New paradigm of the renin-angiotensin system: the receptor-associated prorenin system

○ Atsuhiro Ichihara (Keio University School of Medicine, Tokyo)

Blockade of the renin angiotensin system (RAS) with angiotensin-converting enzyme inhibitors and angiotensin II type 1 receptor blockers has been reported to have a protective effect on end-organ damage in the patients with diabetes and hypertension, even if they have a suppressed circulating RAS represented by a low plasma renin activity. This suggests that the patients with diabetes and hypertension may have the enhanced tissue RAS despite the suppressed circulating RAS. However, the circulating RAS-independent regulation mechanism of tissue RAS remained unclear. Previous studies showed that increased plasma prorenin levels predict development of retinopathy and microalbuminuria in diabetic patients, suggesting that prorenin may contribute to the development of diabetic microvascular complications. Recent discoveries of human (pro)renin receptor in 2002 and non-proteolytic activation of prorenin in 2003 led us to find that non-proteolytic activation of prorenin by (pro)renin receptor plays a pivotal role in the regulation of tissue RAS and end-organ damage in diabetic animals. More recently, studies showed that (pro)renin receptor itself contributes to the end-organ damage through angiotensin II-independent mechanisms. In the symposium, we plan to discuss the role of a new paradigm of the RAS, the receptor-associated prorenin system, in the development and progression of end-organ damage in diabetes and hypertension.