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# Angiotensin type 2 receptor (AT<sub>2</sub>R) and receptor Mas: a complex liaison

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## Abstract

The angiotensin type 2 receptor (AT<sub>2</sub>R) and the receptor Mas are components of the protective arms of the renin–angiotensin system (RAS), i.e. they both mediate tissue protective and regenerative actions. The spectrum of actions of these two receptors and their signalling mechanisms display striking similarities. Moreover, in some instances, antagonists for one receptor are able to inhibit the action of agonists for the respective other receptor. These observations suggest that there may be a functional or even physical interaction of both receptors. This article discusses potential mechanisms underlying the phenomenon of blockade of angiotensin-(1–7) [Ang-(1–7)] actions by AT<sub>2</sub>R antagonists and vice versa. Such mechanisms may comprise dimerization of the receptors or dimerization-independent mechanisms such as lack of specificity of the receptor ligands used in the experiments or involvement of the Ang-(1–7) metabolite alamandine and its receptor MrgD in the observed effects. We conclude that evidence for

a functional interaction of both receptors is strong, but that such an interaction may be species- and/or tissue-specific and that elucidation of the precise nature of the interaction is only at the very beginning.

**Abbreviations:** ACE, angiotensin-converting enzyme; aCSF, artificial cerebrospinal fluid; AngI etc., angiotensin I etc. Ang-(1–7), angiotensin-(1–7); AT1R etc., angiotensin type 1 receptor etc; C21, Compound 21; ET-1, endothelin-1; GPCR, G-protein-coupled receptor; HEK, human embryonic kidney; icv, intracerebroventricular; IRAP, insulin regulated aminopeptidase; MCAO, middle cerebral artery, causing transient occlusion; MrgD, Mas-related G-protein-coupled receptor; PGE2, prostaglandin E2; PGI2, prostaglandin I2; RAS, renin–angiotensin system; SHP, Src homology 2 domain-containing protein tyrosine phosphatase; SHR, spontaneously hypertensive rat

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## Keywords

angiotensin type 2 receptor (AT2R), Mas receptor, renin-angiotensin system (RAS)

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