Modulation of ion selectivity in the proximal tubule paracellular shunt pathway by claudin-2

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Summary

Claudin-2 is one of the tight junction proteins expressed in proximal tubule, but its role in paracellular shunt pathway Na/Cl transport is unknown. Therefore, we generated mice lacking *claudin-2* by gene targeting disruption and compared morphological and functional features between the *claudin-2* knockout (KO) mice and their wild-type (WT) mice. Light microscopic findings exhibited that there were no significant differences between the two groups of the kidneys. Both ultrathin section electron microscopic images and freeze fracture replicae showed that tight junction strands indeed existed in the proximal tubule from the KO mice, and there were no prominent differences of the proximal tubule tight junction and proximal tubule cells between the two groups. Next, we isolated and perfused proximal tubule S2 segments from both groups of the kidneys to estimate the permeability ratio of Na to Cl. In the tubule of the WT mice, when the luminal perfusate was abruptly changed to the low NaCl solution, transepithelial voltage (Vt) deflected to the positive direction, and the tubule was more permeable to Na than to Cl. In sharp contrast, in the tubule of the KO mice, Vt deflected to the negative direction upon abrupt reduction of the luminal NaCl concentration, and the tubule was more permeable to Cl than to Na. The transpithelial resistance in the tubule from the KO mice was significantly greater than that of the WT mice. The fractional excretion of Na or Cl was not significantly different between the two groups. We conclude that claudin-2 contributes to Na selectivity in the paracellular shunt pathway of the mouse proximal tubule.