Speaker : Prof. Saurabh Ghosh, Human Genetics Unit, ISI Kolkata

Date : 20th August, Wednesday

Time : 4:00pm - 5:00pm

Venue : Indian Statistical Institute (ISI), Chennai Centre
SETS (Society for Electronic Transactions and Security),
MGR Knowledge City, CIT Campus, Taramani.
(Landmark: Near IITM Research Park/ Ginger Hotel)

Title : Population-based Association Mapping Of Quantitative Traits: Stratification Issues And Family-based Alternatives

Abstract:

Clinical end-point traits are often defined in terms of quantitative precursors (e.g., systolic blood pressure for hypertension, fasting glucose levels for Type 2 Diabetes, etc.) It has been argued that analyzing the quantitative precursors instead of the binary clinical end-points may be a statistically a more powerful strategy to identify novel genomic regions harboring genes that modulate the underlying complex trait. It is now well established that population stratification can result in spurious association findings in genetic case-control studies. Thus, it is of interest to evaluate the adverse effects of population stratification on the analyses of quantitative traits. The two popular statistical tests of association for quantitative traits using population level data are ANOVA and Kruskal-Wallis. We have theoretically shown that neither genetic heterogeneity nor phenotypic heterogeneity alone can affect the false positive rate of either of the tests. However, if the data comprise subpopulations with different allele frequencies at the marker locus of interest as well as different phenotypic means or distributions, the rate of false positives will be elevated. We have also carried out extensive simulations under different genetic models and probability distributions of quantitative traits to assess the extent of increase in the rate of false positives in the presence of population stratification. The classical Transmission Disequilibrium Test (TDT) for binary traits circumvents the problem of population stratification as it tests for allelic association in the presence of linkage. We propose a simple logistic regression based test for transmission disequilibrium in the context of quantitative traits that can be analytically shown to be statistically equivalent to the TDT for binary traits. We perform Monte-Carlo simulations under a wide spectrum of genetic models and probability distributions of the quantitative trait values to evaluate the power of the proposed procedure and compare with the FBAT approach with identical data. We find that our method yields more power than FBAT if we suitably incorporate trios with both parents heterozygous in our likelihood. The method can be easily extended to incorporate multivariate phenotypes. We apply our method to analyze externalizing symptoms, an alcoholism related endophenotype from the Collaborative Study on the Genetics Of Alcoholism (COGA) project.

Please forward this notice to anyone who you think may be interested.