LUXEMBOURG INSTITUTE OF HEALTH

PRESS RELEASE

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Dr Jekyll & Mr Hyde found in your gut

Friend or foe? New study uncovers two sides of a potential probiotic

A new study led by Prof Mahesh S. Desai of the Luxembourg Institute of Health sheds light on the complex relationship between gut bacteria, pathogens and diet. The research team investigated which bacteria commonly found in the gut could potentially help a pathogen that infects the gut, and how this interaction is shaped by dietary habits. Their findings reveal a surprising duality: A. muciniphila, a bacterium considered a potential probiotic, can either bolster (Dr. Jekyll) or weaken (Mr. Hyde) the gut's defenses against harmful bacteria depending on the intake of dietary fiber. This research underscores that friendly bacteria in the gut synergize with pathogens in the face of a fiber-deprived diet, which calls for considering a holistic approach when designing probiotic interventions.

In a cutting-edge study set to redefine our understanding of gut microbiota dynamics, researchers from the Luxembourg Institute of Health Department of Infection and Immunity, have uncovered a fascinating duality within a popular mucus-eating, bacterium *Akkermansia muciniphila*¸ which is considered as a potential probiotic for the management of Type 2 diabetes and obesity. Published in the prestigious journal Molecular Systems Biology, the research, led by Desai, sheds light on the "Dr Jekyll and Mr. Hyde" persona of this bacterium, showcasing its ability to be either beneficial or detrimental to our ability to resist pathogen infections depending on dietary context.

The study, published as a cover story of the June issue of Molecular Systems Biology, delves into the intricate relationship between gut microbiota composition, dietary fiber intake, and susceptibility to enteric pathogens. Through a series of meticulous experiments using gnotobiotic mice harboring a synthetic human microbiota, the researchers demonstrated that *A. muciniphila* plays a pivotal role in modulating infection dynamics of the gut mucosal pathogen *Citrobacter rodentium*, which is a model for human enteropathogenic and enterohaemorrhagic *Escherichia coli*.

"*What we've uncovered is truly remarkable*," says Desai. "*A. muciniphila, often hailed as a next-generation probiotic, exhibits a Janus-like behaviour, acting as both a facilitator or a protector against enteric pathogens. This dichotomy underscores the nuanced interplay between gut microbes, dietary factors, and host health.*"

The research elucidates that under conditions of dietary fiber deprivation, *A. muciniphila* renders the host more vulnerable to mucosal pathogen colonization by increasing mucus penetrability. However, on a fiber-sufficient diet, the presence of *A. muciniphila* paradoxically reduces pathogen load, highlighting its context-dependent beneficial effects.

"*Our findings challenge conventional wisdom surrounding the role of* A. muciniphila *in gut health*," explains Dr. Mathis Wolter, who is the first author on the study. "*While it's widely regarded as a potential probiotic, our study emphasizes the importance of considering dietary context in harnessing its beneficial effects.*"

The implications of this research extend beyond the realm of gut health, offering insights into the broader dynamics of microbial ecology and disease susceptibility. By identifying *A. muciniphila* as a potential biomarker species for predicting susceptibility to enteric pathogens, the study paves the way for targeted interventions to mitigate the burden of foodborne infections.

"*As we navigate the complex landscape of human health, understanding the intricate interplay between diet, microbiota, and disease is paramount*," adds Desai. "*Our research highlights the need for a nuanced approach to probiotic therapies, taking into account the context-dependent nature of microbial interactions.*"

The publication of this seminal research in Molecular Systems Biology marks a significant milestone in the field of systems biology and microbiome research, offering fresh insights into the multifaceted dynamics of the gut ecosystem. The study can be found under the full title: "*Diet-driven differential response of Akkermansia muciniphila modulates pathogen susceptibility*"(https://www.embopress.org/doi/full/10.1038/s44320-024-00036-7).

Funding and collaborations

The study was a result of the doctoral thesis work of Dr. Mathis Wolter, a former PhD student of Prof. Desai. Two postdoctoral researchers from Prof. Desai`s team, Dr. Erica Grant and Dr. Marie Boudaud, also made important contributions to the study as co-authors. The research was carried out in collaboration with Prof. Eric Martens` laboratory at University of Michigan Medical School, Ann Arbor, USA. This work received funding from Luxembourg National Research Fund (FNR), United States National Institutes of Health, Fulbright Commission, Fondation du Pélican de Mie et Pierre Hippert-Faber, under the aegis of the Fondation de Luxembourg and European Commission Horizon 2020 Marie Skłodowska-Curie Actions.

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.

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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

Press contact:

Arnaud D'Agostini

Head of Marketing and Communication

Luxembourg Institute of Health

Tel: +352 26970-524

Email: communication@lih.lu