Chemical imaging on liver steatosis using synchrotron infrared and ToF-SIMS microspectroscopies

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Fatty liver or steatosis is a frequent histopathological change. It is a precursor for steatohepatitis that may progress to cirrhosis and in some cases to hepatocellular carcinoma. In this study we addressed the in situ composition and distribution of biochemical compounds on tissue sections of steatotic liver using both synchrotron FTIR (Fourier transform infrared) and ToF-SIMS (time of flight secondary ion mass spectrometry) microspectroscopies. FTIR is a vibrational spectroscopy that allows investigating the global biochemical composition and ToF-SIMS lead to identify molecular species in particular lipids. Synchrotron FTIR microspectroscopy demonstrated that bands linked to lipid contribution such as -CH3 and -CH2 as well as esters were highly intense in steatotic vesicles. Moreover, a careful analysis of the -CH2 symmetric and anti-symmetric stretching modes revealed a slight downward shift in spectra recorded inside steatotic vesicles when compared to spectra recorded outside, suggesting a different lipid environment inside the steatotic vesicles. ToF-SIMS analysis of such steatotic vesicles disclosed a selective enrichment in cholesterol as well as in diacylglycerol (DAG) species carrying long alkyl chains. Indeed, DAG C36 species were selectively localized inside the steatotic vesicles whereas DAG C30 species were detected mostly outside. Furthermore, FTIR detected a signal corresponding to olefin (C=C, 3000-3060 cm−1) and revealed a selective localization of unsaturated lipids inside the steatotic vesicles. ToF-SIMS analysis definitely demonstrated that DAG species C30, C32, C34 and C36 carrying at least one unsaturated alkyl chain were selectively concentrated into the steatotic vesicles. On the other hand, investigations performed on the non-steatotic part of the fatty livers have revealed important changes when compared to the normal liver. Although the non-steatotic regions of fatty livers exhibited normal histological aspect, IR spectra demonstrated an increase in the lipid content and ToF-SIMS detected small lipid droplets corresponding most likely to the first steps of lipid accretion.

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