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Editorial

Inhibitory Effects of Beneficial Bacteria on Recruitment and Function of Bone Marrow Cells in a Mouse Model of Chronic Allergic Asthma

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Asthma is a chronic inflammatory disorder of the airways in which different inflammatory /immune cells and mediators play a role [1-2]. Mast cells are crucial in inducing both the early and late allergic responses and these cells are involved in chronic inflammation [3]. We and others showed that potentially beneficial bacteria can suppress allergic inflammatory responses in acute allergic asthma models. Therefore we investigated the therapeutic effects of long term-treatment with two different beneficial bacterial strains (*Bifidobacterium breve, B. breve* and *Lactobacillus rhamnosus, L. rhamnosus*) on the recruitment and function of bone marrow cells in a murine model of chronic allergic asthma. Our preliminary data demonstrate that oral treatment of mice with *B. breve* and *L. rhamnosus*, leads to reduced responsiveness of bone marrow-derived mast cells (BMMC) to antigen-IgE-mediated degranulation. An interesting finding was that the bone marrow of control chronic allergic mice was deprived from mast cell progenitors, as the number of bone marrow cells isolated from this group was very low and no BMMC could be obtained. This could be caused by the inflammatory status of these animals as described in previous studies [4-5]. Oral treatment of mice with *B. breve* and *L. rhamnosus* prevented the depletion of bone marrow cells during the allergic inflammation elicited in the airways of chronic allergic mice. These bacterial strains were equally active as treatment with the reference treatment (budesonide). Long-term treatment of chronic asthmatic mice with *B. breve* and *L. rhamnosus* resulted in a significant inhibition of antigen-IgE-mediated degranulation in mast cells cultured *in vitro* from bone marrow from these animals. Interestingly, BMMC from *B. breve*-treated mice showed almost completely suppression of IgE-mediated degranulation as compared to BMMC cultured from bone marrow of "healthy" controls. This greatly reduced responsiveness of the cultured BMMC could not be explained by reduced maturation. *L. rhamnosus* treatment decreased the relative number of c-Kit-positive BMMC to some extent and it tended to decrease the relative number of FcεRI-positive BMMC in chronic allergic mice as compared to "healthy" controls. Yet, an even greater decrease was found in BMMC from the budesonide-treated group, while these BMMC are not compromised in their response to IgE-receptor cross-linking. The mechanism by which these potentially beneficial bacteria reduced mast cell degranulation still needs further investigation. An interesting finding was that *in vitro* co-culture of *B. breve* with BMMC obtained from bone marrow cells of "healthy" controls or budesonide-treated chronic allergic mice reduced antigen-specific response of BMMC and decreased degranulation by almost 50% compared to the control BMMC in these groups. Yet, the antigen-specific response of BMMC obtained from bone marrow cells of *B. breve*- or *L. rhamnosus*-treated chronic allergic mice was not attenuated by *in vitro* co-culture with *B. breve*. The inhibitory effects of *B. breve* and *L. rhamnosus* on mast cell degranulation are more likely to be caused by the induction of epigenetic changes, because during the differentiation of bone marrow into mast cells there is no contact with bacteria or bacterial components. A previous *in vitro* study demonstrated epigenetic effects of a different strain of *B. breve* on the intestinal mucosal immune system by reducing histone acetylation and enhancing DNA methylation [6].

We demonstrate that oral treatment of chronic allergic mice with *B. breve* or *L. rhamnosus* prevents recruitment of bone marrow cells during inflammation and has long-term inhibitory effects on mast cell progenitors. Our preliminary findings suggest that inhibition of IgE-

mediated mast cell degranulation might be a component of the systemic immunomodulatory effects of *B. breve* and *L. rhamnosus* and this may contribute to the anti-allergic effects of these beneficial bacteria. It remains to be established how these bacteria influence degranulation, by inducing changes in mast cell progenitor phenotypes or by interfering with gene expression or signaling pathways in these cells.

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