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Poster presentation

The elusive β_2 subunit of sGC

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NO's major physiological receptor is the soluble guanylyl cyclase (sGC). sGC exist as heterodimers of 2 subunits, α/β. Heterodimerization between both the α and β subunit is essential for sGC's enzymatic activity. Five subunits, termed α_1, α_2, α_{2i}, β_1 and β_2, have been identified so far; however, there are only two functional enzyme forms, α_1/β_1 and α_2/β_1, that appear to form in vivo at the protein level. The β_2 sGC subunit is the most obscure isoform of all the subunits and its physiological relevance is until now unresolved. Here we clearly show a ubiquitous expression of sGCβ_2 in wildtype mice. Cloning of this subunit revealed a 45 base pairs shorter splice variant in the 7th exon along with the predicted sGCβ_2 mRNA. This shorter variant is expressed along with the sGCβ_2 in all major organs. To further characterize the role of this subunit, we have generated a sGCβ_2 knockout mice and backcrossed by speed-congenics. The heme NO binding domain (HNOB), comprising exons 5, 6 and 7 were deleted. Analysis of the knockout mice revealed no transcripts of sGCβ_2 in all the major organs suggesting the sGCβ_2 knockout mice are complete knockouts. These animals have been backcrossed by marker assisted backcrossing (speed congenics), with over 98 percent of the C57/BL6J (recipient) background incorporated. The phenotypic analysis of these knockout mice will help unravel the role of this subunit in the NO/cGMP cascade.