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Molecular Mechanism of Aldosterone Action on Epithelial Sodium Channel (ENaC)

Yoshinori Marunaka, Noriko Yokoyama, Naomi Niisato, Hiroaki Miyazaki, Shegekuni Hosogi, Mitsuoki Hashiba, Takahiro Yamada, Tamotsu Hashimoto

Department of Molecular Cell Physiology, Graduate School of Medical Science,
Kyoto Prefectural University of Medicine

Summary

It has been considered that the activity of ENaC mainly depends on the number of ENaC at the plasma membrane. Previously we have reported that stimulation with aldosterone decreases the rate of ENaC endocytosis. In this study we have quantified the abundance and localization of ENaC in raft domain as well as plasma membrane with/without aldosterone stimulation. Aldosterone stimulates increases in full-length ENaC and cleavaged of ENaC in cells. Localization of full-length ENaC in raft domain increases following stimulation with aldosterone, although aldosterone has no effect on the localization of the cleavaged form of ENaC. On the other hand the increase in cleavaged form of ENaC at the plasma membrane is obvious in response to aldosterone stimulation. Furthermore the localization of full-length ENaC at the plasma membrane is not altered by stimulation with aldosterone. Depletion of cholesterol from the raft domain diminishes the aldosterone action, suggesting important roles of the raft domain in the regulation of ENaC activity. We have also demonstrated that the modification of ENaC such as ubiquitination and phosphorylation occurs in raft domain. Together, these data demonstrate the important roles of the lipid raft domain on the regulation of ENaC trafficking/activity.