

Scientists closer to solving mystery of why lean people get fatty liver disease

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First author Dr Fei Chen and lead researchers Associate Professor Mohammed Eslam and Professor Jacob George. Credit: The Westmead Institute for Medical Research

Researchers from The Westmead Institute for Medical Research (WIMR) have discovered how fatty liver disease develops in lean people, aiding the development of potential treatments for these patients.

Fatty [liver](#) disease—a condition characterised by a build-up of fat in the liver—affects a quarter of the world's population. Although it commonly develops in overweight and obese people, many individuals with a body-mass index of less than 25kg/m² will develop the disease, and tend to have worse outcomes compared to obese patients.

Professor Jacob George, co-lead researcher of the study said, "Cases of lean [fatty liver disease](#) are considered a bit of a mystery, as we don't know how and why the disease develops and progresses.

"Our research team compared the metabolism, gut bacteria and genetic profiles of patients with lean and non-lean fatty liver disease to determine factors that contribute to disease development and

progression.

"Interestingly, lean fatty liver patients have a very distinct metabolism compared to non-lean ones, which can explain some of the differences we see in disease progression.

"Compared to non-lean patients, lean patients had higher levels of [bile acids](#), which play a role in the digestion of fats, and a protein called fibroblast growth factor 19 (FGF19). Bile acids and FGF19 increase energy expenditure, which can explain why lean individuals with fatty liver disease stay lean. This suggests that lean patients with a fatty liver may have an 'obesity-resistant' profile, and better adaptation to an excess intake of calories."

Associate Professor Mohammed Eslam, co-lead researcher added, "Importantly, the favourable profile of lean patients did not protect them from liver fat accumulation.

"We also identified changes in particular gut bacteria and novel genes that can influence the development of fatty liver disease in lean patients. For example, we identified that a variant in the gene TM6SF2, previously linked to fatty liver disease, is more common in lean patients."

Without treatment, fatty liver disease can result in liver scarring, liver cirrhosis and, in severe cases, liver failure.

Associate Professor Mohammed Eslam said, "The metabolic adaptive mechanisms in lean fatty liver disease tend to be lost in the late stages of the disease. This could explain why these patients have worse disease outcomes compared to their obese counterparts."

"Now that we know more about the metabolic profile and processes behind [fatty liver disease](#) in lean people, we can work towards more targeted treatments for these patients."

Professor George concluded, "Our research is now focused on understanding more about the condition, so that we can prevent its progression, and develop more personalised treatment regimens."

More information: Fei Chen et al, Lean NAFLD : A Distinct Entity Shaped by Differential Metabolic Adaptation, *Hepatology* (2019). DOI: [10.1002/hep.30908](https://doi.org/10.1002/hep.30908)

Provided by Westmead Institute for Medical Research

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