

# **“Two Issues in Genome-wide Association Studies: Incorporating Modes of Inheritance and Use of Hardy-Weinberg Disequilibrium”**

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## **Abstract**

Genome-wide association studies (GWAS) are an enormously popular method of searching for the genetic bases of complex diseases. One common method of analysis is to consider multiple modes of inheritance per single nucleotide polymorphism (SNP) and report the smallest p-value, or compute the genotype- and allele-based tests and again report only the smallest p-value. The first portion of this seminar demonstrates via simulation that such approaches increase the type I error rate, as expected. Power is also compared for several such statistics after properly controlling the type I error rates at 5%. Another issue in the analysis of GWAS is how to use deviations from Hardy-Weinberg Equilibrium (HWE) as measures of association with disease. The second portion of this presentation proposes new statistics which consider differential rates of HWE deviation, via the inbreeding coefficient, between cases and controls. These statistics are contrasted with tests based on assessing differential rates of homozygosity in affecteds and unaffecteds. Multi-locus versions of these test statistics are applied to four GWAS of Parkinson's disease, age-related macular degeneration and heroin addiction.