

ALLERGY, GENETICS

TRUE, FALSE, TRUE, FALSE, TRUE, FALSE, FALSE

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While [some of my earlier co-workers](#) continue to praise the achievements of GWAs, [some other earlier co-authors](#) now show that the common variants thrown on the current GWA chips are leading to false associations (politely called “synthetic” associations)

We propose as an alternative explanation that variants much less common than the associated one may create “synthetic associations” by occurring, stochastically, more often in association with one of the alleles at the common site versus the other allele. Although synthetic associations are an obvious theoretical possibility, they have never been systematically explored as a possible explanation for GWAS findings. Here, we use simple computer simulations to show the conditions under which such synthetic associations will arise and how they may be recognized. We show that they are not only possible, but inevitable... by occurring, stochastically, more often in association with one of the alleles at the common site versus the other allele. Although synthetic associations are an obvious theoretical possibility, they have never been systematically explored as a possible explanation for GWAS findings. Here, we use simple computer simulations to show the conditions under which such synthetic associations will arise and how they may be recognized. We show that they are not only possible, but inevitable...

The proof comes with a sickle cell anemia study

For sickle cell anemia, a total of 179 SNPs reached genome-wide significance ($p < 5 \times 10^{-8}$), encompassing an ~2.5-Mb region on chromosome 11p15.4 ... The region contains dozens of genes and dozens of visually discernable LD blocks in HapMap YRI population. The top association signal (rs7120391, $p = 1.1 \times 10^{-136}$) is 9 kb from OR51V1, which is very near the causal gene, HBB ... Clearly, highly significant association signals can travel across multiple LD blocks to distant genomic regions.

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