**Subject:** Dissertation Defense - Nicholas Minster, PhD in Bioinformatics & Computational Biology
**Date:** Thursday, April 9, 2026 at 5:10:19 PM Eastern Daylight Time
**From:** SSB Faculty List on behalf of Diane St. Germain
**To:** SSB-FACULTY-LIST-L@LISTSERV.GMU.EDU

Dissertation Defense Announcement
To: The George Mason University Community

**Candidate:** Nicholas Minster

**Program:** PhD in Bioinformatics and Computational Biology

**Date:** April 24, 2026

**Time:** 9:00 A.M. Eastern Time (US and Canada)

**Location:** via Zoom

Join Zoom Meeting

https://gmu.zoom.us/j/98027176964?pwd=uZrQaIzMc5gapFmOrAsKXC21nq3hVC.1

Meeting ID: 980 2717 6964
Passcode: 099630
One tap mobile
+13017158592,,98027176964#,,,,*099630# US (Washington DC)
+12678310333,,98027176964#,,,,*099630# US (Philadelphia)

Dial by your location
+1 301 715 8592 US (Washington DC)
+1 267 831 0333 US (Philadelphia)
Meeting ID: 980 2717 6964
Passcode: 099630
Find your local number: https://gmu.zoom.us/u/adicUgmxkm

**Committee Chair:** Dr. M. Saleet Jafri

**Committee members:** Dr. Ancha Baranova, Dr. James C. Thompson

**Title:** Parkinson's Disease Through Peripheral Proteomics: Cross-Cohort

Diagnosis, Severity Modeling, and Biological Grounding from a Leakage-Safe Multi-Omics Framework

## Abstract:

Parkinson's disease affects over ten million people worldwide, yet diagnosis remains clinical and occurs after substantial neurodegeneration. This dissertation develops an interpretable, leakage-safe machine learning framework for PD biomarker discovery using matched whole-blood RNA sequencing and targeted plasma proteomics from the AMP-PD consortium, with PPMI and PDBP as training and external validation cohorts. A 32-protein diagnostic classifier achieves external AUROC = 0.8724, while whole-blood RNA yields only modest discrimination and no fusion strategy improves on proteomics alone. Unsupervised subtyping of residualized transcriptomic data produces stable partitions that lack clinical separation, demonstrating that cluster stability alone is insufficient for biological interpretability. A continuous severity model using Ridge regression on plasma proteins generalizes across cohorts (Spearman $\rho = 0.507$), with enrichment converging on cell–matrix adhesion and integrin signaling and genetic anchoring identifying overlap with PD risk loci. An exploratory Mendelian randomization analysis using UKB-PPP cis-pQTL instruments demonstrates feasibility for genetically anchoring severity-associated proteins, with ENPP5 showing directional concordance across MR, severity association, and bootstrap importance. Across all studies, plasma proteomics consistently outperforms transcriptomics under cross-cohort transfer, with biological themes converging on extracellular signaling, immune regulation, and cell–matrix adhesion.

###