The proof is in the poo: S'pore study links gut health to fatty liver disease

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Scientists have found a protein in the gut that acts like a "middleman", connecting your lunch, your gut bacteria and your liver health.

By examining stool samples, the team, led by Nanyang Technological University, found that people with higher levels of this protein tend to develop fatty liver disease later in life.

The study, headed by Andrew Tan, an associate professor and vice-dean of innovation and enterprise at the Lee Kong Chian School of Medicine (LKCMedicine), focused on angiopoietin-like 4, a protein found in the gut that can cause a leaky gut, a condition in which the gut becomes overly porous.

This allows bacteria from the gut to travel directly to the liver, where they can trigger inflammation and the build-up of fat.

The researchers used not only preclinical models but also human data collected from three patient cohorts from Singapore, Thailand, China and India. The whole exercise took between three and four years and provided the team with a window into how diet can affect the liver, Tan said.

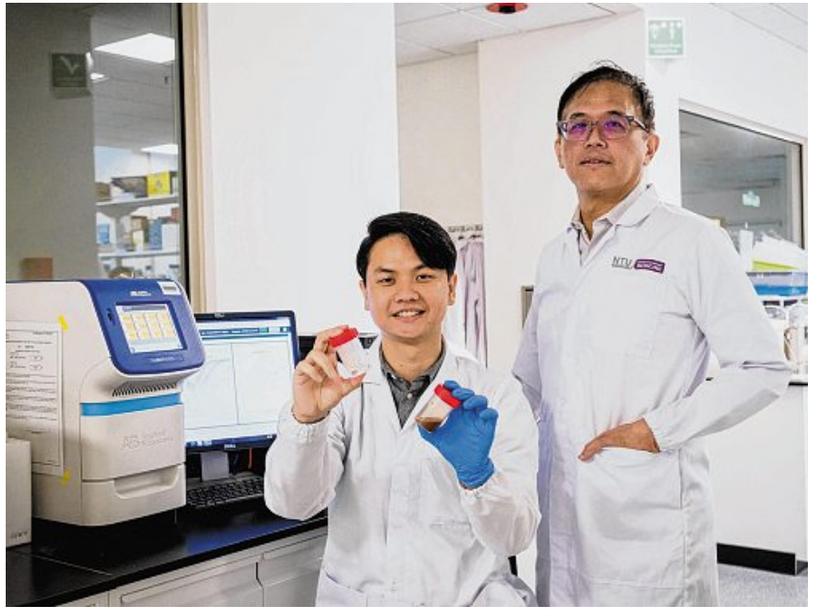
"We know what we eat changes the bacteria in the gut, so we intentionally picked these three countries that are very different in their dietary intakes... and, hopefully, similar to that of Singapore. We took faecal samples from patients in the different disease states to measure the protein levels. It turned out to be a very good marker for gut health, unlike blood markers," he said.

LKCMedicine doctorate student Damien Chua said doctors used to think fatty liver primarily affects the liver itself, "but actually the damage starts early on in the gut".

"They tend to use serous markers from blood samples, but we found from our cohort studies that these do not actually align properly, so they were not as robust as we thought they were. With our biomarkers from faecal samples, we are also able to look at a different aspect of what constitutes a leaky gut," said Chua, who is also the principal investigator of the research.

"In this regard, our research has not only changed the way we think about the relationship (between leaky gut and fatty liver), but also provided a new way to test for such signs in patients," he added.

The new findings, published in Nature Communications, a peer-reviewed scientific journal, on May 22, help researchers understand early gut-liver changes before they develop into more serious liver diseases such as fatty liver and liver cancer.



The team, including LKCMedicine researchers Andrew Tan (right), who helmed the study, and Damien Chua, found that people with higher levels of a protein found in the gut tend to develop fatty liver disease later in life. PHOTO: NTU

The findings are also relevant to Singapore, where fatty liver disease is a growing health issue. According to Annals, the official journal of the Academy of Medicine in Singapore, the local disease burden for non-alcoholic fatty liver disease was projected to rise from about 1.49 million in 2019 to 1.8 million by 2030.

This increase is alarming because most patients are either asymptomatic or do not have elevated liver enzyme levels.

"When we saw the recent NUH (National University Hospital) paper that identified the people with the risk, (we felt) what we are doing is complementary. They need to focus not only on the liver but also on gut changes through stools. When you do that, you actually have an early intervention – before the disease gets established," Tan said.

The NUH researchers found that a specific genetic change that results in fatty liver, when combined with metabolic conditions like diabetes and obesity, is linked to a higher risk of liver cancer. They also found that men with what is commonly known as a "beer gut" are up to nine times more likely to develop the most common type of primary liver cancer called hepatocellular carcinoma.

"Just imagine that 30 per cent or 40 per cent of Singaporeans are developing fatty liver disease – the number is huge and the cost is going to be very high for medical intervention. Looking at stools is an easier way for monitoring patients," he added.

Tan said one way to do so was to piggyback on Healthier SG, which shifts the focus of healthcare from reactive treatments to proactive preventive care.

"At this stage, we are examining how the gut biomarker test can be streamlined into a routine clinical test before it can be considered for programmes such as Healthier SG.

"The biomarker can already be detected using PCR (polymerase chain reaction) machines commonly found in clinical laboratories. Once a stool sample has been collected and processed, it would not be too difficult to incorporate the test into existing diagnostic workflows," he said.

The researchers are also working with organisations in China and Thailand to further validate the findings, such as measurements before and after treatments, and with NTU engineering colleagues to develop a microfluidic device version in the near future.

"This could make the test easier to use and more suitable for wider deployment in time," Tan added.

Under the Healthier SG screening protocol, doctors collect stool samples using the faecal immunochemical test kit, a non-invasive screening tool that detects microscopic amounts of blood, an early sign of colorectal cancer or precancerous growths in the colon.

"We should leverage the test because it is already collecting stool samples and integrating one more test would make it accessible... It is one sample and you can test for different states, much like with blood. There is actually a lot more information from faecal material that could be tested," he said.

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