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System-Based Proteomic Analysis of the Interferon Response in Human Liver Cell

Hookeun Lee, Wei Yan, Eugene C. Yi, Xiao-Jun Li, Andrew Keller, Jimmy Eng, Paul Shannon, David Reiss, Tim Galitski, Michael G. Katze* and Ruedi Aebersold
Institute for Systems Biology, Seattle, WA 98103, USA.
*Department of Microbiology and Washington National Primate Research Center,
University of Washington, Seattle, WA 98195, USA.

With the completion of the genome sequencing of a number of species, major focus of biological researches is currently on how the information in these sequences might be interpreted in terms of structure, function, and control of biologic systems and processes. Quantitative proteome analysis, the global analysis of protein expression, is increasingly being used as a method to study perturbation-induced changes in protein profiles. Here, we present a global quantitative proteomic analysis of human hepatoma cells (Huh7) in the presence and absence of interferon-alpha (IFN) treatment using the isotope coded affinity tag (ICAT) method and tandem mass spectrometry (MS/MS) to examine liver specific responses to IFN playing a critical role in host anti-viral defense and being an essential component of current therapies against Hepatitis C Virus (HCV), a major cause of liver disease worldwide. In three sub-cellular fractions we identified a total of more than 1364 proteins with pH 0.4, corresponding to a 95% confidence level. Among these, 54 were induced by IFN and 24 were repressed by more than 2-fold, respectively. These IFN regulated proteins were associated with the functions they performed including antiviral defense, immune response, cell metabolism, signal transduction, cell growth, and cellular organization. To analyze this proteomics dataset, we utilized several system biology data mining tools, including Gene Ontology via the GoMiner program and the Cytoscape bioinformatics platform. Integration of the quantitative proteomics with global protein interaction data using the Cytoscape platform led to the identification of several novel and liver-specific key regulatory components of the IFN response which may be important in regulating the interplay between HCV, interferon, and the host response to virus infection.

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Systems Biology at KRIBB: From Atoms to Cells

YOON, Tae-Sung
Systemic Proteomics Research Center, Korea Research Institute of Bioscience & Biotechnology.

Understanding complexity inherent in biological systems at the atomic details will lead to practical innovations in medicine, drug discovery and bioengineering. X-ray crystallography has been the tool to provide the atomic structure of proteins and continued to play its role in structural genomics. Systems biology can be regarded as a metaphor for in silico biology to render the cellular and physiological meaning to atomic components and to allow the control over biological process at the systems level. Capitalizing on our strength in X-ray crystallography, we aim to carry out a targeted structural genomics program, and to develop and operate high-throughput synchrotron X-ray beam lines and associated facilities. Rendering the cellular context to our structural genomics effort, we have implemented a protein profiling method based on 2D-Differential Gel Electrophoresis (DIGE) and MALDI-TOF/tandem mass spectrometry. Unlike mRNA profiling method limited in profiling over time, our protein profiling effort is unique to provide the profiling over time and sub-cellular spaces (cytosol, mitochondria, and nucleus) simultaneously to reveal post-translational modifications as well as translocations implicated in important biological processes such as programmed cell death. Spatiotemporal protein profiling experience and *in silico* model building opportunity will be discussed.