Bevin Gangadharan et al., J Mol Biomark Diagn 2014, 5:2
http://dx.doi.org/10.4172/2155-9929.S1.022

OMICS Group Conferences
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5th International Conference on
Biomarkers & Clinical Research
April 15-17, 2014 St. Hilda's College - University of Oxford, UK

Discovery of novel biomarker candidates for liver fibrosis in hepatitis C patients using proteomics

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Liver biopsy is the reference standard for assessing liver fibrosis and no reliable non-invasive diagnostic approach is available to discriminate between the intermediate stages of fibrosis. Therefore suitable serological biomarkers of liver fibrosis are urgently needed. We used proteomics to identify novel fibrosis biomarkers in hepatitis C patients with different degrees of liver fibrosis. Proteins in plasma samples from healthy control individuals and patients with hepatitis C virus (HCV) induced cirrhosis was analysed using a proteomics technique: two dimensional gel electrophoresis (2-DE). This technique separated the proteins in plasma samples of control and cirrhotic patients and by visualizing the separated proteins we were able to identify proteins which were increasing or decreasing in hepatic cirrhosis. 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. 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. These markers are currently being further validated using a large clinical cohort. 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 obtained his D.Phil under the supervision of Prof. Nicole Zitzmann at the University of Oxford where he carried out the first ever gel-based proteomics study to discover novel biomarkers for liver fibrosis. He has more than a decade of experience in proteomics and biomarker discovery and first started in this field in 2000 at Smithkline Beecham looking at depletion of albumin in plasma, an important approach in biomarker discovery. He has published in several peer-reviewed journals and has two patents on novel biomarkers for liver fibrosis. He is on the editorial board for Biomarker Research and gives proteomics lectures to students in the Department of Biochemistry at the University of Oxford.

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