Uncovering Epistatic Variants in Gene Expression Studies

WEDNESDAY, May 13, 2015, at 8:45 AM
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ABSTRACT

In the quest to determine genetic causes of complex traits, researchers continue to be interested in the potential effects of epistasis, or gene-gene interaction. However, the available data and computational resources have precluded the possibility of detecting epistasis in human disease until recently. Even now, the statistical methods and computations need to be improved in order to generate more reliable results. In a recent paper in Nature Genetics, Hemani et al. (2014) presented one approach to investigate the effects of epistasis in a data set. Nevertheless, there are several problems with their paper that we explore here. After a discussion of these problems, we indicate some of the main issues that must be confronted when searching for epistasis, namely the large dimension of the search space with its associated power challenges and statistical tests that are robust to transformations and the linkage disequilibrium between the tag and causal single nucleotide polymorphisms (SNPs). We present possible candidates for a reasonable approach to addressing these issues by providing ways to reduce the search space and a statistical test for interaction.