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Reconstructing integrative molecular bayesian networks from metabolomics and other omics data

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Abstract

GWAS have identified thousands of candidate variations for human diseases. However, distinguishing causal variations from a plethora of candidates is a big challenge. Even though meta-analyses of GWAS identified high confident candidates, it is still not clear what are mechanisms of these variations contribute to human diseases. To achieve comprehensive understanding of these candidate variations, we need a complete biological context within which to interpret potential functions of these variations. We developed RIMBANet, a general Bayesian network framework to integrate diverse types of data such as DNA variation and RNA expression data. Cells employ multiple levels of regulation, including transcriptional and translational regulation, that drive core biological processes and enable cells to respond to genetic and environmental changes. Metabolites represent the direct output of protein-mediated cellular processes, endogenous metabolite concentrations can closely reflect cellular physiological states, especially when integrated with other molecular-profiling data. We extended the framework to integrate more data types: endogenous metabolite concentration, miRNA expression variation, DNA mutations and DNA copy number variations, DNA-protein binding, protein-metabolite interaction, protein-protein interaction data, and more, to construct probabilistic causal networks that elucidate the complexity of cell regulation. The goals of our integrative analysis are not only to find causal regulators, but to uncover mechanisms by which these predicted causal regulators affect genes and metabolites whose transcriptional profiles, proteomic profiles or metabolite profiles are linked to phenotype differences. We applied the integrative approach to human GWAS results and other human data to elucidate mechanisms of metabolic diseases and cancers.

Biography

Jun Zhu (www.mssm.edu/profiles/jun-zhu) is a professor in Genetics and Genomic Sciences, Icahn School of Medicine at Mount Sinai. He obtained his bachelor degree in Electronic Engineering in Tsinghua University in China, Master degree in Computer Sciences and Ph.D in Biomedical Sciences from State University of New York at Albany. He has working experiences in both biotech companies (Amgen and Merck Co.) and academic institutes. He has pioneered constructing integrative causal network in Bayesian network framework, which resulted multiple publications in high profile journals such as Nature, Nature Genetics, and Genome Research.