## The transient receptor potential (TRP) ion channels: recent progress

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Mammalian TRP channel proteins are six transmembrane (6TM) cation-permeable channels that may be grouped into TRPC, TRPV, TRPM, TRPA, TRPP and TRPML subfamilies. Selected functional properties of TRP channels from each subfamily will be summarized. TRP channels are cation channels with polymodal activation properties. By integrating multiple concomitant stimuli and providing signal amplification through calcium permeation and membrane depolarization, TRP channels function in cellular sensing. Other than overall sequence homology, basic channel architecture and cation selectivity, there are no particular features defining the TRP family. Cooperativity intrinsic to TRP channels may result in allosteric coupling of distinct activation stimuli, blurring the definition of 'activator' *versus* 'modulator'. The established modes of activation for expressed TRP channels may be divided into:

**1. Receptor activation.** G protein coupled receptors and receptor tyrosine kinases that activate phospholipases C (PLC) can modulate TRP channel activity in at least three ways: a) hydrolysis of phosphatidylinositol (4,5) bisphosphate (PIP2); b) production of diacylglycerol (DAG); or c) production of inositol (1,4,5) trisphosphate (IP3) and subsequent liberation of calcium from intracellular stores.

**2. Ligand activation.** Ligands that activate TRP channels may be broadly classified as: a) exogenous small organic molecules, including synthetic compounds and natural products (capsaicin, icilin, 2-APB); b) endogenous lipids or products of lipid metabolism (diacylglycerols, phosphoinositides, eicosanoids, anandamide); c) purine nucleotides and their metabolites (ADP-ribose, βNAD+); or d) inorganic ions, with calcium and magnesium being the most relevant. It seems likely that endogenous molecules that function as TRP channel ligands remain to be discovered.

**3. Direct activation.** Changes in ambient temperature are strongly coupled (Q10 > 10) to opening of TRPV1-TRPV3 and TRPM8. Other cellular signaling mechanisms such as regulation by $Ca^{2+}$/calmodulin have also been demonstrated to modulate TRP channel activity.

**4. Channel availability** by translocation also regulates TRP channel function. For several different TRP channels, insertion of vesicles containing TRP proteins into the plasma membrane regulates the number of functional channels.