Angiotensin II Type 2 Receptor Effects: Lesson From a Human Model of Vascular Hyporeactivity. Letter Regarding Kemp et al

Angiotensin II (Ang II) regulates a broad spectrum of cardiovascular and renal processes ranging from vasoconstriction to inflammatory processes, including atherosclerosis and vascular ageing. Ang II determines most of its effects via activation of 2 G-protein–coupled receptors with opposite effects: the type 1 (AT, R) and the type 2 receptors (AT, R).

The relationships and interactions between AT, R and AT, R signals, their roles in the control of vascular tone and cardiovascular remodeling, and the underlying mechanisms are complex and remain to be defined fully.

Kemp et al have added another relevant piece of evidence in this field through an elegant study in an animal model of AT, R stimulation recently published in the journal. These authors have, in fact, demonstrated that AT, R stimulation via the specific non-peptide AT, R agonist compound-21 (C-21) increased the urinary sodium excretion without affecting the mean arterial blood pressure and the renal hemodynamics. This effect has been shown to be dependent on a bradykinin-nitric oxide-cyclic guanosine monophosphate pathway. Finally, the authors demonstrated that in a rat model of Ang II–dependent hypertension, the intrarenal monophosphate pathway. Finally, the authors demonstrated that AT, R mediated vasodilation, a main effector of AT2R signaling, whose protein expression is blunted by the AT2R inhibitor PD123319 in fibroblasts.

We suggest that the relevance of the data provided by Kemp et al in an animal model is supported by the results of our studies in a human model of endogenous AT, R stimulation and blunted Ang II signaling via AT, R, the Bartter/Gitelman (BS/GS) syndromes.

BS/GS syndromes are rare diseases caused by gene defects in specific kidney transporters and ion channels and are characterized by the activation of the renin–angiotensin–aldosterone system with high plasma levels of Ang II, and aldosterone, yet normotension or hypotension, hyporesponsiveness to pressor agents and the activation of antithrombotic and antiremodeling defenses. Patients with BS/GS syndromes likely represent a human model of in vivo endogenous antagonist of Ang II signaling via AT, R as suggested by the reduced expression of the a subunit of Gq protein, of the p63RhoGEF, and of downregulation of RhoA/Rho-kinase system, and by the upregulation of the regulator of G protein signaling-2 and of the nitric oxide system.

None.

Disclosures

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References
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