Search for Haplotype-Interactions That are Susceptible to Type 1 Diabetes Using Unphased Genotype Data

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The pathogenic equation for type 1 diabetes presents a complex interrelation of genetic and environmental factors, most of which have yet to be identified. Simultaneous identification of these genetic factors using unphased genotype data has received increasing attention in past few years. Several approaches have been described, such as the modified transmission/disequilibrium test procedure, the conditional extended transmission disequilibrium test, and the stepwise logistic-regression procedure. These approaches are limited either by being restricted to family data or by ignoring so-called haplotype interactions between alleles. To overcome this limit, this report provides a general method to identify the haplotype blocks that interact to define the risk for a complex disease based on unphased genotype data. The principle underpinning the proposal is minimal entropy. The performance of our procedure is illustrated for both simulated and real data. In particular, for a set of Dutch type 1 diabetes data, our procedure suggests some novel evidence of the interactions between and within haplotype-blocks, which are across chromosomes 1, 2, 3, 4, 5, 6, 7, 8, 11, 12, 15, 16, 17, 19, and 21. The results demonstrate that by considering interactions between potential disease haplotype blocks, we may succeed in identifying disease-predisposing genetic variants that might otherwise have remained undetected.

Running title: Haplotype-Interactions

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