

In situ lipidomic analysis of non alcoholic fatty liver by cluster TOF-SIMS imaging

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Mass spectrometry imaging has been used to map liver biopsies of several patients suffering from nonalcoholic fatty liver disease. This steatosis is characterized by an accumulation of triacylglycerols and diacylglycerols in the liver. Using time-of-flight-secondary ion mass spectrometry (TOF-SIMS) with a bismuth cluster ion source, it has been possible to map lipids in situ at the micrometer scale and to simultaneously characterize their molecular distribution on liver sections. Accumulation of triacylglycerols, diacylglycerols, monoacylglycerols, fatty acids, with the apparition of myristic acid, together with a dramatic depletion of vitamin E and a selective macrovacuolar localization of cholesterol are observed in steatosis areas of fatty livers compared to control livers. These ion species are concentrated in small vesicles having a size of a few micrometers. Moreover, very fine differences in lipid localizations, depending on alkyl acid chain lengths of diacylglycerols and fatty acids, have been found after careful scrutiny of the ion images. Finally, TOF-SIMS has revealed lipid zonation in the normal human liver and accumulation of very similar lipids to those detected in areas of the fatty livers, which are not characterized as steatotic ones by the histological control performed on serial tissue sections.

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