28) Possible Participation of Angiotensin II Receptor Subtype 1 in Development of Hypertension. Nobuyuki Oda, Yasundo Yamasaki, Yoshihisa Nozawa, Akihiro Haruno and Naosuke Matsuura. Immunological and Cardiovascular Research Lab. Taiho Pharmaceutical Co., Ltd. Saitama, 357.

The activation of calcium channels and/or the renin-angiotensin system contribute to the development of hypertension. Recently angiotensin II receptors have been divided into two subtypes (AT1, AT2) by using selective antagonists and the vasoconstrictive action of angiotensin has been suggested to be mediated by AT1 receptors. In the present study, we examined the possible contribution of angiotensin II (Ang II) receptor subtype 1 (AT1) in male spontaneously hypertensive rats (SHR) and male Wistar Kyoto rats (WKY).

Radioligand receptor binding assay (^{125}I Ang II) was used to determine the number of receptors and to characterize the percentages of AT1 receptors in the aorta at three developmental ages: 3, 6 and 30 weeks old. DuP 753, a selective Ang II receptor antagonist, blocked [^{125}I] Ang II binding in the aorta membrane in a biphasic manner, indicating the presence of high-affinity (AT1) and low-affinity (AT2) sites for this agent.

In WKY, the systolic blood pressure was 96.6 ± 11.1 , 134.9 ± 5.5 and 161.1 ± 10.9 mmHg at the three developmental ages. In SHR, the systolic blood pressure increased with ages, and 95.6 ± 8.8 , 149.7 ± 7.2 and 219.7 ± 16.0 mmHg, in 3, 6 and 30 weeks old, respectively. The number of Ang II receptors (Bmax) decreased with ages in both WKY and SHR (Bmax= 3W:150.1, 6W:61.6 and 30W:41.6 in WKY and 3W:116.5, 6W:78.7 and 30W:43.2 fmol/mg protein in SHR). However, the percentage of AT1 to total Ang II receptors increased with ages in both WKY and SHR (percent of AT1= 3W:22.3, 6W:39.0 and 30W:61.9% in WKY and 3W:49.0, 6W:58.7 and 30W:86.7% in SHR). Furthermore, the number of AT1 receptors (Bmax $\times$ percent of AT1) was higher (57.1, 46.2 and 37.5 fmol/mg protein) than that of WKY (33.5, 24.0 and 25.8 fmol/mg protein) at every ages examined. Interestingly that the percentages of AT1 receptors to total Ang II receptors was high even at a young age when high blood pressure had not yet developed.

These results suggest that activation of vascular renin-angiotensin system in SHR participated in the development of hypertension.