Oxygen dependent regulation of TRP channel function

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The transient receptor potential (TRP) gene superfamily encodes calcium-permeable non-selective cation channels broadly expressed in most tissues in the body. Members of the TRP channel superfamily play distinctive roles of polymodal cellular sensors which respond to a diverse range of extracellular and intracellular stimuli, including second messengers, chemicals, temperature, mechanical stimulation, and osmolality. Recent research suggests that several members of TRP superfamily contribute to physiological responses to changes in redox state and levels of molecular oxygen by regulating cellular electrical activity and calcium signalling. Molecular mechanisms of redox- and oxygen-sensing of TRP channels range from indirect activation by reactive oxygen and nitrogen species through intracellular messengers (TRPM2), modification of cysteine free sulfhydryl groups (TRPA1, TRPV1 and TRPC5), to proline hydroxylation (TRPA1). We have recently shown that the activity of another TRP family member, TRPV3, is also regulated by hydroxylation, but on a single asparaginyl residue within the conserved intracellular N-terminal ankyrin repeat domain, by an asparaginyl hydroxylase. TRPV3 was originally characterised as a warm temperature sensor, but is also found to be activated by endogenous and exogenous chemical ligands. It has been implicated in pathologies associated with dermatitis, pruritus, inflammation, ischaemia and wound healing.