73) Atrial Natriuretic Polypeptides in Rat Heart and Plasma. Kazuwa Nakao^{1,2}, Makoto Sakamoto¹, Narito Morii¹, Akira Sugawara¹, Mitsuaki Suda¹, Masanori Shimokura³, Yoshiaki Kiso³, Masahiro Kihara⁴, Yukio Yamori⁴, and Hiroo Imura¹.
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Following the discovery of natriuretic and diuretic action of rat atrial extracts, multiple forms of natriuretic and diuretic polypeptides have been isolated from rat and human atrial extracts. α -rat atrial natriuretic polypeptide (α -rANP) is a 28-amino acid polypeptide which is a counterpart of α -human atrial natriuretic polypeptide (α -hANP) isolated from human atria by Kangawa and Matsuo (Biochem Biophys Res Commun 118: 131, 1984) and corresponds to the C-terminal 28 amino acids of β -rANP (5K) and γ -rANP (13K). An atrial peptide identical to α -rANP was also purified from rat atria by Flynn et al. (Biochem Biophys Res Commun 117: 859, 1983). This atrial peptide or α -rANP has a single amino acid replacement of methionine by isoleucine at the position 12 when compared with α -hANP. In order to elucidate the pathophysiological significance of these atrial natriuretic polypeptides, we have set up a radioimmunoassay (RIA) for α -ANP which can recognize α -hANP and α -rANP equally (Nakao et al: Biochem Biophys Res Commun in press, 1984, Sugawara et al: This Meeting, 1984).

In the present study, we have investigated α -rANP-like immunoreactivity (α -rANP-LI) in male Wistar rat heart and whether or not α -rANP-LI is present in the rat plasma.

The dilution curve of rat atrial extracts was parallel to the standard curve of the RIA for α -ANP. A large amount of α -rANP-LI was present in the rat atrium and the concentrations of α -rANP-LI in the right auricle, left auricle and non-auricle part of the atrium are 506 ± 26 ng/mg, 409 ± 19 ng/mg and 109 ± 17 ng/mg (the mean $\pm$ SE), respectively. Little was found in the rat ventricle (<50 pg/mg). Thus, the concentration of α -rANP-LI in the right auricle was the highest in the atrium and about 1.2 times higher than that in the left auricle.

High performance gel permeation chromatography (HP-GPC) coupled with the RIA demonstrated that α -rANP-LI in the rat atrium showed two peaks, one major peak and one minor peak. The major peak emerged at the elution position of γ -rANP (13K) and the minor peak, 3K-5K α -rANP-LI, was located at the elution position consistent with that of β -rANP. There was little immunoreactivity at the position of α -rANP. These results along with the previous report on bioactivity of γ -rANP suggest that γ -rANP is not only a precursor of β - and α -rANP, but an important component of atrial natriuretic polypeptides.

A significant concentration of α -rANP-LI was also detected in the rat plasma (approximately 1-3 ng/ml). This finding indicates that atrial natriuretic polypeptides act as circulating hormones. Further studies on the nature of α -rANP-LI in the rat plasma are ongoing in our laboratory.

In summary, large amounts of natriuretic polypeptides exist in the rat atrium, especially in the auricle. γ -rANP, a high molecular weight form, is a major component of α -rANP-LI in the rat atrium. A high concentration of α -rANP-LI is present in the rat plasma, suggesting that α -rANP-LI is released into the bloodstream from the atrium and circulates as a natriuretic and diuretic hormone.