Mapping the triglyceride distribution in NAFLD human liver by MALDI imaging mass spectrometry reveals molecular differences in micro and macro steatosis

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Abstract

Hepatic lipid accumulation, mainly in the form of triglycerides (TGs), is the hallmark of non-alcoholic fatty liver disease (NAFLD). To date, the spatial distribution of individual lipids in NAFLD-affected livers is not well characterized. This study aims to map the triglyceride distribution in normal human liver samples and livers with NAFLD and cirrhosis with imaging mass spectrometry (MALDI IMS). Specifically, whether individual triglyceride species differing by fatty acid chain length and degree of saturation correlate with the histopathological features of NAFLD as identified with classical H&E. Using a recently reported sodium-doped gold-assisted laser desorption/ionization IMS sample preparation, 20 human liver samples (five normal livers, five samples with simple steatosis, five samples with steatohepatitis, and five samples with cirrhosis) were analyzed at 10-μm lateral resolution. A total of 24 individual lipid species, primarily neutral lipids, were identified (22 TGs and two phospholipids). In samples with a low level of steatosis, TGs accumulated around the pericentral zone. In all samples, TGs with different degrees of side-chain saturation and side-chain length demonstrated differential distribution. Furthermore, hepatocytes containing macro lipid droplets were highly enriched in fully saturated triglycerides. This enrichment was also observed in areas of hepatocyte ballooning in samples with steatohepatitis and cirrhosis. In conclusion, macro lipid droplets in NAFLD are enriched in fully saturated triglycerides, indicating a possible increase in de novo lipogenesis that leads to steatohepatitis and cirrhosis.

Keywords Fatty acid/synthesis; Imaging mass spectrometry; Lipids; Non-alcoholic fatty liver disease; Triglycerides