Stimulation of the histamine 4 receptor with 4-methylhistamine modulates the effects of chronic stress on the Th1/Th2 cytokine balance (Article)

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Abstract

Alterations to the immune system caused by stress have been considered to markedly increase the risk for immune-related diseases such as cancer and autoimmune disorders. We investigated the potential anti-stress effects of the histamine 4 receptor (H4R) agonist, 4-methylhistamine (4-MeH), in a murine stress model. Mice were placed in 50ml conical centrifuge tubes for 12h followed by a 12h rest. The effects of treatment with 4-MeH (30mg/kg, i.p., twice daily) for 2 days were assessed. At 2 days after physical restraint, mice were sacrificed and tissues harvested. We evaluated the effects of 4-MeH treatment on CD4+ T cell production, and intracellular IFN-γ and IL-4 expression in these cells. We also assessed IL-1β, IFN-γ, TNF-α, and IL-4 mRNA expression as well as IFN-γ, TNF-α, GITR, Ox40 and IL-4 protein expression in the spleen. The results showed that 4-MeH treatment of stressed mice results in a substantial increase in the CD4+ T cells as well as in IFN-γ production by these cells. Compared to both untreated and stressed controls. In contrast, IL-4 expression decreased significantly following 4-MeH treatment of mice. Moreover, stimulation of the H4R resulted in up-regulated expression of IL-1β, IFN-γ and TNF-α mRNAs and decreased the expression of IL-4. Western blot analysis confirmed decreased protein expression of IFN-γ, TNF-α, GITR, Ox40 and increased IL-4 in the SC group and treatment of mice with 4-MeH reversed these effects. Our results confirm the significant impact of chronic stress on T cell function and production of Th1/Th2 mediators H4R. © 2014 Elsevier GmbH.

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Author keywords

4-Methylhistamine dihydrochloride, Chronic stress, Cytokines, Histamine 4 receptor, Protein and mRNA expression levels

Indexed keywords

EMTREE drug terms: 4 methylhistamine, CD134 antigen, gamma interferon, glucocorticoid induced tumor necrosis factor receptor, histamine H4 receptor, interleukin 1beta, interleukin 4, messenger RNA, tumor necrosis factor alpha, 4-methylhistamine, gamma interferon, glyceraldehyde 3 phosphate dehydrogenase (NADP), histamine agonist, histamine derivative, histamine receptor, IL1B protein, mouse, interleukin 1beta, interleukin 4, messenger RNA, tumor necrosis factor alpha

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