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The role of poly(ADP-ribose) polymerase-1 inhibitor in carrageenan-induced lung inflammation in mice (Article)

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Abstract

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Increasing indication is unveiling a role for poly(ADP-ribose) polymerase (PARP)-1 in the regulation of inflammatory/immune responses. The aim of the present study was to determine the potential anti-inflammatory effects of PARP-1 inhibitor 5-aminoisoquinolinone (5-AIQ) to explore the role of PARP-1 inhibitor in a mouse model of carrageenan-induced lung inflammation. A single dose of 5-AIQ (1.5mg/kg) was administered intraperitoneally (i.p.) 1h before λ-carrageenan (Cg) administration. We assessed the effects of 5-AIQ treatment on $CD25^+$, $GITR^+$, $CD25^+GITR^+$, $IL\text{-}17^+$ and $Foxp3^+$ cells which were investigated using flowcytometry in pleural exudates and heparinized blood. We also evaluated mRNA expressions of IL-6, TNF-α, IL-1β, IL-10, CD11a, l-selectin (CD62L), ICAM-1, MCP-1, iNOS and COX-2 in the lung tissue. We further examined the effects of 5-AIQ on the key mediators of inflammation, namely COX-2, STAT-3, NF-kB p65, PARP-1, IkB-α and IL-4 protein expression in the lung tissue using western blotting. The results illustrated that the numbers of T cell subsets, $IL\text{-}17^+$ cytokine levels were markedly increased and $Foxp3^+$ production decreased in the Cg group. Furthermore, Cg-induced up-regulation of adhesion molecules, pro-inflammatory mediators and chemokine expressions. Western blot analysis revealed an increased protein expressions of COX-2, STAT-3 NF-kB p65 and PARP-1 and decreased IkB-α and IL-4 in the Cg group. PARP-1 inhibitor via 5-AIQ treatment reverses the action significantly of all the previously mentioned effects. Moreover, histological examinations revealed anti-inflammatory effects of 5-AIQ, whereas Cg-group aggravated Cg-induced inflammation. Present findings demonstrate the potent anti-inflammatory action of the PARP-1 inhibitor in acute lung injury induced by carrageenan. © 2014 Elsevier Ltd.

SciVal Topic Prominence

Topic: Poly(ADP-ribose) Polymerases | Poly Adenosine Diphosphate Ribose | polymerase-1 PARP-1

Prominence percentile: 98.254

Author keywords

Carrageenan | Inflammatory mediators | Lung tissue | PARP-1 inhibitor | Pleural exudate

Indexed keywords

EMTREE drug terms:

5 aminoisoquinolinone | antiinflammatory agent | carrageenan | cyclooxygenase 2 | I kappa B alpha | inducible nitric oxide synthase | intercellular adhesion molecule 1 | interleukin 10 | interleukin 17 | interleukin 1beta | interleukin 4 | interleukin 6 | L selectin | lymphocyte function associated antigen 1 | malonaldehyde | messenger RNA | monocyte chemotactic protein 1 | nicotinamide adenine dinucleotide adenosine diphosphate ribosyltransferase 1 | nicotinamide adenine dinucleotide adenosine diphosphate ribosyltransferase 1 inhibitor | STAT3 protein | transcription factor FOXP3 | tumor necrosis factor alpha | unclassified drug | 5-aminoisoquinolinone | autacoid | cell adhesion molecule | cyclooxygenase 2 | cytokine | enzyme inhibitor | forkhead transcription factor | Foxp3 protein, mouse | glucocorticoid induced tumor necrosis factor receptor | inducible nitric oxide synthase | interleukin 17 | interleukin 2 receptor alpha | isoquinoline derivative | messenger RNA | nicotinamide adenine dinucleotide adenosine diphosphate ribosyltransferase | Tnfrsf18 protein, mouse

EMTREE medical terms:

adult | animal experiment | animal model | animal tissue | antiinflammatory activity | Article | CD25+ T lymphocyte | concentration (parameters) | controlled study | cytokine production | female | flow cytometry | gene expression | lipid peroxidation | lung parenchyma | lymphocyte count | mouse | mouse model | nonhuman | pleura fluid | pleurisy | pneumonia | protein expression | single drug dose | T lymphocyte subpopulation | upregulation | Western blotting | animal | antagonists and inhibitors | Bagg albino mouse | biosynthesis | drug effects | enzymology | gene expression regulation | genetics | metabolism | pathology | pneumonia | regulatory T lymphocyte

Species Index:

Mus

MeSH:

Animals | Carrageenan | Cell Adhesion Molecules | Cyclooxygenase 2 | Cytokines | Enzyme Inhibitors | Female | Forkhead Transcription Factors | Gene Expression Regulation | Glucocorticoid-Induced TNFR-Related Protein | Inflammation Mediators | Interleukin-17 | Interleukin-2 Receptor alpha Subunit | Isoquinolines | Lipid Peroxidation | Mice, Inbred BALB C | Nitric Oxide Synthase Type II | Pneumonia | Poly(ADP-ribose) Polymerases | RNA, Messenger | T-Lymphocytes, Regulatory

Chemicals and CAS Registry Numbers:

carrageenan, 9000-07-1, 9049-05-2, 9061-82-9, 9064-57-7; I kappa B alpha, 151217-48-0; inducible nitric oxide synthase, 501433-35-8; intercellular adhesion molecule 1, 126547-89-5; L selectin, 126880-86-2; malonaldehyde, 542-78-9; nicotinamide adenine dinucleotide adenosine diphosphate ribosyltransferase, 58319-92-9;

5-aminoisoquinolinone; Carrageenan; Cell Adhesion Molecules; Cyclooxygenase 2; Cytokines; Enzyme Inhibitors; Forkhead Transcription Factors; Foxp3 protein, mouse; Glucocorticoid-Induced TNFR-Related Protein; Inflammation Mediators; Interleukin-17; Interleukin-2 Receptor alpha Subunit; Isoquinolines; Nitric Oxide Synthase Type II; Poly(ADP-ribose) Polymerases; RNA, Messenger; Tnfrsf18 protein, mouse

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Drug manufacturer:

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