Bilateral Scientific & Technological Cooperation Belgium–China: Biomarker of Liver Fibrosis and Liver Cancer: From Molecular Biology to Clinical Perspectives

[1-1] Non-invasive (serum) markers in the diagnosis of liver fibrosis

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The stellate cell is the key regulator cell in the development of liver fibrosis and cirrhosis. After an injury (which can be viral, toxic, auto-immune or metabolic), the stellate cell gets activated and produces an increase in the extracellular matrix in the liver; this can lead to fibrosis and cirrhosis. Patients with severe liver fibrosis and/or end stage liver cirrhosis can suffer from jaundice, bleeding from oesophageal varices, development of ascites and hepatic encephalopathy and carry a risk to develop a hepatocellular carcinoma. Liver transplantation is at this moment the only ‘curative’ option. If a liver transplantation is not possible, these fibrosis related complications often lead to the death of the patient. Although the diagnosis of liver fibrosis is made by an invasive liver biopsy, this ‘golden standard’ carries a substantial number of complications and inter- and/or intra agreement correlations are not optimal. Recently the interest for non-invasive (serum) markers for liver fibrosis have been studied. The features of an ideal marker for liver fibrosis are:

- Liver specific
- Levels not influenced by alterations in liver, renal or reticuloendothelial function
- Measurement of one of more of the following processes
  - Stage of fibrosis
  - Activity of matrix deposition
  - Activity of matrix removal
- Easy to perform

Actually there are direct and indirect markers of liver fibrosis. A direct marker is a marker of matrix turnover with relationship to ECM deposition and removal. Indirect markers use ‘standard’ laboratory test which have not necessary direct correlation to matrix turnover. However these actual markers (direct and indirect), although promising, lack performance in earlier stages of fibrosis. They also need validation by independent groups. Liver stiffness measurement by elastography is an alternative promising non-invasive technique to distinguish mild from severe fibrosis.

[1-2] Insight into new markers and diagnostic models on hepatocellular carcinoma

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The incidence of hepatocellular carcinoma (HCC) is increasing worldwide. The overall survival of patients with HCC is grim because most patients are diagnosed late, when curative treatment is not possible. So early diagnosis of hepatocellular carcinoma (HCC) is still a great challenge for clinical practice. Image techniques as well as pathological examination are expensive or invasive and operator dependent. Obviously, serum markers of HCC are desperately required so as to make early diagnosis and patient’s follow up practical. The ideal biomarkers should be sensitive, specific, noninvasive, reproducible, inexpensive and acceptable to patients. Up to now, the so called tumor markers like AFP, liver enzymes, cytokines as well as some special glycoproteins, though helpful, are not sensitive and specific enough for HCC early diagnosis.

On the other hand, the knowledge on independent predictors of HCC is increasing. These predictors include virus infection, BMI (body mass index), diabetes, low platelet count or some special genotypes of predisposing genes. The establishment of several interesting predictive diagnostic models on liver fibrosis/cirrhosis suggests that mathematical predictive model, based on large sample size and follow up study, might be of higher sensitivity, specificity and feasibility in clinical application. According to our preliminary research, here we suggest to pay attention to the establishment and application of this kind of multiparameter diagnostic models clinically, so as to improve the early diagnosis of HCC in a more economical and feasible way.

In summary, although many studies of newer tumor markers as well as independent predictors have been published, the existing comments on these markers have many limitations. These newer markers, including GPC-3, GP73, AFP-L3, as well as our suggested putative multiparameters diagnostic models should be evaluated further in properly designed collaborative longitudinal studies.

[1-3] The Ras inhibitor farnesylthiosalicyclic acid (FTS) prevents nodule formation and development of preneoplastic foci of altered hepatocytes in rats

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Background and Aims: Aberrant activation of oncopgenes, such as Ras, likely contributes to the development of hepatocarcinoma (HCC) making Ras a target for cancer therapy. We evaluated in vivo the effect of intraperitoneal injection of the Ras inhibitor S-trans, transfarnesylthiosalicyclic acid (FTS) on Ras activation and the development of preneoplastic liver lesions in rats repeatedly injected with diethylnitrosamine (DEN).

Methods and Results: FTS prevents the development of macroscopic liver nodules and reduces liver expression and overall surface of the tumour marker GSTp as assessed by Western blotting and immunohistochemistry. FTS abrogates