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[redacted]amine 4 receptor with 4-methylhistamine modulates the effects of chronic stress on the Th1/Th2 cytokine balance (Article)

Ahmad, S.F.[a], Zoheir, K.M.A.[a,b], Ansari, M.A.[a], Korashy, H.M.[a], Bakheet, S.A.[a], Ashour, A.E.[a], Attia, S.M.[a,c]

[a]Department of Pharmacology and Toxicology, College of Pharmacy, King Saud University, PO Box 11451, Riyadh, Saudi Arabia
[b]Department of Cell Biology, National Research Centre, Cairo, Egypt
[c]Department of Pharmacology and Toxicology, College of Pharmacy, Al-Azhar University, Cairo, Egypt

Abstract

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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.

SciVal Topic Prominence

Topic: Receptors, Histamine | Histamine | receptor H4R

Prominence percentile: 87.380

Reaxys Database Information

View Compounds

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

EMTREE medical terms:

adaptive immunity | animal cell | animal experiment | animal model | animal tissue | Article | CD4+ T lymphocyte | chronic stress | controlled study | cytokine production | down regulation | drug effect | drug mechanism | gene expression regulation | IFN gamma gene | IL 1beta gene | IL 4 gene | immobilization stress | immunomodulation | male | mouse | nonhuman | protein expression | T lymphocyte activation | Th1 Th2 balance | TNF alpha gene | upregulation | Western blotting | animal | Bagg albino mouse | biosynthesis | blood | drug effects | exercise | genetics | immunology | lymphocyte activation | lymphocyte count | physiological stress | spleen | Th1 cell | Th1 Th2 balance | Th2 cell

MeSH:

Animals | Glyceraldehyde 3-Phosphate Dehydrogenase (NADP+) | Histamine Agonists | Interferon-gamma | Interleukin-1beta | Interleukin-4 | Lymphocyte Activation | Lymphocyte Count | Male | Methylhistamines | Mice | Mice, Inbred BALB C | Receptors, Histamine | Restraint, Physical | RNA, Messenger | Spleen | Stress, Physiological | Th1 Cells | Th1-Th2 Balance | Th2 Cells | Tumor Necrosis Factor-alpha | Up-Regulation

Chemicals and CAS Registry Numbers:

4 methylhistamine, 36507-31-0; gamma interferon, 82115-62-6; histamine H4 receptor, 272100-58-0; glyceraldehyde 3 phosphate dehydrogenase (NADP), 9028-92-6;

4-methylhistamine; Glyceraldehyde 3-Phosphate Dehydrogenase (NADP+); Histamine Agonists; IL1B protein, mouse; Interferon-gamma; Interleukin-1beta; Interleukin-4; Methylhistamines; Receptors, Histamine; RNA, Messenger; Tumor Necrosis Factor-alpha

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Ahmad, S.F.; Department of Pharmacology and Toxicology, College of Pharmacy, King Saud University, PO Box 11451, Riyadh, Saudi Arabia

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