Titel des Beitrags: From proteomic multimarker profiling to interesting proteins: thymosin-α(4) and kininogen-1 as new potential biomarkers for inflammatory hepatic lesions.

Abstract: Despite tremendous efforts in disclosing the pathophysiological and epidemiological factors associated with liver fibrogenesis, non-invasive diagnostic measures to estimate the clinical outcome and progression of liver fibrogenesis are presently limited. Therefore, there is a mandatory need for methodologies allowing the reasonable and reliable assessment of the severity and/or progression of hepatic fibrogenesis. We here performed proteomic serum profiling by matrix-assisted laser desorption ionization time-of-flight mass spectrometry in 179 samples of patients chronically infected with hepatitis C virus and 195 control sera. Multidimensional analysis of spectra allowed the definition of algorithms capable to distinguish class-specific protein expression profiles in serum samples. Overall about 100 peaks could be detected per single spectrum. Different algorithms including protein peaks in the range of 2000 and 10,000 Da were generated after pre-fractionation on a weak cation exchange surface. A specificity of 93% with a sensitivity of 86% as mean of the test set results was found, respectively. The nature of three of these protein peaks that belonged to kininogen-1 and thymosin-α(4) was further analysed by tandem mass spectrometry (MS)/MS. We further found that kininogen-1
mRNA was significantly down-regulated in cirrhotic livers. We have identified kininogen-1 and thymosin-?-4 as potential new biomarkers for human chronic hepatitis C and conclude that serum profiling is a reliable technique to identify hepatitis-associated expression patterns. Based on the high throughput capability, the identified differential protein panel may serve as a diagnostic marker and warrants further validation in larger cohorts.