UNC
GILLINGS SCHOOL OF
GLOBAL PUBLIC HEALTH

BIOSTATISTICS SEMINAR

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Systematic tissue-specific functional annotation of the human genome and its applications in post-GWAS analysis

Continuing efforts from large international consortia have made genome-wide epigenomic and transcriptomic annotation data publicly available for a variety of cell and tissue types. However, synthesis of these datasets into effective summary metrics to characterize the functional non-coding genome remains a challenge. Here, we present a statistical framework to produce high-resolution, single tissue annotations through integration of diverse epigenomic and transcriptomic data. After validating our annotations with a catalog of known tissue-specific non-coding elements, we apply our method using data from 127 different cell and tissue types to present an atlas of enrichment across 45 different complex traits. Additionally, we use our annotations in an in-depth case study of late-onset Alzheimer's disease (LOAD). Our analyses suggest a strong connection between LOAD heritability and genetic variants contained in regions of the genome functional in monocytes. We show that the localization of SNPs to monocyte-functional regions is a pattern of inheritance shared with Parkinson's disease. Finally, we introduce a principled framework to estimate annotation-dependent genetic covariance using GWAS summary statistics. We demonstrate its effectiveness through dissecting the shared genetic architecture between LOAD and amyotrophic lateral sclerosis, another major neurodegenerative disease. Overall, we show that integrated genome annotations at the single tissue level may be a valuable tool for understanding the etiology of complex human diseases

Thursday, February 23, 2017
3:30 pm - 4:30 pm
Blue Cross Blue Shield Memorial Auditorium
0001 Michael Hooker Research Center