morinaga

# Human-Residential Bifidobacteria:

## A Probiotic Naturally Selected for the Human Body

Human-Residential Bifidobacteria™





# What is HRB?

HRB（Human-Residential Bifidobacteria）are bifidobacteria that coevolved with human, coexisted with human, naturally resides in human gut.
We are connected to HRB through our gut, and HRB are connected to our health — and our future.

**Three key takeaways from this white paper**

- Why HRB are “partners chosen by humans”.
- Human health and the science of HRB （breast milk-based selection, co-evolution, metabolites, and more）.
- How to use the HRB story for product development and marketing communication.

# Why HRB “now”?

Advances in medicine and technology have made it possible to treat many diseases. Precisely because of this, people’s interests are shifting toward “prevention before illness,” “maintaining health,” and “healthy aging.”

In this context, the microbiome has gained attention as a critical factor in health. With the advent of next-generation sequencing, research has accelerated, countless microorganisms have been identified, and the colonic microbiome is now considered a community of roughly 40–100 trillion microorganisms spanning hundreds of species. This is comparable to — or even exceeds — the number of human cells in the body（∼37 trillion）, and how these microbes influence human health has become a major focus.

Recent research is also expanding beyond microbial species and genes to include microbial metabolites. As a result, it is increasingly reported that gut microbes may be involved not only in general gut health, but also in cognition, immunity, skin health, and mental well-being.

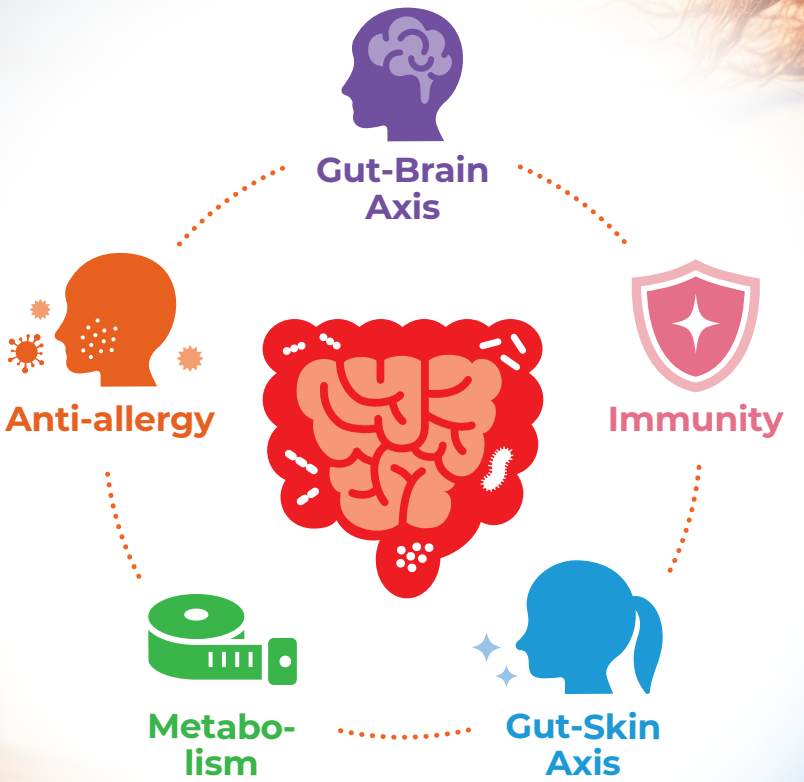
HRB（bifidobacteria present in the human gut）have likewise been reported to contribute to a wide range of health areas. However, HRB are fundamentally different from broadly used “probiotics” such as general bifidobacteria and lactic acid bacteria. HRB are partners that have accompanied us since the time of our ancestors, and they are deeply involved across life stages — infancy, adulthood, and old age — supporting our health through multiple HRB types. In this white paper, we introduce what HRB are, and the roles HRB play across the human lifespan.










Gut-Brain Axis
Immunity
Gut-Skin Axis
Metabo-lism
Anti-allergy

# Symbiosis with Microorganisms

Across nature, animals and plants have long used microorganisms that are useful for their own survival strategies. For example, plants and soil bacteria can form mutualistic symbioses: plants provide sugar, while microbes assist with nutrient uptake and growth.

Symbiosis is also seen in animals. It is said that gut microbes are involved in enabling koalas to eat eucalyptus leaves containing poison, and it is  widely known that gut microorganisms contribute to fiber breakdown and fermentation that help pandas digest bamboo.

In humans, the counterpart of these relationships is the colonic microbiome that includes HRB. Over a long history, humans have “selected” HRB as gut partners. This story is described concretely in the next section.



# HRB and Human Coexistence

We are connected to HRB through our gut, and HRB are connected to our health — and our future.

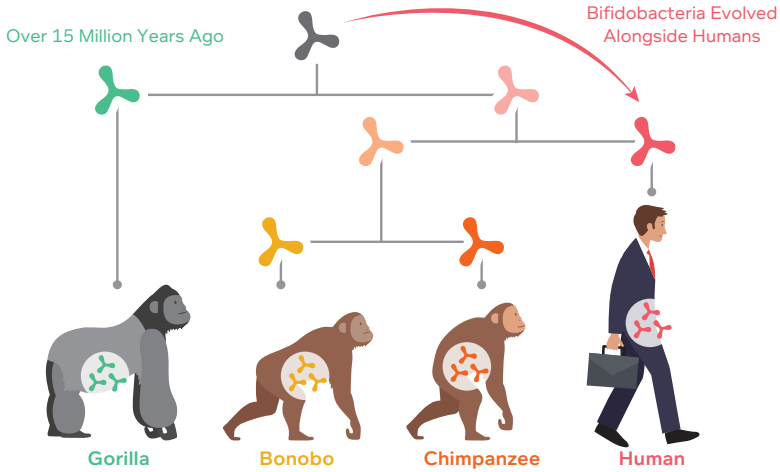
Bifidobacteria — including HRB and non-HRB — are currently classified into more than 100 species, and the species that inhabit the gut are thought to differ by host（e.g., primates, rodents, birds, insects）. This reflects long-term adaptation to distinct intestinal environments over time, leading to diversification.

Recent reports leveraging large-scale genetic information suggest that bifidobacteria（HRB）have co-evolved with humans since the era of hominoids around 15 million years ago, without being eliminated [1,2].

The key point here is that HRB are not simply “trendy microbes,” but organisms that have adapted to the human gut over a long time. Viewing HRB as “natural and reassuring partners for humans” provides a strong axis for both probiotic product concepts and communication.

## Investigating the Gut Flora of Great Apes：
## The History of Bifidobacteria in Humans

The fact that we have coevolved for 15 million years is evidence that individuals harboring Bifidobacterium have maintained an evolutionary advantage, suggesting that Bifidobacterium living in humans.




**Bifidobacteria Have Been Our Partners for Over 15 Million Years!**

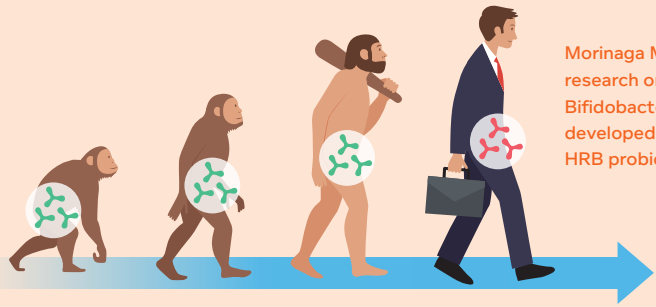
Moeller et al., *Science*. (2016) Segre and Salafsky, *Science*. (2016)

### Human-Residential Bifidobacteria（HRB）

***B. infantis, B. bereve, B. longum, B. bifidum,* etc.**

**non-Human-Residential Bifidobacteria（non-HRB）**

***B. animalis, B. lactis, B. pseudolongum, B. thermophilum, B. magnum,* etc.**



Morinaga Milk focuses its research on Human-Residential Bifidobacteria（HRB）and have developed a premium range of HRB probiotics strains.

# The Science of HRB

## 1 Selection by Breast Milk

One major difference observed in HRB genomes involves carbohydrate – metabolism – related genes. HRB that inhabit infants possess many genes associated with metabolizing human milk oligosaccharides（HMOs）found in breast milk.

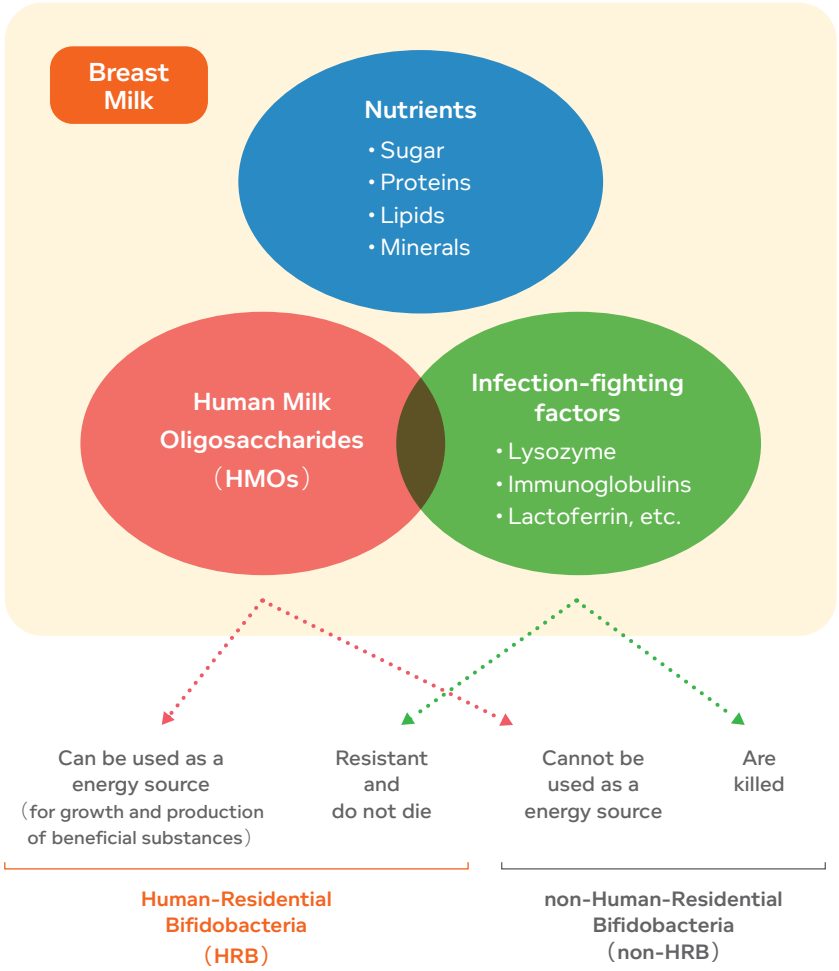
In growth studies conducted in breast milk, HRB（e.g., *B. longum* and *B. breve*）showed growth, whereas many non-HRB strains decreased below the detection limit [3].

Furthermore, regarding tolerance to antimicrobial components in breast milk（e.g., lysozyme）, HRB are reported to show high tolerance, while non-HRB lacked such tolerance [3,4,5].

In other words, humans are exposed to microbes immediately after birth and begin forming a gut microbiome, but for bifidobacteria to become members of the human microbiome, they must pass selection pressures imposed by breast milk. HRB can be considered “special” bifidobacteria that have passed this selection.



## The Relationship between Breast Milk and Bifidobacteria is an Example of Long-term Coevolution

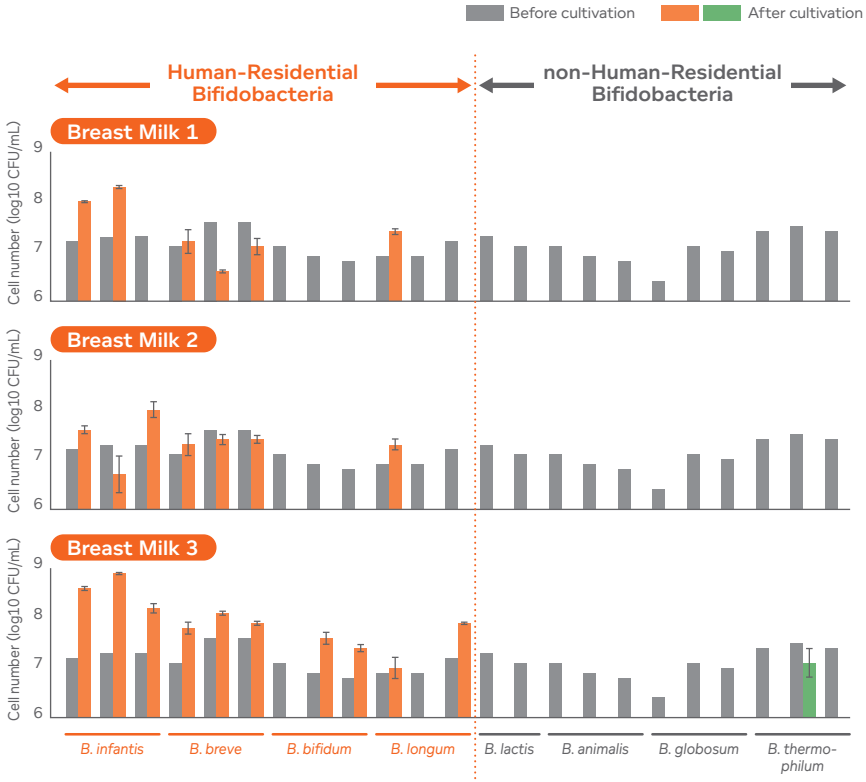



Wong et al., *J Hum Nutr Food Sci.* (2018)

## The Only Bacteria that can Thrive in Human Breast Milk are "Bifidobacteria Found in Infants."

**In vitro studies :**

Investigation of the growth potential of various *Bifidobacterium* strains in human breast milk




**The *Bifidobacterium* species natrually resident in infants and young children multiplied in breast milk.**

**The *Bifidobacterium* species not natrually resident in humans died off in breast milk.**

Minami et al., *Beneficial Microbes.* (2016)

## 2 Characteristics of HRB Metabolites （Acetic acid）

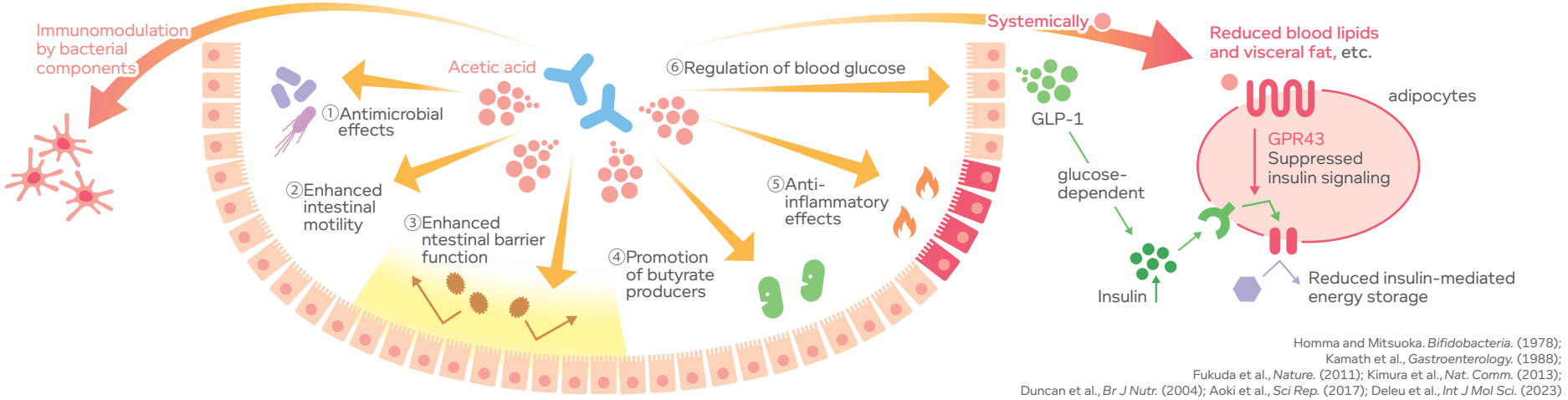
Next, let's take a closer look into HRB metabolites.

Acetic acid is widely known as a typical metabolite of bifidobacteria. The ability to produce acetic acid clearly differs from lactic acid bacteria and is an important hallmark of bifidobacteria. Because HRB are members of the genus *Bifidobacterium*, they also produce acetic acid.

Health-promoting functions reported for acetic acid produced in the colon include:

1. Suppression of harmful bacteria in the microbiome and suppression of putrefactive byproduct formation
2. Anti-inflammatory effects
3. Immune activation
4. Enhancement of intestinal barrier function
5. Serving as a substrate（"food"）for butyrate-producing bacteria
6. Blood glucose control via gut-hormone secretion and GLP-1（glucagon-like peptide-1）

### The Diverse Functions of Acetic Acid




Homma and Mitsuoka. *Bifidobacteria.* (1978);
Kamath et al., *Gastroenterology.* (1988);
Fukuda et al., *Nature.* (2011); Kimura et al., *Nat. Comm.* (2013);
Duncan et al., *Br J Nutr.* (2004); Aoki et al., *Sci Rep.* (2017); Deleu et al., *Int J Mol Sci.* (2023)

Bifidobacteria require nutrients to function effectively as probiotics.

Therefore, consuming HRB as probiotics — aligned with the human digestive and absorptive processes — can support concept development that is intuitive and convincing to consumers. HRB are special bifidobacteria that naturally exist in the human large intestine and have maintained a symbiotic relationship with humans by cleverly utilizing components that humans "did not absorb"（such as dietary fiber and sugars）to produce beneficial components for the host [6].



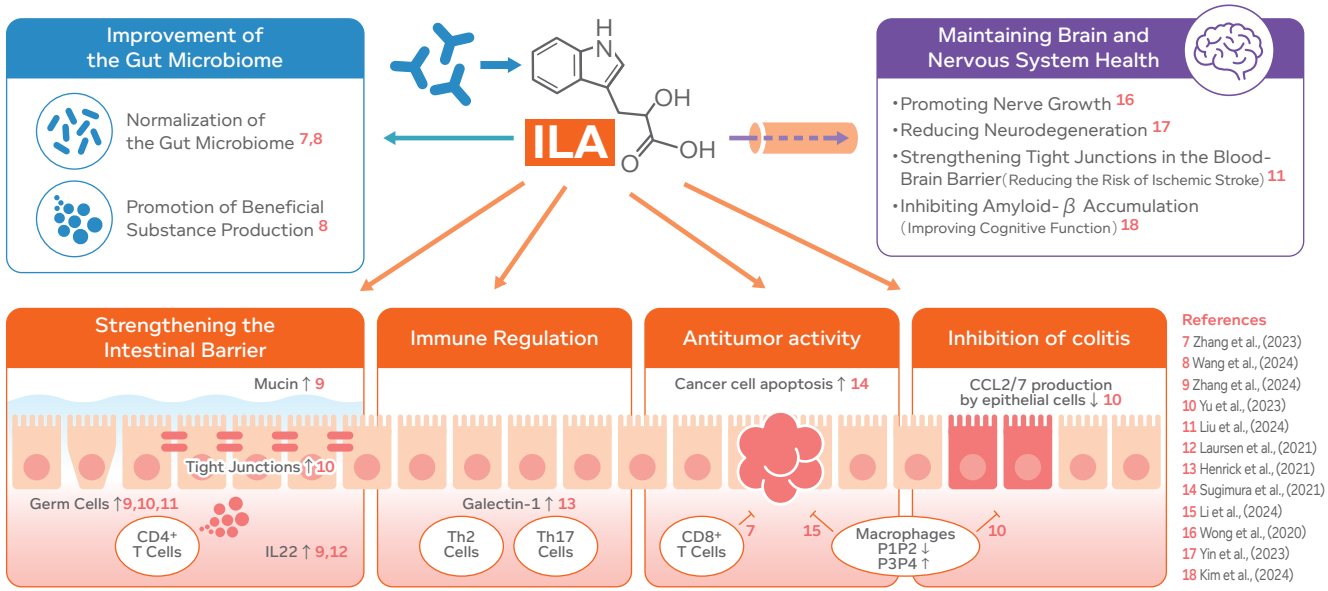
## 3 Characteristics of HRB Metabolites (ILA)

Recent studies have drawn attention to indole compounds produced by gut microbes as biologically active substances with antioxidant and anti-inflammatory activities. Indole-3-lactic acid (ILA), one such compound, has been reported to be produced at high levels by certain HRB.

ILA has been associated with multiple functions in research reports, including microbiota improvement [7,8], intestinal barrier reinforcement [9,10,11,12], immune modulation [13], anti-tumor effects [7,14,15], suppression of colitis [10], and maintenance of brain/neurological health [11,16,17,18].

### Bifidobacteria Highly Produce ILA

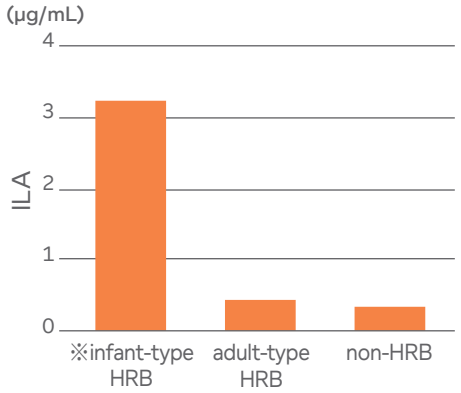
#### The Effects of ILA in Living Organisms





References
7 Zhang et al., (2023)
8 Wang et al., (2024)
9 Zhang et al., (2024)
10 Yu et al., (2023)
11 Liu et al., (2024)
12 Laursen et al., (2021)
13 Henrick et al., (2021)
14 Sugimura et al., (2021)
15 Li et al., (2024)
16 Wong et al., (2020)
17 Yin et al., (2023)
18 Kim et al., (2024)


#### ILA production by Bifidobacteria




This represents the average values of 10 infant-type strains, 4 adult-type strains, and 5 non-HRB strains, respectively.

※Infant-type HRB : *B. breve, B. bifidum, B. infantis, B. longum*

Sakurai et al., *Microorganisms.* (2019)

**Indole-3-lactic acid (ILA): Research suggests that tryptophan catabolic metabolites produced by the gut microbiota are important signaling molecules in the microbial community and play an important role in regulating host-microbe interactions as well as intestinal and systemic homeostasis.**

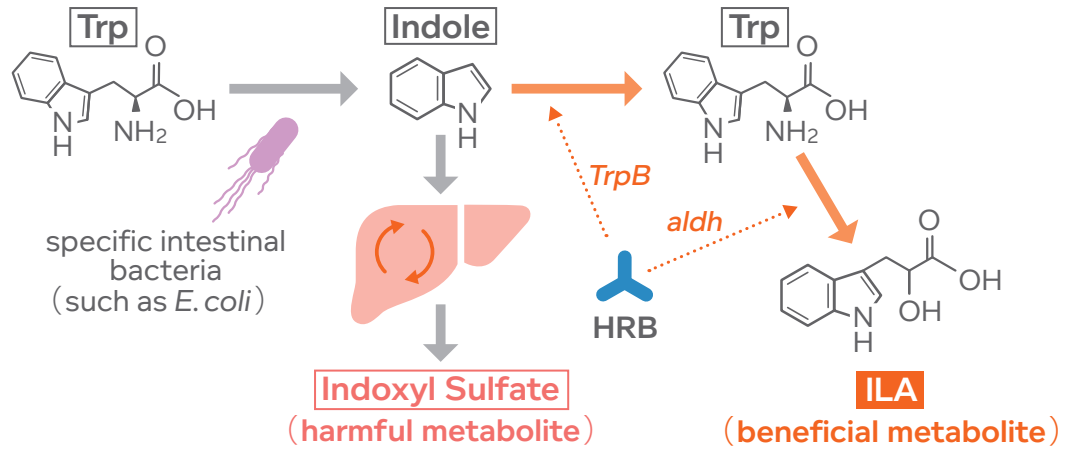
Beyond these functions, recent findings on HRB-related metabolic pathways are also noteworthy. Tryptophan that reaches the colon can be converted to indole by certain gut bacteria. Indole is further metabolized in the liver into indoxyl sulfate, a representative uremic toxin. Under normal kidney function, indole and related metabolites are excreted in urine; however, with reduced kidney function, they can accumulate in blood, and indole / indoxyl sulfate have been implicated in the progression of renal failure.

HRB are also expected to play an important role in this metabolic pathway. In vitro studies have shown that HRB possess two key genes involved in indole conversion and can metabolize indole and related intermediates into ILA, which is useful to humans. Furthermore, genomic analysis of 960 high-quality strains（11,943 strains）registered in the NCBI database revealed that only 95 strains possessed both the *trpB* and *aldh* genes, and all of these were HRB [19].

These observations may suggest that HRB help keep the colon “clean” while supporting host health, and could be a clue to understanding why humans and HRB have maintained a symbiotic relationship over evolutionary time.

We are confident that as HRB research continues to advance, the characteristics, roles, and metabolites of HRB will become clearer and HRB will gain even more attention as probiotics that support human health.

## HRB Convert Indole to ILA




**In vitro experiments suggested that HRB convert indole produced by *Escherichia coli* into tryptophan（Trp）and then into indole-3-lactic acid（ILA）.**

**HRB contain genes that convert indole, a precursor of uremic toxin, to beneficial ILA**

Yong et al., *Gut Microbes*. (2024)

## 4 Characteristics of HRB Metabolites（Folate）

HRB are reported to produce more folate when compared with non-HRB [20].

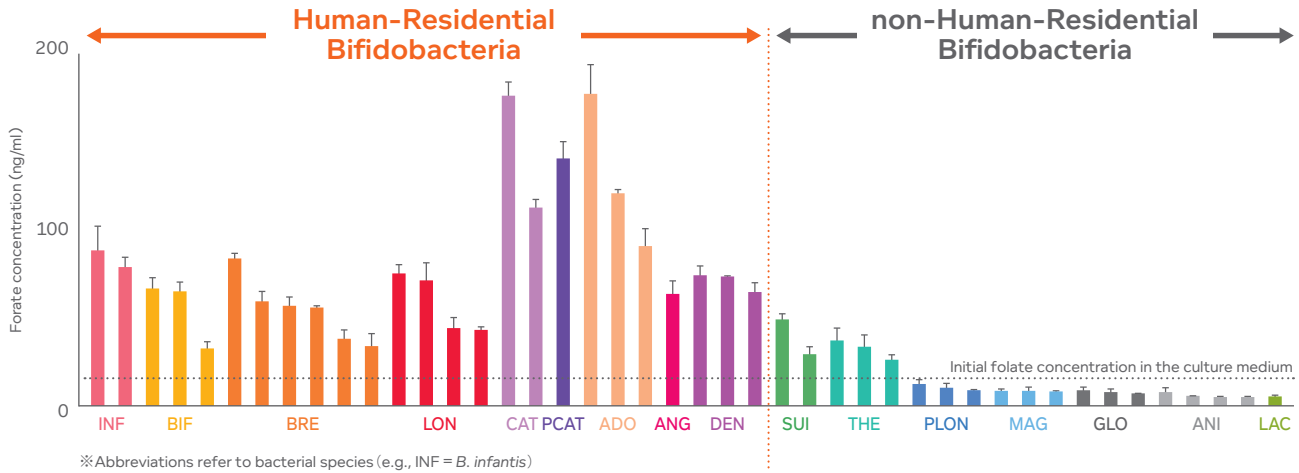
Folate is an essential vitamin for cellular growth and metabolism, and is particularly important for infants, children, pregnant women, and older adults. Folate deficiency is associated with neural tube defects, megaloblastic anemia, and cardiovascular diseases.

Because folate is primarily absorbed in the small intestine, one may question whether folate produced in the colon has meaningful effects. The following findings have been reported for colonic folate :

1. Folate can be absorbed in the human colon; in a clinical study, approximately 46% of colon-delivered folate was reported to be absorbed [21].
2. Folate in the colon has been reported to be involved in proliferation and maintenance of colonic epithelial cells and in maintaining DNA stability [22].

Because HRB act in the colon, the alignment between the site of production and the site of action is an important point.

### Differences in Vitamin B12（Folic Acid）Production




※Abbreviations refer to bacterial species (e.g., INF = *B. infantis*)

**In vitro studies :**

Measurement of folic acid concentration in the culture supernatant after anaerobic cultivation of each *Bifidobacterium* strain

※Folic acid is a water-soluble vitamin belonging to the B vitamin group. Together with vitamin B12, it plays a role in aiding the production of red blood cells.

**HRB found in humans produce higher amounts of folic acid**

Sugahara et al., *Biosci Microbiota Food Health*. (2015)

# “Microbial Relay”

A concept called the “microbial relay” can help communicate part of the complex functions of gut microbes in a way that is understandable to consumers and can also provide hints for product development.

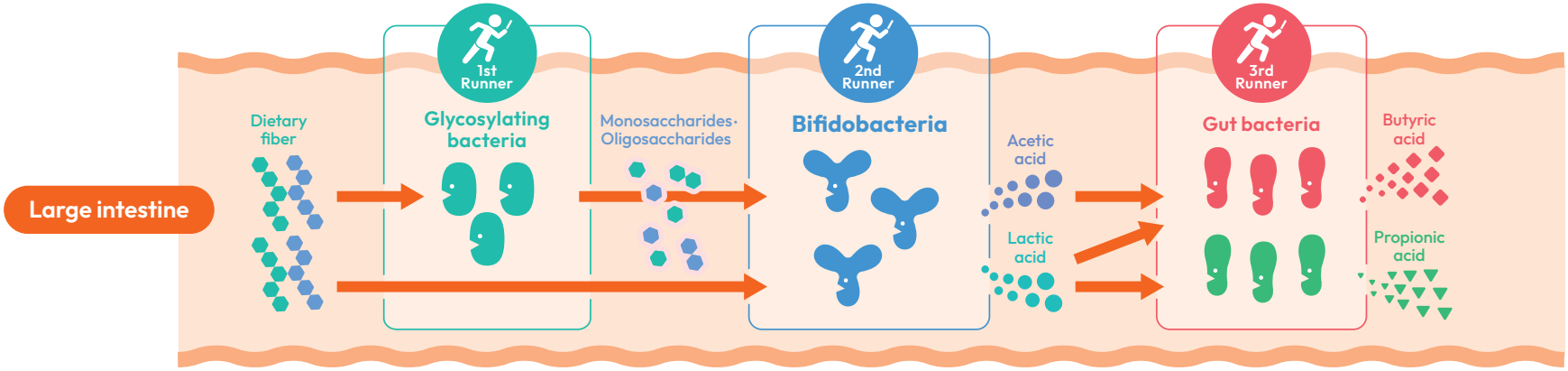
The “microbial relay” describes how gut microbes share work and pass fiber-derived metabolites like a baton:

- **First runner :** saccharifying microbes（e.g., *Bacillus subtilis* natto and koji molds）break down dietary fiber into sugars.
- **Second runner :** bifidobacteria and lactic acid bacteria use sugars to produce lactic acid（lactic acid bacteria＋bifidobacteria）and acetic acid（bifidobacteria）.
- **Third runner :** Propionate-producing bacteria utilize lactate to produce propionate and acetate, while butyrate-producing bacteria utilize acetate or lactate to produce butyrate.

The second runner plays a crucial role by passing the “baton”（metabolites）to the third runner. Therefore, in addition to consuming dietary fiber as a microbial substrate, it is important to take care of the second step.

HRB function in the second step, and some human-selected HRB（e.g., *B. longum* subsp. *longum*）also have the capability of taking up dietary fiber-derived components [6].

This framework helps consumers understand otherwise invisible microbial functions and strengthens the rationale for concepts such as “combining dietary fiber with HRB” or “coadministering HRB with butyrate-producing bacteria” in product development.



# Life Stages and HRB

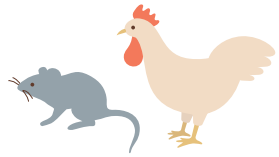
## 1 Life Stages and HRB（general）

HRB abundance in the gut is also known to change across life stages. As described in “Selection by breast milk,” the microbiome of newborn infants undergoes selection through breastfeeding. Actinomycetota（including HRB）are abundant during the pre-weaning period and decrease after weaning.

This is thought to reflect developmental and dietary changes that alter the nutrients reaching the colon, leading to shifts in the microbiome. During adulthood, changes are small, while in old age Actinomycetota including HRB tend to decrease [22,23].

### Species of Bifidobacteria and Their Habitats

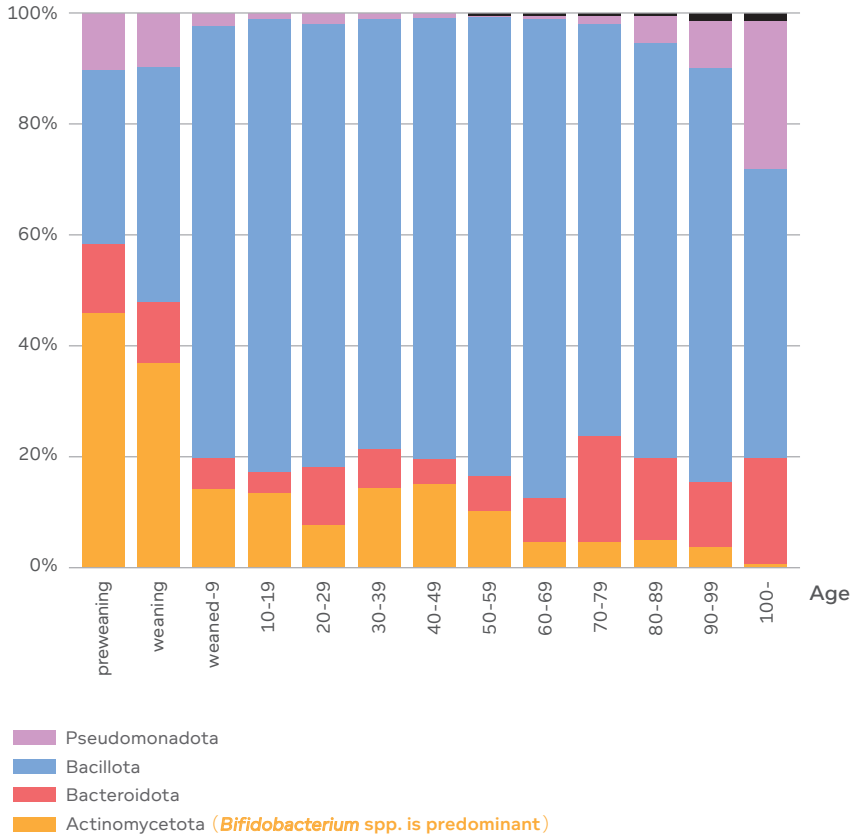
**Currently, more than 100 species of Bifidobacteria have been identified. ▶ They can be classified as follows based on their habitats**

| Human-Residential Bifidobacteria（HRB） | | non-Human-Residential Bifidobacteria（non-HRB） |
|---|---|---|
| Early life  | Adulthood  | Others  |
| *B. breve* | *B. adolescentis* | *B. animalis* |
| *B. longum* | | *B. lactis* |
| *B. bifidum* | *B. pseudocatenulatum* | *B. thermophilum* |
| *B. infantis* | *B. angulatum* | *B. magnum* |

# Bifidobacteria as Important Factor for Health

## A KEY MEMBER IN THE HUMAN GUT MICROBIOTA

Bifidobacteria are abundant in infants before weaning, then decrease with age and are linked to disease development across the lifespan [23,24].

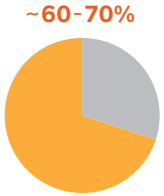



Odamaki et al., *BMC Microbiol.* (2016)

**Early life**

- NEC
- Allergies
- Infections
- Gut problems
- Obesity

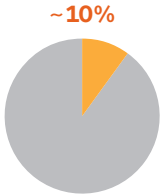





**Adulthood**

- Gut problems（e.g.IBS, IBD, etc.）
- Allergies
- Obesity
- Infections

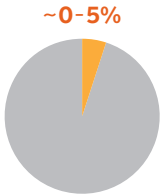





**Old age**

- Bowel problems
- Weaken immunity
- Infections
- Cognitive impairment
- Metabolic disorders






Bifidobacteria　Others

Arboleya et al., *Front Microbiol.* (2016)

## 2 Life Stages and HRB（infancy）

The high abundance of HRB in the infant gut is thought to have important implications — for example, in allergy risk.

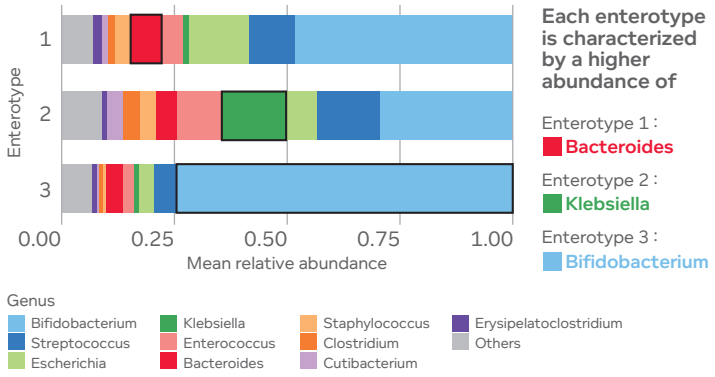
Data also suggest that the risk of developing food allergies is determined early in life. Food allergies typically occur when the immune system becomes sensitized to specific food proteins. Sensitization often begins before 7 months of age, and in Europe and the United States, 10–20% of children are already sensitized by 6 months. To prevent food sensitization, it is crucial to build a robust immune system during this early window. One study found that when *Bifidobacterium* was the predominant enterotype at 1 month of age, the incidence of egg white sensitization and future food allergies was significantly lower [29].

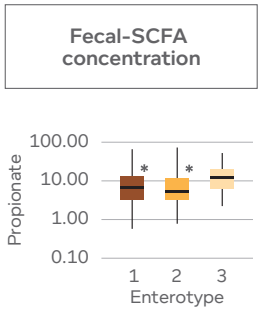
However, some studies comparing the gut microbiota of infants based on feeding methods have reported that infants breastfed have bifidobacteria as the dominant gut microbiota, while infants fed formula tend to have a significantly lower proportion of bifidobacteria [29].

Therefore, in premium infant formula design, there is growing attention on HMOs and HRB that can effectively utilize HMOs — such as *B. infantis* M-63.

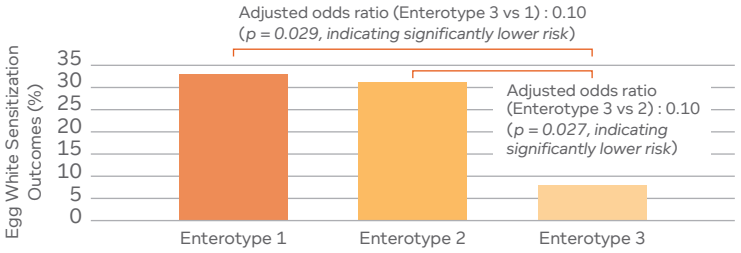
### Neonatal Gut Microbiota and Allergy

#### Characteristics of microbiota at 1 month age




#### Food sensitization development at 2 years old




When *Bifidobacterium* is the predominant enterotype at 1 month old, there is lower rates of egg white allergen sensitization and food allergies in the future.

Shibata et al., *J Allergy Clin Immunol*. (2025)

## 3 Life Stages and HRB（adulthood to older age）

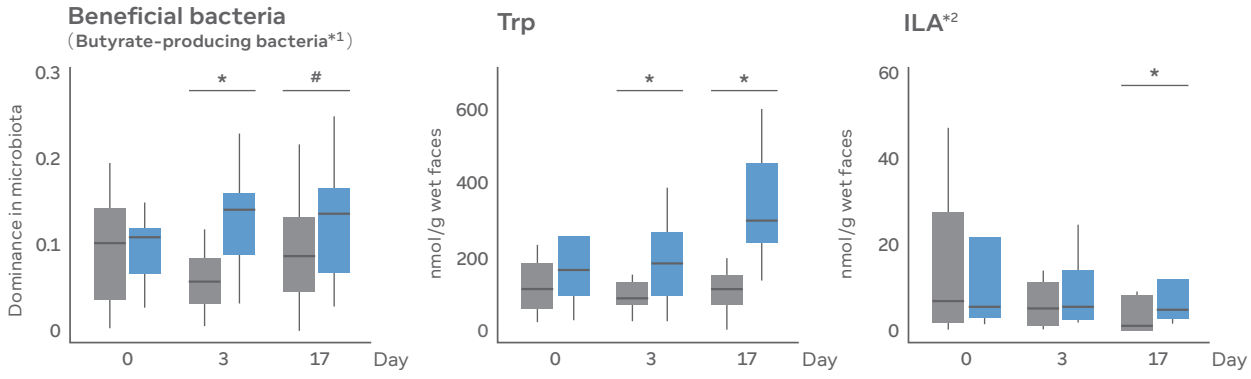
Across life stages, HRB species composition also changes from infancy to adulthood. For example, *B. breve* and *B. infantis* are infant-associated HRB, whereas *B. longum* is detected across a wide range of ages, including both infants and adults.

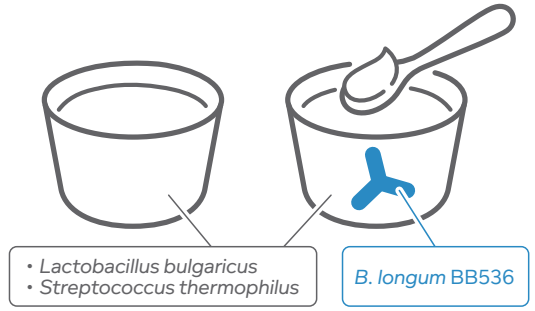
This may reflect differences in HRB characteristics and roles.

For instance, *B. longum* BB536 — a longum strain detected across many generations — has been reported to have strong bowelregulating effect [25,26,27] and interactions with other gut microbes [27], suggesting broad adaptability to the human gut.

### Impact of *B. longum* BB536 on the Gut Environment

Study design：Double-blinded RCT study
Subjects：34 of healthy adults
Duration：17 days
Test food：Placebo yogurt or Yogurt with BB536, 100g/day（= **BB536 2 billion** CFU/day）




Ejima et al., *Nutrients*. (2024)

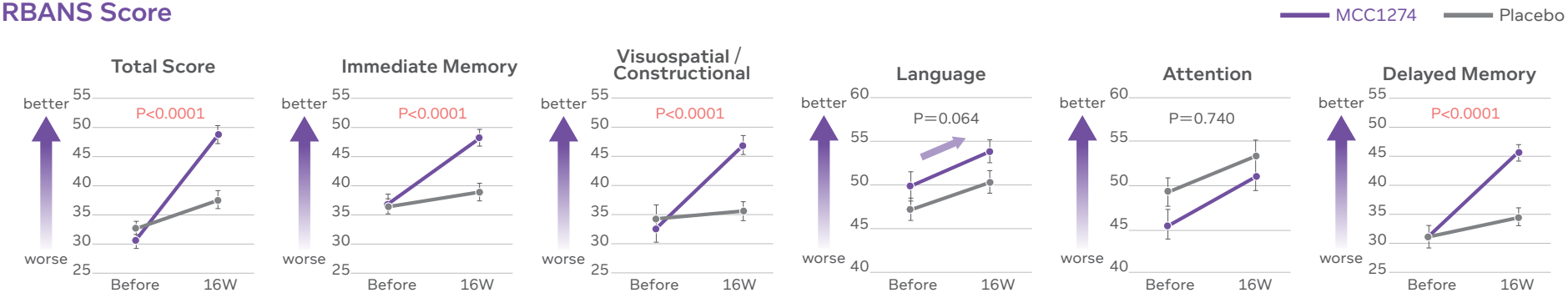
**Consumption of yogurt containing BB536 increased butyrate-producing bacteria in the gut and Trp and Trp metabolites in stool.**
**▶BB536 intake has a beneficial effect on regulating the intestinal environment.**

Meanwhile, *B. breve* MCC1274, an infant-associated HRB species, showed improvements in cognitive function scores in a study involving individuals suspected of MCI aged 50 to under 80 [28]. The story that a special “infant-type” HRB may help protect health in later life could capture strong interest among people concerned about aging.

## Improving Memory Function by MCC1274

Study design：RCT Study
Subjects：More than MMSE 22 points and suspected of MCI（Age 50 to 80, 80 people）
Dosage：Capsule with ***B. breve* MCC1274 20 billion CFU/day** vs Placebo capsule, 16 weeks

### RBANS Score




Xiao et al., *J Alzheimers Dis.* (2020)

**For those suspected of mild cognitive impairment（MCI）,**
**significant improvement of the cognitive function score by MCC1274 was observed**

# Convey a Message with HRB Logo

The HRB logo was developed by Morinaga Milk Industry Co., Ltd. to express the idea that “Humans are connected to HRB through the  intestines — and HRB are also connected to people’s health and future.”

The orange color abstractly represents how HRB can brighten and support people’s health and future.

Across a variety of touchpoints where Morinaga Milk Industry Co., Ltd.’s HRB strains are used, the HRB logo helps communicate the value and story of HRB to consumers.

For example, a consumer may notice this logo on a product package or website and think, “Is this different from ordinary bifidobacteria?” That curiosity can lead them to your brand’s product website, where they can discover the HRB story and value, feel empathy for the concept, and become a fan of your product. This is the kind of world the HRB logo is designed to enable.




## Benefits of the HRB Logo

For product development teams :
It helps express the HRB story and philosophy, and can be leveraged in consumer communication.

For consumers :
It provides an opportunity to learn about a deeper relationship between humans and the microbiome — beyond general probiotics — and to choose an option that feels more natural and reassuring for humans.

# Related White Paper Highlight

For deeper insights into HRB strains — including detailed functions and scientific evidence — please explore our white paper library at : https://morinagamilk-ingredients.com/resources/




Brain Health




Metabolic Health



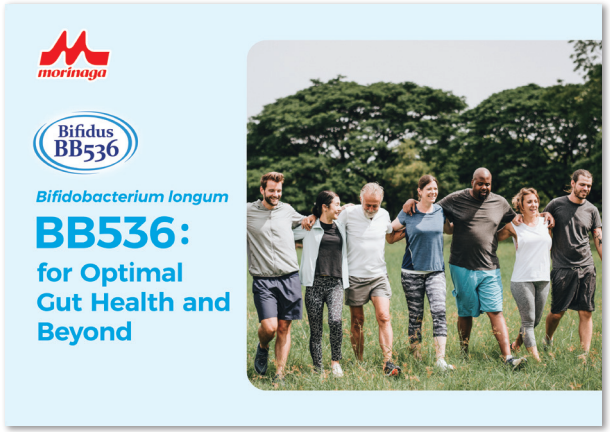

Gut Health




Cognitive Health and Healthy Aging




Metabolic Health and Healthy Aging




Gut Health and Beyond

# Morinaga Milk as your partner for NPD

With its unique postbiotic and practical knowledge of applications, Morinaga Milk is ready to assist partner food companies with the new product development of different types of foods, including dietary supplements, functional foods, and functional beverages.

Start your journey today by contacting us of find out how Morinaga Milk's Probiotics and Postbiotics ingredients, can help you appeal to smarter consumers.

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