Dr. Laura Harris – ICER REU Faculty Talk

Title: Gene Expression and Pathway Activity Meta-Analysis of SARS-CoV Infection in Lungs

Background: Severe Acute Respiratory Syndrome (SARS) coronavirus (CoV) infections are a critical public health threat through their pandemic spread. This novel research involves meta-analysis of mRNA expression data to identify gene expression and pathway activity changes from SARS (SARS-CoV, MERS-CoV, and SARS-CoV2) infections by comparing gene or pathway signatures.

Methods: Gene signatures (T-score ranked gene lists) from comparing 37 human and mouse lung cultures or samples 48hrs post SARS and mock infection are generated. The signatures represent 29 SARS-CoV infections across seven different strains with varying virulence (icSARS, Urbani, MA15, ΔORF6, BAT-SRBD, ΔNSP16, and ExoNI), five MERS-CoV infections, and three SARS-CoV2 infections. Gene signatures are converted to pathway signatures (lists ranked by normalized enrichment score) with Gene Set Enrichment Analysis (GSEA) from the 7573 Gene Ontology Biological Process gene sets. For both gene and pathway signatures, positive and negative panels are defined from the intersection of leading-edges identified by GSEA between two icSARSvsmock signatures. This meta-analysis compares icSARS panels to 37 signatures via GSEA to find the intersection of leading-edges to find common genes and pathways.

Results: For both gene and pathway signatures, enrichment is observed consistently between icSARS positive gene and pathway panels and all SARS signatures (GSEA $p<0.001$). Inconsistent enrichment is observed for the icSARS negative panels. Identified leading-edges from icSARS positive panel comparisons find five common genes and 11 common pathways across all SARS signatures regardless of variation, suggesting these genes and pathways are associated with SARS infection. Identified genes and pathways are involved in immune response.

Conclusion: This GSEA-based meta-analysis identifies genes and pathways with and without reported associations with SARS infections, highlighting this approach's predictability and usefulness in identifying molecular changes associated with SARS infections that may have therapeutic potential.