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Immunobiology
Volume 220, Issue 3, 1 March 2015, Pages 341-349

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

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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

Funding details

Funding sponsor	Funding number	Acronym
King Saud University		KSU
Deanship of Scientific Research, King Faisal University		DSR, KFU

Funding text

The authors are grateful to the College of Pharmacy Research Center and the Deanship of Scientific Research, King Saud University, Riyadh, Saudi Arabia for the financial support.

ISSN: 01712985
CODEN: ZIMMD
Source Type: Journal
Original language: English
DOI: 10.1016/j.imbio.2014.10.014
PubMed ID: 25457414
Document Type: Article
Publisher: Elsevier GmbH

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