Gut microbiota harnessed as tool to diagnose diseases, promising results for fatty liver diagnosis

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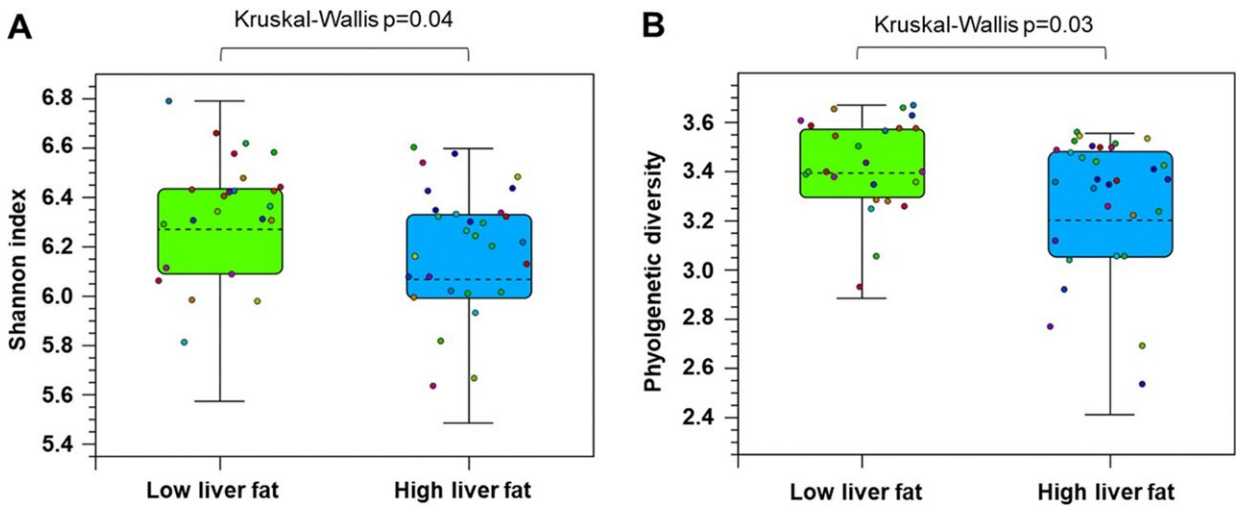

The diversity of the gut microbiota in the low (n = 25) and high (n = 37) liver fat groups. (A) Shannon index, a measure of alpha-diversity indicating species diversity. (B) Phylogenetic diversity. The data are shown as mean ± 95 CI, with the dots indicating diversity in individual samples. Statistical differences between the groups are shown above the panels (Kruskal-Wallis test). Credit: *mBio* (2023). DOI: 10.1128/mbio.02663-22

A recent study at the University of Jyväskylä (Finland) published in February in *mBio* compared the gut microbiota and gut-derived metabolites between healthy controls and individuals with fatty liver.

The results revealed that certain microbial metabolites are associated with liver fat content.

The fact that the gut microbiota associates with many diseases, has raised the hope that they could be used for diagnostic purposes. One of the progressing research fields is the analysis of gut-derived metabolites that are manufactured by the microbes from the food.

Fatty liver disease is the most common chronic liver disease world-wide, especially in individuals with obesity, and it predisposes to cardiovascular diseases. The recent study compared the gut microbiota and gut-derived metabolites between healthy controls and individuals with fatty liver. The study was conducted in collaboration with the Universities of Helsinki, Eastern Finland and Indiana, as well as the International Agency of Cancer Research (WHO).

The researchers found that individuals with fatty liver had, for instance, more degradation products of the amino acid leucine and histidine, as well as less of testosterone in their feces.

"These could be useful gut microbiota-derived biomarkers for diagnosing fatty liver disease," says Senior Lecturer Satu Pekkala from the University of Jyväskylä. "We are currently analyzing new data to determine whether these biomarkers could also be used to identify fatty liver patients that can be treated with personalized diet."

The most interesting finding in the blood samples was that the individuals with fatty liver had higher levels of caffeine and its metabolites, even though both groups consumed the same amount of coffee.

A failure in caffeine metabolism can reflect lower activity of cytochrome enzymes in the liver. These enzymes are important

degraders of drugs and nutrients, and therefore their role should be studied more to understand the importance of these enzymes and fatty liver in overall health.

More research is coming

By going through the existing literature for a review article published in March in the *International Journal of Molecular Sciences*, Pekkala noticed that the studies on the fecal metabolites in fatty liver disease were rather scarce.

Pekkala also observed that, surprisingly, many research findings were contradictory, and only Pekkala's recent study in *mBio* considered the diet in the analyses.

"Because the microbes digest the food that we eat, it cannot be known whether the metabolite differences between healthy controls and patients with fatty liver are solely due to dietary differences," Pekkala explains. "So that the microbial biomarkers could be used for diagnostics, more research in larger populations is needed, and most importantly diet should be considered among other confounding factors."

Pekkala's research team is already conducting such studies and new studies are being planned.

More information: Anastasiia Driuchina et al, Identification of Gut Microbial Lysine and Histidine Degradation and CYP-Dependent Metabolites as Biomarkers of Fatty Liver Disease, *mBio* (2023). DOI: 10.1128/mbio.02663-22

Satu Pekkala, Fecal Metagenomics and Metabolomics Identifying Microbial Signatures in Non-Alcoholic Fatty Liver Disease, *International Journal of Molecular Sciences* (2023). DOI: 10.3390/ijms24054855