Aquaporin water channels: From atomic structure to clinical medicine

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Physiologists have long recognized that plasma membranes of red cells and certain epithelia exhibit high water permeability. The molecular identity of membrane water channels eluded identification until a 28 kDa membrane protein was discovered. When expressed in amphibian oocytes, the new protein, AQP1, made the cells highly permeable to water with inhibition by $HgCl_2$ and low Arrhenius activation energy. The molecular structure resembles an hourglass with an external chamber and an internal chamber linked by 3Å diameter channel that allows trans-membrane passage of water but not ions or larger solutes. Aquaporins with similar structures have been found in all life forms. Thirteen known human aquaporins have been identified and characterized for physiological functions and potential roles in human diseases. Humans lacking Colton blood group antigens have no AQP1 protein and exhibit defective urine concentration and reduced fluid exchange between capillaries and interstitium in lung. AQP2 is the vasopressin activated water channel in renal collecting duct principal cells and has been linked to nephrogenic diabetes insipidus. AQP4 has been implicated in brain edema, and an extracellular epitope is the antibody recognition site in neuromyelitis optica. Mistargeting of AQP5, normally expressed in the apical membranes of salivary and lacrimal gland acini, can occur in Sjogren's syndrome. AQP0 resides in lens fiber cells and has been linked to familial cataracts. Aquaglyceroporins have slightly wider pore structures and are permeated by water plus glycerol. AQP3 in basal levels of dermis contributes to skin integrity. AQP7 facilitates glycerol release from adipocytes during fasting, and AQP9 provides glycerol uptake by hepatocytes for conversion to glucose. Aquaporins are present in plant tissues and microbes where functional roles are being established in malaria and other infectious diseases. Applications of this knowledge are being sought for prevention and treatment of diseases.