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Hughes Lab Seminar
"Transcription factors operate across disease loci, with EBNA2 implicated in autoimmunity"

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Abstract:

Explaining the genetics of many diseases is challenging because most associations localize to incompletely characterized regulatory regions. Using new computational methods, we show that transcription factors (TFs) occupy multiple loci associated with individual complex genetic disorders. Application to 213 phenotypes and 1,544 TF binding datasets identified 2,264 relationships between hundreds of TFs and 94 phenotypes, including androgen receptor in prostate cancer and GATA3 in breast cancer. Strikingly, nearly halfof systemic lupus erythematosus risk loci are occupied by the Epstein-Barr virus EBNA2 protein and many coclustering human TFs, showing gene-environment interaction. Similar EBNA2-anchored associations exist in multiple sclerosis, rheumatoid arthritis, inflammatory bowel disease, type 1 diabetes, juvenile idiopathic arthritis and celiac disease. Instances of allele-dependent DNA binding and downstream effects on gene expression at plausibly causal variants support genetic mechanisms dependent on EBNA2. Our results nominate mechanisms that operate across risk loci within disease phenotypes, suggesting new models for disease origins.

Friday, May 18, 2018 | Noon (12 PM)
James D. Friesen | Cecil C. Yip Red Seminar Room
Host: Timothy R. Hughes, PhD