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A Study of Human Immune Cell Responsiveness, One of the Factors Associated with Aging

Bifidobacteria May Help Suppress Excessive Inflammatory Responses

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For more than 50 years, Morinaga Milk has conducted a broad range of research—from basic to applied—on the diverse health benefits of Human-Residential Bifidobacteria (HRB),[*1] the bifidobacteria that reside in the human gut. In this study, we gained new insight into how gut bifidobacteria may help regulate inflammatory responses. The findings were published in the international journal *iScience* on June 30, 2026.

This study's findings can be summarized in two key points:

- People with a higher abundance of bifidobacteria in the gut tend to have immune cells that are less likely to show excessive inflammatory responses (Figure 1, left).
- Immune cells that have been exposed to bifidobacteria-derived components are less likely to show excessive responses to subsequent inflammatory stimuli (Figure 1, right).

Together, these results suggest that gut bifidobacteria may influence the inflammatory responsiveness of human immune cells and may help regulate excessive inflammatory responses. Recent studies have reported that persistent low-grade inflammation, often referred to as chronic inflammation,[*2] is associated with aging and may contribute to a range of diseases. These findings suggest that bifidobacteria may help maintain a balanced inflammatory response and, in turn, support the maintenance of health.

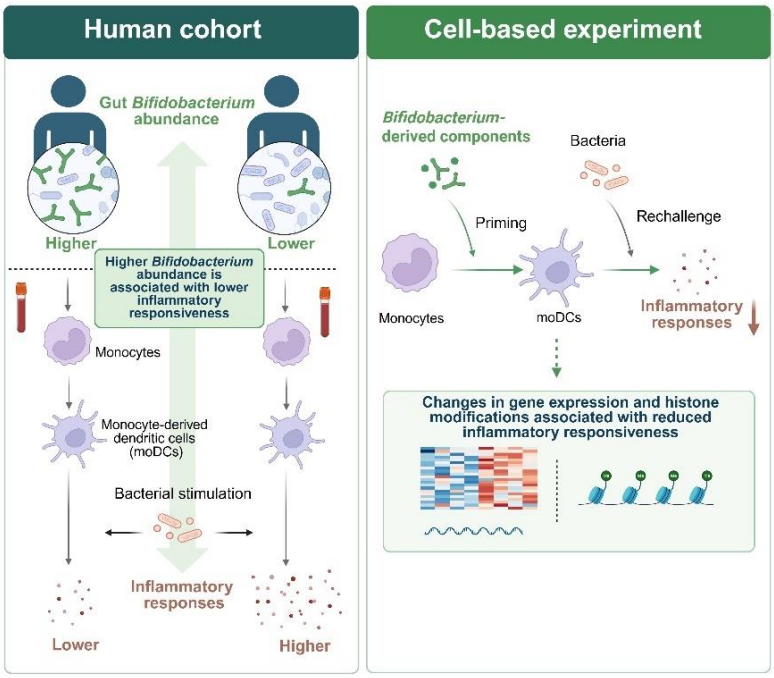

Figure 1. Conceptual overview of the study

1. Research Background

As part of the body's normal defense system, immune cells respond not only to pathogens but also to components derived from a wide range of bacteria, including beneficial bacteria such as bifidobacteria. These responses can lead to the production of substances involved in inflammation. However, when inflammatory responses become excessive or persist over time, they may have negative effects on health. The strength of these responses varies from person to person. In addition to individual factors such as age and individual biological differences, environmental factors, including diet and the gut microbiota, may also play a role. In particular, growing evidence suggests that the gut microbiota may influence immune cells beyond the gut and help shape how they respond to stimuli. However, it has remained unclear which gut bacteria are associated with differences in the inflammatory responsiveness of human immune cells and what mechanisms may underlie these associations.

Bifidobacteria are beneficial bacteria commonly found in the human gut. Previous research suggests that they may help maintain immune balance and modulate inflammatory responses. In this study, we examined the relationship between the gut microbiota and the inflammatory responsiveness of immune cells in healthy adults. We also investigated whether components derived from bifidobacteria could alter the subsequent inflammatory responsiveness of human immune cells.

2. Research Results

(1) Higher gut bifidobacterial abundance was associated with lower inflammatory responsiveness in immune cells

We collected blood samples from 50 healthy adults and generated monocyte-derived dendritic cells (moDCs)[*3] from blood monocytes. These cells produce inflammation-related substances in response to bacterial stimuli and are used to study the inflammatory responsiveness of immune cells. We then stimulated the moDCs with either *B. longum* or *L. paracasei* and examined whether differences in the cells' responses among participants were associated with differences in their gut microbiota.[*4] Among the gut bacteria examined, the relative abundance of bifidobacteria was associated with the inflammatory responsiveness of the moDCs. Participants with a higher relative abundance of bifidobacteria in the gut tended to have moDCs that produced lower levels of IL-6, IL-8, and other inflammation-related substances, suggesting lower inflammatory responsiveness (Figure 2; Figure 1, left).

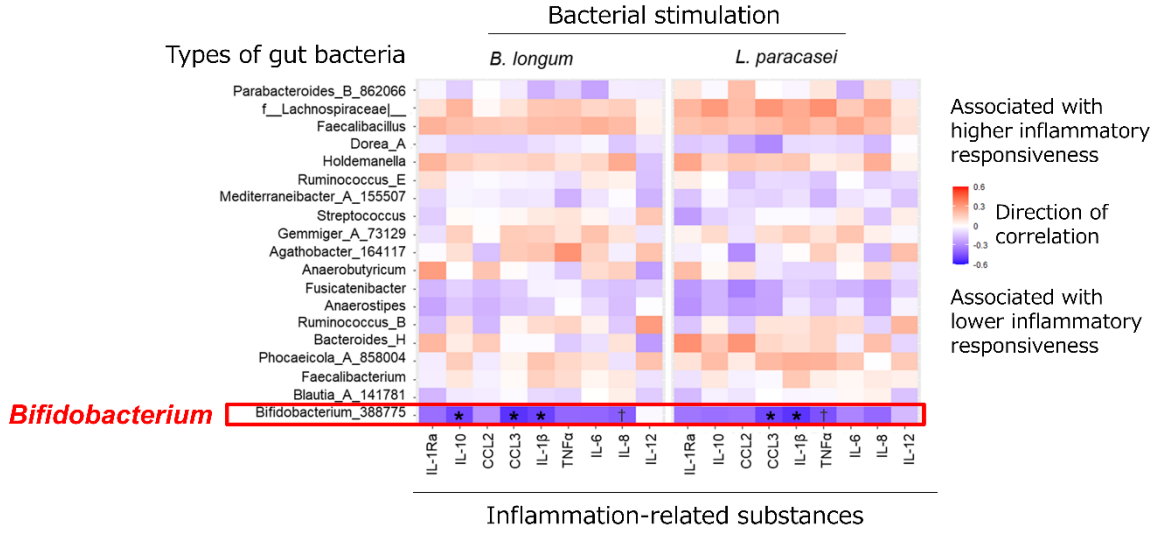

Figure 2. Association between gut bacteria and inflammatory responsiveness

Figure 2 uses color to show the associations between the 19 types of gut bacteria listed on the vertical axis and the inflammatory responsiveness of moDCs. The analysis included gut bacteria with an average relative abundance of 1% or more across the 50 participants. Purple indicates that people with a higher abundance of a given gut bacterium tended to show lower inflammatory responsiveness, while red indicates a tendency toward higher inflammatory responsiveness. An asterisk indicates a statistically significant association (*$p < 0.05$).

(2) Bifidobacteria-derived components may affect gene-regulatory mechanisms and help regulate excessive inflammatory responses

Next, we used cell-based experiments to examine whether components derived from bifidobacteria could alter the inflammatory responsiveness of moDCs. Previous exposure to certain stimuli can change how strongly immune cells, including moDCs, respond to later inflammatory stimuli. Such changes in responsiveness are thought to help maintain a balanced inflammatory response and may help prevent excessive inflammation from persisting. We therefore examined whether prior exposure to bifidobacteria-derived components could influence this balance.

The moDCs that had previously been exposed to bifidobacteria-derived components produced lower levels of inflammation-related substances than control cells that had not been exposed to these components, even when subsequently stimulated with Gram-positive or Gram-negative bacteria[*5] (Figure 3; Figure 1, right). Further analysis also identified changes in histone modifications,[*6] which are involved in regulating gene activity.

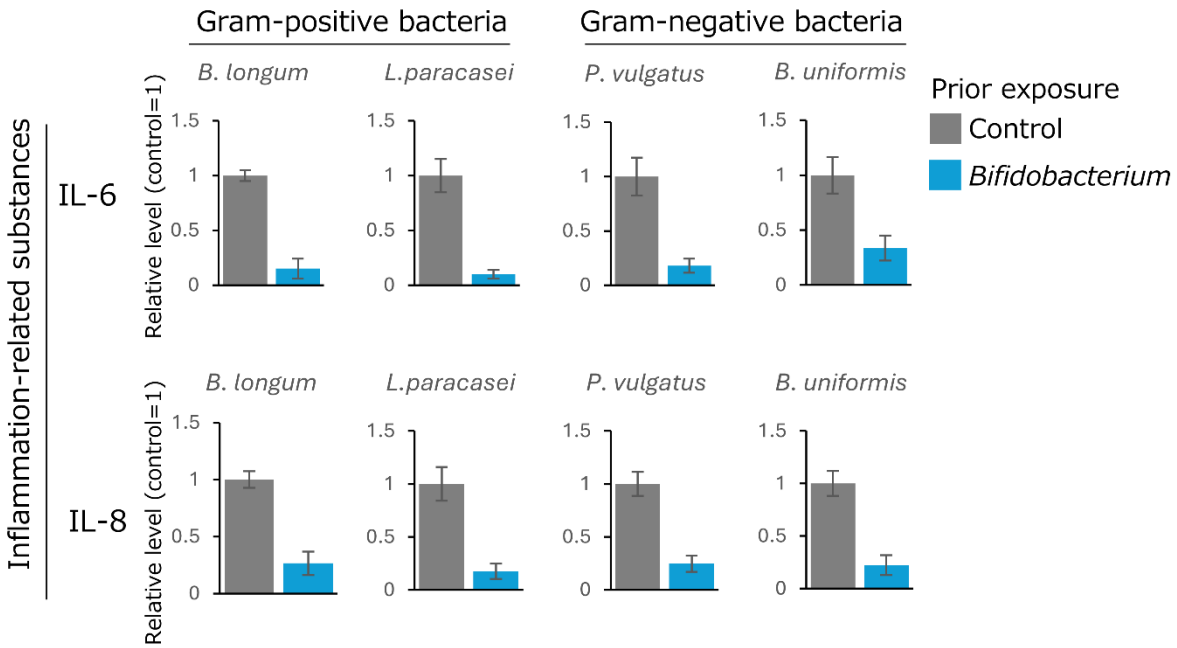

Figure 3. Changes in the inflammatory responses of immune cells following prior exposure to bifidobacteria-derived components (adapted from a figure in the paper)

3. Summary and Future Outlook

Bifidobacteria are known to have a variety of health benefits that originate in the gut.[*7] The findings of this study suggest that gut bifidobacteria may influence the inflammatory responsiveness of immune cells and help regulate excessive inflammatory responses. Morinaga Milk has also previously reported that combining the consumption

of plain yogurt containing *Bifidobacterium longum* BB536 with improvements in diet and exercise habits may slow the pace of biological aging.[*8]

Aging is influenced by many factors, including chronic inflammation. We believe that the present findings provide an important foundation for further understanding how bifidobacteria may contribute to maintaining human health, including their potential role in modulating inflammatory responses linked to aging. Morinaga Milk will continue to investigate how bifidobacteria influence inflammatory responses and pursue research and development aimed at future product applications that support human health.

Reference information

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

More than 100 species of bifidobacteria have been identified to date. The species commonly found in the human gut generally differ from those found in other animals. Morinaga Milk focuses its research and development on bifidobacteria that naturally reside in the human gut and refers to species that characteristically inhabit the human intestinal tract as "Human-Residential Bifidobacteria" (HRB). Evidence suggests that these bifidobacteria have coevolved with human ancestors for more than 15 million years. We believe that this long history of coevolution highlights the important role that HRB may play in human health.

***2 Chronic inflammation**

Inflammation is a necessary response that helps protect the body from injury and infection. When low-grade inflammation persists over a long period, it is known as chronic inflammation. Chronic inflammation may cause few noticeable symptoms, but it tends to become more common with age and has been linked to various age-related changes in the body and health concerns.

***3 Monocyte-derived dendritic cells (moDCs)**

Monocyte-derived dendritic cells are dendritic-cell-like immune cells generated by culturing blood monocytes under specific conditions. Because they produce inflammation-related substances in response to stimuli such as bacteria, they are used to study the inflammatory responsiveness of immune cells. In this study, monocytes isolated from the blood of healthy adults were differentiated into monocyte-derived dendritic cells, and their inflammatory responses to bacterial stimulation were evaluated.

***4 Association between the inflammatory responsiveness of immune cells and the gut microbiota**

Spearman's rank correlation analysis was performed to examine whether the inflammatory responses of immune cells were associated with the relative abundance of different gut bacteria. This statistical method shows the strength and direction of an association based on the rank order of two variables. Values closer to +1 indicate a stronger tendency for the two variables to change in the same direction, while values closer to −1 indicate a stronger tendency for them to change in opposite directions. Values closer to 0 indicate little or no clear association.

***5 Gram-positive and Gram-negative bacteria**

Based on differences in cell-surface structure, bacteria are broadly divided into two main types: Gram-positive and Gram-negative bacteria. Gram-positive bacteria have a thick cell wall, whereas Gram-negative bacteria have an outer membrane containing LPS (lipopolysaccharide). Both types can stimulate immune cells and trigger the production of inflammation-related substances.

***6 Histone modification**

Histones are proteins around which DNA is wound, and they help regulate how genes work. The attachment of chemical marks to histones is called histone modification. Depending on the pattern of these modifications, genes can become more or less likely to be expressed. This study suggested that bifidobacteria-derived components may affect histone modifications in immune cells and influence the activity of genes involved in inflammatory responses.

***7 Health effects of bifidobacteria**

Bifidobacteria are beneficial bacteria known to help maintain a healthy gut environment, and they have been reported to support regular bowel movements and digestive health. Research is also underway into how their activity in the gut may contribute to immune function and other aspects of overall health.

***8 Clinical trial of plain yogurt containing *Bifidobacterium longum* BB536**

This study investigated the effects on aging of a program combining the daily consumption of plain yogurt containing *Bifidobacterium longum BB536*, an HRB strain, with improvements in diet and exercise habits. After three months, indicators reflecting the pace of aging suggested that biological aging may have slowed.

Short-term responsiveness of DNA methylation–based aging biomarkers to a multimodal intervention comprising exercise and dietary guidance involving daily consumption of yogurt containing *Bifidobacterium longum* BB536: an exploratory randomized controlled trial. *Aging* (2026).

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