Aquaporins in Health and Disease

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Aquaporins are integral membrane proteins which mediate rapid water transport across cell membranes in the kidney and other organs. Four Aquaporins are known to play important functional roles in the kidney : aquaporin-1(in proximal tubule and thin descending limb of Henle), aquaporin-2(in apical plasma membrane of collecting duct principal cells), aquaproin-3(in basolateral plasma membrane of connecting tubule, cortical collecting duct and outer medullary collecting duct), and aquaporin-4(in basolateral plasma membranse of outer medullary and inner medullary collecting ducts). Among the aquaporins, aquaporin-2(the vasopressin-regulated water channel) is most important for control of water excretion by the kidney. Vasopressin regulates aquaporin-2 in two distinct modes : 1) Short term regulation, and 2) Long term regulation. Short term regulation of aquaporin-2 is achieved through the action of vasopressin to regulate exocytosis of aquaporin-2-bearing vesicles to the apical plasma membrane, a process mediated in part by specialized vesicle-targeting receptors in the vesicular membrane and the plasma membrane. Long term regulation is achieved through the action of vasopressin(working through cyclic AMP) to regulate the aquaporin-2 gene, producing more aquaporin-2 in the cell with long term exposure of the collecting duct cells to high circulating levels of vasopressin. Investigations of the role of altered regulation of aquaporin-2 in several pathophysiological states have been carried out, demonstrating specific defects in either the short-term or long-term regulatory processes. These pathophysiological states include : 1) central diabetes insipidus; 2) hereditary nephrogenic diabetes insipidus; 3) primary polydipsia; 4) syndrome of inappropriate antidiuretic hormones secretion; 5) acquired nephrogenic diabetes insipidus (lithium-induced, hypokalemic, hypercalcemic, and post-obstructive); and 6) extracellular fluid volume expanded states(congestive heart, cirrhosis and nephrotic syndrome).