Aquaporin 2

Aquaporin 2 (AQP2) is found in the apical cell membranes of the kidney's collecting duct principal cells and in intracellular vesicles located throughout the cell.

It is the only aquaporin regulated by vasopressin.

The basic job of aquaporin 2 is to reabsorb water from the urine while its being removed from the blood by the kidney. Aquaporin 2 is in kidney epithelial cells and usually lies dormant in intracellular vesicle membranes. When it is needed, vasopressin binds to the cell surface vasopressin receptor thereby activating a signaling pathway that causes the aquaporin 2 containing vesicles to fuse with the plasma membrane, so the aquaporin 2 can be used by the cell.

This aquaporin is regulated in two ways by the peptide hormone vasopressin:

short-term regulation (minutes) through trafficking of AQP2 vesicles to the apical region where they fuse with the apical plasma membrane long-term regulation (days) through an increase in AQP2 gene expression. This aquaporin is also regulated by food intake. Fasting reduces expression of this aquaporin independently of vasopressin.

Mutations in this channel are associated with nephrogenic diabetes insipidus, which can be autosomal dominant or recessive. Mutations in the vasopressin receptor cause a similar X-linked phenotype.

Lithium, which is often used to treat bipolar disorder, can cause acquired diabetes insipidus (characterized by the excretion of large volumes of dilute urine) by decreasing the expression of the AQP2 gene.

The expression of the AQP2 gene is increased during conditions associated with water retention such as pregnancy and congestive heart failure.

Arystarkhova et al. report that FXYD1 (phospholemman), better known as a regulator of Na,K-ATPase, has a role in AQP2 trafficking. Daytime urine of Fxyd1 knockout mice was more dilute than WT despite similar serum vasopressin, but both genotypes could concentrate urine during water deprivation. FXYD1 was found in IMCD. In WT mice, phosphorylated FXYD1 was detected intracellularly, and vasopressin induced its dephosphorylation. We tested the hypothesis that the dilute urine in knockouts was caused by alteration of AQP2 trafficking. In WT mice at baseline, FXYD1 and AQP2 were not strongly co-localized, but elevation of vasopressin produced translocation of both FXYD1 and AQP2 to the apical plasma membrane. In kidney slices, baseline AQP2 distribution was more scattered in the Fxyd1 knockout than in WT. Apical recruitment of AQP2 occurred in vasopressin-treated Fxyd1 knockout slices, but upon vasopressin washout, there was more rapid reversal of apical AQP2 localization and more heterogeneous cytoplasmic distribution of AQP2. Notably, in sucrose gradients, AQP2 was present in a detergent-resistant membrane domain that had lower sedimentation density in the knockout than in WT, and vasopressin treatment normalized its density. We propose that FXYD1 plays a role in regulating AQP2 retention in apical membrane, and that this involves transfers between raft-like membrane domains in endosomes and plasma membranes [1].

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Arystarkhova E, Bouley R, Liu YB, Sweadner KJ. Impaired AQP2 trafficking in Fxyd1 knockout mice: A role for FXYD1 in regulated vesicular transport. PLoS One. 2017 Nov 20;12(11):e0188006. doi:

10.1371/journal.pone.0188006. eCollection 2017. PubMed PMID: 29155857.