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Genetic Architecture of Complex Traits: What have we learnt from Genome-wide Association Studies?

ABSTRACT

Recent genome-wide association studies have led to the identification of many susceptibility loci for a variety of complex traits of quantitative and qualitative nature. Although a large fraction of heritability of many of the individual traits still remain unexplained, there are now enough discoveries to begin assessing the “genetic architecture” of polygenetic traits in an empirical fashion. In the first part of this talk, I will describe a set of descriptive tools that can use data from existing studies to estimate the number of underlying susceptibility loci for a trait and the distributions of various related parameters, such as effect sizes and allele frequencies,. These methods are applied to analyze data for a variety of traits to estimate the number of undiscovered susceptibility loci, sample size required for future studies for further discoveries, potential utility of additional discoveries for risk-prediction and to examine the relationship between effect-size and allele frequencies. In the second part of the talk, I will describe a novel approach to meta-analysis that can combine association signals from a set of heterogeneous, but possibly related, phenotypes to explore common genetic links between them. An application of the method is illustrated using data from GWAS of 30,000 cases and 30,000 controls across six different cancer sites.