

INVITED LECTURE H18

Integrative analysis of the liver proteome as a strategy for liver disease biomarker discovery

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We are using a combination of methodologies applied to human and mouse liver and plasma samples, obtained from healthy controls or associated with liver fibrosis or cancer. The proteomic methodologies include:

- comprehensive characterization of the liver proteome by separating intact proteins by 2D-HPLC followed by SDS-PAGE. Approximately 200 fractions are generated and analyzed by LC MS/MS. This approach was applied to the HUPO Liver Proteome Project reference sample. We identified 8149 non-redundant proteins and 472 protein groups, each identified with 3 or more peptides and with a ProteinProphet probability ≥ 0.9 (error rate $\sim 1\%$). Transcriptomic analysis of the same sample identified 10082 expressed genes. Comparison between the transcriptomic and the proteomic data sets will be presented.
- comprehensive characterization of the plasma proteome. We are using a combination of immunodepletion of abundant proteins and 3-D protein separation as described above. Depletion of highly abundant proteins results in loss of important proteins. We have identified as many as 141 proteins and protein fragments bound to immunodepleted abundant proteins.
- selective isolation of peptides that are N-glycosylated in the intact protein. We have characterized 356 glycopeptides so far.

Integration of this collection of data sets identified proteins for which expression and/or post-translational modifications are associated with liver diseases.