

Poster presentation

Open Access

Lack of NO-mediated NANC relaxation in mice deficient in NO-sensitive guanylyl cyclase

Dieter Groneberg*, Doris Koesling and Andreas Friebe

Address: Institut für Pharmakologie, Ruhr-Universität Bochum, Bochum, Germany

Email: Dieter Groneberg* - dieter.groneberg@rub.de

* Corresponding author

from 3rd International Conference on cGMP Generators, Effectors and Therapeutic Implications
Dresden, Germany. 15–17 June 2007

Published: 25 July 2007

BMC Pharmacology 2007, 7(Suppl 1):P24 doi:10.1186/1471-2210-7-S1-P24

This abstract is available from: <http://www.biomedcentral.com/1471-2210/7/S1/P24>

© 2007 Groneberg et al; licensee BioMed Central Ltd.

The NO/cGMP signal transduction pathway plays an important role in the control of smooth muscle function. NO-sensitive guanylyl cyclase (NO-GC) is the main target of the messenger molecule NO produced by NO synthases. Stimulation of NO-GC by NO results in the synthesis of the second messenger cGMP. cGMP-mediated activation of cGMP-dependent protein kinase leads to the phosphorylation of various target proteins which finally induce the relaxation of smooth muscle. Several smooth muscle-containing tissues are innervated by non-adrenergic non-cholinergic (NANC) neurons. Release of NO from these neurons is known to mediate relaxation.

Recently, we deleted NO-GC in mice on the genomic level. Lack of GC-NO abolishes NO-dependent relaxation of smooth muscle resulting in hypertension and gastrointestinal dysfunction. The GI dysmotility reduces the life expectancy as many mice die due to peritonitis and perforation of the gastrointestinal wall. We hypothesized that the absence of NO-GC as the receptor for the NANC transmitter NO is the reason for this phenotype.

The importance of NO-GC in NANC relaxation was investigated in organ bath experiments using a pharmacological approach and electrical field stimulation (EFS). Neither physiological concentrations of NO donors nor EFS at low frequencies led to NANC relaxation of gastric fundus or sphincters (pylorus and lower esophageal sphincter) from GC-KO mice. This lack of NO-mediated NANC relaxation was corroborated in non-gastrointesti-

nal tissue using penile corpus cavernosum. Taken together, we think that NO-GC is indispensable for NO-mediated NANC relaxation.