Chapter 14

Web Text Box 1

Changing the channel: the different types of potassium channel

In the book we refer to “potassium channels” and give little indication of the range of types and behaviors of the potassium channel family. In fact there are approximately 50 genes coding for potassium channel subunits, while extensive alternative splicing (In Depth 5.1 on book page 76) vastly increases the number of potential protein products. The functional channel (usually) comprises four oligomers (e.g. Example 9.1 on book page 141) and since there is every reason to suspect that channels in cells can be heterotetramers as well as homotetramers (that is, the four subunits of a single channel can be different gene or splice products) there are potentially millions of different working channel designs. The potassium channel genes are divided into a number of families:

Voltage gated potassium channels are similar to sodium channels in that they switch to an open state when the membrane is depolarized. Some, like sodium channels, then inactivate and have to spend some time at a negative voltage to recover from inactivation. They are common in nerve cells, where they help to terminate the action potential. Subtle differences in the voltage dependence and speed of activation, inactivation and recovery from inactivation mean that nerve cells expressing different types of voltage gated potassium channel show different patterns of action potential firing upon stimulation.

Calcium activated potassium channels open when the cytosolic calcium concentration rises. Some have an integral calcium binding site; others are regulated by the calcium-binding protein calmodulin (book page 149). As well as being important in nerve and muscle cells they play important roles in other cells. For example, the flow of liquid across many gland epithelia is driven by potassium movement out of the cells through calcium activated potassium channels that open when the gland cells are stimulated by agonists that raise cytosolic calcium (by the mechanisms described in book pages 253-254).

Inward rectifier potassium channels are a disparate group that share the property that certain cytosolic cations (including a molecule first crystallized by Anton van Leeuwenhoek (book page 1) from sperm and therefore called spermine) try to accompany potassium through the channel when the electrochemical gradient for potassium is outward, but they are too large and instead block the channel. In contrast when the electrochemical gradient for potassium is inward potassium moves in unhindered. This property of passing current better in one direction than another is called rectification.

One of the most clinically important of the inward rectifier potassium channels is the ATP gated channel found in pancreatic β cells. When the glucose concentration in the blood increases these cells make more ATP, which blocks the channels. The β cells therefore depolarize (because since there are fewer open potassium channels, the new steady state voltage must lie further away from the potassium equilibrium voltage such that each potassium channel carries a larger outward current to balance a relatively constant inward current carried by sodium and calcium) and fire action potentials, opening voltage gated calcium channels. The inward movement of calcium triggers the exocytosis of insulin. ROMK (Example 9.1 on book page 141, Medical Relevance 14.3 on page 246) is another member of the inward rectifier family.

Two pore channels are poorly named – they should really be called two-oligomer channels. An ancestral potassium channel gene has been duplicated so that a single gene now encodes a polypeptide that folds into two domains, each of which is homologous to one oligomer of a typical potassium channel. Thus only two oligomers are necessary to form a complete channel. Many two-pore channels simply stay open all the time, without being dramatically affected by voltage or extracellular stimuli. They are therefore often the channels responsible for the high potassium permeability of the plasma membrane in resting, unstimulated cells.

For more detail see Benarroch. 2009. Neurology, 72:664 and Johnston et al. 2010. J. Physiol. 588:3187.