

DETECTION OF NOVEL BIOMARKERS OF LIVER CIRRHOSIS BY HIGH PERFORMANCE PROTEOMICS

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Since more than 10 years, the word PROTEOME catches the attention of more and more researchers in the life science field. At about the same time the term high throughput proteome analysis came up with the intention to analyse all proteins in a complex protein mixture in parallel. Thus, a huge amount of data can be produced from a single sample and the following analysis and validation becomes the time limiting step. However, the limited number of available biomarkers for diagnosis, status of the disease, therapy control and prediction of the course of the disease demands for new efforts in finding new ones. Especially, proteomics raises high expectations in finding new and reliable biomarker for human diseases.

Hepatic cirrhosis is a life-threatening disease arising from different chronic liver disorders. Major causes for hepatic cirrhosis are chronic hepatitis B&C infection or abuse of alcohol. Chronic hepatitis C causes at least ~20% developing liver cirrhosis within 40 years. To date only liver biopsy allows a reliable evaluation of the course of hepatitis C by grading inflammation and staging fibrosis, and thus serum biomarkers for hepatic fibrosis with high sensitivity and specificity are needed.

In order to identify new candidate biomarkers for hepatic fibrosis, we performed a proteomic approach of microdissected cirrhotic septa and liver parenchyma cells. In cirrhotic septa we detected an increasing expression of cell structure associated proteins including actin, tropomyosin, calponin, transgelin and human microfibril associated glycoprotein 4 (MFAP-4). The expression of tropomyosin, transgelin and MFAP-4, an extracellular matrix associated protein, were further evaluated by immunohistochemistry. Tropomyosin and microfibril associated glycoprotein 4 demonstrated high serum levels in patients with hepatic cirrhosis of different etiologies. A quantitative analysis of MFAP-4 serum levels in a large number of patients (n=130) revealed MFAP-4 as novel candidate biomarker with high diagnostic accuracy for prediction of non-diseased liver vs cirrhosis as well as stage 0 vs stage 4 fibrosis.

Thus, **high performance proteomics** is the basic principle for reliable results which allows us to discover new biomarker candidates for liver cirrhosis using minute amounts of patients' material. How to reach this goal will be presented in the lecture.

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