論文審査の要旨

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Role of musclin in the pathogenesis of hypertension in rats

高血圧の発症におけるマスクリンの関与

Background & Aims

Musclin is a novel skeletal muscle-derived secretory factor found by the signal sequence trap of mouse skeletal muscle cDNAs. Musclin possesses a homologous region to the natriuretic peptide family. Thus, musclin is thought to bind with the natriuretic peptide clearance receptor (NPR-C). However, the role of musclin in vascular regulation remains unclear. In this study, the applicant tried to investigate direct effect of musclin on vascular tone and to clarify its role in hypertension using the spontaneously hypertensive rats (SHR).

Resluts

The applicant found that musclin induced vasoconstriction in aortic strips isolated from wistar kyoto (WKY) or SHR in a concentration-dependent manner. The response in SHR was more marked than that in WKY. In SHR, musclin expression was higher than in WKY. Moreover, the blood pressure was raised by injection of musclin into the rats. The blood pressure in SHR and WKY were decreased after treatment with anti-musclin antibody. Although NPR-C expression in SHR was higher than in WKY, anti-NPR-C antibody treatment partially abolished the vasoconstriction caused by musclin. The vasoconstriction induced by musclin appeared to be calcium-dependent. Finally, they found that both musclin-induced vasoconstriction and musclin expression were more pronounced in SHR as compared to WKY.

Discussions

In the *in vitro* studies, musclin could trigger blood vessel contraction. Injected musclin to both WKY and SHR could lead the blood pressure increase. But blood pressure of only SHR was decreased by treatment with anti-musclin antibody. However, musclin-induced aortic vasoconstriction was partially reduced by NPR-C antibody. It is suggested that musclin may have its own specific receptor and could also partially activate NPR-C rat.

Conclusions

Taken together, their results demonstrated that musclin has the ability to induce vasoconstriction, thereby increasing the blood pressure in rats. This is the first report on the role of musclin in blood pressure regulation. Musclin may be a new pharmacological target in the treatment of hypertension.

本研究は、Musclin が血管平滑筋細胞において、生理的及び病理的条件下でも血管収縮及び、血圧調節に関与している可能性を示唆しており、高血圧の新規治療法の開発にもつながる重要な知見を報告している点で非常に興味深い。よって本研究は学位論文として十分な価値を有するものと判定した。