

College of Arts and Sciences  
Department of Statistics  
University of South Carolina

# Statistics Colloquium

## Identifying individual risk rare variants using protein structure-guided local tests

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Rare variants are of increasing interest to genetic association studies because of their etiological contributions to human complex diseases. Due to the rarity of the mutant events, rare variants are routinely analyzed on an aggregate level. While aggregation analyses improve the detection of global-level signal, they are not able to pinpoint causal variants within a variant set. To perform inference on a localized level, additional information, e.g. biological annotation, is often needed to boost the information content of a rare variant. Following the observation that important variants are likely to cluster together on functional domains, we propose a protein structure guided local test (POINT) to provide variant-specific association information using structure-guided aggregation of signal. Constructed under a kernel machine framework, POINT performs local association testing by borrowing information from neighboring variants in the three-dimensional protein space in a data-adaptive fashion. Besides merely providing a list of promising variants, POINT assigns each variant a p-value to permit variant ranking and prioritization. We assess the selection performance of POINT using simulations and illustrate how it can be used to prioritize individual rare variants in PCSK9 associated with low-density lipoprotein in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) clinical trial data.

**THURSDAY**  
**August**  
**30**  
**2018**

**2:50 p.m. – 3:50 p.m.**

LeConte College 210

Refreshments will be served in the  
Faculty Lounge, LeConte 213

4:00 p.m. – 4:30 p.m.

Check out the Statistics Department  
home page at [www.stat.sc.edu](http://www.stat.sc.edu) for  
upcoming colloquium information.



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