Subject: Dissertation Defense - Claire Weber, PhD Biosciences
Date: Tuesday, June 18, 2024 at 10:45:08 AM 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: Claire Weber

Program: PhD Biosciences

Date: Wednesday July 3, 2024

Time: 11:00 AM Eastern Time (US and Canada)

Location: Via Zoom

Join Zoom Meeting

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97451955294@zoomcrc.com

Committee chair: Dr. Alessandra Luchini

Committee members: Dr. Donald Seto, Dr. Karl Fryxell, Dr. Iosif Vaisman, Dr. Emily Y. Chew

Title: “Integrative Multi-omics Investigation of Biomarkers for Age-Related Macular Degeneration”

Abstract:

Age-related macular degeneration (AMD) is a progressive and potentially blinding eye disease without a cure and limited therapeutic options. It is the leading cause of blindness in high-income countries and loss of central vision causes substantial decline in overall quality of life. This study explored the multifactorial nature of AMD through integrative multi-omics analysis using data from the Age-Related Eye Disease Studies (AREDS) and AREDS2 and the Framingham Offspring Eye Study (FOES) as a complementary cohort. The goal was to identify molecular biomarkers and bio-pathways most strongly associated with AMD, particularly the late stages, across the omics.

We applied Cox proportional hazards with mixed effects models to longitudinal serum metabolomes from AREDS and AREDS2 with an outcome of late AMD. With AREDS serum proteomics we used linear mixed effects models with an outcome of late AMD. For 13 cross-sectional omics datasets in FOES we applied limma generalized linear regressions with an outcome of any AMD. In each cohort, enrichment analysis was run for FDR significant metabolites, proteins, or genes. Integrative pathway enrichment was performed to find jointly significant biomarkers across cohorts and omics types.

We found significant alterations in the serum of AMD patients, where enriched broad pathways included metabolism of lipids, amino acids, and nucleotides; apoptosis; angiogenesis, and others. Specific lipids appearing repeatedly in results and shared across the three cohorts were glycerophosphocholines and sphingosines or sphingomyelins, in both protective and risk directions of association with late AMD.

This comprehensive analysis highlights the significant overlap in immune and inflammatory responses across different data sets in late AMD. By finding significant commonalities from three large-scale cohorts, this work enhances our understanding of AMD's underlying mechanisms and highlights the potential for high throughput, omics-based medicine that could transform its management and treatment.

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