KSN 2021
FULLY VIRTUAL MEETING
September 02 (Thu) - 05 (Sun)

Abstract Submission No. : 9103

Vasopressin-independent pathways for aquaporin-2 activation in the kidney

Tae-Hwan Kwon
Kyungpook National University, Korea

The kidney collecting duct (CD) is the renal tubular segment, in which the osmolality and volume of the final urine are established. This process makes urine concentrated under the arginine vasopressin (AVP) stimulation and contributes to body water homeostasis. AVP binds to the arginine vasopressin receptor 2 (AVPR2) and mediates transcellular water reabsorption across the CD principal cells. The signaling cascade regulates the water channel protein aquaporin-2 (AQP2). Specifically, AVP induces the intracellular trafficking of AQP2-expressing vesicles to the apical plasma membrane, thereby, increasing the osmotic water permeability of CD cells. Moreover, AVP stimulates the transcription of the *Aqp2* gene, inducing the AQP2 protein abundance. However, AVP-independent mechanisms for the AQP2 trafficking to the plasma membrane are also present. This can be achieved by bypassing AVPR2 signaling and inducing AQP2 accumulation in the membrane. There are two categories: 1) intracellular cAMP elevation by either activating other GPCRs or inhibiting phosphodiesterases; and 2) cAMP-independent pathways. Endogenously expressed G-protein-coupled receptors (GPCRs) besides AVPR2 are present in the renal CD that naturally couple to GαS to increase cAMP levels and regulate AQP2 expression. There are several potential candidates, including the prostaglandin E receptors (EP2 and EP4), β3-adrenergic receptor (β3-AR), calcitonin receptor, secretin receptor, and TGR5 (bile acid-activated membrane receptor). Alternatively, there are GPCRs that do not couple to GαS and cAMP pathways but regulates AQP2 expression, including frizzled receptor and EGF receptor. In addition, AQP2 protein abundance is regulated by post-translational modification, e.g., ubiquitination or RNA interference. This talk deals mainly with AVP-independent regulation of AQP2, which could provide new insights into the treatment of hereditary nephrogenic diabetes insipidus associated with mutations of either *AVPR2* or *AQP2* gene.