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Probiotics: Every gut reacts differently

A study by the University of Bern and Inselspital, Bern University Hospital, has shown in mice that the effectiveness of a probiotic in alleviating intestinal inflammation depends on the animals' existing gut microbiota. The same four-strain bacterial mixture was significantly more effective in some animals than in others. These findings could pave the way for tailoring probiotic treatments more closely to individual gut microbiomes.

Trillions of bacteria inhabit the gut. Among other functions, they break down components of our food and produce substances that are important for the intestinal lining. Probiotics contain living microorganisms intended to support this ecosystem. They are used, for example, in the treatment of irritable bowel syndrome and are being studied in relation to chronic inflammatory bowel diseases such as Crohn's disease and ulcerative colitis. In these conditions, the composition and function of the gut microbiota can change, and probiotics may help relieve symptoms such as bloating, abdominal pain and irregular bowel movements. Probiotics are available as dietary supplements, and some probiotic microorganisms are also found in fermented foods such as yogurt and kefir. Their effects, however, can vary considerably: while some people benefit, others experience little or no improvement. The reasons for these differences are still only partly understood.

A research team led by Prof. Dr. Bahtiyar Yilmaz from the University Clinic for Visceral Surgery and Medicine at Inselspital, Bern University Hospital, and the Department for BioMedical Research (DBMR) at the University of Bern, set out to investigate the role of the existing gut microbiota in the efficacy of probiotics. The researchers tested a mixture of four bacterial strains in mice with experimentally induced intestinal inflammation. Their findings show that the existing community of gut bacteria influences how effective the probiotic is. The study has recently been published in *Cell Reports*.

Bern as a research hub for personalized microbiome medicine

"Bern is home to outstanding research at the intersection of gastrointestinal medicine, microbiome research and precision medicine," says study leader Yilmaz. "This combination enables us to investigate not only the composition of the microbiome, but also its functions and its impact on intestinal diseases." For the study, the researchers tested a probiotic mixture containing four bacterial strains in mice with different gut microbiota. The mixture was administered either preventively or after inflammation had already developed. "We wanted to determine not only whether the mixture was effective, but also under which conditions," explains Yilmaz. "In particular, we were interested in whether the existing bacterial community served as a baseline for treatment."

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The researchers also analyzed the composition of the gut microbiota, and the metabolic products present in the gut. In a further experiment, they transferred gut microbiota from treated mice to germ-free animals to determine whether the transferred microbiome contributed to the animals' differing responses to the probiotic.

The probiotic needs the right environment

The most pronounced protective effect was observed when the probiotic was administered before the onset of inflammation. In the groups that responded to treatment, the mice lost less weight, showed fewer signs of illness, and experienced less tissue damage. Their gut microbiota was more diverse and remained more stable throughout the inflammatory process. When treatment began only after inflammation had developed, the effect was less pronounced. It also diminished during repeated episodes of inflammation, despite continued administration. "This suggests that both the initial state of the gut and the timing of probiotic treatment may be critical" explains co-first author Göktuğ Özkurt, a doctoral student at the DBMR at the University of Bern.

What also differed between the groups was the metabolic activity of the gut microbiome. Where the probiotic was effective, many inflammation-related changes in metabolites shifted back towards a healthy profile. The researchers also found higher levels of butyrate and propionate – short-chain fatty acids that, among other functions, help support the intestinal lining. "Our results show that an effective probiotic helps the existing gut microbiota maintain its functions and partially recover from inflammation" says Jiaqi Li, co-first author of the study and a former doctoral student at the DBMR at the University of Bern.

A foundation for more targeted probiotics

The findings are currently limited to a mouse model of chemically induced intestinal inflammation. "They do not show that the mixture tested is effective in people with chronic inflammatory bowel disease nor do they yet provide a way of identifying which probiotics are best suited to which patients" Yilmaz notes. It remains to be determined whether an unresponsive gut microbiota can be specifically modified to make it respond to a probiotic. "The key question going forward is not only which probiotic is administered, but also which gut microbiota it encounters," says Yilmaz. The researchers will now validate their findings in further mouse studies and prospective clinical trials. High-resolution genetic analyses and measurements of bacterial gene activity should help identify the strains and functions that are critical to the response. They will also investigate whether unresponsive gut communities can be specifically modified.

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Department for BioMedical Research (DBMR)

The Department for BioMedical Research (DBMR) of the Faculty of Medicine of the University of Bern was founded in 1994 by the University of Bern and the Inselspital, University Hospital Bern. The DBMR is divided into 14 research programs with around 100 participating individual laboratories and several independent research laboratories whose research span all biomedical areas. To bridge the gap between the laboratory and the bedside, the DBMR promotes clinical research with a strong emphasis on the development of translational approaches, the use of "omics" and other cutting-edge technologies, and extensive collaboration between laboratory-based and patient-centered clinical research. The DBMR is also committed to the promotion of young Scientists. Further information: https://www.dbmr.unibe.ch/index_eng.html

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