Circulating Lipidomic Signature To Identify Nonalcoholic Fatty Liver Disease

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BACKGROUND

Fatty liver disease (or steatohepatitis) is often associated with excessive alcohol intake or obesity, but also has other causes such as metabolic deficiencies including insulin resistance and diabetes. The causation of a fatty liver results from triglyceride fat accumulation in vacuoles of the liver cells resulting in decreased liver function, and possibly leading to cirrhosis or hepatic cancer. Non-alcoholic fatty liver disease (NAFLD) represents a spectrum of disease occurring in the absence of alcohol abuse. There is a clinical need for a simple test to identify individuals with nonalcoholic fatty liver disease (NAFLD) in the population. While circulating lipids have been used for this purpose, the large number of analytes within the human lipidome makes it cumbersome to utilize this approach for high throughput screening.

TECHNOLOGY DESCRIPTION

Researchers at UC San Diego have developed new invention that uses plasma lipid data that are predictive for NAFLD. Often, non-alcoholic fatty liver (NAFL), the milder form of NAFLD, remains unnoticed due to unchanged plasma levels of liver enzymes, the current diagnostic tool for NAFL. This invention identified a lipid panel that is highly predictive of NAFL. In addition, a subset of lipids can be used to specifically discriminate between NAFL and nonalcoholic steatohepatitis (NASH), the severe form of NAFLD. It uses blood plasma samples from adult patients with varying phenotypes of NAFLD and samples of healthy control subjects (N =389). Plasma samples were utilized for lipid measurement of eicosanoids, sterols, ceramides, and sphingomyelins using multiplex technologies based on UPLC-mass spectrometry. Akaike Information Criterion (AIC) was used to select lipids for constructing diagnostic models.

APPLICATIONS

This invention provides a lipid panel that is highly predictive of NAFL and can be used on a biological sample from blood, plasma and serum. The final model using a defined panel of lipids showed high discriminatory performance between NAFLD and healthy controls as well as NAFL and NASH. This prediction model may allow the development of a non-invasive “point-of-care” test to diagnose NAFLD and identify patients who may need further evaluation for the presence of NASH.

ADVANTAGES

This new invention generates and uses plasma lipid data that are predictive for NAFLD. Often, non-alcoholic fatty liver (NAFL), the milder form of NAFLD, remains unnoticed due to unchanged plasma levels of liver enzymes, the current diagnostic tool for NAFL.

STATE OF DEVELOPMENT

The prototype used blood plasma samples from adult patients with varying phenotypes of NAFLD and samples of healthy control subjects (N = 389). Plasma samples were utilized for lipid measurement of eicosanoids, sterols, ceramides, and sphingomyelins using multiplex technologies based on UPLC-mass spectrometry. We used AIC to select lipids for constructing diagnostic models. This selection of lipids is able to predict NAFLD with a c-statistic of 0.995% (95% confidence interval (CI) = 0.982, 0.999). The sensitivity was 97% (95% CI = 95, 99) at 95% specificity, and the positive and the negative predicted values (PPV, NPV) were 91% and 99% at NAFLD prevalence of 30%.

INTELLECTUAL PROPERTY INFO

This technology is patent pending and available for licensing and/or research sponsorship.

RELATED MATERIALS


PATENT STATUS

Patent Pending