S7-01

Preparation of Human Protein Tyrosine Phosphatase (PTP) Array: A Novel Screening Tool for Selective PTP Inhibitors

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Protein tyrosine kinase (PTK) and protein tyrosine phosphatase (PTP) catalyze phosphorylation and dephosphorylation on tyrosine in the cellular proteins. In human, 90 PTKs and 107 PTPs have been identified, but the majority of their biological functions remain unclear. PTPs have been recently implicated in many human diseases such as cancer, diabetes, inflammation, and obesity, leading them to be of medicinal interest. Selective PTP inhibitors are of great interest not only for therapeutic agents but also for chemical tools to study PTP themselves. To search chemical library for selective PTP inhibitors, we have developed a high-throughput screening system (HTS). The HTS utilizes PTP array with a fluorophobic chemical probe as a reference ligand, allowing library-to-library screening. We have therefore cloned about 90 human PTPs and successfully expressed more than 60 clones in bacterial overexpression systems. The purified proteins will be printed on a glass plate to afford human PTP arrays. The inhibitory activity of tested compounds will be measured by a competitive binding to each PTP in the array with the reference ligand.

S7-02

LC-MS/MS Proteomics in Drug Target Identification and Validation

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Proteomics has become a major tool in pursuing drug discovery and development in the pharmaceutical industry. In order to be successful in proteomic drug discovery projects, careful sample preparation, robust mass spectrometry platforms, and bioinformatics tools to improve the proteomics workflow and efficiency of target/biomarker candidate selection are all important. The Aventis US proteomics has established robust high-throughput LC-MS/MS platforms to be applied to all proteomics drug discovery projects including target identification, pathway elucidation, and biomarker discovery. Using these systems, unique and differentially expressed proteins separated by 1D- or 2D-gel separation and membrane proteins in protein complex samples can be accurately identified with a reasonable throughput. In this presentation, our approaches for proteomic target identification and pathway elucidation and some lessons from the two different project areas will be discussed.