学位論文抄録

The interaction of vasopressin V1a and V2 receptor in renal tubules under the low pH conditions

(低pH下での腎尿細管内バソプレシンV1aとV2受容体の相互作用の検討)

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Abstract of the Thesis

Background and Purpose: Arginine-vasopressin (AVP) plays a key role in the urine concentration mechanism via the vasopressin V2 receptor (V2R) and aquaporin 2 (AQP2) in the kidney. It is well known that V2R is localized on the basolateral side and the V1a receptor (V1aR) is distributed on the luminal side of the collecting ducts. Previously, we have reported an increase of V1aR mRNA and decrease of V2R mRNA in the collecting duct under chronic metabolic acidosis. However, the regulatory mechanism of V2R in acidic conditions has not been determined yet. The purpose of the present study is to investigate the regulatory mechanism of V2R and the effect of V1aR stimulation on V2R expression under acidic conditions.

Methods: The effect of changes in pH on V2R promoter activity was investigated using the LLC-PK_1 cell line stably expressing rat V1aR (LLC-PK_1/rV1aR). LLC-PK_1/rV1aR cells were incubated under alkaline, normal and low pH conditions (pH 7.6 - 6.7) after the transfection of rat V2R (rV2R) promoter-luciferase vector. The effect of low pH on V2R expression was also examined at the transcription, mRNA, and protein levels in LLC-PK_1/rV1aR cells. The MAPK and PKA inhibitors were using to see the intracellular signaling pathways how to effect on the rV2R promoter activity in low pH conditions.

Results: The rV2R promoter activity was significantly increased at 12 hr after the incubation in low pH conditions, which was sustained for 24 hr. The mRNA and protein expressions of V2R were also increased in low pH conditions. V1aR stimulation suppressed rV2R promoter activity in pH dependent manner. PKA and JNK inhibitors suppressed the rV2R promoter activity both in neutral and low pH conditions without FBS. However, JNK inhibitor prevented the increase of V2R promoter activity only in low pH conditions in the presence of FBS.

Conclusions: V2R expression is increased at the transcriptional, mRNA, and protein levels in LLC-PK_1/rV1aR cells under the low pH conditions. Acidic condition-induced V2R enhancement was suppressed by V1aR stimulation, suggesting the crucial role of V1aR for water and electrolytes homeostasis in acidosis.