LUXEMBOURG INSTITUTE OF HEALTH

PRESS RELEASE

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Food allergies: a "gut feeling"

LIH scientists elucidate a functional link between diet, intestinal mucus-eating microbes and food allergy

In a ground-breaking study published in the prestigious journal "Nature Microbiology", the Nutrition, Microbiome and Immunity research group of the LIH Department of Infection and Immunity (DII) showed how a diet low in fibre leads to the proliferation of the mucolytic bacterium Akkermansia muciniphila *in the gut. This is in turn associated with a damaged gut mucosal barrier, an inflammatory state and consequently, an increased sensitivity to food allergens. The findings therefore open up innovative possibilities to employ the gut microbiota as a therapeutic or preventive target to tackle food allergies, which have been recognised as a rising global epidemic.*

The gut microbiome, i.e. the "friendly" microbial community naturally present in the gastrointestinal tract, is known to play an important role in preventing the emergence of sensitivities to food allergens. Alterations in the gut microbiome, caused for instance by high-fat and low-fibre diets, have therefore been linked to the rising prevalence of food allergies, although little is known about how specific gut bacteria affect the tolerance to food allergens. The LIH research team therefore aimed to identify such causal links to facilitate our mechanistic understanding of how the interactions between diet and gut microbes regulate food allergy.

The intestinal mucosal barrier lining the interior of the gut, and particularly the mucus layer, acts as a first line of defence against pathogens, allows efficient nutrient absorption and promotes tolerance to food antigens. "*We therefore hypothesised that dietary fibre deprivation can result in a change in microbiome composition, and specifically in the increase of mucolytic gut microbes, leading to the breakdown of the barrier and, consequently, to an inflammatory state in the gut, which predisposes the host to enhanced allergen sensitisation*", says Prof Mahesh Desai, head of the Nutrition, Microbiome and Immunity group, and leader of the study.

Using mouse models, the team compared the effects of a fibre-free and a fibre-rich diet on the gut microbiome composition. They found that an increase in the abundance of mucus-degrading bacteria, particularly *Akkermansia muciniphila*, in the gut of fibre-deprived mice is associated with altered immune responses that predispose the host to developing food allergies. Allergen sensitisation, however, is generally known to take place in the small intestine. "*Our results suggest hitherto undescribed innate immune pathways of allergen sensitisation in the large intestine, which are dependent on the increase in mucus-degrading bacteria in a diet-dependent manner*", says Prof Desai. In addition, the scientists observed an increase in bacteria coated with antibodies in the large intestine. "*These antibody-coated*

bacteria, together with the leaky gut barrier, in turn generate a mucosal inflammatory state in the colon that promotes pathways leading to food allergy", he adds.

The presence of *A. muciniphila* was found to be a necessary condition to increase the severity of allergic symptoms in sensitised mice, regardless of their diet, demonstrating the causal role of this specific type of mucolytic bacterium in increasing susceptibility to allergens induced by fibre deprivation. These results suggest that there could be several other such "biomarkers" indicative of allergic reactions that could be identified in the microbiome of food allergic patients. Modulating such biomarkers with dietary interventions could therefore help alleviate the symptoms and thus reduce the burden of food allergy. "*I am convinced that this study will change the paradigms in food allergy!*", says Prof. Markus Ollert, Director of the DII and a collaborator on this study.

"*Overall, our study strongly supports the emerging view that food allergy consists of a vast array of different 'endotypes', i.e. subtypes characterised by distinct immune mechanisms influenced by environmental triggers such as diet and ensuing changes in the composition of the gut microbiome*. *Diet- and microbiota-based therapies will therefore play an important role in managing such food allergy endotypes in a truly personalised manner",* highlights Prof Desai. The research team is now keen to translate these research findings to a cohort of food allergic patients, in order to identify additional food allergy-promoting gut microbes. Interestingly, changes in the composition of the gut microbiome, mucosal barrier degradation and gut inflammation are also hallmarks of an array of intestinal disorders, including Irritable Bowel Syndrome (IBS) and Inflammatory Bowel Disease (IBD), and of extra-intestinal autoimmune diseases, like Alzheimer's Disease, Multiple Sclerosis, Rheumatoid Arthritis, Type 1 diabetes and even Parkinson's Disease. *"Understanding the role of the various components of the microbiome and how their functions are affected by external factors like diet therefore becomes the key to preventing and treating a broad range of afflictions, from food allergies to neurodegenerative diseases, thereby giving our work a highly translational dimension with an enormous therapeutic potential for many patients around the world",* he concludes.

The study was performed with former PhD candidate Dr. Amy Parrish, and Dr. Marie Boudaud, in Prof. Desai's team. It benefited from the collaboration with other LIH researchers, namely Prof. Markus Ollert, Mr. Oliver Hunewald and Dr. Antonio Cosma. The original paper was published in the renowned journal Nature Microbiology with the full title "Akkermansia muciniphila exacerbates food allergy in fiber-deprived mice".

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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