BIOSTATISTICS SEMINAR

BIOMARKERS AS NETWORKS, NOT INDIVIDUAL LOCI

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ABSTRACT

Much of bioinformatics and genomics is now focused on methods to assemble measurements into models of networks and pathways within the cell. These pathway maps will provide essential information as doctors struggle to interpret the flood of genetic and clinical data that can now be collected for a patient. We are working in several areas that we believe will be critical for assembling network models and for using them in a clinical setting:

1. Mapping the genetic network underlying the response to DNA damage. Failure of cells to respond to DNA damage is a primary step in the onset of cancer and is a key mechanism of environmental toxicity. We will describe our ongoing efforts to apply ChIP-sequencing and synthetic-lethal screens to map how the cell's transcriptional network is remodeled by DNA-damaging conditions.

2. Network-based biomarkers for disease diagnosis and personalized medicine. Genetic biomarkers are typically thought of as individual genes and proteins. However, we have shown that networks can also serve as powerful biomarkers and in many cases are more predictive than any individual gene. This “network-based” biomarker approach has shown improved accuracy in diagnosis of breast and lung cancer as well as NF-kB activation state.

3. Protein network comparative genomics. We are developing a library of standard approaches for comparing protein interaction networks across species, conditions, and network types. We are working with Dr. Sumit Chanda at the Burnham Institute to identify protein networks essential for HIV infection and how these differ from RNA and DNA viruses.

For professional distribution of our network-based technologies, we are developers of the Cytoscape platform, an Open-Source software environment for visualization and analysis of biological networks and models (http://www.cytoscape.org/).

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