



**BIOINFORMATICS 2016 FALL SEMINAR SERIES**

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<http://bioinformatics.udel.edu/Seminars/Current>

**MONDAY, November 7, 2016  
12:00pm**

**Webinar :**

<https://nemours.webex.com/nemours/j.php?MTID=mbf9c470f660b31d93e473fd3eab78a15>

## **System Genetics Approaches to Understand Metabolic Diseases**

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**ABSTRACT:** Systems genetics is an approach to understand the flow of biological information that underlies complex traits. It uses a range of experimental and statistical methods to quantitate and integrate intermediate phenotypes, such as transcript, protein or metabolite levels, in populations that vary for traits of interest. Systems genetics studies have provided the first global view of the molecular architecture of complex traits and are useful for the identification of genes, pathways and networks that underlie common human diseases. Given the urgent need to understand how the thousands of loci that have been identified in genome-wide association studies contribute to disease susceptibility, systems genetics is likely to become an increasingly important approach to understanding both biology and disease.

Many genetic variants influence complex traits by modulating gene expression, thus altering the abundance of one or multiple proteins. Here we introduce a powerful strategy that integrates gene expression measurements with summary association statistics from large-scale genome-wide association studies (GWAS) to identify genes whose cis-regulated expression is associated with complex traits. We leverage expression imputation from genetic data to perform a transcriptome-wide association study (TWAS) to identify significant expression-trait associations. We applied our approaches to expression data from blood and adipose tissue measured in ~3,000 individuals overall. We imputed gene expression into GWAS data from over 900,000 phenotype measurements to identify 69 new genes significantly associated with obesity-related traits (BMI, lipids and height). Many of these genes are associated with relevant phenotypes in the Hybrid Mouse Diversity Panel. Our results showcase the power of integrating genotype, gene expression and phenotype to gain insights into the genetic basis of complex traits.