# A genome-wide association study of carotid atherosclerosis in HIV-infected men.

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**Abstract**

**BACKGROUND:** The role of host genetics in the development of subclinical atherosclerosis in the context of HIV-infected persons who are being treated with highly active antiretroviral therapy (HAART) is not well understood.

**METHODS:** The present genome-wide association study (GWAS) is based on 177 HIV-positive Caucasian males receiving HAART who participated in the Fat Redistribution and Metabolic Change in HIV Infection (FRAM) Study. Common and internal carotid intima-media thicknesses (cIMT) measured by B-mode ultrasound were used as a subclinical measure of atherosclerosis. Single nucleotide polymorphisms (SNPs) were assayed using the Illumina HumanCNV370-quad beadchip. Copy Number Variants (CNV) were inferred using a hidden Markov Model (PennCNV). Regression analyses were used to assess the association of common and internal cIMT with individual SNPs and CNVs, adjusting for age, duration of antiretroviral treatment, and principal components to account for potential population stratification.

**RESULTS:** Two SNPs in tight linkage disequilibrium, rs2229116 (a missense, nonsynonymous polymorphism (Ile to Val)) and rs7177922, located in the ryanodine receptor (RYR3) gene on chromosome 15 were significantly associated with common cIMT (P-
value < 1.61 x 10). The RYR gene family has been known to play a role in the etiology of cardiovascular disease and has been shown to be regulated by HIV TAT protein.

**CONCLUSION:** These results suggest that in the context of HIV infection and HAART, a functional SNP in a biologically plausible candidate gene, RYR3, is associated with increased common carotid IMT, which is a surrogate for atherosclerosis.

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