

MEETING ABSTRACT

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# Contribution of the NO-GC isoforms to airway responsiveness

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From 7th International Conference on cGMP Generators, Effectors and Therapeutic Implications  
Trier, Germany. 19-21 June 2015

Hyperreactivity of airways to bronchoconstrictive agents is a common feature of reactive airway diseases. In addition to its established role on vascular smooth muscle tone, the NO/cGMP pathway is also expected to balance the contractile responses of airway smooth muscle. The NO-sensitive guanylyl cyclase (NO-GC) which forms cyclic GMP in response to NO holds a key position in this pathway and exists in two isoforms, NO-GC1 and NO-GC2, which both have been identified in bronchial and pulmonary blood vessels smooth muscle.

Here we determined the contribution of the NO-GC isoforms to the regulation of airway resistance. Airway resistance was determined in a whole body plethysmography chamber in conscious mice deficient in either NO-GC1 or NO-GC2 in response to methacholine and serotonin inhalation. L-NAME was applied to NO-GC KOs to analyse the effect mediated by the remaining NO-GC isoform and to WT to inhibit both isoforms to see a possible synergistic or antagonistic action. The ganglionic blocker hexamethonium was used to differentiate bronchial and neuronal pathways.

Preliminary results indicate that both NO-GC isoforms contribute to airway responsiveness.

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Published: 2 September 2015

doi:10.1186/2050-6511-16-S1-A67

Cite this article as: Mergia et al.: Contribution of the NO-GC isoforms to airway responsiveness. *BMC Pharmacology and Toxicology* 2015 16(Suppl 1):A67.

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