ONTOLOGY-DRIVEN AND NETWORK–ENABLED SYSTEMS BIOLOGY CASE STUDIES

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Abstract:

ABSTRACT Zhong Yan ONTOLOGY-DRIVEN AND NTEWORK–ENABLE SYSTEMS BIOLOGY CASE STUDIES With the progress in high-throughput technologies and bioinformatics in recent years, it is possible to determine to what extent genetic or environmental manipulation of a biological system affects the expression of thousands of genes and proteins. This study requires a shift from the conventional pure hypothesis-driven approach to an integrated approach--systems biology method. Systems biology studies the relationships and interactions between various parts of a biological system. It allows individual genes or proteins to be placed in a global context of cellular functions. This analysis can answer the question of how networks of genes/proteins, differentially regulated respond to genetic or environmental modification, are placed in the global context of the protein interaction map. In this project, we establish a protein interaction network-based systems biology approach, and use the method for two case studies. In particular, our systems biology studies consist of the following parts: (1) Analysis of mass-spectrometry derived proteomics experimental data to identify differentially expressed proteins in different genetic or environmental conditions; (2) Integration of genomics and proteomics data with experimental results, the molecular context of protein-protein interaction networks and gene functional categories; (3) Visual interpretation of molecular networks. Our approach has been validated in two case studies by comparing our discoveries with existing findings. We also obtained new insights. In the first case study, the proteomes of cisplatin-sensitive and cisplatin-resistant ovarian cancer cells were compared and we observed that cellular physiological process is significantly activated in cisplatin-resistant cell lines, and this response arises from endogenous, abiotic, and stress-related signals. We found that cisplatin-resistant cell lines demonstrated unusually high level of protein-binding activities, and a broad spectrum of across-the-board drug-binding and nucleotide-binding mechanisms are all activated. In

the second case study, we found that the significantly enriched GO categories included genes that are related to Grr1 perturbation induced morphological phenotype change are highly connected in the GO sub-network, which implies that Grr1 could be affecting this process by affecting a small core group of proteins. These biological discoveries support the significance of developing a common framework of evaluating functional genomics and proteomics data, using networks and systems approaches.

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