37) **Pathophysiological role of a Novel Vasopressin Receptor (V_p) in isolated SHRSP nephron segments.** Kyu Yong Jung, Keiichi Shimamura, Satoru Sunano, and Hitoshi Endou. Department of Pharmacology, Faculty of Medicine, University of Tokyo, Bunkyo-ku, Tokyo 113; and Research Institute of Hypertension, Kinki University, Sayama, Osaka 589.

In addition to renin-angiotensin-aldosterone system, vasopressin (or AVP) is also considered as an important regulator in hypertension. AVP coupled with V_2 receptor activates adenylate cyclase, and thus synthesized cAMP regulates sodium and water reabsorption in thick ascending limb of Henle's loop and collecting tubule, respectively. Recently, we have found a novel vasopressin receptor (V_p) in isolated normotensive rat early proximal tubule (S_1). Majority (about 90%) of AVP receptor subtypes in S_1 is V_p , and that in medullary thick ascending limb of Henle's loop (MTAL) and outer medullary collecting tubule (OMCT) is V_2 . V_p stimulation by AVP inhibits ATP consumption presumably by inhibiting sodium pump. From these observations, this study was aimed to investigate role(s) of V_p receptor under several stages of hypertension using isolated SHRSP nephron segments.

S_1 , MTAL and OMCT were isolated from collagenase-treated kidney of young (4-5 weeks) and adult (12-14 weeks) WKY and SHRSP. AVP (10^{-7} M)-induced intracellular free calcium ($[Ca^{++}]_i$) change was measured using Fura-2. In order to investigate a role of AVP (10^{-7} M) in ion transport, cellular ATP content was measured by microchemiluminescence method.

AVP transiently increased $[Ca^{++}]_i$ in adult WKY S_1 , MTAL and OMCT. AVP-induced $[Ca^{++}]_i$ transient in adult SHRSP S_1 was significantly attenuated compared to adult WKY S_1 . When adult WKY S_1 and MTAL were incubated with AVP in the presence of Na^+ and absence of exogenous substrates, cellular ATP content in MTAL was significantly low compared to control, whereas the reversed result was obtained in S_1 . These results indicate that AVP (V_2) receptor in MTAL stimulates ATP-consuming active ion transport, but AVP (V_p) receptor in S_1 inhibits this. Interestingly, AVP did not change the cellular ATP content in adult SHRSP S_1 . Similar to WKY MTAL, cellular ATP in SHRSP MTAL was significantly lowered by AVP. Moreover, AVP-induced $[Ca^{++}]_i$ mobilization was also significantly attenuated in dehydrated rat S_1 . On the other hand, a role of V_p receptor investigated in young WKY and SHRSP revealed that AVP-induced $[Ca^{++}]_i$ transient in OMCT was similar to adult WKY and SHRSP. However, $[Ca^{++}]_i$ increase by AVP in young SHRSP S_1 was slightly decreased compared to young WKY S_1 .

From these results, it is suggested that stimulation of V_p receptor inhibits ATP-consuming active ion transport in normotensive rat S_1 . However, lack of V_p receptor responsiveness in SHRSP might lead to increase ion V_p transport, and thus to augment cellular volume expansion. And then, this study concludes that V_p receptor could be considered as one of regulators for the development of hypertension in SHRSP.