The University of Chicago
Department of Statistics

Master's Seminar

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The Feasibility of a Genome-Wide Linkage Study of a Large Asthma Pedigree

TUESDAY, July 31, 2007 at 3:00 PM
110 Eckhart Hall, 5734 S. University Avenue

ABSTRACT

In this study, the feasibility of a genome-wide linkage analysis of a large asthma pedigree was investigated. Simulations were undertaken to assess the power, resolution, and ways to achieve maximum information with minimum genotyping using single-nucleotide polymorphism (SNP) markers. The software package Allegro was used to carry out nonparametric linkage analyses and genotype data simulation.

To elucidate the test power and resolution, simulations were performed under 33 inheritance models, using 100 replicates per model. The results indicated that for most models, there is no sufficient power to detect a disease locus with information provided by this pedigree. The most powerful model, a near-Mendelian dominant model with the disease allele frequency at 0.01, had 85% power to detect a disease locus at the nominal significance level of 0.01, but only 35% power at the level of 0.0001. Most models didnt provide fine resolution to detect a disease locus. For the optimal model described above, the average of the distances from the estimated disease locus to the true disease location was 4.46 centiMorgan, and the average length of the confidence regions was 12.45 centiMorgan.

Simulation to investigate the available information was carried out with Affymetrix GeneChip 10K SNP markers on Chromosome 22. Several replicates of simulated genotype data were analyzed. The results showed that current pedigree data provide sufficient information using SNP markers.

In conclusion, the pedigree described in this manuscript can be used for detecting linkage only for genetic models with large genotype relative risks (GRR), and the confidence regions that will result from a successful linkage study would likely be too large for a straightforward positional cloning project. Additionally, the current pedigree data provide sufficient information when genotyping is carried out with SNP markers.

Information about building access for persons with disabilities may be obtained in advance by calling Karen Gonzalez (Department Administrator and Assistant to Chair) at 773.702.8335 or by email (karen@galton.uchicago.edu).