

Scientists Identify Three Types of Fatty Liver Disease

From mild to severe, the different types can help predict the risk of NAFLD progression to cirrhosis and liver cancer.

January 6, 2025 By [Sukanya Charuchandra](#)

Looking at two separate Chinese cohorts, researchers identified three different molecular subtypes linked to the risk of advancing non-alcoholic fatty liver disease (NAFLD), according to study results published in [Science Translational Medicine](#).

NAFLD, which is now known as [metabolic dysfunction-associated fatty liver disease \(MASLD\)](#), and its more severe form, metabolic dysfunction-associated steatohepatitis (MASH, formerly known as NASH), are responsible for a growing proportion of advanced liver disease worldwide. Over time, fat buildup in the liver can trigger inflammation, leading to fibrosis, [cirrhosis](#) and [liver cancer](#).

The new terminology emphasizes the link with obesity, diabetes and other metabolic abnormalities. The first medication for MASH, [Rezdiffra \(resmetirom\)](#), was approved last year, but management still largely relies on lifestyle changes such as weight loss and exercise.

While various classifications of fatty liver disease have been recommended, identifying the risk of disease progression is less well defined. Jingjing Ding, PhD, of the Third Military Medical University in China, and colleagues sought to better classify disease types to help predict those at risk for progression.

First, the team used multiple tests, from whole-genome sequencing to multiomics profiling, to identify molecular subtypes of fatty liver disease. They collected and analyzed blood, urine and liver tissue samples from 103 people to look for molecular differences indicative of disease severity and progression.

The researchers found three distinct types of NAFLD. The first type, named NAFLD-mSI, was characterized by less steatosis (liver fat accumulation) and mild symptoms. People with this type had higher levels of two enzymes, CYP1A2 and CYP3A4, that limited the buildup of fat in the liver.

In people with the second type, dubbed NAFLD-mSII, liver fat accumulation was associated with the presence of more macrophages, a type of immune white blood cell, in the organ. This group was at greater risk for cirrhosis,

People with the third type, called NAFLD-mSIII, showed greater expression of cancer-related genes and were at higher risk for hepatocellular carcinoma (HCC), the most common type of liver cancer.

After identifying these molecular subtypes, the researchers validated them in a different cohort of 92 people with NAFLD treated at three Chinese hospitals.

“These findings may aid in understanding the molecular features underlying NAFLD heterogeneity, thereby facilitating clinical diagnosis and treatment strategies with the aim of preventing the development of liver cirrhosis and HCC,” wrote the researchers.

The different molecular subtypes may help explain why existing treatments do not work equally well for all patients.

“This lack of consistency is likely attributed to the high heterogeneity of human NAFLD, because the susceptibility to developing NAFLD is highly variable and influenced by a variety of risk factors, including aging, genotype, sex, ethnicity, dietary intake, bile acid metabolism and insulin resistance,” they suggested.

“By targeting these molecular subtypes of NAFLD through precision medicine strategies, it may be possible to reduce imprecision in NAFLD diagnosis and pharmacotherapy, potentially preventing its progression into cirrhosis and hepatocellular carcinoma in the early stages,” they concluded.

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