NAFLD

Profiling NAFLD—liver gene expression and DNA methylation patterns to characterize disease severity

Altered gene expression and methylation patterns can distinguish patients with advanced NAFLD from those with mild disease, according to new research published in both *Gastroenterology* and *Hepatology*. These profiles have potential as noninvasive biomarkers in population-based screening to detect those at the highest risk of progressive disease, as well as providing vital new clues into disease pathogenesis.

In both studies, patients with NAFLD were split into two groups according to severity of fibrosis upon histological analysis. Individuals were classified as having mild or advanced disease; that is, those at low or high risk of developing clinically significant liver disease, respectively. Then, RNA and DNA was extracted from biopsy samples to facilitate transcriptomic and methylomic analysis.

In the first study, 69,247 CpG sites were found to be differentially methylated in

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patients with advanced ($n = 23$) versus mild ($n = 33$) disease, with the majority being hypomethylated (76% versus 24% hypermethylated). Altered expression and methylation was observed for genes involved in wound healing, fibrogenesis and carcinogenesis. “The methylome–transcriptome analysis is the first of its kind in NAFLD to be done from noncancerous human livers,” highlights author Cynthia Moylan.

In the second study, a microarray was used to analyse gene expression patterns in patients with mild ($n = 40$) or advanced ($n = 32$) NAFLD. The findings were validated in a second, independent cohort ($n = 17$). A 64-gene expression profile could be used to reproducibly distinguish

patients with severe NAFLD from those with mild disease. Furthermore, a 20-gene subset of this gene signature correlated with NAFLD severity, independently of other factors known to influence NAFLD progression. Importantly, analysis revealed increased expression of genes involved in cell adhesion, tissue remodelling and/or regeneration, and Hedgehog target genes.

The authors now plan to use these new findings to “inform both basic, mechanistic studies of fibrosis development in NAFLD as well as clinical outcomes associated with disease.”

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Original articles Murphy, S. K. *et al.* Relationship between the methylome and transcriptome in patients with non-alcoholic fatty liver disease. *Gastroenterology* doi:10.1053/j.gastro.2013.07.047 | Moylan, C. A. *et al.* Hepatic gene expression profiles differentiate pre-symptomatic patients with mild versus severe nonalcoholic fatty liver disease. *Hepatology* doi:10.1002/hep.26661