Shared genetic association between a disease and a quantitative trait: evidence for a common causal variant?

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Following the recent success of genome-wide association studies in uncovering disease associated genetic variants, the next challenge is to understand how these variants affect molecular pathways. A way to address this issue is to obtain quantitative measures of molecular traits that can be correlated with the presence of disease associated variants. A promising set of quantitative molecular traits are expression trait loci (eQTL), quantifying the level of gene expression, which have already provided evidence of widespread association with Single Nucleotide Polymorphisms (SNPs). As a consequence, some eQTL associations are found in the same genomic region as a disease variant. The key question to plan further functional experiments is whether an overlap between a disease and an eQTL association map is consistent with the presence of a single common causal SNP. Here we derive a formal test of this hypothesis. This test amounts to testing whether the vectors of coefficients are proportional in two independent regressions. We will explore the power of the test as well as its robustness to the presence of outliers in the eQTL measurement. We will then apply this statistical test to compare an eQTL map associating in humans the expression of the gene RPS26 in the 12q13 region with another map associating this same region with T1D susceptibility.