FUNCTIONAL IMPORTANCE OF THE SOLUBLE GUANYLYL CYCLASE 11
ISOFORM IN VASORELAXATION
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Of the two active soluble guanylyl cyclase (sGC) isoforms (α1β1 andα2β1), the α1β1 isoform is predominantly present in vascular tissue and is therefore believed to play a dominant role in vasorelaxation. This was investigated on aortic and femoral artery segments isolated from sGCα1−/− mice and their wild type littermates and by measuring of the cGMP level and sGC enzyme activity. The functional importance of sGCα1β1 was demonstrated by a significantly reduced response to acetylcholine, sodium nitroprusside (SNP), NO-gas, YC-1 and BAY 41-2272 in arteries of sGCα1−/− mice. However, those substances still had a substantial relaxing effect in these arteries, indicating that not only sGCα1β1 is involved in vasorelaxation. The non-upregulation of the sGCα2 gene and the non-significant increase in cGMP-level in response to SNP, do not support the involvement of the minor sGCα2β1 isoform and thus rather suggest (an) sGC-independent mechanism(s). The similarity in the response to the cGMP-analogue 8-pCPT-cGMP between wild type and sGCα1−/− mice, indicates that the sGCα1−/− mice are not more sensitive towards cGMP. The response to the phosphodiesterase type-5 inhibitor, T-1032 was nearly abolished in the arteries of the sGCα1−/− mice, indicating that in those mice there is no accumulation of basal cGMP produced by sGCα2β1. Again those findings are against the importance of sGCα2β1. On the other hand, the inhibition of the nitric oxide-induced relaxation and cGMP production in the sGCα1−/− mice by ODQ suggest that sGCα2β1 is functionally active. This is also suggested from the significant increase in sGC activity in the sGCα1−/− mice after addition of BAY-41-2272. It is concluded that besides sGCα1β1, also sGCα2β1 and/or(an) sGC-independent mechanism(s) has a substantial role in nitric oxide-related vasorelaxation.