BMC Pharmacology

BioMed Central

Poster presentation

Open Access

Relaxation of vascular smooth muscle by the cGMP-kinase substrate IRAG

Dominik Bernhard*[1], Franz Hofmann[1] and Jens Schlossmann[2]

Address: [1]Institut für Pharmakologie und Toxikologie, TU-München, Germany and [2]Institut für Pharmakologie und Toxikologie, Universität Regensburg, Germany

Email: Dominik Bernhard* - Bernhard@ipt.med.tu-muenchen.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):P8 doi:10.1186/1471-2210-7-S1-P8

This abstract is available from: http://www.biomedcentral.com/1471-2210/7/S1/P8

Intracellular signalling by NO/cGMP-dependent protein kinase type I (cGKI) relaxes smooth muscles thereby modulating e.g. vascular tone. An important mediator of this signalling cascade is the inositol 1,4,5,-trisphosphate receptor I (IP_3 RI) associated protein cGMP kinase substrate (IRAG). This protein forms a trimeric complex together with the cGMP kinase Iβ and the IP_3 RI. Recently, it was shown that the relaxation of hormone-contracted aortic smooth muscle by cGMP was abolished in IRAG $^{\Delta 12/\Delta 12}$ mutant mice with a disrupted IRAG-IP_3 RI interaction site [1]. Now we investigated whether IRAG might regulate the vascular tone in small vessels. NO-mediated relaxation of isolated arteria tibialis was nearly absent in the IRAG mutant. Moreover, the relaxing effect of IRAG on NO-mediated dilation of resistance vessels in perfused hind limbs of mutant mice was abolished.

To analyze the in vivio function of IRAG/IP_3 RI interaction, we finally recorded blood pressure in conscious, freely moving animals via implanted radiotelemetric devices. After application of NO-donors blood pressure decrease was clearly diminished in IRAG$^{\Delta 12/\Delta 12}$ mutants compared to control mice.

These data suggest that IRAG is essential for NO/cGMP-dependent relaxation of vascular smooth muscle.

References

1. Geiselhoringer A, Werner M, Sigl K, Smital P, Worner R, Acheo L, Stieber J, Weinmeister P, Feil R, Feil S, Wegener J, Hofmann F, Schlossmann J: **IRAG is essential for relaxation of receptor-triggered smooth muscle contraction by cGMP kinase.** *EMBO J* 2007, **23:**4222-4231.