High prevalence of the ApoE Arg145Cys dyslipidemia at-risk polymorphism in African-derived populations

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Background:
Apolipoprotein E (ApoE), a protein component of blood lipid particles, plays an important role in lipid transport and delivery. Single polymorphisms in residues 112 and 158 define the common E2, E3 and E4 alleles. In a study of Qatari, we observed that 17.4% of the African-derived genetic subgroup were heterozygotes for the rare Arg145Cys (R145C) variant that functions as a dominant trait with incomplete penetrance associated with dyslipidemia. Based on this, we hypothesized that the R145C polymorphism may be common in African-derived populations.

Methods:
The prevalence of the R145C variant worldwide was assessed in the 1000 Genomes Project (1000G) and then in 1012 Caucasians and 1226 African-Americans in New York City. Lipid profiles of the Qatari and New York R145C+ heterozygotes were compared to controls.

Results:
R145C+ Qatari heterozygotes had higher triglyceride levels compared to Qatari controls (p <0.007). The 1000Gs data demonstrated that the R145C polymorphism is rare in non-African derived populations, but present in 4.9-12.3% of Sub-Saharan African-derived populations. The R145C polymorphism was rare in New York City Caucasians (1/1012, 0.1%), but strikingly, 53 (4.3%) of 1226 New York City African-Americans were R145C+ heterozygotes, with an average of 52% higher fasting triglyceride levels compared to African-American R145C- controls (p <0.002).

Conclusions:
Based on these observations, there are likely to be millions worldwide derived from Sub-Saharan Africans that are ApoE R145C+. While larger epidemiological studies will be necessary to determine the long-term consequences of this polymorphism, the available evidence suggests it is a common cause of a mild triglyceride dyslipidemia.