ABSTRACT

Bacillus clausii (BC) is a probiotic widely used in Italy since the 1960s for viral diseases in children and antibiotic-associated diarrhea. Clinical trials have shown BC is useful in mucosal protection and generation in recurrent respiratory infections in children. (1) This probiotic has been demonstrated to exert immunomodulatory activity. However, a few reports have examined whether the anti-allergic mechanisms of probiotics are associated with hypoxia signaling.

Methods: Forty-two BALB/c mice were randomly assigned to six experimental groups: normal saline control, ovalbumin (OVA) with aluminum hydroxide gel (alum adjuvant: Thermo, Waltham, MA, USA) in 20 μl saline on days 0 and 14. After systemic sensitization, mice were orally administered with Lactobacillus paracasei (LP) or Bacillus clausii (BC), a probiotic derived from mudflats, had anti-inflammatory effects compared to the control group. After LP treatment, the number of CD4+ and CD8+ infiltrated cells was significantly increased in the lungs compared to the LP group (P < 0.05, Figure 2A). OVA-induced allergic airway inflammation through regulation of the hypoxia signaling pathway, whose effect is quite comparable to that of Lactobacillus paracasei (LP) administration, one of the most well-known probiotic strains.

RESULTS

In this study, we demonstrated that administration of BC attenuated allergic airway inflammation through regulation of the hypoxia signaling pathway, whose effect is quite comparable to that of Lactobacillus paracasei (LP) administration, one of the most well-known probiotic strains.

METHODS AND MATERIALS

Animals: Six-week-old female BALB/c mice.

Sensitization and Challenge. For the induction of allergic asthma, mice in the OVA group were sensitized with an intraperitoneal injection of 20 μg OVA (Sigma-Aldrich, St. Louis, MO, USA) in aluminum hydroxide gel (alum adjuvant; Thermo, Waltham, MA, USA) in 20 μl saline on days 0 and 14. On day 15, all animals were challenged with 20% aerosol OVA (Sigma-Aldrich, St. Louis, MO, USA) in 20 μl saline. After systemic sensitization, mice were orally administered with Lactobacillus paracasei (LP) or Bacillus clausii (BC), a probiotic derived from mudflats, had anti-inflammatory effects compared to the control group. After LP treatment, the number of CD4+ and CD8+ infiltrated cells was significantly increased in the lungs compared to the LP group (P < 0.05, Figure 2A). OVA-induced allergic airway inflammation through regulation of the hypoxia signaling pathway, whose effect is quite comparable to that of Lactobacillus paracasei (LP) administration, one of the most well-known probiotic strains.

Administration of probiotics: OVA-induced allergic asthmatic mice were orally administered with LP or BC, at 1 x 10^9 or 5 x 10^8 CFU/ml each. We performed differential cell counting on bronchoalveolar lavage fluid (BALF), lung histopathology, serum total and OVA-specific IgG1 and IgG2a, level of Th2 cytokines (IL-4, IL-5, IL-13) in BALF, and pulmonary gene expression, quantitative PCR for home oxygen signaling (HO-1 and HIF-1α) and immune-mediators for three mice.

Results: Compared to the OVA group mice, OVA-sensitized mice treated with LP or BC showed significantly reduced numbers of eosinophils and neutrophils in the BALF (P < 0.05). Both probiotics also significantly reduced pulmonary inflammation and eosinophil infiltration. Mice in the LP or BC group had a substantially lower level of IL-4 and IL-5 in BALF, and decreased IL-4 and IL-5 expression in the lung parenchyma. Real-time PCR and immunohistochemistry showed that HO-1 and BC could significantly suppress HO-1 and HIF-1α expression in asthmatic mice (P < 0.05). Conclusion: BC can attenuate murine allergic asthma via downregulation of HO-1 and HIF-1α, whose anti-inflammatory effect is comparable to that of LP.

Figure 1. Study protocol for induction of asthma/ rhinitis and oral administration of probiotics (LP or BC).

In conclusion, this study demonstrates that BC attenuates asthma symptoms in a murine model of asthma. Furthermore, we found that BC might play a role in the HIF-1α pathway-mediated pulmonary allergic hyperreactivity, which probably results in immune dysregulation.

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RESULTS

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CONCLUSIONS

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REFERENCES


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