



UNC  
GILLINGS SCHOOL OF  
GLOBAL PUBLIC HEALTH

## **BIostatISTICS SEMINAR**

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**Ann Arbor, MI**

### **Set-based Tests for Genetic Association and Gene-Environment interaction**

Characterizing genetic association and gene-environment interaction related to complex diseases has received considerable attention in the last decade. To reduce the burden of multiple comparisons and improve power, many genetic association studies have now considered an alternate or supplementary analytic approach towards jointly testing the effect of all genetic variants in a biologically defined set, such as a gene, pathway or specific genome region as opposed to a one-at-a-time single variant analysis. In this talk, I will briefly introduce a set of random field based tests for genetic association. Then I will introduce a statistical framework for set-based inference for gene-environment interaction with longitudinally measured quantitative traits and propose a generalized score type test. The test is robust to misspecification of within subject correlation and has enhanced power compared to existing alternatives, particularly in presence of a temporal trend and modest number of repeated measures. Unlike tests for marginal genetic association, set-based tests for gene-environment interaction face the challenges of fitting a potentially misspecified and high-dimensional main effect model. We show that the proposed test is robust to main effect misspecification of an environmental exposure and genetic variables under the gene-environment independence condition. When genetic and environmental factors are related, the method of sieves is further proposed to eliminate potential bias due to a misspecified main effect of a continuous environmental exposure. A weighted principal component analysis approach is developed to perform dimension reduction when the number of genetic variants in the set is large relative to the sample size. These general issues are also relevant to a cross-sectional analysis.

**Thursday, February 18, 2016**  
**3:30 pm - 4:30 pm**  
**Blue Cross Blue Shield Memorial Auditorium**  
**0001 Michael Hooker Research Center**