Systems Biology Research Symposium
Oral Presentation Session

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Network Approaches to Elucidate the Molecular Basis of Disease

Bing Zhang and Jing Li

Department of Biomedical Informatics, Vanderbilt University School of Medicine, Nashville, TN 37232, USA
Presenter's email address: bing.zhang@vanderbilt.edu

Accumulating evidence suggests that biological systems are composed of functional modules of interacting molecules. It has been argued that an understanding of a cell might be better achieved by investigating, not individual genes, RNAs, or proteins, but the networks and functional modules. In deed, protein interaction network-based approaches have been developed and successfully applied on the prediction of protein functions, prioritization of candidate disease genes, and classification of cancer metastasis etc. Here we employed graph theoretical approaches to identify network modules, and used the modular information to facilitate transcriptomics and proteomics data analyses in disease studies.
Despite the promise of gene expression signatures in disease diagnosis and prognosis, extracting and understanding the underlying biology highlighted by these signatures remain significant challenges. We constructed gene co-expression network from large-scale microarray gene expression data sets, identified co-expression modules from the networks, and correlated the modules with disease outcomes. Because genes in each co-expression module are likely to be co-regulated by common transcriptional programs, we further identified *in silico* transcriptional regulators that may underlie the dysregulated transcriptional programs.
Besides microarray gene expression profiling, shotgun proteomics has emerged as a promising technology for protein identification with remarkable applications in discovering disease biomarkers. However, challenges remain in protein assembly and biological interpretation of the assembled proteins. Current protein assembly pipelines treat proteins as independent entities. Usually, only individual proteins with strong experimental evidence are reported, while many possible proteins of potential biological interest are eliminated because of insufficient experimental evidence. In biomarker studies, this may prevent us from identifying important biomarker candidates. Taking into consideration the functional relationship among proteins as embedded in protein interaction networks, we have developed a protein interaction network-assisted complex-enrichment approach (CEA) to rescue eliminated but possible proteins. Applying CEA on a breast cancer data set rescued the products from some well-known breast cancer genes. Moreover, CEA generates a network view of the proteins and helps reveal the modular organization of proteins that may underpin the molecular mechanisms of the disease.

Key words: network, module, disease biomarker, gene regulation, shotgun proteomics, cancer