Identification of Parkinson's Disease-Associated SNP-SNP Interaction Using Interaction Analysis by Chi-Square (IAC)

Chu, Sidney

Parkinson's disease (PD) is a progressive neurodegenerative disease that affects an estimated seven to ten million people worldwide. During the past ten years, Genome-Wide Association Studies (GWAS) have been successful in identifying genetic variants (SNP) associated with genetic predisposition of different diseases, including Parkinson's disease. Despite the numerous achievements made in identifying single-locus disease-associations, more is still needed to be done in exploiting epistasis in order to solve the problem of missing heritability. Recent computational methods have low productivity in identifying such interactions; most statistical frameworks do not have the power to detect significant interactions under non-significant main effects, or even if they do, computational burdens slow down the research process. This novel statistical framework, IAC, reduces 98% of redundant search space and computational intensity with biologically plausible constraints — helping to detect interactions between different loci at seemingly low sample sizes. After applying this method on 532 different simulation experiments, IAC's efficiency exceeded that of conventional methods (such as univariate analysis/regression models). One dominant-dominant interaction between two SNPs previously unidentified with conventional models in the same Parkinson's disease dataset (a coverage of 408,803 unique genome-wide SNPs) was successfully exploited with IAC. Furthermore, both SNPs are located on the introns of genes NRP2 and LRVN respectively and may hint on an higher-order genetic interaction. IAC will be instrumental in shaping the way we understand the genetic susceptibility of PD and other complex diseases, paving the way for more effective pharmaceutical solutions.

Awards Won:

Fourth Award of $500