BMC Pharmacology

POSTER PRESENTATION Open Access

Function of IRAG and the phosphorylation of the $InsP_3R$-I for the NO/cGMP-dependent inhibition of platelet aggregation

Katharina Salb*, Elisabeth Schinner, Jens Schlossmann

From 5th International Conference on cGMP: Generators, Effectors and Therapeutic Implications
Halle, Germany. 24-26 June 2011

Background

Precondition for activation and aggregation of platelets is a rise in intracellular calcium concentration which can be inhibited by activation of the NO/cGMP/cGKI signalling cascade. The cGMP-dependent Kinase I (cGKI) is assembled in a macrocomplex with the Inositoltrisphosphate receptor I ($InsP_3R$-I) and the Inositoltrisphosphate receptor associated cGMP kinase substrate (IRAG).

Results

We investigated the relevance of IRAG and the cGKI stimulated phosphorylation of the calcium channel $InsP_3R$-I for the NO/cGMP-dependent inhibition of platelet aggregation and adhesion.

After incubation with different agonists (collagen, thrombin, TxA2) we performed aggregation experiments with platelets of WT and IRAG-KO mice, thereby the IRAG-KO platelets aggregated stronger than the WT platelets. After preincubation with NO/cGMP the inhibition of aggregation was decreased in IRAG-KO platelets compared to WT platelets. Furthermore, GPIIb/IIIa-mediated adhesion of platelets to fibrinogen could only weakly be inhibited in IRAG-deficient platelets contrary to WT platelets. The cGKI-mediated stimulation of $InsP_3R$-I phosphorylation showed an equal increase in WT and IRAG-KO platelets.

Conclusion

These results revealed that IRAG plays an important role in the NO/cGMP-dependent inhibition of platelet aggregation. However, the cGMP-stimulated phosphorylation of $InsP_3R$-I is not necessary for the inhibition of platelet aggregation.

Published: 1 August 2011

doi:10.1186/1471-2210-11-S1-P58
Cite this article as: Salb *et al.*: Function of IRAG and the phosphorylation of the $InsP_3R$-I for the NO/cGMP-dependent inhibition of platelet aggregation. *BMC Pharmacology* 2011 **11**(Suppl 1):P58.

* Correspondence: katharina.salb@chemie.uni-regensburg.de
Department of Pharmacology and Toxicology, University of Regensburg, Germany