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A lipidomic analysis for Non-Alcoholic Steatohepatitis (NASH)

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Background: The mechanism underlying the transition from simple steatosis to the more severe form NASH remains unclear thus far.

Aim: To investigate the lipidomic profile alteration during the transition of non-NASH to NASH in human livers, and to identify hepatic lipid biomarkers which can discriminate between NASH and non-NASH liver samples.

Materials & Methods: Two independent sets (n=119 and n=106) of liver tissue samples collected from transplantation donors without heavy alcohol intake and viral hepatitis were characterized for histology. Lipidomic profiling was conducted for both sample sets. Liver tissues were classified as non-NASH or NASH. For lipidomic analyses, we use the first set as a discovery set (n=119) and the other as a validation set (n=106). A multivariate analysis was performed to identify lipids that discriminate NASH and non-NASH samples accurately. Elastic net logistic regression along with 10-fold cross validation was used. Validation was conducted using lipidomics data of 106 liver tissue samples obtained independently from another data set.

Results: We found that 75 phospholipids are significantly different between NASH and non-NASH samples in the discovery set ($p<0.01$), among which 52 (69%) remained significant in the validation set ($p<0.05$). The majority of these lipids are phosphatidylcholines (PCs) and ester phosphatidylcholines (ePCs). 10 lipids ($p<0.01$) were found to discriminate NASH versus non-NASH accurately, with an AUROC (Area under the Receiver Operating Characteristic) curve = 0.89. The same 10-lipid signature produced an AUROC of 0.92 in the validation set, with 3 lipids remained significant ($p<0.05$). By focusing on these 3 lipids that are significantly associated with NASH in both sets, we observed an AUROC of 0.83 and 0.82 in the discovery and validation data set, respectively.

Conclusion: Our study highlighted the important role of phosphatidylcholines in the development of NASH. Further investigation of these lipids among larger biopsy-proven NASH samples as well as in serum samples are warranted.

Biography

Parul Verma is a Graduate Research Assistant at School of Chemical Engineering, Purdue University, USA. She completed her BTech in Chemical Engineering at Indian Institute of Technology in India.

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