Integrative network analysis reveals novel insights of disease mechanisms

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There are multiple ways to perturb key pathways leading to disease initiation and progression. Large scale genetic/genomic studies have been conducted to uncover driver events of diseases such as germline or somatic mutations, gene fusion or translocations, methylation or other epigenetic changes, copy number alterations, gene expression changes. However, molecular mechanisms through which these driver events lead to diseases are not clear in most of cases. We developed methods to leverage multiple data types available in the studies. We previously developed an analytical procedure, Reconstructing Integrative Molecular Bayesian Networks (RIMBANET) (1), to reveal pathways linking causal events to disease phenotypes. This integrative approach has been successfully used in dissecting causal relationships in complex human diseases such as diabetes and obesity, cardiovascular disease, neurodegenerative diseases, and multiple types of cancers including breast cancer, hepatocellular carcinoma, prostate cancers (2). We showed that integration of diverse types of data with gene expression data can improve network accuracy with the directed network representing biologically meaningful causal relationships as opposed to sheer statistical relationships. We also showed that activities of functional units (3) (such as subnetworks) are more robust in predicting disease progression (4) or more important in understanding multiple genes and pathways interactions regulating progression of complex diseases.

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