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Pancreatic and Hepatic Fibrosis: Remarkable Similarities

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Quantification of liver fibrosis by non invasive means is a major challenge that has stimulated the search for new approaches. The prognosis and clinical management of chronic liver diseases are highly dependent on the extent of liver fibro¬sis, as complications mainly occur in patients in the advanced stages. This is particularly true in patients with chronic hepatitis C (HCV). Liver biopsy with METAVIR analysis is the gold standard for assessing liver fibrosis associated with HCV [1-3]. It is an invasive and expensive procedure that is not well accepted by many patients especially when repeated exam¬inations are needed. Moreover, its accuracy in assessing fibrosis is questionable, as reproducibility is poor due to sampling errors, and even in adequately sized spec¬imens, intra-observer and inter-observer discrepancies are seen [4-7]. Our research shows that a special type of blood test which we have developed, the 'Fibrogenic Stimulation Index' (FSI), can identify patients with liver fibrosis. The FSI assesses the stimulation of proliferation of fibroblasts and hepatic stellate cells (HSCs), the key cell involved in hepatic fibrosis, in response to patients' sera samples. The FSI is a cell based assay of fibrosis that assesses the ability of patients' sera samples to stimulate proliferation of selected target cells. The type of fibrosis to be assessed is matched with a specific target cell. The FSI is a noninvasive test which uses patients' sera samples in an *in vitro* assay which can detect and quantify the degree of fibrosis based on a patient's blood sample. Our data suggests that FSI correlates with procollagen type III peptide (P-III-P) another measure of hepatic fibrosis and that both the FSI and P-III-P correlate with METAVIR fibrosis score. Further study in the larger cohort of HCV patients indicates that FSI is a positive predictor of fibrosis in HCV patients. We were the first to reported on the role for platelet derived growth factor (PDGF) in experimental models of hepatic fibrosis [8,9] and we showed that PTX blocked fibrosis via an effect on PDGF and that this occurred by blocking phosphorylation of c-jun on serine 73 [10]. We began investigations of non alcoholic steatohepatitis (NASH) mediated fibrosis [11,12] and reported that ribavirin but not interferon inhibited fibrosis also associated with HCV and that this effect was mediated by the block of phosphorylation of c-jun on ser 73 and resulted in decreased synthesis of collagen and hepatic stellate cell (HSC) proliferation [13]. We reported that PTX decreased NASH sera-stimulated FSI (our patented diagnostic test for fibrosis using HSCs as the target cell) and c-Jun phosphorylation as assessed by ^{3}H-thymidine incorporation and Western analysis respectively, such that NASH patient sera stimulated HSC proliferation and increased phosphorylated c-Jun in HSCs and that PTX significantly decreased NASH patient sera stimulated HSC proliferation and decreased NASH sera-stimulated phosphorylated c-Jun in HSCs [14]. Our recent published [15] and unpublished data indicate that PTX decreased the FSI; that the FSI correlates well with the METAVIR fibrosis score in HCV patients and may be predictive of fibrosis in this cohort; this intellectual property is patented [16]. Pancreatic fibrosis shows remarkable though not surprising similarities to hepatic fibrosis. From the Binkley and colleagues early studies on molecular basis of pancreatic fibrosis [17] to the more recent studies of Krantz and colleagues on the molecular understanding of the role of TGFβ in this disorder [18]; the diseases run in parallel. It would be exciting to work more closely with those who are making such great advances in the area of pancreatic fibrosis and facilitate the development of novel therapeutics that could potentially cure both.

References

1. Poynard T, Yuen MF, Ratziu v, Lung Lai C (2009) Viral hepatitis C. Lancer 362: 2095-2100.
2. Bonny C, Rayssiguier R, Ughetto S, Aublet-Cuvelier B, Baranger J, et al. (2003) Medical practices and expecrations of general practitio¬ners in relation to hepatitis C virus infection in the Auvergne region. Gastroenterol Clin Biol 27: 1021-1025.
3. Bedossa P, Dargere D, Paradis V (2003) Sampling variability of liver fibrosis in chronic hepatitis C. Hepatology 38: 1449-1457.
4. Maharaj B, Maharaj RJ, Leary WP, Cooppan RM, Naran AD, et al. (1986) Sampling variability and the influence on the diagnostic yield of percutaneous needle biopsy of the liver. Lancet 1: 523-525.
5. Regev A, Berho M, Jeffers LJ, Milikowski C, Molina EG, et al. (2002) Sampling error and incraobserver variation in liver biopsy in patients with chronic HCV infection. Am J Gastroenterol 97: 2614-2618.
6. Soloway RD, Baggenstoss AH, Schoen field LJ, Summerskill WH(1971) Observer error and sampling variability tested in evaluation of hepatitis and cirrhosis by liver biopsy. Am J Dig Dis 16: 1082-1086.
7. Abdi W, Millan JC, Mezey E(1979) Sampling variability on percutaneous liver biopsy. Arch Intern Med 139: 667-669.
8. Peterson TC, Isbrucker RA (1992) Fibroproliferation in liver disease, role of monocyte factors. Hepatology 15: 191-197
9. Peterson TC (1993) Pentoxifylline Prevents Fibrosis in an Animal Model and Inhibits Platelet Derived Growth Factor Driven Proliferation of Fibroblasts. Hepatology 17: 486-493.
10. Peterson TC, Peterson MR, Robertson HA, During M, Dragunow M (2002) Selective down regulation of c-jun expression by pentoxifylline and c-jun antisense interrupts PDGF signalling: pentoxifylline inhibits phosphorylation of c-jun on serine 73. Mol Pharmacol 61:1476-1488.
11. Le TH, Caldwell SH, Redick JA, Sheppard BL, Davis CA, et al. (2004) The Zonal Distribution of Megamitochondria with Crystalline Inclusions in Early and Advanced NASH. Hepatology 39: 1423-1429.
12. Caldwell SH, Osaim A, Chang C, Davis C, Hespenheide E, et al. (2005) Nanalcoholic Fatty Liver (NAFL): Overview. In NASH and Nutritional Therapy. pp 1-43. Editor K.Okita, Springer-Verlag, New York.
13. Verma-Gandhu M, Peterson MR, Peterson TC (2007) Effect of fetuin, a TGF β antagonist and pentoxifylline, a cytokine antagonist on hepatic stellate cell function and fibrotic parameters in fibrosis. Eur J Pharmacol 572: 220-227.
14. Khan F, Peltekian KM, Peterson TC (2008) Effect of interferon, ribavirin, pentoxifylline and IL- 18 antibody on hepatitis C sera-stimulated hepatic stellate cell proliferation. J Interferon Cytokine Res 28: 643-651.

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15. Peterson TC, Khan F, Caldwell S, Peltekian KW, Utility of the Fibrogenic Stimulation Index (FSI) in Documenting Fibrosis in Non-Alcoholic Steatohepatitis (NASH). Clin Exp Med J 2009 1st Fatty Liver Congress, abst.

16. Peterson TC (1999) Uses for pentoxifylline and functional derivatives/ metabolites thereof. United States Patent # 5,985,592. Issued November 16.

17. Binkley CE, Zhang L, Greenson JK, Giordano TJ, Kuick R (2004) The Molecular basis of pancreatic fibrosis; Common Stromal Gene Expression in Chronic Pancreatitis and Pancreatic Adenocarcinoma Pancreas 29: 254–263.

18. Krantz SB, Shields MA, Dangi-Garimella S, Cheon EC, Barron MR (2011) MT1-MMP Cooperates with KrasG12D to Promote Pancreatic Fibrosis through Increased TGF-β Signaling. Mol Cancer Res 9: 1294-1304.