31) Alterations of Atrial Natriuretic Peptide (ANP) Binding Sites in Spontaneously Hypertensive Rats. Masaki Kurihara, Keisuke Tsutsumi, Teruaki Kawano, Masami Niwa*, Masayori Ozaki*, Kazuo Mori and J.M. Saavedra**. Department of Neurosurgery, *Department of Pharmacology 2, Nagasaki University School of Medicine, Nagasaki 852, Japan. **LCS, NIMH, USA.

INTRODUCTION: Atrial natriuretic peptide (ANP) has been suggested to play a role in the regulation of blood pressure and fluid homeostasis. The action of ANP could be mediated through specific ANP receptors in the kidney, adrenal gland, vasculature and possibly in discrete brain nuclei and pituitary gland (Needleman, et al.: Hypertension, 1985). An increased plasma content of ANP has been reported in SHR after the development of high blood pressure (Gutkowska et al.: Hypertension, 1986), and also the lower number of ANP binding sites in the subfornical organ (SFO) has been shown in 4- and 14-week-old SHR. In this study, to elucidate the characteristics of ANP receptors in SHR, we further examined in the some other tissues of SHR using in vitro quantitative autoradiography (Israel et al.: Brain Res, 1984).

MATERIALS AND METHODS: Male 4- and 14-week-old SHR and WKY were used. Systemic blood pressure was 89 ± 8 mmHg and 94 ± 5 mmHg (mean $\pm$ S.E.M., $n=8$) in 4-week-old WKY and SHR, and of 14-week-old WKY and SHR was 125 ± 10 mmHg and 194 ± 12 mmHg ($p < 0.01$), respectively. ANP binding sites were labeled in vitro by incubating consecutive frozen (16 μ m-thick) sections with 3-[125 I]-iodotyrosyl 28 rat ANP $_{99-126}$ and quantified by autoradiography followed by computerized densitometry and comparison with 125 I-standards (Kurihara et al.: BBRC, 1987).

RESULTS AND DISCUSSION: The SHR had the lower number of ANP binding sites in the SFO and choroid plexus at the age of 4 and 14 weeks and smooth muscle layer of thoracic aorta at 4-week-old examined, when compared to age-matched WKY. Furthermore, SHR had undetectable ANP binding sites in the sympathetic ganglia (superior cervical and stellate), pituitary gland and lymphoid organs, where WKY showed specific high affinity binding sites. The adrenal zona glomerulosa of 4- and 14-week-old SHR and kidney glomeruli and olfactory bulb of 4-week-old SHR showed no significant differences in the binding sites as compared to those of age-matched WKY. The lower number of ANP binding sites also was found in SFO and choroid plexus of stroke-prone SHR as compared to those of age-matched WKY. ANP $_{99-126}$ -induced cyclic GMP production in the isolated lymphocytes as well as stellate ganglia from SHR was not only found in a dose-dependent manner, but also the magnitudes in that production was the similar to those found in WKY, indicating the discrepancies between specific ANP binding and its effect on cyclic GMP production. In addition, tissues which showed the lower or undetectable number of ANP binding sites in SHR had high affinity binding sites for ANP $_{111-126}$ in WKY. Although ANP $_{111-126}$ effectively competed for specific binding sites in some tissues of WKY, this fragment was not agonist and did not antagonize the ANP $_{99-126}$ -induced increase in cyclic GMP. Thus, our results suggest that SHR has a genetic defect in the one of subtypes of ANP receptors, which may not be coupled to guanylate cyclase.