morinaga

HRB, a game-changing probiotics solution for healthy living

Morinaga Milk offers a range of natural, human-compatible, science-backed probiotic ingredients to support healthy living, from gut health to better immunity, healthy weight, and happy mood.

Let's discover more.

At a glance

What consumers want and why

Health-conscious consumers are interested in natural functional ingredients that possess extensive clinical efficacy to address fundamental health problems (e.g., digestion, obesity, allergies, immunity).

It is not only strain-specificity but also the residential origin of the probiotics that matter.

Changing the game with Morinaga Milk's HRB probiotics

Ever since the 1960s, Morinaga Milk has been researching Human-Residential Bifidobacteria (HRB), inspired by the fact that bifidobacteria are the predominant bacteria residing the intestines of breastfed infants. With more than 50 years of research on bifidobacteria, Morinaga Milk has developed four main HRB probiotic strains:

B. longum BB536, *B. breve* M-16V, *B. infantis* M-63, and *B. breve* B-3.

Morinaga Milk's HRB probiotics are strains of bifidobacteria of high compatibility with humans. They are clinically demonstrated to be beneficial for humans in various targeted health areas.

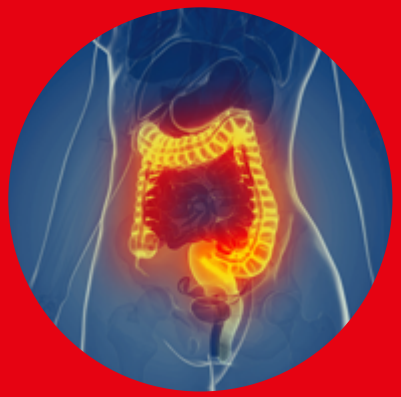
Product innovation with Morinaga Milk's HRB probiotics

Innovative applications help a probiotic product to stand out from the crowds. However, it is impossible to achieve with low stability profiles of a probiotic ingredient. Overage and cost-effectiveness are other issues to be resolved.

Morinaga Milk's HRB probiotics are the super-natural probiotic ingredients that can deliver your desired results and help you appeal to smarter consumers. They can be incorporated into a broad range of delivery formats.

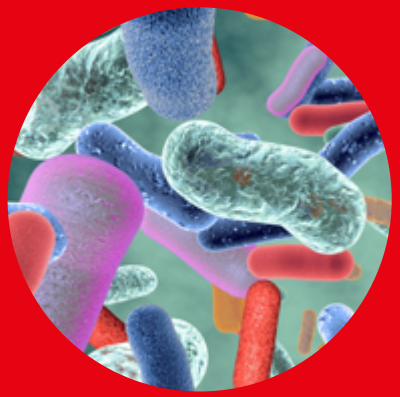
Living longer and living healthier?

People worldwide are living longer than ever before. A longer life provides us with opportunities to pursue our life goals and new activities. Nevertheless, how to stay healthy and age gracefully remain an open question. Modern lifestyles bring their perils. Over the last several decades, our diets have become unhealthy. Many of us live a poor lifestyle with high stress, physically inactive, poor sleep quality, and antibiotics use. These risk factors have resulted in an ever-increasing prevalence of chronic conditions and health problems, including obesity, diabetes, cancer, cardiovascular disease, inflammatory bowel disease, and mental disorders.



The number of inflammatory bowel disease (IBD) increased 84 percent, from 3.7 million in 1990 to 6.8 million in 2017.
(The Lancet Gastroenterology and Hepatology, 2019)

The prevalence of obesity has increased worldwide in the past ~50 years, reaching pandemic levels.
(WHO, 2019)



The prevalence of allergic diseases worldwide is rising dramatically in both developed and developing countries. Hundreds of millions of subjects worldwide suffer from rhinitis, and it is estimated that more than 300 million have asthma.
(WHO, 2019)

Unraveling the gut microbiome

The gut microbiome is a hot topic for everyone. There are trillions of microorganisms live inside our gastrointestinal tract, and these microbial companions play crucial roles in maintaining our health. They help maintain our gut health. They assist our immune system in developing and functioning well, and they very probably also have a role over certain diseases, like obesity, allergies, and mental disorders. Any disturbances in its composition and functionality may predispose some health disorders such as metabolic syndrome, colorectal cancer, obesity, diabetes, and allergies.

On a day-to-day basis, our diet and lifestyle are, without a doubt, influencing our microbial companions. How to maintain healthy gut microbiota is undoubtedly a key trend now. In this regard, supplementation of probiotics – live microbes that, when consumed in adequate amount, confer a health benefit on the host, has drawn a lot of attention. Among the common probiotic agents, bifidobacteria are one genus of these beneficial bacteria that you probably do not want to miss out on your product development.

Why do we need bifidobacteria?

Members of *Bifidobacterium* are among the first colonizers of the human gut and represent one of the most abundant genera in the healthy breast-fed infant gut [1]. The prevalence of bifidobacteria in the human gut is of substantial importance to human health across the lifespan. Bifidobacteria play essential roles in regulating intestinal, immunological, and metabolic systems. These include the production of short-chain fatty acids and vitamins, immune system development, and maintenance of gut homeostasis [2].

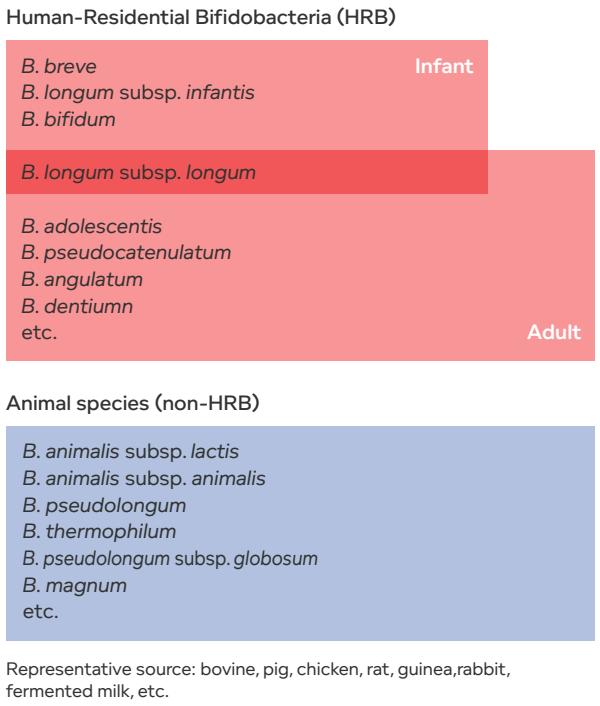
Unsurprisingly, the levels of bifidobacteria decrease in older adults and within several diseases. Given these facts, supplementation of the beneficial commensal bifidobacteria would help maintain intestinal homeostasis and immune balance, conferring beneficial effects on human health.

Are your probiotics "natural" ?

Recently a growing number of consumers scrutinize ingredients and additives present in the food and supplement products to ensure the product is safe before purchase. In response to this consumer's preference, nutrition and supplement manufacturers are developing so-called Clean Label products while food stores specializing in organic/wholesome foods are increasing. Like organic or "free-from" foods and supplements, products only with natural ingredients are preferred by health-conscious consumers, who see artificial ingredients as unhealthy or even harmful. This trend has spread among people who use food supplements or functional foods too. However, few people pay much attention to the origin of the ingredients when it comes to probiotics, presumably because they think probiotics are naturally occurring and not artificial. However, the truth is a bit more complicated than that, and arguably, not all probiotics are "natural" ingredients for human consumption. Here is the story.

The latest research studies show that bifidobacteria species can be split into two groups; those that naturally reside in the human intestines and those that are not. The former is called Human-Residential Bifidobacteria (HRB), while others who are the natural inhabitants of animal intestines, sewage, or foods are called non-HRB. HRB and non-HRB can have substantial differences in their genetic and physiological functions. They display variations in their ecological adaptation and functionality among species [3].

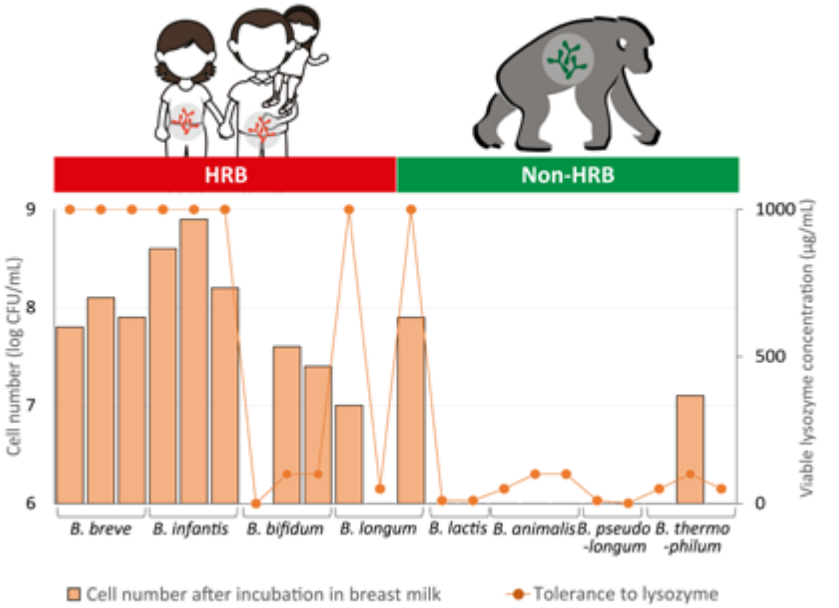
Among HRB, *B. breve*, *B. longum* subsp. *infantis*, *B. longum* subsp. *longum* and *B. bifidum*, the dominant species in the infant's intestines, are referred to as infant-type HRB [4], whereas *B. adolescentis*, *B. catenulatum*, *B. pseudocatenulatum*, *B. longum* subsp. *longum*, etc. The dominant species in the adult intestines are referred to as adult-type HRB. On the other hand, non-HRB species encompass *B. animalis* subsp. *animalis*, *B. animalis* subsp. *lactis*, *B. thermophilum*, *B. pseudolongum*, etc., among which, some species show a strict ecological adaptation to a particular animal gut [5].



Representative source: bovine, pig, chicken, rat, guinea,rabbit, fermented milk, etc.

No doubts.
The natural choice of mother's milk cannot be wrong.

Morinaga Milk's HRB:
Naturally selected
by human breast milk



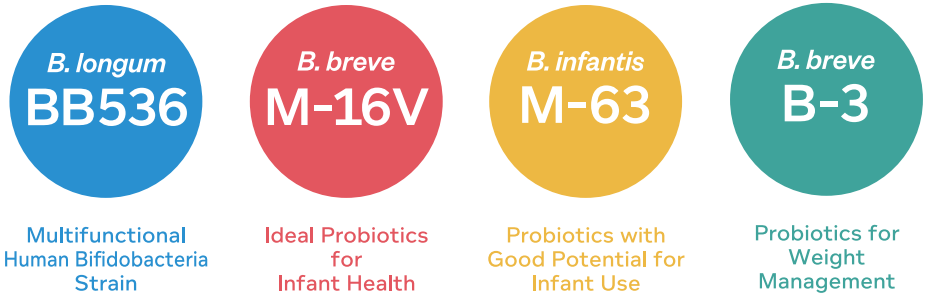
This graph was reproduced from Minami et al., 2016. Beneficial Microbes.

Accumulating evidence has found that only those HRB commonly found in the infant gut microbiome are compatible with human breast milk. These infant-type HRB strains can utilize human milk oligosaccharides (HMOs). They are also highly tolerant of lysozyme - a natural antibacterial factor found in human breast milk [6,7]. These characteristics allow HRB species to colonize the infant gut, contributing to lifelong health across the lifespan. The findings show that HRB species are natural and ideal for human consumption, and this concept of 'HRB species are suitable for human consumption' is Morinaga Milk's philosophy.

Now is the right time to change our conversation around probiotics bifidobacteria. In addition to strain-specificity, a bacterium's residential origin could also determine how it interacts with a human host and contributes to different health effects.

Better functionality. Better probiotics

Human strains for human use



HRB strains are naturally selected by human breast milk for a good reason. The research discovered that only HRB species are capable of certain physiological functions. One of them is the capability to produce folate – an essential vitamin for cell growth and metabolism that is particularly important for infants, children, pregnant women, and the silver population. Folate deficiency is associated with neural tube defects, megaloblastic anemia, and cardiovascular disease.

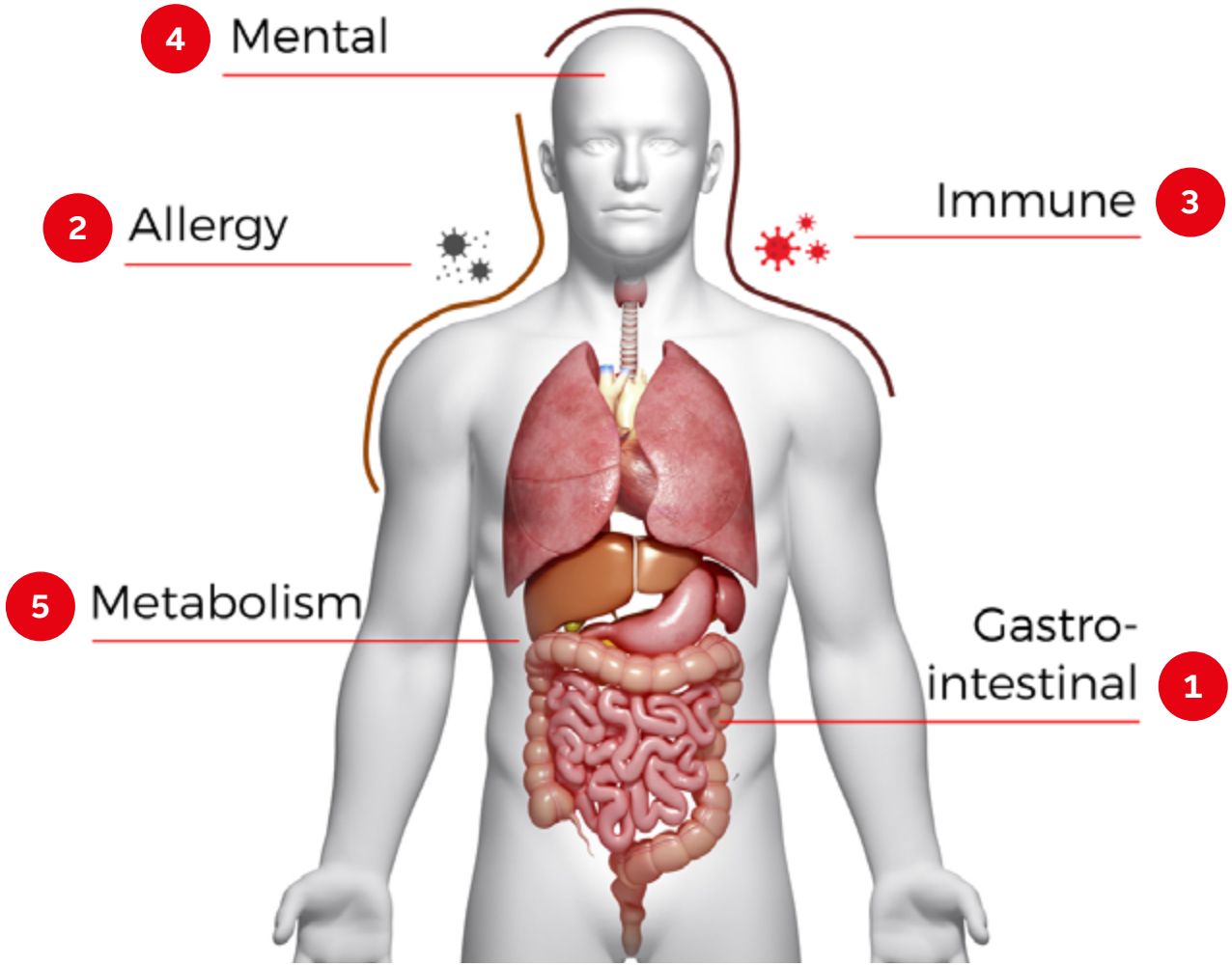
Unlike non-HRB, HRB strains (e.g., *B. longum* BB536) are exceptionally superior at producing folate and improving blood hemoglobin levels and mean corpuscular volumes [8]. Such function is crucial for the human host's well-being, as humans cannot make folate independently but must obtain it via intestinal absorption from exogenous sources, such as the diet and the gut microbiota. With that said, folate-producing HRB strains (e.g., *B. longum* BB536) could more efficiently confer protection against folate-deficiency related disorders.

Moreover, certain HRB species are particularly effective at eliminating the potentially harmful food-derived opioid peptides (e.g., human milk and bovine milk-derived β-casomorphin-7 and wheat gluten-derived α-gliadorphin-7) [9]. These partially digested peptides derived from food proteins are associated with many health complications in sensitive individuals, including sudden infant death syndrome, allergies, celiac disease, autism, and type I diabetes. Therefore, these HRB strains (e.g., *B. infantis* M-63) could more efficiently confer protection against potential health complications triggered by food-derived opioid peptides.

The latest research also discovered that certain strains of HRB have better functional capacity at producing indole-3-lactic acid (ILA) [10], a unique metabolite derived from tryptophan. ILA has been reported to involve in the regulation of the immune system and has an anti-inflammatory effect. More recently, we found that ILA could promote neuronal cell differentiation for healthy development [11]. Given these facts, ILA-producing HRB strains (e.g., *B. longum* BB536, *B. breve* M-16V, and *B. infantis* M-63) could confer better functional benefits to the human host.

Altogether, the scientific findings demonstrate that HRB species are ideal probiotics for consumption by humans at all ages, especially infants, and are more beneficial for promoting human health.

Morinaga Milk's HRB:
Your lifelong health partner



1 Gastrointestinal health

The gut microbiota is an essential determinant of intestinal homeostasis and health. Studies have shown that gut dysbiosis is associated with several diseases in humans, including gastrointestinal and metabolic disorders. Probiotics have historically been used to improve gastrointestinal health. However, not all probiotics are the same. What has been studied and shown with regards to a specific strain cannot be extrapolated to another.

Morinaga Milk's HRB strain *B. longum* BB536 has long been recognized as one of the most effective probiotic strains for improving gastrointestinal conditions. Mounting clinical evidence has shown that consumption of *B. longum* BB536 in various formats can alleviate the frequency of defecation and fecal characteristics in healthy adults with constipation [12].

B. longum BB536 has also been reported to modulate gut motility and normalize defecation frequency in hospitalized elderly patients aged >65 years receiving enteral tube feedings.

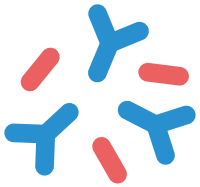
In two double-blind placebo-controlled human intervention studies, administration of *B. longum* BB536 (at both low and high doses of 2.5×10^{10} and 5×10^{10} CFU per day, respectively) for 16 weeks significantly improved the gut conditions of elderly patients as compared to placebo [13].

Another clinical study involving 32 healthy Japanese adults, who were the carriers of enterotoxigenic *Bacteroides fragilis* (ETBF), revealed a positive impact of *B. longum* BB536 on the intestinal environment [14]. ETBF has been suggested to be associated with acute and persistent diarrheal disease in patients with inflammatory bowel disease (IBD) and colorectal cancer development[15]. Ingestion of yogurt containing *B. longum* BB536 ($\geq10^8$ CFU/g, 160g per day) had a discernible effect on the cell numbers of ETBF in the gut microbiota of healthy adults. This finding indicates the ability of *B. longum* BB536 to eliminate the opportunistic ETBF pathogens in the gut microbiota and to condition the intestinal environment.

Enterotoxigenic *Bacteroides* fragilis (ETBF)

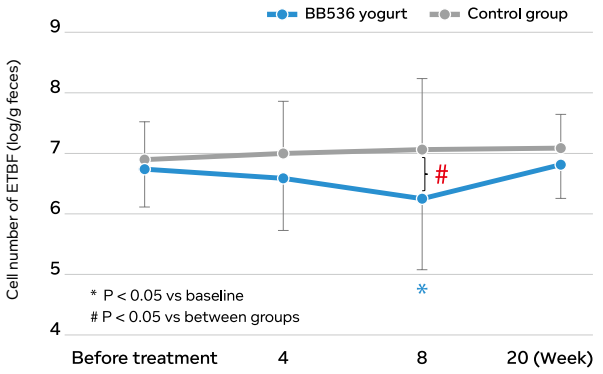
- Inflammatory Bowel Disease (IBD)
- Colorectal cancer

BB536 supplementation



- Eliminate ETBF
- Conditioning gut environment
- Maintain healty gut microbiota

BB536 significantly reduced ETBF numbers



This graph was reproduced from Odamaki et al., 2012. Anaerobe.

2 Anti-allergy

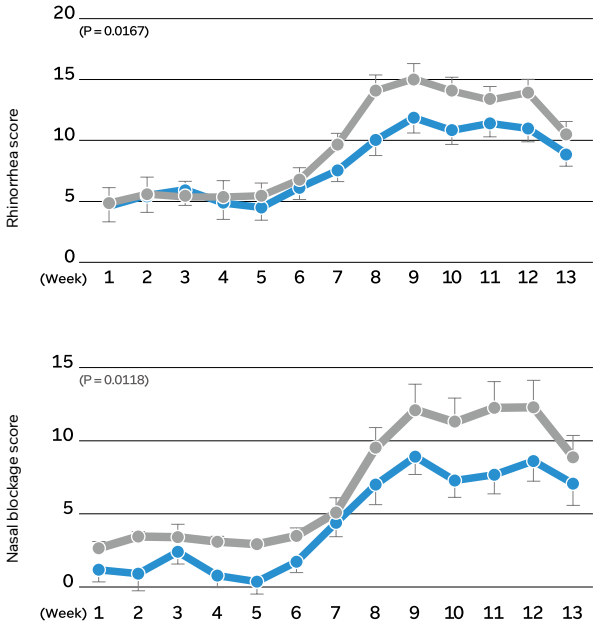
The prevalence of allergic diseases worldwide is rising dramatically in both developed and developing countries. Studies have demonstrated the beneficial effects of probiotics on allergies, but their efficacy depends on the strain used.

Morinaga Milk's HRB strains *B. longum* BB536, *B. breve* M-16V, and *B. infantis* M-63 have been extensively studied to alleviate allergic conditions in different target populations, including infants, children, and adults.

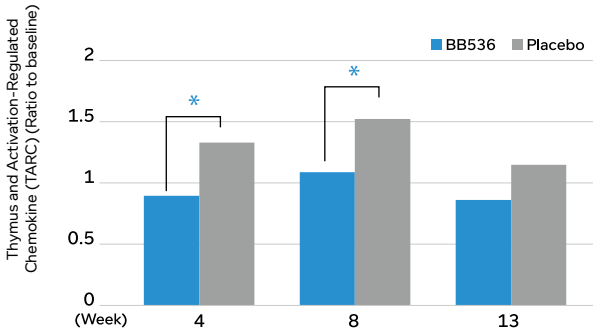
A remarkable RCT study involves 44 adults with allergic rhinitis induced by Japanese cedar pollen (i.e., Japanese cedar pollinosis) has exemplified the functional benefits of *B. longum* BB536 on alleviation of allergies. The subjects who received *B. longum* BB536 powder at a dose of 5×10^{10} CFU/2 g twice daily for 13 weeks during the pollen season in 2005, which was the most massive season within the past ten years, showed a significant improvement in all symptoms associated with Japanese cedar pollinosis when assessed on the medical score. They tended to have improved immune functions [16]. *B. longum* BB536 significantly rebalanced the T-helper type 2 (Th2)-skewed immune response that was occurred along with pollen dispersion.

Another RCT study involving 40 Italian children (4–17 years) treated with probiotics mixture containing three Morinaga Milk's HRB probiotic strains, *B. longum* BB536 (3×10^9 CFU), *B. infantis* M-63 (1×10^9 CFU), and *B. breve* M-16V (1×10^9 CFU), for eight weeks has also revealed a significant improvement in pollen-induced allergic rhinitis [17]. Administration of probiotic mixture protected the children against pollen-induced allergic reactions and improved their quality of life, for which these parameters were worsened in the placebo group.

Allergic symptom scores



Effect on Th2-skewed immune balance



This graph was reproduced from Xiao et al., 2006. Clinical and Experimental Allergy.

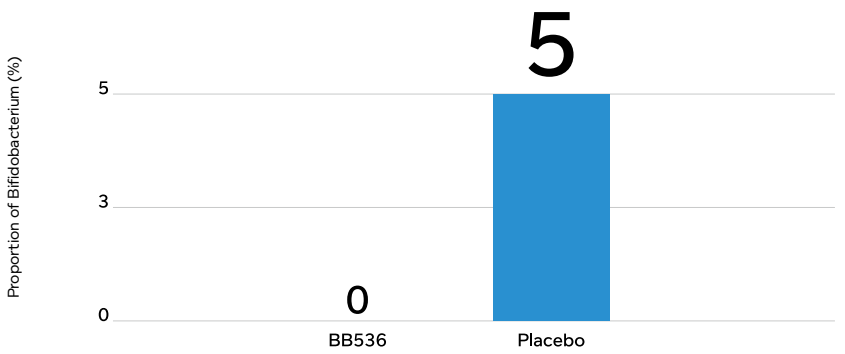
3 Immunity

Immunity is the primary mechanism of host defense against infectious agents. It functions to protect us from foreign invaders and the illnesses they cause. To function well, it requires balance and harmony. It is crucial to have an optimally functioning immune system for healthy living at every life stage.

Morinaga Milk's HRB probiotics strain *B. longum* BB536 could improve seniors' waning immunity and enhance their resistance to pathogenic viruses. Administration of *B. longum* BB536 to seniors with influenza vaccination (two weeks prior to vaccination and continued up to 14 weeks) was shown to potentiate the innate immunity where the natural killer (NK) cell activity and neutrophil activity were reduced in the placebo group, while they were maintained in the BB536 group [18]. As a result, the incidence of influenza virus infections is reduced in seniors supplemented with *B. longum* BB536.

In another clinical study, the ingestion of *B. longum* BB536 powder (5×10^9 CFU/day) in healthy pre-school children (aged 2-6 years) for ten months during the high-prone season of upper respiratory illnesses in Malaysia shortened the duration of clinical symptoms. *B. longum* BB536 shows promise in protecting children against the incidence of upper respiratory infections [19].

Number of subjects contracted influenza infection



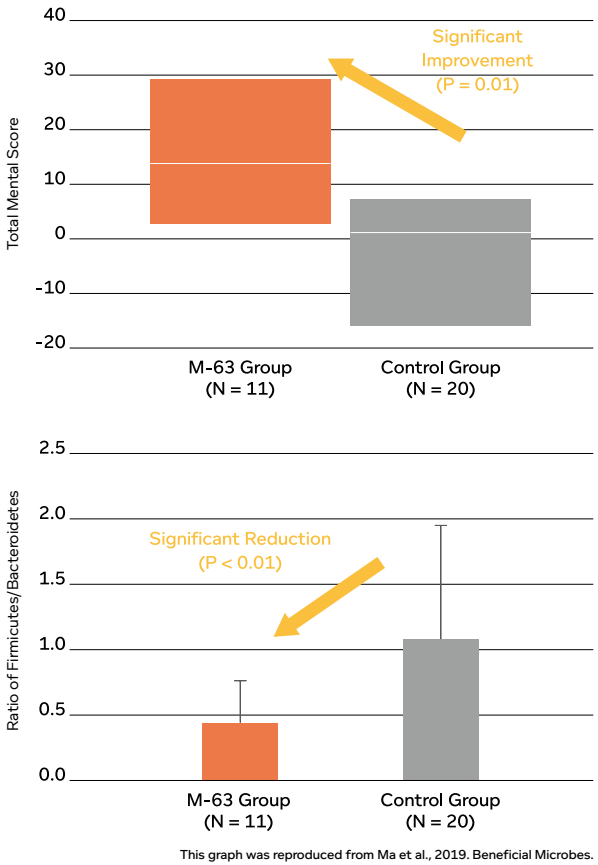
This graph was reproduced from Namba et al., 2010. Bioscience, Biotechnology and Biochemistry.

4 Mental health

Tapping into the booming fascination with the microbiome-gut-brain axis, Morinaga Milk's HRB strain *B. infantis* M-63 is clinically demonstrated to improve the mental state in adults with irritable bowel syndrome (IBS). It is unclear how mental health status (stress, anxiety, and depression) and IBS are related or which one comes first, but studies show they can happen together. The gut and brain are linked where the gut microbes could communicate with the brain and vice versa. The perturbation of this bidirectional communication system has been shown to exacerbate vulnerability to a range of health complications, including IBS and mood disorders.

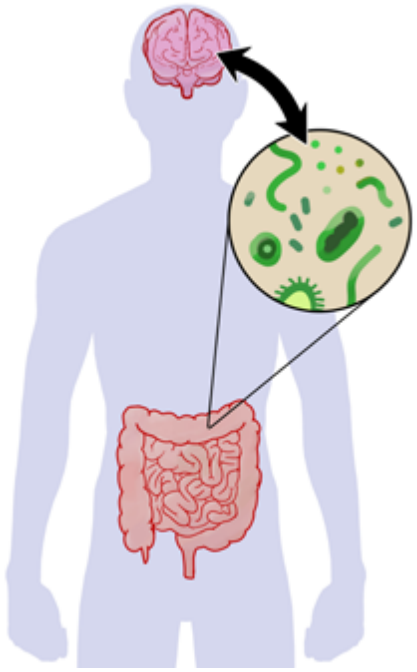
In a clinical study, individuals in a community who developed IBS after major floods were given *B. infantis* M-63 (1×10^9 CFU/sachet/day) for three months. As compared to the control, subjects who consumed *B. infantis* M-63 had significant improvement in their mental health scores and gut microbial balance [20]. The study implicates that *B. infantis* M-63 could help improve the mental health of adults with IBS condition.

Improvement of Mental State in Subjects with Irritable Bowel Syndrome



This graph was reproduced from Ma et al., 2019. Beneficial Microbes.

Microbiome gut brain axis

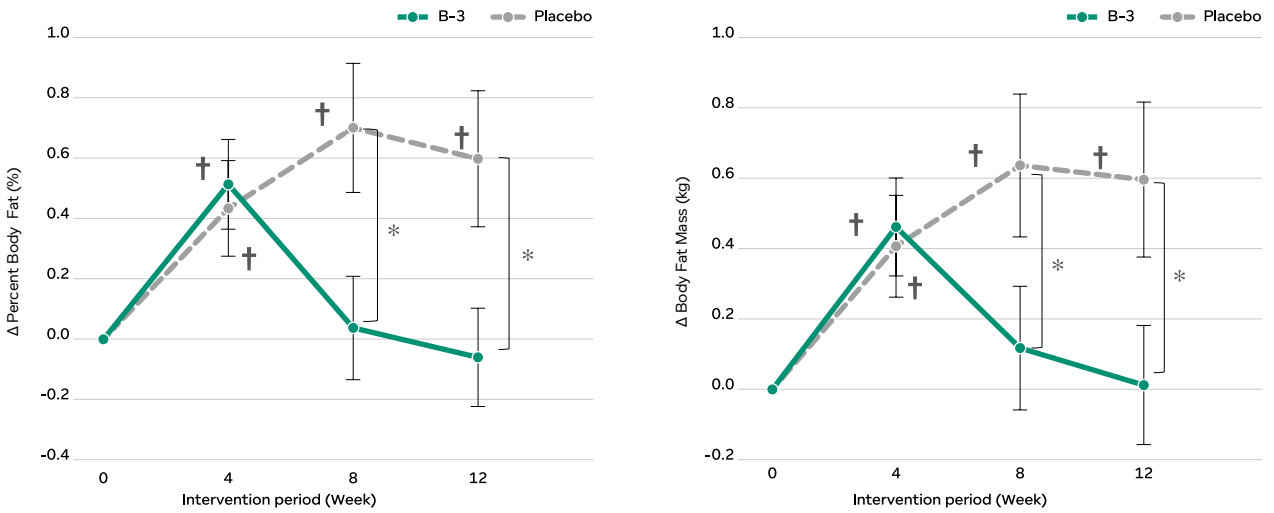


5 Metabolic health

In addition, the altered gut microbiota is associated with metabolic syndrome, occurring in most obese individuals. Gut microbiota may contribute to the establishment of metabolic diseases via the onset of chronic low-grade inflammatory processes. In this instance, Morinaga Milk's HRB probiotics strain *B. breve* B-3 has been shown to possess attractive beneficial effects in maintaining healthy body weight.

In an RCT study, healthy adults with BMI 25-30 kg/m² who taken *B. breve* B-3 (2×10^{10} CFU/day) for 12 weeks had a significant reduction in their body fat percentage and body fat mass as compared to the placebo [21]. Clinical findings and mechanistic studies reveal that *B. breve* B-3 potentially improves intestinal barrier function [22], preventing metabolic inflammation [23] and metabolic syndrome development [24].

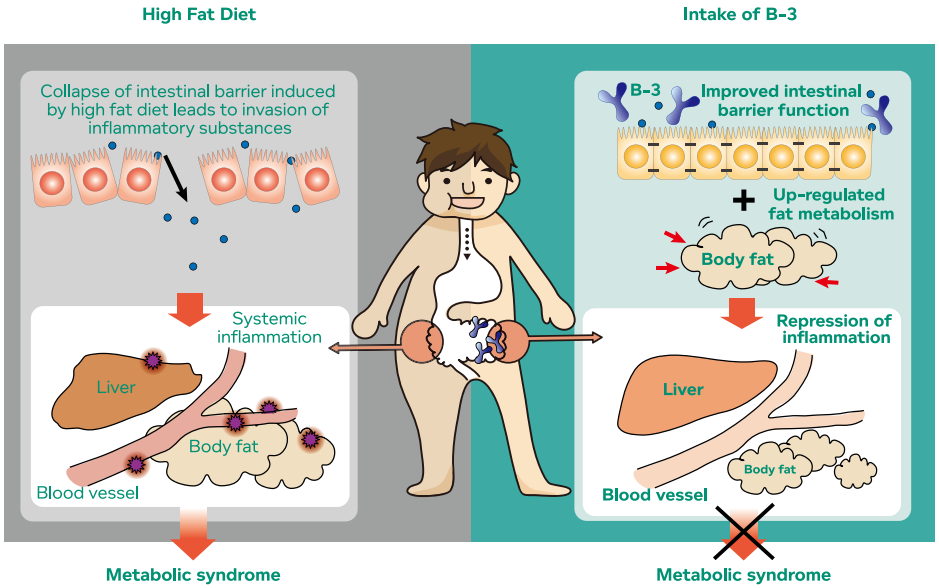
Administration of B-3 (20 billion CFU/day) reduced body fat in pre-obese adults.



Comparison between groups:
Covariance analysis adjusted with the value of 0 week, †P < 0.05 / Intragroup comparison: paired t test, * P < 0.05

This graph was reproduced from Minami et al., 2018. Bioscience of Microbiota, Food and Health .

Proposed Mechanism of Action of B-3



Changing the game of probiotics supplement

As explained above, HRB strains are unique and natural probiotics genuinely suitable for human consumption. When health-conscious consumers know of HRB and the market demand for such probiotics increases, it will almost definitely become a norm to choose HRB as probiotics for food and supplement products. Even the time might come when HRB probiotics drive Non-HRB strains out of the market in the future, and probiotics food and supplements with HRB is the standard product. Therefore, if you have a plan to develop a new product of food/supplement with probiotics right now, you might want to consider incorporating Morinaga Milk's HRB probiotics before your competitors develop such a product ahead of you.

Morinaga Milk's HRB probiotics are the super-natural probiotic ingredients that delivered your desired results with a rigor safety and efficacy profile. They possess excellent stability profiles with a long shelf life that made them attractive probiotic ingredients for innovative product development. Probiotics stability has been a hurdle in food and supplements product development where delivery forms and packaging are crucial. Innovative applications help a probiotic product to stand out from the crowds. Morinaga Milk's HRB probiotics can be incorporated into a wide range of delivery formats, including bulk powder, room-stable chewable tablets, sachets, sticks, oil drops, yogurt, formula milk, ice cream, chocolate, cereals, etc. and have excellent survival rate during the complete shelf life. With that said, cost efficiency can be achieved by adding lower overage.

Morinaga Milk's HRB probiotics also have a well-consolidated regulatory status that guarantees the strains have been manufactured according to the higher standards. The strains *B. longum* BB536 and *B. breve* M-16V have the FDA-notified GRAS status for general foods and infants use. *B. infantis* M-63 and *B. breve* B-3 acquire the self-affirmed GRAS status. These probiotic strains have also been clinically tested effectively, even combined with certain other probiotic strains, prebiotics, and lactoferrin.

Innovate with Morinaga Milk's HRB probiotics

Morinaga as your partner for NPD

Since the 1960s, Morinaga Milk Industry Co., Ltd. has been researching the safety, functional health benefits, and mechanisms of action of probiotic bifidobacteria to better understand their role in maintaining human health. With its unique HRB probiotic strains and practical knowledge on applications, Morinaga is ready to assist food companies with the new product development of a different type of foods, including dietary supplements, functional foods and infant nutrition.

Start your journey today by contacting us to find out how Morinaga's HRB probiotics can help you appeal to smarter consumers.

Contact

Morinaga Milk Industry Co., Ltd.
International Division

Chyn Boon Wong

chynboon020@morinagamilk.co.jp
+81 3-3798-0152

www.linkedin.com/company/morinaga-probiotics-center
www.morinagamilk.co.jp/english
www.bb536.jp/english/index.html

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