Poster presentation

Cardiovascular and gastrointestinal function of IRAG

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Background

Signalling by NO/cGMP is very important for regulation of vascular tone and gastrointestinal motility. One important signalling pathway of cGMP-dependent protein kinase type I (cGKI) is mediated by IRAG (IP₃ Receptor Associated cGKI substrate) which is highly expressed in smooth muscle of cardiovascular and gastrointestinal tissue. In order to elucidate the physiological role of IRAG we generated IRAG knockout mice by targeted deletion of exon 3. These mice show an enlarged gastrointestinal tract including pylorus stenosis.

Results

Exogenous and endogenous NO and cGMP stimulation relaxes hormone induced contraction of wild type aortic vessels as well as gastrointestinal tissues of colon and jejunum. This effect is significantly reduced in IRAG – deficient animals. Furthermore, activation of particulate guanylyl cyclase by atrial natriuretic peptide (ANP) shows a reduced relaxing effect in IRAG knockout tissue strips. The expression levels of other cGKI substrates and the NO-induced cGMP synthesis are not affected in these tissues from IRAG KO mice.

Conclusion

These results indicate that IRAG signalling is essential for smooth muscle relaxation by NO/cGMP and ANP/cGMP.