Introduction

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We are delighted to present this special issue celebrating the anniversary of the Transmission Disequilibrium Test (TDT) [1, 2]. In this introduction, we list a few reasons why we think that the TDT belongs in the pantheon of great statistical genetics methods.

- (1) The method is simple. For trios in which the father, mother, and affected child all have genotype data, the TDT may easily be calculated by counting the number of times a heterozygous parent transmits one allele and not the other, across all trios. These numbers may be tallied in a table, as was demonstrated in the 1993 publication [see table 2 of 1]. The counts are entered into a formula to calculate the TDT statistic, and for a sufficiently large sample size, the significance of the statistic is determined using the null distribution of the TDT, which is a central chi-square with 1 degree of freedom.
- (2) The method is widely used. The TDT has been applied to hundreds of studies involving the mapping of disease genes. Genetic disorders to which TDT methods have been applied include insulin-dependent diabetes mellitus [1], psoriasis [3–6], Graves disease [7], schizophrenia [8, 9], bipolar disorder [10], autism [11, 12], and many others. The method is considered so essential to family-based association testing that it is routinely implemented in comprehensive statistical genetics analysis programs (e.g., GENEHUNTER [13], PLINK [14]).

- (3) The method has inspired several methodological extensions/investigations. Since the publication of the original TDT statistic in 1993, there have been hundreds of papers investigating methodological issues regarding the TDT. If one types the key words 'transmission disequilibrium test' and 'method' into Pubmed, over 200 papers are returned (as of February, 2008). Extensions of the TDT method include those that allow for untyped parents [15], multiple alleles at a locus [16, 17], discordant sibs [18], quantitative traits [19, 20], and haplotypes [21], to name a few.

In this issue of Human Heredity, we present additional methodological and empirical investigations of the TDT statistic. We hope you enjoy reading the articles and that you find them useful in your research.

Finally, we wish to thank Drs. Warren Ewens and Richard Spielman for their guidance and support of this special issue. We dedicate this issue to them and to Dr. Ralph McInnis.

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