

MEETING ABSTRACT

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Contribution of the NO-GC isoforms to airway responsiveness

Evanthia Mergia^{1*}, Stefanie Köhler-Bachmann², Michelle Puschkarov², Doris Koesling¹

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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.

Authors' details

¹Institute of Pharmacology, Ruhr-University Bochum, Bochum, Germany.

²Department of Experimental Pneumology, Ruhr-University Bochum, Bochum, Germany.

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* Correspondence: mergia@evanthia.de

¹Institute of Pharmacology, Ruhr-University Bochum, Bochum, Germany
Full list of author information is available at the end of the article

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