Intrarenal renin-angiotensin system and salt-dependent hypertension in patients with CKD

Akira Nishiyama, MD, PhD, FAHA (akira@kms.ac.jp)

Departments of Pharmacology,
Faculty of Medicine, Kagawa University, Kagawa, Japan

Abstract

The renin-angiotensin system (RAS) plays a critical role in the regulation of blood pressure and body fluid homeostasis. In addition to its physiological roles, angiotensin II (AngII) induces inflammation, cell growth, mitogenesis, apoptosis, migration, and differentiation, regulates the gene expression of bioactive substances, and activates multiple intracellular signaling pathways, all of which contribute to renal tissue injuries. In the kidney, all of the RAS components are present and intrarenal AngII is formed by independent multiple mechanisms. In particular, a series of our studies have revealed that intrarenal angiotensinogen plays a predominant role in the regulation of AngII production in the kidney. Consequently, AngII is compartmentalized in the renal interstitial fluid and the proximal tubular compartments with much higher concentrations than those existing in the circulation. Recent evidence has also revealed that inappropriate activation of the intrarenal RAS is an important contributor to the pathogenesis of hypertension and renal injury. For example, circulating plasma AngII levels are reduced in CKD patients with salt-dependent hypertension; however, intrarenal RAS is activated by inappropriately augmentation of angiotensinogen in the kidney. Thus, it is necessary to understand the mechanisms responsible for independent regulation of the intrarenal RAS. In this symposium, I will briefly summarize our current understanding of independent regulation of the intrarenal RAS and discuss how inappropriate activation of this system contributes to the development of salt-dependent hypertension on patients with CKD. We will also discuss the possible biomarker of the intrarenal RAS.