Abstract of Presentation

Note: This paper should be typed in "Times New Roman" of 12pt.

Presentation Title(Should be no more than 20 words):

Clinical Proteomics in Hepatobiliary Diseases -From Bench to Practice-

Abstract :

There is growing interest in proteomic studies allowing for identification of disease related proteins in a variety of clinical fields. We have conducted comprehensive proteome analyses using gel-based and gel-free methods to discover and identify novel diagnostic markers for hepatobiliary diseases.

Hepatocellular carcinoma (HCC), the most common form of primary hepatic malignancy, is a common cancer in many countries and is the fourth leading cause of cancer death in Japan. Early diagnosis of HCC is mainly done by means of imaging modalities, Pathological diagnosis is considered in equivocal cases. However, the distinction between benign and malignant tumors is not easy and novel immunohistochemical markers are necessary. Using agarose two-dimensional fluorescence difference gel electrophoresis, we analyzed surgically resected HCC tissues. The fluorescence volumes of more than 100 protein spots were significantly different between tumor and non-tumor tissues. Among them, increased expression of clathrin heavy chain (CHC) and decrease of formiminotransferase cyclodeaminase (FTCD) were noteworthy and these changes were confirmed by immunoblotting and immunohistochemistry. It was shown that CHC and FTCD were useful to distinguish early HCC from benign tumors such as regenerative nodule or focal nodular hyperplasia Immunostaining of CHC and FTCD could make substantial contributions to the early diagnosis of HCC in which definite diagnosis can not be made with imaging studies alone.

Excessive consumption of alcohol leads to a variety of organ injuries including the liver and the pancreas. Since personal and verbal reporting of alcohol use is not necessarily accurate, objective markers to assess alcohol consumption are required. The currently available markers, however, are limited in terms of sensitivity and specificity for screening excessive alcohol drinkers.

Therefore, we used the SELDI-TOF MS and MALDI-TOF MS technologies to generate comparative protein profiles of the consecutive serum samples obtained during abstinence from a total of 16 chronic alcoholic patients hospitalized for a rehabilitation program. Among a number of proteins or peptides altered during abstinence, we focused on a 5.9 kD peak, that had been downregulated on admission and the expression of which remarkably increased after abstinence. It was noteworthy that these changes were also seen in nonresponders of gamma-glutamyltransferase.(GGT).

Detecting proteins and peptides that are present at quite low levels in human serum (so-called deep proteome), as potential disease biomarkers, is complicated by a few highly abundant proteins. One promising strategy is the removal of these abundant proteins interfering with the analysis of the deep proteome. On the other hand, albumin and other abundant proteins bind a number of low-molecular-weight molecules, including proteins and peptides. Appropriate procedures that can selectively analyze those low-molecular weight peptides remain to be established. Furthermore, the majority of serum proteins are more or less glycated. Glycomic characterization of serum proteins will also be required for comprehensive search for novel biomarkers..