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Sorting nexin 27 regulates the lysosomal degradation of AQP2 protein in kidney collecting duct

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Objectives: We recently demonstrated that vacuolar protein sorting-associated protein 35 (Vps35), a component of the retromer complex, interacts with the carboxyl terminus of aquaporin-2 (AQP2c), and depletion of Vps35 was associated with decreased AQP2 trafficking and increased lysosomal degradation of AQP2 (Am J Physiol Renal Physiol, 2016; 311: F1294). Sorting nexin 27 (SNX27), a PDZ domain-containing protein, is known to cooperate with the retromer complex in the recycling of early endosome to the plasma membrane.

Methods: Since AQP2c has the class I PDZ-interacting motif (X-Thr/Ser-X-Φ), we aimed to examine whether SNX27 could play a role in the regulation of AQP2 trafficking and protein abundance in the kidney collecting duct cells.

Results: Immunohistochemistry of rat kidneys revealed that SNX27 was diffusely labeled throughout the cytoplasm in the collecting ducts cells. Co-immunoprecipitation assay demonstrated that SNX27 interacted with AQP2 in rat kidney inner medulla. The role of SNX27 in the dDAVP-induced AQP2 trafficking and AQP2 protein abundance was examined in mouse kidney cortical collecting duct mpkCCDc14 cells under siRNA-mediated knockdown of SNX27. Cell surface biotinylation assay revealed that dDAVP-induced translocation of AQP2 to the apical plasma membrane was not changed under SNX27 knockdown. dDAVP-induced AQP2 up-regulation was significantly blunted in the cells with SNX27 knockdown. During the withdrawal period (3 h) after dDAVP stimulation, the decrease of AQP2 protein abundance in the cells with SNX27 knockdown was attenuated by lysosomal inhibition with chloroquine co-treatment.

Conclusions: Taken together, SNX27 is an interacting protein with AQP2 and is likely to act as a component of the AQP2 sorting machinery after endocytosis, partly by regulating the lysosomal degradation of AQP2 protein abundance.