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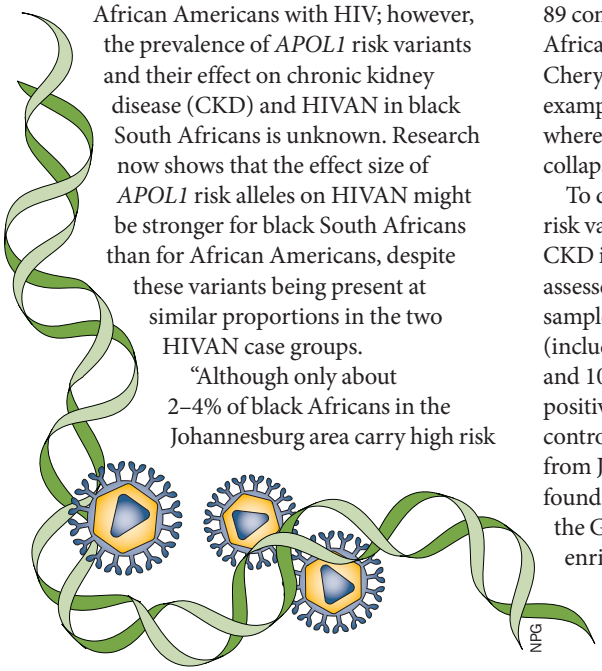
GENETICS

Strong association of *APOL1* risk variants with HIV-associated nephropathy in black South Africans



The *APOL1* G1 and G2 risk variants contribute to the increased risk of HIV-associated nephropathy (HIVAN) in African Americans with HIV; however, the prevalence of *APOL1* risk variants and their effect on chronic kidney disease (CKD) and HIVAN in black South Africans is unknown. Research now shows that the effect size of *APOL1* risk alleles on HIVAN might be stronger for black South Africans than for African Americans, despite these variants being present at similar proportions in the two HIVAN case groups.

"Although only about 2–4% of black Africans in the Johannesburg area carry high risk *APOL1* genotypes, nearly 80% of those with HIVAN carried two risk alleles, giving an extremely high odds ratio for HIVAN of 89 compared with an odds ratio of 29 in African Americans," explains researcher Cheryl Winkler. "This represents a striking example of a gene–environment interaction where HIV interacts with *APOL1* to cause collapsing glomerulopathy."

To determine the influence of *APOL1* risk variants on HIV and other forms of CKD in South Africans, Kasembeli *et al.* assessed *APOL1* genotypes in biopsy samples from 116 patients with CKD (including 38 patients with HIVAN) and 108 controls without CKD (54 HIV-positive controls and 54 population controls) of black African ancestry from Johannesburg. The researchers found that the combined frequency of the G1 and G2 risk alleles was highly enriched in patients with HIVAN (90.6%) compared to HIV-positive controls (20.8%) and population controls (18.4%). Similarly, 78.9% of patients with HIVAN were homozygous (G1/G1 or G2/G2) or compound heterozygous (G1/G2) for the risk alleles compared with 3.7% of HIV-positive controls and 1.9% of population controls. They found no association between *APOL1* genotype and other forms of CKD regardless of HIV status.

"There are so many unanswered questions to address," says Winkler. "A first step in Africa is to quantify the prevalence of *APOL1* risk factors among different populations and ethnic groups to ascertain the public health impact of these variants on CKD."

Susan J. Allison

Original article Kasembeli, A. N. *et al. APOL1* risk variants are strongly associated with HIV-associated nephropathy in black South Africans. *J. Am. Soc. Nephrol.* doi:10.1681/ASN.2014050469