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Physiological Roles of Moesin, a Membrane Cytoskeletal Cross-Linker in the Renal Salt and Water Reabsorption

Ryo Hatano, Kotoku Kawaguchi, Shinji Asano

Department of Molecular Physiology, College of Pharmaceutical Sciences,
Ritsumeikan University

Summary

Electrolytes as Na^+, K^+, and Cl^- have a vital role in maintaining body fluid homeostasis. Kidney is an essential organ to keep these electrolytes balance in the body and several ion transporters and channels play pivotal roles in keeping electrolytes balance. Although more than 50 % of Na^+ filtered in the glomerulus are reabsorbed in the proximal tubules via Na^+ transporters as Na^+-dependent glucose cotransporter, Na^+/H^+ antiporter, Na^+-phosphate cotranspoter and so on, this process seems to be required for the reabsorption of nutritions but not the regulation of body fluid balance. In the thick ascending limb of Henle (TALH), 20 to 40 % Na^+ are reabsorbed by NKCC2 (Na-K-Cl cotransporter 2), which plays essential roles in the reabsorption of electrolytes and volume balance regulation. Despite of the physiological importance of NKCC2 in the regulation of NaCl homeostasis, the molecular mechanisms for its membrane trafficking are not elucidated. Recently, Carmosino *et al.* reported that Moesin, which is a member of ERM (Ezrin-Radixin-Moesin) family, plays an important role in the apical membrane trafficking of NKCC2 by *in vitro* experiments. Thus, we examined the physiological importance of Moesin in the regulation of renal function by using moesin deficient mice. We found that moesin deficient mice exhibited the significant increase in the fractional urinary excretion of electrolytes (Na^+, K^+, and Cl^-), whereas total urinary contents of these electrolytes were not different between Wild type and Moesin deficient mice. Furthermore, Moesin deficient mice showed moderate hypotensive phenotype and significantly reduced glomerular filtration rate, suggesting the possible compensation for the urinary loss of electrolytes. Immunofluorescent analysis also indicated the reduced apical surface expression of NKCC2 in Moesin deficient mice. In summary, our study suggests that Moesin plays an important role in the maintaining the apical surface expression of NKCC2 in TALH and regulation of the electrolyte reabsorption *in vivo*.