Save The Date: Friday, January 30, 2026

11 am (EST), 8 am (PST) and 5 pm (CET)

Dear IGES members,

IGES hosts regular virtual journal clubs throughout the year to increase IGES members' familiarity with emerging and classic literature in genetic epidemiology and to foster discussion and networking among members. This month's journal club evaluates a Proteome-Wide Association Studies (PWAS) approach that incorporates trans SNPs via an intermediate GWAS step, improving protein prediction accuracy and enabling reproducible associations with lipid and blood cell traits in large cohorts. Make plans to attend our next meeting!

Title: "Proteome-Wide Association Study Using Cis and Trans Variants and Applied to the Women's Health Initiative Study" (*Genet Epidemiol*. 2024 Oct;48(7):310-323).

Article: https://doi.org/10.1002/gepi.22578

Abstract (adapted from the original abstract):

In most Proteome-Wide Association Studies (PWAS), variants near the protein-coding gene (+/- 1 Mb), also known as cis SNPs, are used to predict protein levels, which are then tested for association with phenotypes. However, proteins can be regulated through variants outside of the cis region. An intermediate GWAS step to identify protein quantitative trait loci (pQTL) allows for the inclusion of trans SNPs outside the cis region in protein-level prediction models. Here, we assess the prediction of 540 proteins in 1,002 individuals from the Women's Health Initiative (WHI), split equally into a GWAS set, an elastic net training set, and a testing set. We compared the testing r2 between measured and predicted protein

levels using this proposed approach, to the testing r2 using only cis SNPs. The two methods usually resulted in similar testing r2, but some proteins showed a significant increase in testing r2 with our method. For example, for cartilage acidic protein 1, the testing r2 increased from 0.101 to 0.351. We also demonstrate reproducible findings for predicted protein association with lipid and blood cell traits in WHI participants without proteomics data and in UK Biobank utilizing our PWAS weights.

Registration link:

https://msm-edu.zoom.us/meeting/register/xxaG-AuOQ7CZa-NM5fOzMg

After registering, you will receive a confirmation email containing information about joining the meeting.

Bio:

Brian Chen is a current 5th-year Biostatistics PhD student at the University of North Carolina at Chapel Hill. His dissertation work focuses on complex disease prediction through genomics and multi-omics data with applications to Alzheimer’s disease and blood cell traits. He has developed methods to improve polygenic risk scores for admixed individuals by incorporating functional annotations. Additionally, he has leveraged deep learning and omics data for phenotype prediction. His other research includes proteomic and metabolomic associations with blood cell traits. Brian was also given the opportunity to intern at Alexion Pharmaceuticals in the summer of 2025, running large-scale simulations.

Do you have any suggestions for interesting topics, papers, or presenters for further talks? Or would you like to support us in organizing the Journal Club? Please contact Dr. Silke Szymczak (silke.szymczak@uni-luebeck.de)

On behalf of the organizing team of the IGES Journal Club,
Silke Szymczak
Heejong Sung
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