BMC Pharmacology

Poster presentation

Reduction of soluble guanylyl cyclase expression in asthma

Andreas Papapetropoulos*[1,2], Davina de CM Simoes[2], Georgia Xanthou[3], Charis Roussos[1] and Christina Gratziou[1]

Address: [1]G.P. Livanos and M. Simou Laboratories, Evangelismos Hospital, Department of Critical Care and Pulmonary Services, University of Athens School of Medicine, Athens, Greece, [2]Laboratory of Molecular Pharmacology, Department of Pharmacy, University of Patras, Patras, Greece and [3]Center for Immunology and Transplantation, Institute for Biomedical Research, Academy of Athens, Athens, Greece

Email: Andreas Papapetropoulos* - apapapet@upatras.gr

* Corresponding author

from 2nd International Conference of cGMP Generators, Effectors and Therapeutic Implications
Potsdam, Germany, 10–12 June, 2005

Published: 16 June 2005

BMC Pharmacology 2005, **5**(Suppl 1):P42 doi:10.1186/1471-2210-5-S1-P42

Soluble guanylyl cyclase (sGC) is a ubiquitously expressed enzyme that is highly expressed in the lung. Stimulation of sGC by nitric oxide (NO) increases the conversion of GTP to cGMP, thereby, causing airway smooth muscle relaxation. To determine whether sGC expression is reduced in an animal model of inflammatory airway disease and, therefore, contributes to airway hyperreactivity (AHR), mice were sensitized and challenged with ovalbumin (OVA). Histological and biochemical analyses confirmed the presence of inflammation in the lungs of OVA-challenged mice that was characterized by increased eosinophil infiltration, mucus production and high interleukin-13 levels. Moreover, OVA-challenged mice exhibited increased airway reactivity to methacholine inhalation. Steady-state mRNA levels for all sGC subunits (α1, α2 and β1) were reduced in the lungs of OVA mice by 60–80%, as estimated by real-time PCR. The changes in sGC expression extended to the protein level where α1, α2 and β1 were reduced by 50–70%, as determined by western blotting. Reduced α1 and β1 expression in animals with asthma was confirmed by immunohistochemistry and showed to occur in epithelial and smooth muscle cells. To study if AHR and/or inflammation occur following sGC inhibition in naïve animals, mice we treated with the selective sGC inhibitor 1H-[1,2,4] oxydiazolo[4,3-ea]quinoxalin-1-one (ODQ). Such treatment led to bronchial hyperreactivity to methacholine. However, in the bronchoalveolar lavage fluid of ODQ-treated mice only a small increase in macrophage number was detected, without changes in IL-13 levels or eosinophil infiltration. We conclude that sGC expression is reduced in an animal model of asthma contributing to the observed AHR.