NEWS RELEASE

Study confirms that consumption of *Lacticaseibacillus paracasei* strain Shirota suppresses upper respiratory tract infections and activates mononuclear phagocytic cells in healthy Japanese office workers

TOKYO, July 18, 2025 - Yakult Honsha Co., Ltd. (President: Hiroshi Narita) carried out a clinical trial which investigated the effects of consuming a milk drink containing *Lacticaseibacillus paracasei* strain Shirota (LcS)*1 on the incidence of upper respiratory tract infections (URTIs)*2 and the impact on immune cells, particularly mononuclear phagocytic cells*3, which play a key role in initiating the immune response, in the blood of healthy office workers.

The trial results indicated the following two points:

Compared with participants who consumed the control unfermented milk drink, those who consumed the milk drink containing LcS showed:

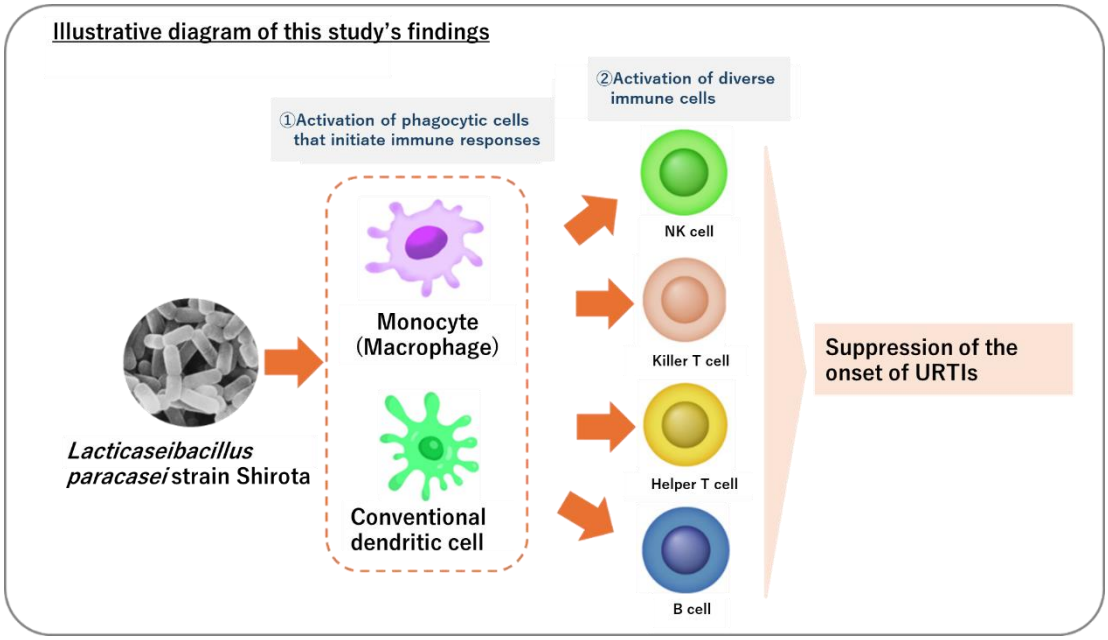
1. **A lower incidence of URTI symptoms.**
2. **Sustained high expression of activation markers on conventional dendritic cells (cDCs)*4 and monocytes*5.**

cDCs and monocytes are known to activate the effector cells of the immune system, including natural killer (NK), T, and B cells. In this study, consumption of the milk drink containing LcS coincided with the suppressed incidence of URTI symptoms. The results suggest that the mechanism of this suppression involves the activation of cDCs and monocytes.

Previous research has shown that LcS promotes health in adults by boosting NK cell activity and maintaining secretory antibody levels in saliva.

The present findings add to this evidence by demonstrating that LcS acts on phagocytic cells and other immune cells to help maintain immune function, thereby contributing to human health.

This study was published in the academic journal *Bioscience of Microbiota, Food and Health* on July 1, 2025.



*1 *Lacticaseibacillus paracasei* strain Shirota was previously classified as *Lactobacillus casei* strain Shirota.

*2 Upper respiratory tract infection (URTI): A collective term for conditions in which viruses or bacteria infect the upper respiratory tract, such as the nasal cavity and throat, causing inflammation. URTIs encompass the common cold, seasonal influenza, and related syndromes.

*3 Phagocytic cells: Immune cells that ingest and digest foreign substances and pathogens. They include dendritic cells and monocytes (macrophages).

*4 Conventional dendritic cells (cDCs): Cells that ingest pathogens or other foreign material and present that information to T cells to initiate adaptive immune responses.

*5 Monocytes: Immune cells that circulate in the bloodstream and remove foreign material. They are also involved in suppressing inflammation and repairing tissue damage.

1. Background

While URTIs are the most common reason people seek medical care worldwide, no definitive therapy exists for removing causative pathogens, with existing treatments merely targeting symptoms. Outbreaks of URTIs also create social problems by increasing healthcare costs through hospital visitations and by reducing people's working days due to sickness-related absences, thereby leading to economic losses.

Lacticaseibacillus paracasei strain Shirota (LcS) is a representative probiotic with nearly 90 years of consumption history. Previous studies have shown that it helps healthy adults maintain wellness by activating NK cells and preventing declines in secretory immunoglobulin A in saliva. However, clinical trials had not clarified whether these beneficial effects were produced by particular immune cell subsets or by activation of the immune system as a whole.

Against this background, the present study focused on phagocytic cell, which initiate immune responses. The aim was to test whether LcS could activate the immune system as a whole and thereby reduce the risk of developing URTIs.

2. Study details

(1) Methodology

Two hundred healthy adults aged 23 to 57 years who mainly worked indoors and considered themselves prone to catching colds were randomly allocated to one of two groups. One group (the "LcS group") consumed one 80-mL bottle per day of a dairy milk drink fermented with 40 billion colony-forming units (CFUs) of LcS; the other group (the "control group") consumed one 80-mL bottle per day of an unfermented milk drink that did not contain LcS (randomized, double-blind, parallel-group trial*6).

During the trial, participants completed questionnaire surveys on URTI symptoms so that effects on URTIs could be assessed. The incidence rate was calculated based on the number of days during which any of the following twelve symptoms occurred: (1) runny nose, (2) stuffy nose, (3) sneezing, (4) coughing, (5) sore throat, (6) sputum, (7) fever, (8) chills, (9) muscular pain, (10) joint pain, (11) headache, and (12) fatigue. The appearance of any symptom from (1) to (6) was classified as "nasopharynx symptoms," and any symptom from (7) to (12) was classified as "whole-body symptoms." Incidence rates were also calculated for each category.

In addition, blood samples were collected at baseline (day 0), day 14, and day 28. Peripheral blood mononuclear cells were isolated, and the expression of the phagocytic-cell activation markers (HLA-DR*8 and CD86*9) was measured using mass cytometry (CyTOF)*7.

*6 Randomized, double-blind, parallel-group trials: Participants are randomly assigned to groups and given test products that either contain or lack the active ingredient. The study is conducted in a double-blind manner, meaning that neither the participants nor the researchers know which product each person is taking. Both groups consume their assigned product concurrently for a fixed period, and the results from each group are analyzed to compare and evaluate efficacy. Results obtained from appropriately conducted randomized, double-blind, parallel-group trials are considered to have high scientific reliability.

*7 Mass cytometry: A technique for analyzing cellular characteristics that combines flow cytometry and mass spectrometry. In mass cytometry, cells are stained with metal-labeled antibodies and then analyzed, which allows many more parameters to be measured simultaneously than with conventional flow-cytometric analysis.

*8 HLA-DR: A member of the human leukocyte antigen (HLA) family and a protein that plays an important role in the immune system. It is expressed on immune cells, such as macrophages, dendritic cells, and B cells. By presenting antigens to T cells, HLA-DR helps initiate adaptive immune responses.

*9 CD86: A protein expressed on macrophages, dendritic cells, and B cells. CD86 plays an important role in activating T cells.

(2) Results

① Consumption of a milk drink containing LcS suppresses the incidence of URTIs

During the 28-day intake period, the incidence rate of URTI symptoms in the LcS group was significantly lower in comparison to the control group (Figure 1A). In particular, the incidence rate from days 15 to 28 was markedly suppressed (Figure 1B). Likewise, the incidence rates of nasopharynx symptoms and whole-body symptoms during the intake period were significantly lower in the LcS group in comparison to the control group (Figure 1C), with the reduction especially pronounced from days 15 to 28 (Figure 1D).

These findings indicate that continuous consumption of a milk drink containing LcS reduces the frequency of URTI symptoms, with the effect becoming more pronounced beginning approximately two weeks after the start of consumption.

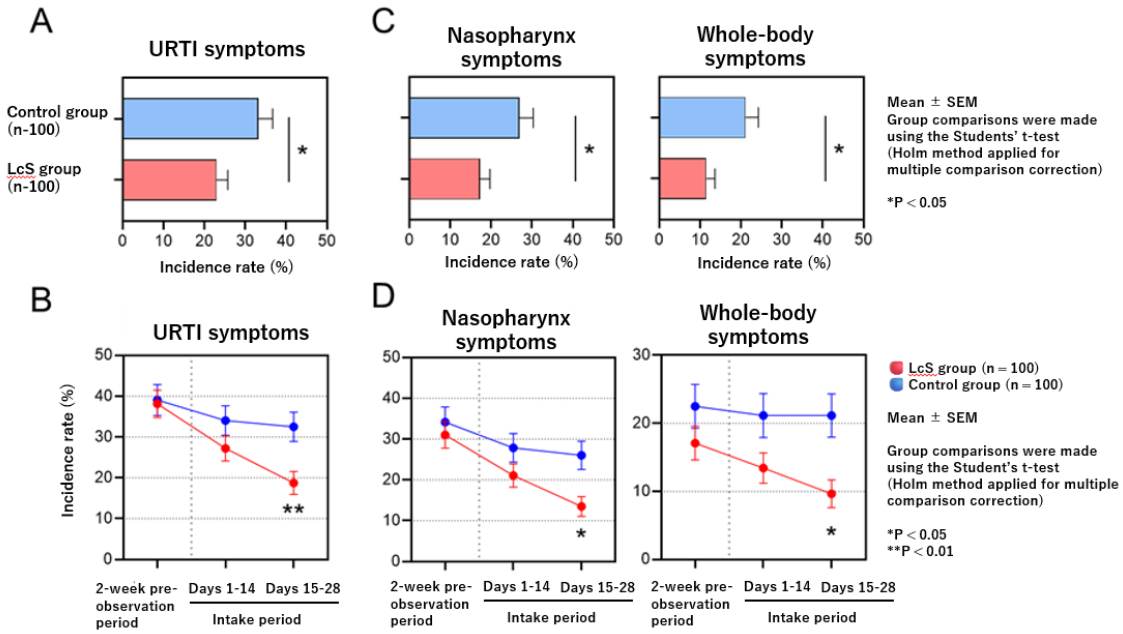


Figure 1: Effect on incidence rate of URTI symptoms

(A, C: Incidence rate on symptoms over 28-day consumption period;

B, D: time-course changes at two-week intervals)

② **Consumption of a milk drink containing LcS maintains high expression of activation molecules on phagocytic cells (conventional dendritic cells and monocytes)**

In the LcS group, the intensity of HLA-DR expression on conventional dendritic cells (cDCs) was significantly higher on days 14 and 28, and the proportion of CD86-positive cDCs was higher on day 14, in comparison to the control group (Figure 2).

Similarly for monocytes, the intensity of HLA-DR expression in the LcS group was significantly higher in comparison to the control group on both days 14 and 28 (Figure 3).

Taken together, these results show that consuming the milk drink containing LcS activates cDCs and monocytes.

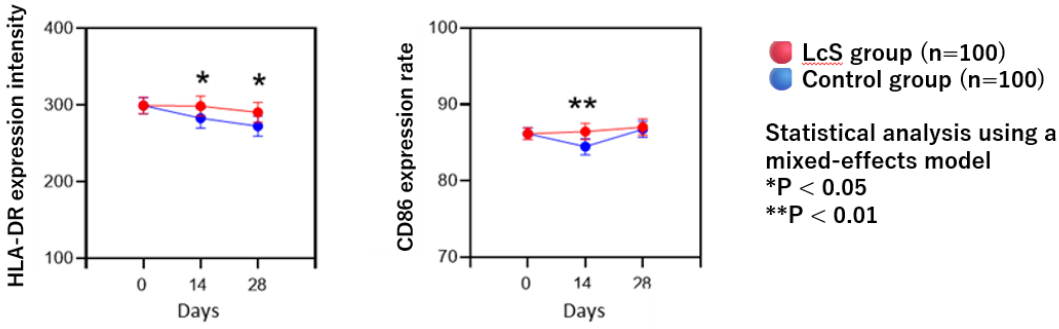


Figure 2: Effects on the expression of activation molecules on cDCs

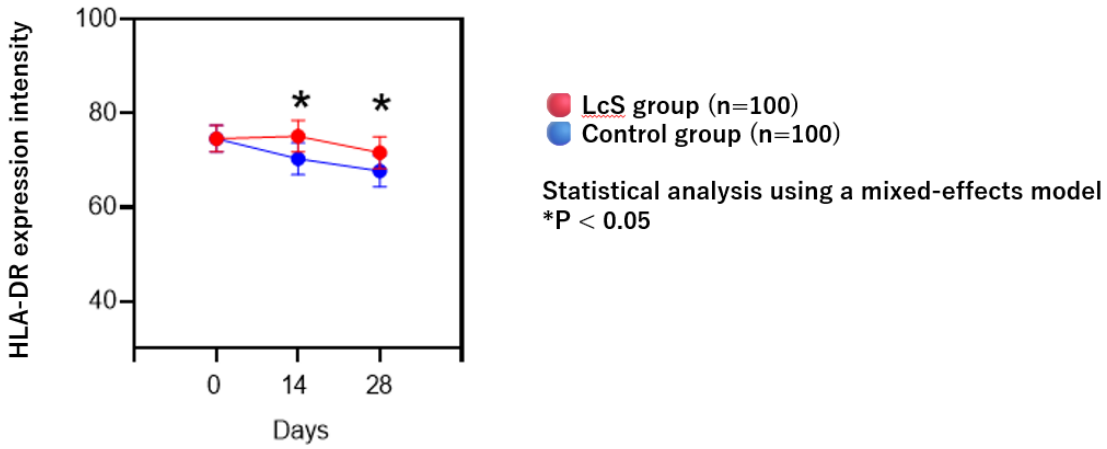


Figure 3: Effect on the expression of activation molecules on monocytes

3. Future prospects

In this study, we demonstrated in a single trial that LcS both suppresses the incidence of URTIs and maintains high expression of activation molecules on cDCs and monocytes.

These findings suggest that LcS acts on dendritic cells and monocytes (the cells that initiate immune responses) to influence the body's overall immune system, and that this action is likely the mechanism by which it confers its health benefit of suppressing the onset of URTIs.

Moving forward, we will further explore the underlying mechanisms involved and use the findings from this trial to enhance the value of our products.

4. Publication information

Name of the journal: *Bioscience of Microbiota, Food and Health*
(https://doi.org/10.12938/bmfh.2025-004)

Title: "*Lacticaseibacillus paracasei* strain Shirota suppresses upper respiratory tract infections and activates mononuclear phagocytic cells in healthy Japanese office workers: a randomized, double-blind, controlled trial"

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