Systematic Survey of Pathways Perturbed in Complex Diseases

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Tissue and pathway enrichment tests are associated with mutations of Body Mass Index (BMI) and Alzheimer's Disease (AD). Researches had shown that AD is correlated with stress-induced changes in lifestyle, such as obesity. The goal of my study is to examine tissue-pathway enrichment associated with both BMI and AD to reveal biological mechanisms and patterns for diseases. I applied loci2path to analyze sets of genomic intervals associated with the traits BMI and AD. To run loci2path, I downloaded the Genome-Wide Association Study (GWAS) data from PheGenI and converted the file into a loci2path (.txt) readable file. Also, in the 49 eQTL sets I generated (each contains about 600,000 eQTL) with only p-values of 49 tissues, the most enriched pathways were initially generated. The pathways (IL2RB, TLR4, CTCF, and GLEEVEC) I identified in Alzheimer's disease may contribute to neurodegenerative diseases. The toll-like receptor 4 (TLR4) signaling pathway has been reported as one of the main triggers of the obesity-induced inflammatory response. The Biocarta MHC, IL3, Lectin, GH, and Insulin pathways have been reported for BMI. The Biocarta Lectin Pathway result is encouraging since one previous study showed that insulin and leptin resistance are related to the dysregulation of energy balance and the induction of a chronic inflammatory status, which has been recognized as important cofactors in cognitive impairment and AD initiation and progression. Our results show different pathways play distinct roles across tissues but are correlated in both BMI and AD. I am currently examining additional traits for their tissue-pathway enrichment.

Awards Won: