



An illustration of gut microbiota, which may be associated with intestinal health.

EXPLORING LINKS BETWEEN PROBIOTICS AND REDUCING OBESITY

In a pre-clinical study, researchers at a university in China and a dairy manufacturer explore mechanisms that could **CONNECT OBESITY REDUCTION AND PROBIOTICS**.

In the human body, microorganisms tend to outnumber human cells ten to one. The microorganisms are largely symbiotic and found throughout the body, though most densely in the digestive tract. In recent decades, research has shown that healthy gut microbiota has been associated with a host of general health benefits, and a number of studies have examined the impact of probiotics on both gut and overall health¹.

Among consumers, enthusiasm for probiotics, whether from natural sources such as yogurt, kefir and fermented vegetables or manufactured supplements, is growing rapidly.

"The COVID-19 pandemic has reframed the status of the

microbiome industry," says Weilian Hung, head of Yili Probiotics Research Centre, an innovation centre within one of China's leading dairy producers, Yili Group, based in Hohhot, Inner Mongolia, China. "Awareness of health has significantly increased, and there is a huge demand for products that can improve gut health and enhance immunity. Probiotics, as representative microbiome products, are receiving unprecedented attention."

While such demand is largely viewed as positive, Hung adds that more probiotics studies are needed to understand the precise mechanisms that connect a healthy gut and a healthy body. Likewise,

more research is required to ensure companies are bringing optimized, scientifically validated probiotics to their customers.

Yili Group has set up 15 innovation centres around the world, and by the end of 2022, Yili was ranked second in the world's dairy industry in terms of the total number of global patent and invention applications.

"This was achieved by setting up high-profile collaborations with prestigious universities and research institutes," Hung says. "In the field of probiotics, we have established close research collaborations with 47 experts from 23 universities, five research institutes, and three hospitals worldwide."

The Yili Probiotics Research Centre in Shanghai is currently collaborating with researchers in screening probiotic strains, studying their properties and developing probiotic products. In one recent project, the centre collaborated with researchers at Sichuan University in Chengdu on a study, published in *Probiotics and Antimicrobial Proteins*², that explored mechanisms that could connect obesity reduction and the administration of probiotics.

PRECLINICAL MODELS

Over the past few decades, the prevalence of obesity and obesity-related conditions, such as type 2 diabetes and cardiovascular diseases, has increased significantly,

particularly in China. According to the International Diabetes Federation, around 12.8% of the Chinese population had diabetes in 2021.

Fang He, a professor in the department of nutrition and food hygiene at Sichuan University, along with researchers at Yili, designed an experiment to investigate the effects of a new strain *Lactocaseibacillus paracasei* K56 (K56) on obesity in mice and explore the underlying mechanisms.

"We speculated that interventions targeting gut microbiota, such as taking probiotics, might play a significant role in the prevention and treatment of obesity," He says. "I have been studying probiotics for 30 years. There are many unclear reports about whether they can help with weight loss. Many say that lactic acid in fermented milk is effective, but it is difficult to provide clear evidence and explain the underlying principles," He says.

The study involved 40 mice, with eight in the control group, and 32 fed a high fat diet. After eight weeks, those in the high fat diet group which had experienced a 40% or more weight gain were separated into another control group and three other groups were fed varying doses of K56. All groups were then tested in a multitude of ways to gauge body mass and composition, fat content, and the expression of key biomarkers, including cholesterol, serum leptin, and importantly fatty acid synthase (FAS).

FAS is an enzyme that catalyses process of fatty acid synthesis — storing fat for future energy, when there is an excess of nutrients. After 10 weeks, He and the team found decreased expression of FAS in the livers of all three groups of mice that had been fed K56. These mice also displayed changes in their gut microbiota.



▲ A Yili researcher (top) is isolating and screening probiotic strains; Yili's headquarters (bottom) in Hohhot, Inner Mongolia, China.

He says that during the study the team had to be careful to prevent with the complex sampling process.

"In the past, only the weight of mice was measured, but now we have access to various detection methods."

To make their findings, the team used a battery of new measurement techniques from western blotting to high-throughput gut microbiota detection technology.

NEW BREAKTHROUGH

In mice, He and his team demonstrated an association between K56 and a reduction in obesity, as measured by body weight, glucose, blood lipids, and insulin-resistance.

Perhaps more significantly, the team also proposed a

mechanism to explain the outcome. They found that K56 mice saw downregulated FAS expression and upregulated insulin sensitivity in the liver. The research team hypothesizes that K56 may have prevented the mice from fat accumulation by regulating the host gut microbiota, promoting host-microbiota interactions, and restoring host metabolic function.

"We are excited to discover that the mice's liver metabolisms of the treatment group increased. This provides scientific evidence that K56 can positively affect the mice's metabolism," He says.

While the study provides potential insight into connections between gut microbiota and obesity, He says more research is

required, particularly for clinical application.

Recently, Yili worked with researchers at Hua Dong Hospital Affiliated to Fudan University in Shanghai to carry out a pilot study³ to investigate the effects of K56 on body fat and metabolism in adult human participants with obesity.

"Obesity is a pressing public health issue," Hung says. "It's our mission to verify probiotic strains that are safe with scalability potential for weight loss."

Yili is also investigating clinical applications beyond obesity. It has developed several new strains of probiotic bacteria — *Bifidobacterium animalis* subsp. *lactis* BL-99 and *Lactocaseibacillus paracasei* ET-22 — which could have potential applications in intestinal health and oral health areas.

Yili has obtained 20 authorized patents for probiotics, published 18 academic papers, and conducted 6 clinical studies involving a total of 1,000 participants. In 2022, it launched YILIFE® — a brand that focuses on research and applications of probiotics — to help consolidate and focus its efforts.

"Yili is looking to work with global partners to drive innovation," Hung says, "Based on consumer needs, we will provide health products and services for various population groups for their entire life. Our aim is to promote high-quality development of the global healthy food industry." ■

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