

Why Networks Matter: Embracing Biological Complexity

John Quackenbush

Harvard TH Chan School of Public Health, Channing Division of Network Medicine of Brigham and Women's Hospital, and Dana-Farber Cancer Institute

One of the central tenets of biology is that our genetics—our genotype—influences the physical characteristics we manifest—our phenotype. But with more than 25,000 human genes and more than 6,000,000 common genetic variants mapped in our genome, finding associations between our genotype and phenotype is an ongoing challenge. Indeed, genome-wide association studies have found thousands of small effect size genetic variants that are associated with phenotypic traits and disease. The simplest explanation is that genes and genetic variants work together in complex regulatory networks that help define phenotypes and mediate phenotypic transitions. We have found that the networks, and their structure, provide unique insight into how genetic elements interact with each other and the structure of the network has predictive power for identifying critical processes in health and disease and for identifying potential therapeutic targets. I will touch on multiple examples illustrating the importance of network models, drawing on my work in cancer, in chronic obstructive pulmonary disease, and in the analysis of data from thirty-eight tissues provided by the Genotype-Tissue Expression (GTEx) project. We will use these to explore the development and progression of disease and new ways to identify therapeutics.