populations were also associated with CRP levels among African American and Hispanic American women in this study. Furthermore, most new CRP-associated variants occur more frequently in African than European populations.

One new CRP-associated genetic variant was identified on chromosome 6p21. This variant of the TREM2 (triggering receptor expressed by myeloid cells 2) gene plays a role in the inflammatory response, and is common in African American women but relatively rare in other populations. The association between this TREM2 variant and CRP levels was validated using an independent sample of African Americans from a separate cohort, which demonstrated that the association may be confined to women. In addition, there was evidence of at least 3 distinct variants of the CRP gene at chromosomal region 1q23. One variant was more common in women of African ancestry, and it was also associated with higher serum CRP levels. The other two gene variants identified were

associated with lower serum CRP levels, and were more common in women with predominantly European, and not African, ancestry.

Among women of Hispanic ancestry, age-adjusted CRP levels were higher in those with greater Native American ancestry, and lower in those with greater East Asian ancestry, even after accounting for differences in body mass index.

Of the approximately 20 genetic loci associated with CRP levels, the majority involve pathways related to immune function or lipid and glucose metabolism, which, investigators contend, may support a connection between inflammation and metabolic dysregulation. CRP levels in African American women are influenced by several genetic factors, many of which are also common to women of European and Asian descent, and others which predominantly occur in African American women. As expression of CRP is largely controlled by the cytokine IL-6, the authors suggest that therapeutic blockade of the IL-6 receptor may have potential for reducing incidence of coronary heart disease in African Americans.

[Reiner AP, Beleza S, Franceschini N, Auer PL, Robinson JG, Kooperberg C, Peters U, Tang H.](#) 2012. Genome-wide association and population genetic analysis of C-reactive protein in African American and Hispanic American women. *Am J Hum Genet.* 91(3):502-12.



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Dr. Alexander Reiner, Public Health
Sciences Division