Lipidomic signature associated with alcoholic hepatitis: characterization of ether-linked glycerophospholipids

C Alonso1, J Micheletta1, A Cano1, J Altamirano1, I Martinez-Arranz1, D Balgoma2, R Batalier2, JM Mato1, J Caballeria1

1. CIC bioGUNE, Ciencia y Tecnología de Bizkaia, Spain. 2. Liver Unit, Hospital Clinic, CIBERehd, IDIBAPS, Barcelona, Spain. 3. Department of Medicine and Nutrition, University of North Carolina, Chapel Hill, NC, USA. 4. CIC bioGUNE, CIBERehd, Parque Científico y Tecnológico de Bizkaia, Spain.

INTRODUCTION

Alcoholic hepatitis (AH) is a severe form of alcoholic liver disease that is characterised by an acute decompensation of liver function that can occur at any stage of the disease in patients with active alcohol consumption.

Although the presence of AH can be suspected on clinical and biochemical grounds, it is difficult to distinguish AH from decompensated alcoholic cirrhosis (DC), making mandatory a liver biopsy. It is an invasive procedure not exempt from complications and sample errors.

The challenge of a non-invasive diagnosis of AH has been addressed in a metabolomic study. We have used a UPLC-MS based metabolomics platform to determine the sera metabolite profile of AH (n=64) and DC (n=45) patients with proven biopsy. Alterations in ether and vinyl ether-linked glycerophospholipid levels have been uncovered, obtaining a characterised signature for AH diagnosis.

METHODS

**Lipidomics Extraction**

- Lipidomics Platform 1: Methanol extract
- Lipidomics Platform 2: CHCl3 / Methanol extract

**LC-ESI(+)TOF**

**UPLC-MS Analysis**

- LC(ESI) TOF (Acetonitrile / Water)
- LC(ESI) TOF (CHCl3 / Methanol)
- LC(ESI) SQD

**Amino acids Platform**

- Derivatized Methanol extract

AH-ASSOCIATED SERUM LIPIDOMIC SIGNATURE

Metabolic profiles of AH and DC serum samples reveal certain disparities between both diseases. Heatmap representation of the serum metabolic profile comparing AH vs DC patients. Colour scale represents log, transformed ion abundance ratios, while grey lines correspond to significant changes (two-tailed Wilcoxon Rank Sum Test). Metabolites are ordered according to their oxyl chain length and unsaturation degree.

AH-PREDICTIVE MODEL

A logistic regression analysis based on the serum metabolic profiles has been performed to generate a model able to separate patients with AH and DC.

The receiver operating characteristic (ROC) curve has been calculated as averages over the leave-one-out cross validation (1000CV) models. The area under the ROC curve is 0.945 ± 0.01 (AUC ± se).

CONCLUSIONS

The current results show evidence for the alterations of ether-linked glycerophospholipids in serum of alcoholic hepatitis patients, which are decreased related to decompensated cirrhosis.

It has been identified a robust serum metabolic signature that reliably and accurately distinguishes patients with severe alcoholic hepatitis from those with decompensated cirrhosis. These results may have noteworthy clinical implications, resolving the necessity of noninvasive biomarkers in the diagnosis of alcoholic hepatitis.