*Editorial Comment*

# Pleiotropic Actions of Angiotensin Receptor Antagonists

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Various angiotensin II type 1 ($AT_1$) receptor–mediated actions of the renin-angiotensin (R-A) system other than the vasopressor action have been reported. Recently, R-A system has been reported to exist in hematopoietic bone marrow cells, and be involved in cell differetiation (*1*). Angiotensin II influences stem cell differentiation in an $AT_1$ receptor–dependent manner, and hematopoietic stem cells are involved in the regeneration and repair of renal cells (*2*, *3*). Indeed, bone marrow–derived renal tubular cells have been shown to have physiological functions. These hematopoietic stem cells are also present in transplanted kidneys (*4*). Thus, the role of R-A system in these stem cells has been attracting attention.

R-A system is also present in mesenchymal stem cells (MSCs) which are precursors of adipocytes (*5*). Promotion of their differentiation into adipocytes is considered to be an event that can trigger metabolic syndrome. During the differentiation of MSCs, angiotensin II production is increased, and the differentiation into adipocytes was inhibited by administration of $AT_1$ receptor antagonists. During this differentiation process, the expression of angiotensin II type 2 ($AT_2$) receptors also increased, suggesting an $AT_2$ receptor–mediated inhibitory effect on adipocyte differentiation.

In addition to the above effect of the R-A system other than that as a blood pressure–regulating hormone, the effect of angiotensin II on renal iron metabolism has recently been reported by Ishizaka *et al*. (*6*) in this issue. They have analyzed the renal iron metabolism–related proteins such as transferrin receptor (TfR), divalent metal transporter (DMT1), ferroportin (FPN) and hepcidin in angiotensin II–infused rats, and have reported that their mRNA expression was increased in respose to angiotensin II–infusion, which increase was inhibited by the administration of angiotensin receptor blocker (ARB). Their present study stimulates further research on new functions of the R-A system, and the role of the R-A system in not only renal tissue but also blood cell components involved in iron metabolism is of interest.

Thus, recent studies of the R-A system have deepened our understanding of the actions of angiotensin receptors on blood cell differentiation and iron metabolism, suggesting the so-called pleiotropic actions of angiotensin receptor antagonists. In view of the increasing clinical use of ARB, it is important for future studies to clarify the pleiotropic actions of ARB by studying more various function of $AT_1$ receptor.

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