Phenomena: How Does Our Cell Membrane Transport Water and Ions?
Maintaining water and ion homeostasis is critically important for cell form and function. Water and ion channels are implicated in several diseases associated with the kidneys, heart, lungs and brain. But how do they work? With the lipid bilayer being largely hydrophobic, how do cells efficiently and effectively achieve the proper homeostasis of polar molecules like water and salt? Read on to find out...

The existence of water channels was predicted as early as the mid-1800s. However, it wouldn’t be until over 100 years later, while studying Rh blood group antigens, that the identity of the hypothesized water channel would be confirmed and revealed by Agre and his team. Agre demonstrated the function of aquaporin by comparing Xenopus oocytes with and without aquaporin. Those with aquaporin swelled significantly in a hypotonic solution... to the point that the oocytes lysed.

Structure of Aquaporin
To date, at least thirteen variants of aquaporin have been found in all organisms, from bacteria to plants and animals. The aquaporin protein is characterized by six membrane-spanning helices and two half helices that collectively form a channel allowing primarily water molecules to move through the largely hydrophobic phospholipid bilayer of the cell. Aquaporins usually form tetramers, with each monomer defining a single pore. Two main constriction sites have been identified in the aquaporin channels. In the center of the pore, two conserved Asn-Pro-Ala motifs (NPA), with two asparagine side chains pointing into the pore, are located at the end of two half helices. The dipoles of the half helices generate an electrostatic barrier in the NPA region, which is essential in ensuring that water molecules and not protons in the form of hydronium ions pass through the channel. Close to the extracellular exit of the channel, the aromatic/arginine (ar/R) constriction region forms the narrowest part of the pore and is therefore assumed to be important in channel selectivity.

Implications: Various aquaporin proteins are especially important in the kidneys, where 150-200 liters of water must be resorbed daily. Alterations in aquaporin expression or function can be rate-limiting for water transport across membranes. Ultimately, they could be a target for therapy in diseases of altered water homeostasis such as diabetes insipidus, edema and glaucoma.

A Tale of Two Channels

Peter Agre & Aquaporin: The Case of the Exploding Frog Eggs!
The 2003 Nobel Prize in Chemistry

Rod MacKinnon & selectivity of the Potassium Channel

Structure of the Potassium Channel

Implications: Potassium channels are important in producing electrical signals in the nervous system, as well as maintaining proper muscle and heart function. Better understanding ion channels like the potassium channels is also useful in drug interaction and targeting studies.

Resources: