The mechanism of the activation of sodium channel by serine protease and the regulation of rat prostasin

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Summary

Abnormal renal physiology plays a central role in virtually all sustained hypertensive states. In Japan, the population of salt-sensitive hypertension is relatively high. There are several mechanisms in the kidney to reabsorb Na from the luminal fluid, for examples, Na co-transporter systems in the proximal tubule, Na/K/2Cl co-transporter in the loop of Henle, Na/Cl co-transporter and Na channel in the distal nephron. Recent report has given a strong impact on the pathogenesis of essential hypertension. Liddle syndrome, in which patients develop a form of genetic hypertension, has been shown to have mutations within the cytoplasmic COOH terminal of the β-and γ-subunits of the epithelial Na channel lead to a hyperactivity of the channel. In patients with essential hypertension, however, significant relation has not detected. Recently, a new Na channel activator, channel-activating protease(CAP1), has been cloned from a *Xenopus* kidney epithelial cell line. We investigated the mechanism of the activation of Na channel and the regulation of rat prostasin.

Phosphatidylinositol-specific phospholipase C clearly separated the prostasin protein. This result suggested that prostasin is glycosylphosphatidylinositol – anchored ptotein. Prostasin is secreted into incubation medium in cultured M-1 cell line. Urinary prostasin secretion was stimulated when rat was given aldosterone by osmotic mini-pump.

Our data suggest that prostasin, a serine protease, was stimulated by aldosterone. Further studies are necessary to clarify whether prostasin and other Na regulatory hormone systems are closely linked or not. It is also interesting whether prostasin is involved in the pathogenesis in essential hypertension.