

Poster presentation

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

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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<sub>3</sub> RI) associated protein cGMP kinase substrate (IRAG). This protein forms a trimeric complex together with the cGMP kinase I $\beta$  and the IP<sub>3</sub> 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<sub>3</sub> 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 vivo function of IRAG/IP<sub>3</sub> 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

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