



## Xuanyao Liu, PhD

Assistant Professor of Medicine  
Assistant Professor of Human Genetics  
University of Chicago

**Friday, September 2, 2022**

**12:00-1:00 pm**

**Biotech Center Auditorium \*or\* via Zoom Link**

<https://uwmadison.zoom.us/j/4974997546>

## Moving beyond cis gene regulation: the next steps to understand complex trait genetics

**Abstract:** Early genome-wide association studies (GWASs) led to the surprising discovery that, for typical complex traits, most of the heritability is due to huge numbers of common variants with tiny effect sizes. Here, we provide a formal model in which genetic contributions to complex traits are partitioned into direct effects from core genes and indirect effects from peripheral genes acting in trans. We propose that most heritability is driven by weak trans-eQTL SNPs, whose effects are mediated through peripheral genes to impact the expression of core genes. In particular, if the core genes for a trait tend to be co-regulated, then the effects of peripheral variation can be amplified such that nearly all of the genetic variance is driven by weak trans effects. Detecting trans-eQTLs is very challenging. To improve the power of detecting trans-eQTLs, we propose a PC-based multivariate association pipeline, trans-PCO, that combines multiple PCs to detect trans-eQTLs of regulatory networks. We showed through simulations and real data applications that trans-PCO is a powerful and reliable tool that detects trans-eQTLs of cellular pathways and networks, which opens up new opportunities to learn the trans-regulatory mechanism of complex traits and diseases.



**School of Medicine  
and Public Health**

UNIVERSITY OF WISCONSIN-MADISON