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Conditional inactivation of the NO-sensitive guanylyl cyclase isoforms ($\alpha_1\beta_1$, $\alpha_2\beta_1$) in mice

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Signalling via NO/cGMP regulates diverse physiological processes such as smooth muscle relaxation, inhibition of platelet aggregation and modulation of neurotransmission. To elevate intracellular cGMP concentrations the signal molecule nitric oxide (NO) binds to the prosthetic heme group of the NO-sensitive guanylyl cyclase (GC), a heterodimeric enzyme composed of one α and one β subunit.

Two different isoforms of the NO-sensitive GC have been shown to exist in vivo; the $\alpha_1\beta_1$ and the $\alpha_2\beta_1$ heterodimer revealing undistinguishable enzymatic properties. Investigation of the tissue distribution of both GC isoforms revealed a major occurrence of the $\alpha_2\beta_1$ isoform in brain, whereas in all other tissues tested, the $\alpha_1\beta_1$ heterodimer was the predominating isoform.

In order to study the NO/cGMP signalling and to analyse the functional significance of the GC isoforms, we have generated conditional knockout mice, in which the gene coding for the α_1- or the α_2-subunit can be deleted using the Cre/loxP system.

Here we report on the phenotypes of mice with deficiency of the α_1- or the α_2-subunit of the NO-sensitive GC in all tissues.