Background: Altered DNA methylation events contribute to the pathogenesis and progression of metabolic disorders, including nonalcoholic fatty liver disease (NAFLD) and Nonalcoholic steatohepatitis (NASH).

Method: Liver tissue (N=3) and paired plasmas (N=3) as well as 47 plasma samples were obtained to identify cell-free DNA based non-invasive biomarkers. We used the genome-wide bisulfite-sequencing (WGBS) to analyze genome-wide methylation in patients with NAFLD and NASH. Meanwhile, WGBS data of normal liver tissues (N=4) and liver cancers (HCC, N=1) from Roadmap and DEEP project were collected to be DNA methylation reference.

Result: Liver hyper-methylated signature shown significant decreasing from NAFL (78%, pool A), low level NASH (73%, pool B), severe NASH (65%, pool C) and liver cancer (58%). We observed methylation level to LINE-1 was only slightly decreased for NAFL and NASH tissue samples compared with normal liver tissue (72% vs 73%) which is significantly higher than HCC (32%) indicating NASH and NAFL are still have far away from HCC.

Conclusion: Our study demonstrated the progressively change of the genome-wide DNA methylation from NAFLD, NASH and HCC. Meanwhile, we identified 50 cell-free DNA methylation biomarker for the fibrosis and cirrhosis surveillance.