Physiological Significance of high Ca^{2+} permeability of thermosensitive TRP channels

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TRP (transient receptor potential) channels are non-selective cation channels having relatively high Ca^{2+} permeability, and comprise six related protein families (TRPC, TRPV, TRPM, TRPA, TRPML, TRPP) in mammals. One subunit of the TRP channel is composed of six transmembrane domains and a pore region with both amino and carboxyl termini on the cytosolic side. Among the huge TRP super family of ion channels, some have been proven to be involved in thermosensation detecting ambient temperatures from cold to hot. There are now eleven thermosensitive TRP channels (TRPV1, TRPV2, TRPV3, TRPV4, TRPM2, TRPM3, TRPM4, TRPM5, TRPM8, TRPA1 and TRPC5) with distinct temperature thresholds for their activation. Structures of TRPV1, TRPV2, TRPM4, TRPM8 and TRPA1 have been clarified in the last several years. We found that some thermosensitive TRP channels make a complex with Ca^{2+} -activated chloride channel, anoctamin1 (ANO1). Interaction between TRPV4 and ANO1 is involved in water efflux in choroid plexus, salivary gland and lacrimal gland epithelial cells. And TRPV1 (TRPA1)/ANO1 interaction was found to be involved in the enhancement of nociceptive signals through further depolarization upon chloride efflux in peripheral sensory neurons. This interaction could be one of the reasons why TRP channels have high Ca^{2+} permeability.