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GENETIC VARIABILITY AND LINKAGE DISEQUILIBRIUM IN DCN, A GENE ASSOCIATED WITH METABOLIC SYNDROME

Dear Editor,

In the article by de Luis et al. (1), the influence of the SNP rs7139228 on resistin concentrations and the presence of metabolic syndrome (MS) in obese subjects was evaluated using a sample of 1003 obese Caucasian subjects, assessing their anthropometric measurements, nutritional intake, biochemical profile, and rs7139228 genotype. The results showed that the A allele of the rs7139228 genetic variant was associated with higher levels of resistin, basal insulin, and insulin resistance, confirming the findings by Onuma et al. (2), as well as the prevalence of MS in obese subjects, an observation not previously reported. The SNP rs7139228 is located in the regulatory region of the decorin (DCN) gene, which is a small proteoglycan, a component of connective tissue that binds to type I collagen fibrils and plays a role in matrix assembly (3).

Given this finding, we believe it is relevant to have a population perspective on the incidence of the risk allele rs7139228-A and its related genotypes (GA and AA). Here, using information from the 1000 Genomes database, we have explored the frequencies of the risk genotypes of this SNP in 26 populations and 5 macro populations (Fig. 1).

There is a clear high variability in the frequencies of the risk genotypes in African populations, where frequencies range from 20 % in African Americans from the Southwest USA to 51.5 % in Kenya (LWK). In the rest of the populations, this frequency ranges from 4.3 % in Colombia (CLM) to 19.6 % in Spain (IBS).

In an exploratory analysis, we also analyzed the linkage disequilibrium (LD) with another 1793 SNPs located in a 60 Kb region around this locus, using the global sample from 1000 Genomes (n = 5008 chromosomes). Using VcfTools (5), we found 10 SNPs

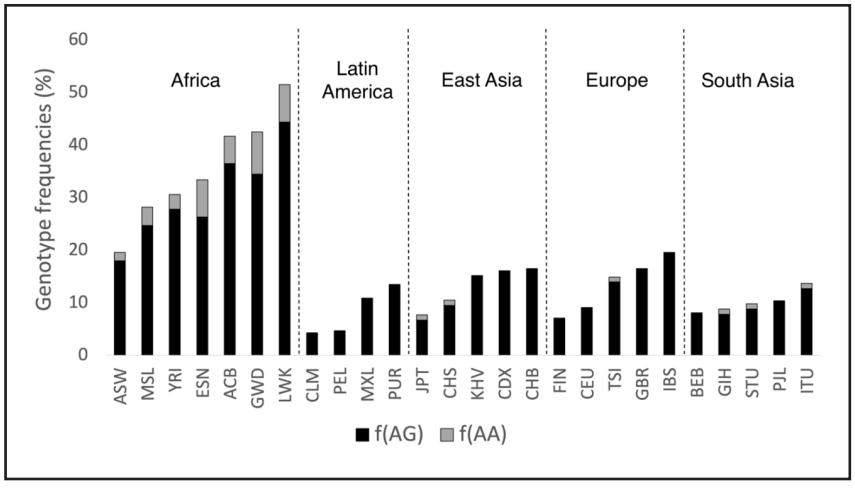

Figure 1.

Frequencies of the risk genotypes of SNP rs7139228 in 26 populations and 5 macro populations. Details of the samples can be reviewed at https://www.internationalgenome.org/ (4).

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with high correlation to rs7139228 ($r > 0.8$), which are candidates to explain the statistical genotype-phenotype association. These SNPs present effects such as: a) intergenic variants (rs7955861, rs73198623, rs57812022, rs530296868, rs1920719, rs1920718, rs190484681, rs111827906), upstream gene variant (rs17018765) and, very importantly, regulatory region variant (rs191730495).

Our observations suggest integrating the population variability of this SNP, incorporating genetic ancestry, and exploring the candidate SNPs proposed here in future genetic association studies involving the DCN gene.

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