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Using the gut microbiome as a health compass

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Machine Learning Model to predict potential NAFLD. Credit: Howell Leung/ Leibniz-HKI

The human microbiome can provide information regarding the risk of non-alcoholic fatty liver disease. This has been discovered by an international team led by the Leibniz Institute for Natural Product Research and Infection Biology-Hans Knöll Institute. The researchers developed a model that can predict the possible course of the disease based on the microbial composition in the intestine. The study is published in *Science Translational Medicine*.

Up to 25% of the global population are affected by non-alcoholic fatty liver disease (NAFLD), in which an increased amount of fat cells form in the liver. It is the most common chronic liver disease in the industrialized countries of the world and, unlike alcoholic fatty liver disease, is not caused by high alcohol consumption. In some people, undetected NAFLD can lead to liver scarring, liver cancer or liver failure.

In a long-term study, an international research team led by Gianni Panagiotou, research group leader for systems biology and bioinformatics at Leibniz HKI, analyzed stool and blood samples from 1200 people who were initially NAFLD-free. "It has already been proven that the microorganisms in the human gut contribute to the development of NAFLD. We wanted to find out if the microbiome of a healthy person could predict whether or not they would develop NAFLD in the future," Panagiotou explains.

When the subjects were re-examined four years later, it was revealed that 90 of them had since developed NAFLD. Samples from those affected were compared to a control group of 90 people who did not have NAFLD at baseline or at the follow-up visit. "Using different methods, we were able to find very subtle differences in the samples we took four years prior," explains first author Howell Leung from Panagiotou's group at Leibniz HKI. "With this data, we were able to develop a model that can predict who will develop NAFLD in the future

based on the microbiome with 80% certainty."

Currently, there are clinical models that use biochemical parameters in the blood to make a prediction with 60% accuracy. "The model we developed combines easily measurable information from the blood with data from the microbiome and can thus increase the reliability enormously," says Panagiotou.

Disease prediction through machine learning

The research team developed a so-called machine learning model—a computer model that is trained to recognize certain patterns in a set of data. The model can then use these patterns to analyze new datasets, and in this case, predict possible non-alcoholic fatty liver disease. "The whole process of developing our model took over three years due to the complexity of the data. However, in the end we were successful and were able to create a useful tool for predicting NAFLD," says Panagiotou.

Late stage non-alcoholic fatty liver disease is irreversible and in the worst cases can even lead to liver cancer. People who already suffer from a precursor or are particularly at risk must therefore be identified early on in order to be able to counteract the disease. "NAFLD is a silent disease. This means that in most cases it is asymptomatic and is usually only detected by chance," explains Gianni Panagiotou. The number of Germans suffering from NAFLD is estimated at around 12 million. People with pre-existing conditions such as type 2 diabetes, obesity, high blood pressure or dyslipidemia are particularly affected by fatty liver disease.

Possible applications and next steps

Using their machine learning model, the researchers have already been able to compare and thus validate their results with patient data from the US and Europe. In the next step, Panagiotou plans to conduct the study globally and use artificial intelligence to integrate even larger data sets into the study.

"I see microbiome-based diagnostics as something that will reach clinical practice and have great potential in the next ten years," says Panagiotou. Early treatment of the risk factors of non-alcoholic fatty liver disease, such as type 2 diabetes, hypertension and obesity, could halt the development of the disease. Therefore, early prognosis is the only way to prevent the disease.

More information: Howell Leung et al, Risk assessment with gut microbiome and metabolite markers in NAFLD development, *Science Translational Medicine* (2022). DOI: 10.1126/scitranslmed.abk0855

Provided by Leibniz-HKI