

## PRESS RELEASE

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### The gut microbiome: a “crystal ball” to predict multiple sclerosis

#### LIH study discovers gut microbial risk factors to predict disease

*In a ground-breaking study, the Nutrition, Microbiome & Immunity research group of the LIH Department of Infection and Immunity (DII) has shed light on the complex relationship in the gut-brain axis between the gut microbiome and a neurodegenerative disease, multiple sclerosis (MS). The new study shows that certain gut microbial factors could predict the susceptibility and progression of this debilitating autoimmune disease. The research, published in the prominent journal Nature Microbiology, identifies microbial “risk factors” or “biomarkers” to predict MS development and severity, with important implications for disease diagnosis and management.*

MS is an inflammatory demyelinating condition affecting an estimated 1.8 million people worldwide. It results from an autoimmune attack on myelin, the fatty insulation surrounding the nerves in the brain and spinal cord, which disrupts the electrical impulses that are sent through the nerves to the rest of the body and results in scars known as plaques or sclerosis. Identifying the parameters that can be used to predict MS disease risk is an important area of research, as little is known about the potential risk predictors. Recently, the gut microbiome has been linked to neurodegenerative diseases, with important differences in its composition being reported in MS patients compared to healthy individuals, although the causal and functional roles of specific microbial risk factors in the onset of the disease remain elusive.

In this context, in order to determine whether MS susceptibility or progression could be predicted by the composition of the gut microbiome, the research team led by Prof Mahesh Desai of the LIH used a pre-clinical model of MS, experimental autoimmune encephalomyelitis (EAE), to investigate the gut microbiome-associated functional responses, as well as how the host immune system is impacted by the gut microbiome. *“This approach allowed us to better examine how individual host–microbe interactions affect disease predictability, thus overcoming the limitations of approaches that only look at the relative abundances of bacterial species between MS-affected and healthy individuals and which cannot explain the observed individual differences in disease susceptibility and progression”,* explains Prof Desai, leader of the Nutrition, Microbiome & Immunity research group at the LIH and lead author of the publication. *“Indeed, making disease-course predictions based on microbiota characteristics is generally possible, but it is not as straightforward as surveying community member presence or abundance.”*

By employing a pre-clinical model of MS in mice of different genetic backgrounds and with distinct complex microbiotas, the researchers shed light on the dual role of a specific bacterium, namely *Akkermansia muciniphila*, whose abundance has been positively correlated with disease in MS patients across multiple MS cohorts in different parts of the world. In the present study, the team studied the causal role of this bacterium and found it to be associated with less severe disease development in mice with certain microbiome compositions, but also with increased disease severity in the presence of other bacteria.

*“These findings suggest that the impact of specific bacteria on MS may depend on the broader microbial community context, and that focusing on combinations of species or microbial networks, rather than single species alone, is essential to predict disease courses across different microbiota compositions”,* he adds. Moreover, the results highlighted substantial interindividual differences in disease progression, even among genetically similar mice with identical microbiota, raising the important question of how personalised disease prediction could be made possible.

Importantly, the team found that when specific ‘reporter bacteria’ get significantly more coated with the host-secreted immunoglobulin A (IgA) before disease onset in a certain individual, that particular individual goes on to develop a more severe disease. These findings therefore suggest the potential of this marker as a prognostic and diagnostic tool, opening up new avenues for personalised diagnostic and therapeutic strategies targeting the gut microbiota.

The study bears important clinical implications. As Prof Desai explains, *“Based on our results, we are currently planning to set up an MS patient cohort at the Centre Hospitalier de Luxembourg in order to translate our findings into clinical practice. This work will also provide crucial insights for the flagship LIH project Clinnova, which features MS as one of its key diseases”*.

The research article was published in the prestigious journal, *Nature Microbiology*, with the full title *“Gut microbial factors predict disease severity in a mouse model of multiple sclerosis”*.

### **Funding and collaborations**

The study included several members of Prof Desai’s research team including researchers Dr Alex Steimle, Dr Mareike Neumann and Dr Erica T Grant. The research was carried out in collaboration with the RIKEN Center for Integrative Medical Sciences, Japan and the Institute for Advanced Biosciences at Keio University, Japan. The study was funded by the Luxembourg National Research Fund, the Fondation du Pélican de Mie et Pierre Hippert-Faber (Fondation de Luxembourg), as well as the Japan Society for the Promotion of Science (JSPS) KAKENHI, JST ERATO, the Lotte Foundation, AMED-CREST, the Food Science Institute Foundation and Astellas Foundation for Research on Metabolic Disorders.

### **About the Luxembourg Institute of Health (LIH)**

*The Luxembourg Institute of Health (LIH) is a public biomedical research organisation focused on precision health and invested in becoming a leading reference in Europe for the translation of scientific excellence into meaningful benefits for patients.*

*The LIH places the patient at the heart of all its activities, driven by a collective obligation towards society to use knowledge and technology arising from research on patient derived data to have a direct impact on people’s health. Its dedicated teams of multidisciplinary researchers strive for excellence, generating relevant knowledge linked to immune related diseases and cancer.*

*The institute embraces collaborations, disruptive technology and process innovation as unique opportunities to improve the application of diagnostics and therapeutics with the long-term goal of preventing disease.*

### **Scientific contact:**

Prof Mahesh S. Desai

Group Leader, Nutrition, Microbiome and Immunity

Department of Infection and Immunity



Luxembourg Institute of Health

E-mail: [mahesh.desai@lih.lu](mailto:mahesh.desai@lih.lu)

**Press contact:**

Arnaud D'Agostini

Head of Marketing and Communication

Luxembourg Institute of Health

Tel: +352 26970-524

Email: [communication@lih.lu](mailto:communication@lih.lu)