

## 論 文 要 旨

### **Role of musclin in the pathogenesis of hypertension in rat.**

李迎霄

Musclin is a novel skeletal muscle-derived secretory factor found in the signal sequence trap of mouse skeletal muscle cDNAs. Musclin possesses a region homologous to the natriuretic peptide family. Thus, musclin is found to bind with the natriuretic peptide clearance receptors. However, the role of musclin in vascular regulation remains unclear. In this study, we aim to investigate the direct effect of musclin on vascular tone and to analyze its role in hypertension using the spontaneously hypertensive rats (SHR). In aortic strips isolated from SHR, musclin induced contractions in a dose-dependent manner. We found that the musclin-induced vasoconstriction was more marked in SHR than in normal rats (WKY). Moreover, this contraction was reduced by blockade of natriuretic peptide receptor C using the ab14355 antibody. Therefore, mediation of the natriuretic peptide receptor in musclin-induced vasoconstriction can be considered. In addition, similar to the natriuretic peptide receptor, expression of the musclin gene in blood vessels was higher in SHR than in WKY. Injection of musclin markedly increased the blood pressure in rats that can be inhibited by anti-musclin antibodies. Musclin-induced vasoconstriction was more pronounced in SHR than in WKY as in its expression. Taken together, these results suggest that musclin is involved in blood pressure regulation. The higher expression of musclin in hypertension indicates that musclin could be used as a new target for the treatment of hypertension in the future.