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Genome wide association study SNPs in the human genome diversity project samples: does selection affect unlinked SNPs with shared trait associations?

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Background

Genome-wide association studies (GWAS) have identified more than 2000 trait-SNP associations and the number continues to increase. GWAS have focused on traits with considerable consequences for human fitness, including many immunological, metabolic, cardiovascular and behavioral phenotypes among others [1]. However, only a few GWAS SNPs seem to have experienced large, rapid, allele frequency changes in the course of human history [2-4]. Given the polygenic nature of complex traits, selection might also exert its influence on them by altering allele frequencies at many associated loci, a possibility that has yet to be explored empirically.

Results

Here we use 38 different measures of allele frequency and eight iHS scores to characterize over 1,300 GWAS SNPs in 53 globally distributed human populations. We apply these same techniques to evaluate SNPs grouped by trait-association. We find that groups of SNPs associated with pigmentation, blood pressure, hematological and autoimmune disease traits exhibit unusual allele frequency patterns and elevated iHS scores in certain geographical locations. We also find that GWAS SNPs are more likely to have unusual allele frequency patterns or elevated iHS scores in Eurasian or East Asian populations than those in Africa, Oceania, or the Americas.

Conclusions

Overall, we believe that our results provide evidence for selection on several complex traits that has caused changes in allele frequency and/or elevated iHS scores at several associated loci. Given the relatively small number of SNPs that have undergone large allele frequency changes in humans, small allele frequency changes at multiple variants linked by trait association might be relatively common, though difficult to detect. Our results also suggest that trait-SNP associations identified in Eurasian samples might not be present in Africa, Oceania, and the Americas, possibly due to differences in linkage disequilibrium patterns. This finding advocates for the inclusion of non- Eurasian and non-East Asia sample populations in future GWAS.

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