The organic germanium compound, Ge-132, has immune-modulating effects. We evaluated the symbiotic effects of Ge-132 with lactobacilli and oligosaccharide (LB/OS) on the immune responses of mice. The highest fecal IgA levels were observed in the mice receiving a low concentration of Ge-132 with LB/OS for 8 weeks. Our data suggest that LB/OS with a low concentration of Ge-132 stimulated the intestinal immunity.

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The organic germ.
Fecal IgA in experiment II was measured after eight weeks of experimental feeding. During the experimental period, fresh feces were collected and freeze-dried after the third week, fifth week and eighth week. The dried feces were mixed with an appropriate volume of PBS-EDTA after being weighed and were centrifuged at 3,000 rpm for 20 min. The resulting supernatant was collected and centrifuged at 10,000 rpm for another 10 min. The IgA levels were then measured by ELISA (Bethyl Laboratories, TX, USA) according to manufacturer’s instructions. All animal experiments were designed and conducted in accordance with the guidelines for animal experiments of the Asai Germanium Research Institute Co., Ltd., and were created in accordance with the guidelines issued by the Japanese Ministry of Education, Culture, Sports, Science and Technology. The data are presented as the mean ± standard error of the mean (SEM). Statistical significance was evaluated by a one-way analysis of variance (ANOVA) with Tukey’s multiple comparisons, and p < 0.05 was considered significant.

We first measured the effects of LB/OS and Ge-132 on the production of IFN-γ, IL-12 and IL-4 in the spleen as indicators of the balance of Th1 and Th2 responsiveness. The cytokine levels in the culture supernatant of splenic cells from the treated mice are shown in Fig. 2. The Cont group showed the highest level of IL-4 among the groups (223.1 pg/mL). The LB/OS group had levels that were approximately half of those detected in the LB/OS (144.2 pg/mL) group, although there were no statistically significant differences among the groups. Similarly, no significant differences were found in the levels of IFN-γ. However, the LB/OS + LGE (5.34 ng/mL) and LB/OS + HGE (6.18 ng/mL) groups had a slightly higher IFN-γ level than the Cont (4.55 ng/mL) and LB/OS (4.06 ng/mL) groups. The level of IL-12 in the LB/OS + HGE group (0.55 ng/mL) was higher than that in the Cont (0.43 ng/mL), LB/OS (0.40 ng/mL) and LB/OS + LGE (0.47 ng/mL) groups. Significant differences were found between the Cont and LB/OS + HGE groups and between the LB/OS and LB/OS + HGE groups. Taken together, the spleen cells from the two groups receiving Ge-132 produced higher levels of IFN-γ than the control and approximately half the amount of IL-4 as the LB/OS group. Although there were no statistically significant differences, these data suggest that Ge-132 and LB/OS might have adjusted the balance of Th1/Th2 cells in favor of Th1. IL-12 produced by antigen-presenting cells is known to act cooperatively with IL-18 to induce the production of IFN-γ.9) IFN-γ and IL-12 showed similar patterns of production among the four groups in this study, so the production of IFN-γ might have been induced by IL-12. Nagura et al. have reported that an intake of raffinose, which is a type of non-digestible oligosaccharide, changed the immune response to promote Th1 or inhibit Th2 responses by increasing IL-12 production by antigen-presenting cells.9) In addition, Ichikawa et al. have reported that Lactobacillus para-casei KW3110 increased IFN-γ mRNA induced by IL-12p40 and IL-12p55 from the CD11b+ and CD11c+ cells of Peyer’s patches.10) These data are consistent with the results of the present study, showing similar effects of oligosaccharide and lactobacilli on LB/OS-treated mice. However, there was no effect on the cytokines related to Th balance by the LB/OS intake without Ge-132. Taniguchi et al. have evaluated the splenic cytokine production by a lactosucrose intake under similar conditions.11) They found similar responses for IFN-γ and IL-4, although IL-4 was decreased by 4 day’s intake
of 5% (w/w) lactosucrose. The rate of decrease was 0.4 for the control group, while our result was 0.35. The deviation in results for both the control group and LB/OS group was too great in this study, showing that there was little effect of LB/OS on general immunity.

Changes in the IgA levels of dry mouse feces over the 8-week administration of the test diet are shown in Fig. 3. The LB/OS + LGE group showed an approximately 3.4 times higher level of fecal IgA than the Cont group after five weeks (514.4 ng/mg of dry feces) and an approximately 2.3 times higher level after eight weeks (642.4 ng/mg of dry feces). Both differences were statistically significant by Tukey’s multiple comparison test, and their respective ANOVA values were p = 5.07 × 10^{-3} and p = 1.32 × 10^{-6}. The LB/OS + HGE group (248.9 ng/mg of dry feces) after eight weeks showed a lower level of IgA in significance than the LB/OS + LGE group. The fecal IgA levels in the fifth and eighth week of test diet administration were high in both the LB/OS and LB/OS + LGE groups. In the eighth week, the LB/OS + HGE group showed the same low value as the Cont group, this data suggesting there was no increase in IgA. Although no significant differences were apparent between the LB/OS group and the LB/OS + LGE group, significant differences were observed between the Cont and LB/OS + LGE groups, suggesting that the symbiotic effects of the LB/OS component and the low concentration of Ge-132 were effective in promoting the secretion of IgA. An increase in IgA secretion induced by the intake of specific lactobacilli and oligosaccharide has been reported.12) It was assumed in this present study that the increase in IgA secretion induced by lactobacilli in the LB/OS group occurred by similar means and that Ge-132 enhanced the antigen presentation, perhaps through an increased TLR function. The mechanism by which the symbiotic effects of Ge-132 and LB/OS resulted in increased IgA secretion is not apparent from this test, although further studies on mucosal epithelial cells related to IgA secretion may provide an insight.

The dose of 50 mg/kg of body weight of Ge-132 used in this study may have been too high for IgA induction in the presence of LB/OS, although the reason for this is unknown from the data. However, LB/OS + HGE may suppress B cell differentiation into Ig-producing plasma cells or suppress IL-21 and/or IL-5 related to a class switching into IgA secreting cells.13) On the other hand, the amount of Ge-132 absorbed in the body is limited to approximately 20–30% and,14) because of the dilution by blood, the amount of Ge-132 distributed to each organ is extremely low.15) It is therefore presumed that the concentration of Ge-132 approached an appropriate level in the group that received the high dose of Ge-132. LB/OS did not affect the Th balance in experiment I, although the dose dependence of Ge-132 with LB/OS was suggested. This effect of Ge-132 concurs with that in the previous report.15) The immune response of general immunity and intestinal immunity is different. Moreover, it is suggested that the intake of Ge-132 for protective and health-promoting purposes in LB/OS + LGE form would be the most effective for activating intestinal immunity. The symbiotic effects of a low concentration of Ge-132 and the LB/OS component may provide assistance in preventing infection with a virus or other pathogen.

Acknowledgment

We express our gratitude to Associate Professor Dr. Kei Sonoyama at the Graduate School of Agriculture of Hokkaido University who evaluated the tests for administering lactobacilli and organic germanium and provided direction prior to conducting this study.

References