

論 文 要 旨

C-type natriuretic peptide modulates permeability of the blood-brain barrier

血液脳関門の透過性に対する
C型ナトリウム利尿ペプチドの関与

Manoj Bohara
(ボハラ マノズ)

C-type natriuretic peptide (CNP) is abundant in brain and is reported to exert autocrine function in vascular cells, but its effect on blood-brain barrier (BBB) permeability has not been clarified yet. Here, we examined this effect. Transendothelial electrical resistance (TEER) of in vitro BBB model, composed of bovine brain microvascular endothelial cells and astrocytes, was significantly dose dependently decreased by CNP (1, 10, and 100 nmol/L). C-type natriuretic peptide treatment reduced both the messenger RNA (mRNA) and protein expressions of tight junction (TJ) protein zonula occludens-1 (ZO-1). The effects on TEER, mRNA, and protein expressions of ZO-1 were mimicked by cyclic GMP (cGMP) analog 8-bromo-cGMP (1 mmol/L) and reversed by protein kinase G (PKG) inhibitor Rp-8-CPT-cGMPS (100 mmol/L), thus implying the role of PKG and cGMP signaling in BBB function. Transcription factor JunD knockdown by small interfering RNA resulted in no change of permeability by CNP. In vivo study of mouse brain by fluorimetric analysis with intravenous administration of sodium fluorescein (40 mg/kg) also showed a significant increase in BBB permeability by CNP (10 nmol/kg, intravenously). These findings suggest that CNP modulates the BBB permeability by altering ZO-1 expression.