

Press release

Leibniz-Institut für Naturstoff-Forschung und Infektionsbiologie - Hans-Knöll-Institut (Leibniz-HKI)

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## What microbes tell us about Nonalcoholic Fatty Liver Disease

Researchers have identified specific gut microbiome signatures that predict bacterial metabolites, which can help differentiate Nonalcoholic Fatty Liver Disease (NAFLD) from non-NAFLD patients. The study, led by an international team including the Leibniz Institute for Natural Product Research and Infection Biology – Hans Knöll Institute (Leibniz-HKI), used machine learning models to analyze large datasets of gut microbiome data. The findings show that these microbial signatures are highly specific and can be used as diagnostic tools for NAFLD.

The study involved analyzing the gut microbiome of patients with NAFLD and comparing it to those without. The researchers found that certain bacterial species and their metabolites were more prevalent in the NAFLD group. These findings are particularly significant because they provide a clear molecular signature for the disease, which can be used for early diagnosis and targeted treatment. The study also highlights the importance of the gut microbiome in liver health and the potential for microbiome-based therapies.

The signatures found are typical specific gut microbiome species and predict bacterial metabolites, that can help differentiate NAFLD from non-NAFLD patients. They allow differentiation from other diseases and are therefore particularly suitable for targeted diagnostics. Supported by machine learning models, the researchers achieved a diagnostic accuracy of over 90 % with the collected data sets.

NAFLD affects up to 40 % of the population in western countries and is one of the most common metabolic diseases worldwide. It is characterized by an excessive storage of fat in the liver cells, which can lead to an approximately 10 % increase in liver weight with a reduced liver function.

Despite intensive research, the exact mechanisms of disease development and its progression (pathophysiology) are not yet fully understood. The gut microbiome appears to play an important role here, as it influences the so-called gut-liver axis and could therefore be significantly involved in the development of NAFLD. An international research team led by the Leibniz Institute for Natural Product Research and Infection Biology – Hans Knöll Institute (Leibniz-HKI) has investigated the question of whether the composition of the microbiome consisting of many different microorganism species, could be an indicator of NAFLD. The study confirmed exactly this: A specific composition of the gut microbiome, in a sense the fingerprint or indeed its signature, could be used in the future as a tool for more precise diagnoses and new forms of therapy for Nonalcoholic Fatty Liver Disease, for example.

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“The occurrence of NAFLD in combination with other metabolic diseases such as type 2 diabetes is a particular challenge, as it makes it difficult to distinguish specific microbiome signatures,” explains the leader of the study Gianni Panagiotou. “We were able to identify signatures that are clearly associated with NAFLD and could enable a differentiated diagnosis.” The composition of the gut microbiome is generally influenced by various factors such as obesity, age, diet, gender or medication.

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In the study, state-of-the-art ecological network analyses were used to decipher how different microorganisms interact in their natural environment, the human gut. These analyses rely on interdisciplinary, data-based, and computer-aided

methods to better understand the relationships between species and their surroundings. The researchers showed that specific microbiome networks are directly linked to the development of NAFLD. These approaches provide not only precise diagnostic insights but also a deeper understanding of the disease mechanisms.

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Therapeutic approaches could be proposed based on these microbiome signatures. For example, it is conceivable that microbial consortia, i.e. selected groups of microorganisms, produced specifically in the laboratory could be used to positively influence intestinal health.

“Our results open up new possibilities for personalized therapy that is precisely tailored to the individual needs of the patient,” says Gianni Panagiotou. He holds the Chair of Excellence in Microbiome Dynamics at the University of Jena and heads the department of the same name at the Leibniz-HKI. His work is dedicated to a central topic of the Cluster of Excellence “Balance of the Microverse”, the understanding of the interactions between microbiomes and their environment.

The results of the study underline the importance of the gut microbiome for the development of new methods in personalized medicine. The combination of genetic, clinical and ecological data opens up new possibilities to better understand and more effectively treat metabolic diseases such as NAFLD.

The study, which was recently published in the journal *Microbiome*, received funding from the German Research Foundation as part of the Jena Cluster of Excellence “Balance of the Microverse” and the Federal Ministry of Education and Research (BMBF) and the European Commission through the Horizon 2020 Research and Innovation Programme, among others.

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