

Using Interactome Networks to Unravel Cellular and Systems Complexity in Human Disease

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Complex cellular systems formed by interactions among genes and gene products (*i.e.* interactome networks) appear to underlie most cellular functions. In the last decade, basic concepts of network biology have been described, emphasizing why cellular networks are important to consider in biology. Importantly, it is becoming increasingly clear that more high quality empirically derived datasets are needed to better describe biological networks and genotype to phenotype relationships. With the explosive growth of sequence information and identification of genetic alterations associated with diseases, a full understanding of genotype-phenotype relationships will require mechanistic descriptions of how interactome networks are perturbed as a result of inherited or somatic disease susceptibilities. To generate the information necessary to eventually address how complex cellular networks relate to biology, we have developed, at the scale of the whole proteome, an integrated approach for modeling protein-protein interaction or “interactome” networks. Our main questions are: How are interactome networks organized at the scale of the whole cell? How can we uncover features underlying this organization? How are interactome networks modified in human diseases such as cancer. And how can we use interactome networks to guide the development of new therapeutic agents?