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Discovery and quantitation of novel liver fibrosis biomarkers in hepatitis C patients

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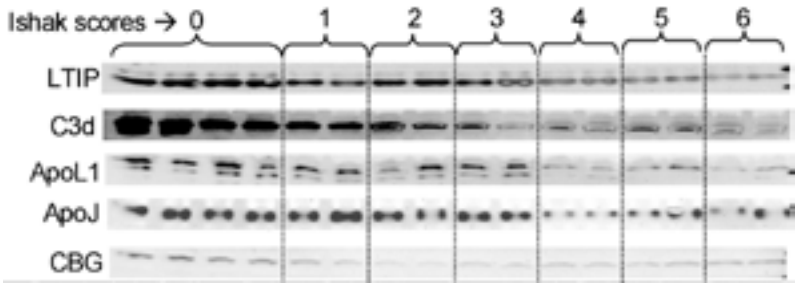
Background: Liver biopsy is the reference standard for assessing liver fibrosis and no reliable serum biomarkers are available to discriminate between the intermediate stages of fibrosis. We used proteomics to identify novel fibrosis biomarkers in hepatitis C patients with different degrees of liver fibrosis.

Methods: Novel liver fibrosis biomarkers were identified by analysing proteins in plasma/serum samples from controls and hepatitis C patients with varying stages of liver fibrosis using a proteomics technique: two dimensional gel electrophoresis (2DE). Identified markers were validated across all Ishak fibrosis stages and compared to the markers used in FibroTest, Enhanced Liver Fibrosis (ELF) test, Hepascore and FIBROSpect by Western blotting. For the most promising biomarkers, an antibody-free assay (parallel reaction monitoring using mass spectrometry) was used which detects tryptic peptides of the biomarkers and their fragments.

Results: Forty four candidate biomarkers for hepatic fibrosis were identified of which 20 were novel biomarkers of liver fibrosis. Western blot validation of all candidate markers using plasma samples from patients across all Ishak fibrosis scores showed that the markers which changed with increasing fibrosis most consistently included lipid transfer inhibitor protein, complement C3d, corticosteroid-binding globulin, apolipoprotein J and apolipoprotein L1. These five novel fibrosis markers which are secreted in blood showed a promising consistent change with increasing fibrosis stage when compared to the markers used for the FibroTest, ELF test, Hepascore and FIBROSpect.



Western blot data for novel HCV fibrosis biomarkers

Conclusion: This study identifies 20 novel fibrosis biomarker candidates. The proteins identified may help to assess hepatic fibrosis and eliminate the need for invasive liver biopsies.

Biography

Bevin Gangadharan is a research associate in the Oxford Antiviral Drug Discovery Unit, University of Oxford headed by Prof. Nicole Zitzmann (http://zitzmannlab.com/). The main focus of his current research is to use proteomics to identify and validate novel serum biomarker candidates for NAFLD. He carried out his DPhil with Prof. Nicole Zitzmann where he identified serum biomarker candidates for liver fibrosis in hepatitis C patients.

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