Transcriptome-based clustering and analysis of NASH patient models reveals cluster-specific signatures and underlying disease mechanisms

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Nonalcoholic steatohepatitis (NASH) is a type of nonalcoholic fatty liver disease (NAFLD) that can progress to cirrhosis, liver failure, and hepatocellular carcinoma. There is currently no FDA-approved pharmacological treatment for NASH, and the standard of care is lifestyle modification, including weight loss, exercise, and dietary changes. NASH is a heterogeneous disease with varying degrees of severity, making it difficult to identify patients who will benefit from treatment and to assess treatment efficacy. Therefore, in order to overcome the difficulty in treatment access due to the heterogeneity of NASH, we conducted a transcriptome analysis of NASH patients and classified the disease model into four clusters based on their transcriptome characteristics. We derived four clusters with disease-specific signatures through the hepatic 164 transcriptome from patients and healthy control, and analyzed the disease mechanism of NASH. Signatures of each cluster show differences in immunity, fibrosis, regulation of transcripton factors, and cell signaling. We validated the efficacy of theses signatures with public data including NASH patients groups and mouse disease models.