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Pathway and network analysis of GWAS and RNA-Seq for schizophrenia

Genome-wide association studies (GWAS) have become a popular approach for searching for common genetic variants which increase susceptibility to complex diseases or traits. At the transcriptome level, RNA sequencing (RNA-Seq) is rapidly emerging as a powerful tool for identifying differentially expressed genes in diseases. Recently, pathway or network-based analysis of genomic datasets has emerged as an alternative but potentially powerful approach to searching for disease causal genes, assuming a complex disease might have resulted from a number of genes which disrupt one or more pathways or protein complexes. We applied several pathway enrichment methods to schizophrenia GWAS datasets including Gene Set Enrichment Analysis (GSEA), hypergeometric test, and a generalized additive model (GAM). At

the network level, we developed a dense module searching (DMS) method to identify candidate subnetworks or genes for complex diseases by integrating the association signal from GWAS datasets into the human protein-protein interaction (PPI) network. Finally, we performed a pathway analysis of schizophrenia RNA-Seq data. We found several pathways that were top ranked and likely associated with schizophrenia by these methods. These pathways are related to metabolism of glutamate, the process of apoptosis, inflammation, and immune system. Our pathway analysis of RNA-Seq data generally supported these findings. Our analysis suggested pathway and network approaches are promising in post-GWAS era and may complement the original analysis of genomics datasets such as GWAS and RNA-Seq.

Biography

Dr. Zhongming Zhao is the Chief Bioinformatics Officer in Vanderbilt-Ingram Cancer Center (VICC), the director of the VICC Bioinformatics Resource Center, and an associate professor in the Departments of Biomedical Informatics, Psychiatry, and Cancer Biology, Vanderbilt University. Dr. Zhao received his Ph.D. degree in human and molecular genetics from the University of Texas Health Science Center at Houston in 2000. He also received three M.S. degrees: genetics (1996), biomathematics (1998), and computer science (2002). He has more than 13 years of bioinformatics and systems biology research experience and published more than 90 papers in these areas. He has served as editor or editorial board member of more than 15 journals and on program committees and sessions chair in international conferences more than 40 times. He received several awards, including the Keck Foundation Post-doctoral Fellowship (twice: 2002, 2003), NARSAD Young Investigator Award (twice, 2005, 2008), the best paper award in the ICIC'08, and Nick Norgan Award for the best paper published in *Annals of Human Biology* during 2009.