

Gene Mapping Strategies Using Linkage and Association Based Methods

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Linkage and association studies are both used to localize susceptibility/trait loci on the genomes of humans and other species. The development of polymorphic markers and the availability of computer software to carry out statistical analysis on large amounts of genetic pedigree data lead to a surge in the mapping and identification of genes for Mendelian traits. Although linkage analysis was highly successful for the mapping of Mendelian diseases this same triumph was not realized for the location and identification of susceptibility genes for complex/common traits. For the mapping of susceptibility genes involved in complex traits the association study design has been resurrected. This study design fell into disfavor due to the frequent occurrence of the inability to replicate findings. Historically the problems which plagued association studies included small sample sizes, the use of a very limited number of marker loci and population substructure and admixture. In the past few years there has been a renaissance in the use of association based studies which has been driven by advances in analysis methods and the ability to quickly and inexpensively genotype single nucleotide polymorphism (SNP) marker loci. In order to overcome problems of population substructure/admixture family based association studies are carried out using trio data (affected children and their parents) and additionally this problem has been alleviated for case-control data by using such methods as genomic control and structured association. Currently many association studies are carried out using large sample sizes and instead of limiting studies to genotyping markers within candidate genes entire genome scans are carried out using large numbers of SNP marker loci (i.e. 500,000). In this presentation an overview will be given of methods used for gene mapping which includes parametric and nonparametric linkage analysis and analysis methods for association studies.