

Applying an Enhancer Lens to Human Disease Genetics

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In this seminar, Dr. Zhu will present three studies to illustrate how enhancers, when coupled with new statistical and computational tools, can improve the discovery and interpretation in GWAS. First, we develop a scalable strategy to identify non-coding elements exhibiting both high levels of cross-species sequence conservation and enhancer-like biochemical activity. Through Bayesian hierarchical modeling of these elements in GWAS, we further showcase the real-world utility of sequence-conserved enhancers in identifying heritability enrichments, likely causal variants, and effector genes for complex diseases. Second, we develop a Bayesian variable selection method to connect enhancers with target genes on the genome scale, using transcriptomic and epigenomic data across diverse tissues and cell types. By combining the identified enhancer-gene linkages with GWAS, we further pinpoint disease associations in the non-coding genome to putative regulatory mechanisms for experimental interrogation. Third, we employ multiplexed CRISPR interference and machine learning to reveal a multi-layer enhancer network that maintains robust gene expression against non-coding mutations. Building on this enhancer network, we further develop an analytical framework to identify non-additive effects of genetic interactions on disease risk. This approach goes beyond standard additivity-only GWAS and enables the construction of interaction-aware polygenic risk scores.

Thursday, February 8, 2024, 3:30-4:30PM Eastern

133 Rosenau Hall

Zoom Link:

<https://unc.zoom.us/j/98423779288?pwd=b0tqYThCQTaxeDdTQ0FRY3RnazdwQT09>

Meeting ID: 984 2377 9288

Passcode: 631794