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Topical Review

TRPs Make Sense

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Abstract. Drosophila flies with the *trp* mutation exhibit impaired vision due to the lack of a specific Ca^{2+} influx pathway in the photoreceptors. The identification of the *trp* gene product as a Ca^{2+}-permeable ion channel and the search for TRP homologues in flies, worms and mammals has opened the way to the discovery of a whole superfamily of cation channels, baptized TRP channels. In contrast to voltage-gated K^+, Na^+, or Ca^{2+} channels, with whom they share their transmembrane architecture, TRP channels are not activated by voltage but by a variety of signals including intra- and extracellular ligands, Ca^{2+}-store depletion and mechanical or thermal stress. Due to the promiscuity of these gating mechanisms, TRP channels are privileged candidates as primary sensing molecules for the recognition and integration of physical and chemical signals from the environment. In this review we discuss recent evidence that implicates members of the TRP superfamily in sensory signal transduction.

Key words: TRP-channels — Cation channels — Ca^{2+} entry — Signal transduction — Sensory functions

Introduction

Ion channels have distinct functions in the signal transduction processes in sensory cells. First, at the level of receptor cells, they translate chemical or physical stimuli from the environment into an electrical signal. Second, they are responsible for the signal transduction from the sensory receptor cell to information-decoding structures in the central nervous system. Several different families of ion channels have been implicated in the primary process of signal recognition: members of the ENaC/ASIC/degenerin superfamily, consisting of Na^+-selective channels with two conserved transmembrane-spanning domains, have been implicated in pain perception, touch reception and proprioception (for a review *see* Kellenberger & Schild, 2002); members of the family of ionotropic purinergic receptors (P2X-receptors) have been implicated in pain reception (Julius & Basbaum, 2001) and mechanosensitivity (Gillespie & Walker, 2001); TREK-1, a member of the 2-pore-domain K^+ channel family, is stimulated by a variety of physical and chemical stimuli, such as membrane stretch, intracellular acidosis and polyunsaturated fatty acids and has therefore been proposed as a "sensory" channel (Honore et al., 2002). In addition, two families of ion channels within the superfamily of cation channels with six transmembrane (TM) domains seem to be especially important for coding the primary steps in mammalian sensory transduction cascades. The first and best-studied family consists of the cyclic nucleotide-gated (CNG) channels, which open upon direct binding of intracellular cyclic nucleotides (cAMP or cGMP) to their C-termini (Broillet & Firestein, 1999). The electrical signals caused by the opening/closing of these channels in rods, cones and olfactory receptor cells are the crucial initial events in mammalian olfactory and visual signal transduction. Recent evidence identifies the novel TRP superfamily as a second important group of channels involved in sensory signal initiation. Based upon the knowledge of the function of the founding *Drosophila* TRP, members of the TRP superfamily were originally thought to mediate predominantly store-dependent and/or PLC-dependent Ca^{2+} influx in non-excitable cells (Friel, 1996; Zhu et al., 1996). However, in the last five years several members of the TRP family have been identified as primary sensors of both physical (e.g., heat, cold, mechanical stress) and chemical (e.g., pH, pheromones, "hot pepper" compounds) external stimuli. In this review, we first provide a brief overview of the nomenclature and structure of the more than 20 mammalian TRP-related proteins, before focussing exclusively on the role of TRPs in sensory physiology.

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Structure and Nomenclature of the TRP Superfamily

The rapid identification of a large number of TRP-related channels during the last years, including more than 20 in humans, has led to considerable confusion as to channel nomenclature, with several TRPs having multiple names or distinct proteins sharing the same name. Moreover, several "TRP-like" proteins display such a limited homology with the founding member of the family, *Drosophila* TRP, that classifying them as genuine members of the TRP superfamily may be somewhat overzealous. This confusion, which is most likely an inevitable side effect of the exciting discovery of a new protein family, has somewhat diminished with the recent consensus on a unified nomenclature for TRP channels (Montell et al., 2002). According to this nomenclature, 20 mammalian TRP-related proteins are classified into three subfamilies: members of the TRPC (C for Canonical) subfamily display the highest homology to *Drosophila* TRP, members of the TRPV subfamily (V for Vanilloid) are more closely related to the Vanilloid Receptor 1 (VR1, now TRPV1), and the TRPMs (M for Melastatin) are most homologous to Melastatin (now TRPM1). The unified nomenclature does not (yet) include the more distally related PKD2 (a protein implicated in polycystic kidney disease; Cai et al., 1999), mucolipin (the product of the gene that is mutated in mucolipidosis patients; Bargal et al., 2000; Sun et al., 2000), or NompC (a mechanosensitive channel found in *Drosophila* and *C. elegans*; Walker, Willingham & Zuker, 2000), although it has been proposed that they are founding members of three additional subfamilies: the TRPPs, TRPMLs and TRPNs, respectively (Montell, 2001). A better understanding of their exact (ion channel) functions may help to determine whether they classify as genuine TRP channels.

It should be noted that the fact that all members of the TRP family are characterized by a similar topology does not necessarily mean that they are all bona fide cation channels. So far, it has been shown for only a few TRP channels (TRPV1, TRPV4 and TRPV5) that mutations in the putative pore region result in changes in permeation properties (Garcia-Martinez et al., 2000; Nilius et al., 2001; Voets et al., 2002). Therefore, the possibility that some of the other TRPs are not channels per se but modulators (or even subunits) of other ion channels has not yet been excluded and is still a reasonable hypothesis until their channel nature has been clearly proven by showing that mutations to their putative pore region result in changes in pore properties.

The transmembrane topology of TRPs is reminiscent of that of voltage-gated and CNG channels: TRP channels consist of six transmembrane spanning helices (TM1–6), cytoplasmic N- and C-termini and a pore region between TM5 and TM6 (Clapham, Runnels & Strübing, 2001). The highest degree of sequence homology between all members of the TRP superfamily is found in the transmembrane segments. Unlike voltage-operated channels, TM4 is not positively charged, which explains the lack of intrinsic voltage dependence of TRP channels. The N-termini of several TRP channels contain multiple ankyrin-binding repeats: 3–6 in TRPCs and TRPVs and as much as 29 in NompC, but no such ankyrin domains are found in the TRPM subfamily. C-terminal to TM6 in TRPCs and TRPMs contain a conserved stretch of 25 amino acids called TRP domain, which starts with the nearly invariant TRP box (EWKFAR; Montell, 2001). This domain is, however, poorly conserved in the TRPV subfamily. The TRPM subfamily is characterized by their relatively long N- and C-termini, and some members have entire enzyme domains linked to their C-termini: an ADP-ribose pyrophosphatase in TRPM2 (Perraud et al., 2001) and an atypical α-kinase domain in TRPM6 and TRPM7 (Nadler et al., 2001; Runnels, Yue & Clapham, 2001). At present, the functional relation between the channel and enzyme activities of these "chanzymes" remains to be fully established.

TRPs and Light

More than 30 years ago a *Drosophila* mutant was discovered that exhibited a transient instead of sustained response to light (Cosens & Manning, 1969). In the rhabdomeres of mutant flies, sustained light induced a transient rather than the normal sustained, plateau-like increase in intracellular Ca^{2+}. The electrical equivalent of this Ca^{2+} signal in the *Drosophila* rhabdomeres is the receptor potential, and the mutant was therefore termed *trp*, for transient receptor potential. About two decades later, the *trp* gene was cloned (Montell & Rubin, 1989) and subsequently shown to code for a Ca^{2+}-permeable cation channel, TRP, the founding member of the TRP family (Hardie & Minke, 1992). Subsequently two additional homologous proteins were identified in *Drosophila*: TRP-like (TRPL; Phillips, Bull & Kelly, 1992) and TRPγ (Xu et al., 2000). These proteins also appear to contribute to light recognition and, at least in expression systems, these three proteins form heteromultimers with novel properties (Niemeyer et al., 1996; Xu et al., 2000). Flies with defects in TRPL were originally reported to be indistinguishable from wild type (Niemeyer et al., 1996), but later it was found that the light response in *trpl* mutant flies displays several anomalies, including changes in cation selectivity of the light-induced current and a reduced response to a light stimulus of long duration (Reuss et al., 1997; Leung, Geng & Pak, 2000). Mutants lacking both TRP and TRPL are completely unresponsive to light (Niemeyer et al., 1996), in-

dicating that TRPγ on its own cannot substitute for the role of TRP and TRPL in generating a light-induced current.

The exact activation mechanism whereby light activates TRP channels in the *Drosophila* eye still remains kind of an enigma (Hardie & Raghu, 2001). There is, however, consensus about the crucial steps upstream of TRP channel gating. Light induces the isomerization of rhodopsin to metarhodopsin, which activates a heterotrimeric G_q protein via GTP-GDP exchange. This causes release of the $G_q\alpha$ subunit, which activates phospholipase C (PLC), generating inositol 1,4,5-trisphosphate (IP_3) and diacyl glycerol (DAG) from phosphatidylinositol 4,5-bisphosphate (PIP_2) (Hardie & Raghu, 2001). The subsequent step(s) leading to TRP activation are still unclear, although a role for IP_3 seems to be unlikely (Acharya et al., 1997). The gating of the TRP channel could be due to the reduction in PIP_2 levels, the rise in DAG or the conversion of DAG into polyunsaturated fatty acids (PUFAs), such as linolenic and linoleic acid, which have been shown to directly activate TRP and TRPL (Chyb, Raghu & Hardie, 1999). Interestingly, *Drosophila* phototransduction depends on the formation of a signaling complex, called a transducisome. This transducisome is formed by a scaffolding protein, INAD (the product of the *inaD* gene, which stands for inactivation no afterpotential), which contains five protein interaction motifs of ~90 amino acids referred to as PDZ domains (Tsunoda et al., 1997). TRP, TRPL, PLC, rhodopsin, protein kinase C (PKC) and calmodulin are all linked together by INAD, thereby ensuring speed of signaling and sensitivity of the photo response (Huber et al., 1996; Chevesich, Kreuz & Montell, 1997; Li & Montell, 2000). Mutations in the genes encoding proteins of the transducisome invariably cause severe defects in light reception. Finally, it should be noted here that, as mentioned in the introduction, light perception in vertebrates occurs through a completely different mechanism involving cGMP, CNG channels and (most likely) no TRP channels.

TRPs and Temperature

At a time when TRP-related channels were thought to be exclusively activated by PLC-dependent and/or store-dependent mechanisms, Caterina et al. (1997) isolated a vanilloid receptor using an expression cloning strategy. Surprisingly, a sequence comparison revealed that the newly cloned receptor, which was initially termed VR1, displayed significant homology with *Drosophila* TRP, mammalian TRPCs and even more with *C. elegans* Osm9 (Colbert, Smith & Bargmann, 1997). As founding member of the TRPV subfamily, VR1 is now renamed TRPV1. TRPV1 was found to be a Ca^{2+}-permeable channel that could not only be activated by vanilloids such as capsaicin and other pungent pepper compounds, but also by temperatures above 43°C (Caterina et al., 1997). The finding that noxious temperature and vanilloids converge upon a single receptor gave a simple molecular explanation for why people classify spicy peppers as "hot". Its activation properties in conjunction with its exclusive expression in small- to medium-diameter neurons within dorsal root, trigeminal and nodose sensory ganglia, made TRPV1 an ideal candidate transducer of noxious thermal and chemical stimuli (Tominaga et al., 1998). This was confirmed in $TRPV1^{-/-}$ mice, which were shown to be severely impaired in the detection of what wild-type mice experience as painful thermal or chemical stimuli, whereas the responses to painful mechanical stimuli where unaltered (Caterina et al., 2000).

Our ability to sense temperatures over a range from <8 to >50°C, and the fact that some cell types in $TRPV1^{-/-}$ mice are still able to sense hot temperature, implied the existence of additional temperature-sensitive channels. This led to the discovery that three additional members of the TRPV family, TRPV2–4, show a steep dependence on temperature. Surprisingly, none of these channels is sensitive to capsaicin. TRPV2 (originally termed VRL-l for vanilloid receptor-like) is activated at significantly higher temperatures than TRPV1, with a threshold of approximately 52°C (Caterina et al., 1999). In contrast to TRPV1, TRPV2 seems to be expressed preferentially in medium- to large-diameter dorsal root ganglion cells, where it may underlie the characteristically high thermal threshold of type I Aδ mechano- and heat-sensitive (AMH) nociceptors. However, significant expression of TRPV2 was also found in other tissues, including lung, spleen and intestine, where it may have a function unrelated to its high threshold temperature sensitivity (Caterina et al., 1999). The recently cloned TRPV3 is the third member of the TRPV subfamily that shows distinct temperature sensitivity (Peier et al., 2002b; Smith et al., 2002; Xu et al., 2002). It is sensitive to innocuous (warm) temperatures and detects temperature changes above ~31–37°C. Expression of TRPV3 was found not only in sensory ganglia but also skin and tongue, making it an excellent candidate for detecting moderate temperatures in these non-neural cell types (Peier et al., 2002b; Smith et al., 2002; Xu et al., 2002).

TRPV4 (formerly known as VR-OAC, TRP12 or OTRPC4) was originally described as a volume-sensitive cation channel (Liedtke et al., 2000; Strotmann et al., 2000; Wissenbach et al., 2000), but recent data indicate that it can also be activated by phorbol esters (Watanabe et al., 2002a) and by warm temperatures (threshold ~27–34°C; Güler et al., 2002; Watanabe

et al., 2002b). TRPV4 is expressed in the anterior hypothalamus, which is known to be involved in temperature sensation (Güler et al., 2002), but also in a variety of other tissues including kidney, cochlea and endothelium (Liedtke et al., 2000; Strotmann et al., 2000; Wissenbach et al., 2000), where its role in temperature sensing remains to be established.

Recently, it was shown that the TRP superfamily not only contains detectors of hot but also of cold temperatures. A member of the TRPM subfamily, TRPM8 (also known as Trp-p8 or CMR1), was shown to be activated by cold temperatures with a threshold of ~25°C and maximal activation around 8°C (McKemy, Neuhausser & Julius, 2002; Peier et al., 2002a). Analogous to the activation of the heat-sensitive TRPV1 by capsaicin, TRPM8 can also be directly activated by cooling agents such as menthol or the more powerful icilin (McKemy et al., 2002; Peier et al., 2002a). Apparently, these substances are sensed as cool because they shift the threshold for activation of TRPM8 to higher temperatures. Like TRPV1, TRPM8 is expressed in a subset of small-diameter neurons in trigeminal and dorsal root ganglia and, at least according to one study, some of these sensory neurons express both channels (McKemy et al., 2002). This finding, although not supported by another study, could provide an explanation for the fact that noxious cold sometimes feels like burning pain. Expression of TRPM8 was also detected outside the sensory system in tissues such as prostate epithelium and in a variety of tumors (McKemy et al., 2002; Peier et al., 2002a). Since in these cases it is unlikely that cold is the trigger for TRPM8 activation, it will be of special interest to search for endogenous menthol-like activators for this channel.

In conclusion, a set of 5 TRPs allows detection of temperatures that almost fully span the range between 8 and 60°C. It is an open question whether this suffices to create all the temperature sensations that we are able to distinguish, or whether additional temperature-sensitive (TRP) channels are to be identified. Clearly, there remains a small gap in the middle range between the thresholds of TRPM8 (~25°C) and TRPV3/TRPV4 (~30°C), and a mechanism for the detection of ultra-cold (<8°C) temperatures is missing. However, as already mentioned above, the temperature sensitivity of at least some of these channels can be modulated, which could further extend the covered temperature range. Moreover, it is well possible that these TRPs form heteromultimers with different temperature sensitivities. Finally, the differential expression of other channel types (e.g., background K^+ channels) and their modulation by temperature may determine the overall excitability and temperature-sensitivity of thermoresponsive neurons (Viana, de la Pena & Belmonte, 2002).

TRPs and Pheromones

Terrestrial vertebrates have evolved two anatomically distinct sets of mechanisms to detect the surrounding chemical world. The main olfactory epithelium (MOE) is located in the posterior recess of the nasal cavity and detects small odorant chemicals carried in the air, which humans perceive as smell (Buck, 1996). As already mentioned in the introduction, smell detection depends on the production of cAMP and the subsequent activation of CNG channels, and will not be discussed further in this review. A second chemical detection unit is the vomeronasal organ (VNO), which is enclosed within a bilateral and tubular-shaped chemosensory structure of the ventral nasal septum in rodents, and has a primary role in the detection of pheromones (Halpern, 1987). In contrast to the MOE, chemical detection in the VNO does not depend on cAMP or CNG channels, suggesting that other channel types are at work.

The finding that TRPC2 (previously named TRP2) is expressed exclusively in the VNO led to the suggestion that it functions as a transduction channel for pheromone sensing (Liman, Corey & Dulac, 1999). This hypothesis was confirmed by generation of TRPC2-deficient mice (Stowers et al., 2002). $TRPC2^{-/-}$ mice are healthy, show no anatomical abnormalities and display normal mating behavior towards females, but completely lack pheromone-induced neuronal activity in the VNO. As a result of the lack of pheromone recognition, mutant male mice do not show the normal aggressive behavior towards other males. Instead, they display sexual behavior towards male intruders, indicating that in the absence of TRPC2, mice are no longer able to discriminate between sexes (Stowers et al., 2002).

Importantly, anatomical evidence shows that VNO function is absent in higher primates and humans, and the TRPC2 gene is a pseudogene in humans (Wes et al., 1995). Apparently, gender discrimination in higher primates and humans depends on visual rather than chemical clues. It is intriguing to speculate that the relatively high occurrence of homosexuality and the absence of overt male-male aggression in (most) humans originate from a defect in the TRPC2 gene during evolution.

TRPs and Sound

Hearing depends on specialized cells in the inner ear, the cochlear hair cells, which are able to translate incoming sound into electrical stimulation of the auditory nerve fibers (Hudspeth, 1997). These hair cells contain flexible hair-like structures at their apical side, the stereocilia, which are connected to each other by tip-links. Excitatory deflections of the hair bundle caused by sound waves traveling through the

cochlea directly gate a nonselective cation channel, the so-called transduction channel, which leads to depolarization of the hair cell, opening of voltage-gated Ca^{2+} channels and neurotransmitter release onto the auditory nerve fibers (Hudspeth, 1997). An analogous mechanism is at work in the vestibular organ, where vestibular hair cells in the semicircular canals sense the movement of our head. Although many genes involved in hair-cell function have been identified, the molecular identity of the transducer channel remains unknown (Gillespie & Walker, 2001). However, two observations indicate that this channel may be related to the TRP family. First, several biophysical properties of the transducer channel are also seen in many TRP channels, including a single-channel conductance of ~100 pS, moderate selectivity for Ca^{2+} ions, which act as permeant blockers, sensitivity to La^{3+} and feedback inhibition by intracellular Ca^{2+} (Kros, Rusch & Richardson, 1992). Second, it was found that the transducer channel responsible for mechanosensation in *Drosophila* bristle mechanoreceptors, which may be considered as rudimentary invertebrate hair cells, is completely abolished in *nompC* mutant flies (Walker et al., 2000). The NompC protein shares significant homology with the TRP superfamily, apart from the unusually large number of ankyrin-binding sites (29!) in its N-terminal part. Although a NompC orthologue was found in *C. elegans* but not in mammalian cells (Walker et al., 2000), these findings indicated that TRP or related channels are good candidates as the transducer channel in mammalian hair cells.

Until now, TRPV4 is the only TRP that has been put forward as a potential constituent of the hair-cell transducer current (Liedtke et al., 2000). This was based on the finding that this channel is highly expressed in the cochlea and can be activated by a mechanical stimulus (i.e., cell swelling). However, TRPV4's biophysical properties do not really match with those of the hair-cell transducer current, and its specific localization in hair cells has not yet been shown. Final identification of the transducer channel will contribute greatly to our understanding of auditory phenomena such as rapid adaptation, and of the pathophysiology of certain hearing disorders.

TRPs and Touch

Until recently, touch sensation was the almost exclusive domain of ion channels within the ENaC/ASIC/degenerin superfamily (Gillespie & Walker, 2001). However, Colbert et al. (1997) found that the *C. elegans osm-9* gene, which codes for a TRPV-type channel expressed in dendrites of some ciliated sensory neurons, is required for osmosensation and nose touch sensation. Additionally, distinct sensory functions in *C. elegans* may arise from combinations of OSM-9 and other members of the so-called OSM-9/capsaicin receptor-related (OCR) family (Tobin et al., 2002). It remains to be proven that TRP channels are also involved in mammalian touch perception. If so, the thermosensitive TRPV3 and the thermo- and osmosensitive TRPV4, which have been detected in skin, keratinocytes and in the hair shaft (Güler et al., 2002; Smith et al., 2002; Xu et al., 2002), appear to be good candidates. The sensory function of TRP channels might also arise from combinations of different channels.

TRPs and Taste

The sensation of taste relies on a wide variety of chemoreceptive molecules in the mouth, mostly concentrated in specialized receptor cells clustered within the taste buds. Salty and sour stimuli are detected by ion channels including members of the ENaC/ASIC/degenerin superfamily and the hyperpolarization-activated, cyclic nucleotide-gated cation channel HCN, whereas bitter, sweet and umami compounds are detected by G-protein-coupled receptors (GPCRs) of the T2R/TRB, T1R and mGluR families, respectively (reviewed in Lindemann, 2001). These GPCRs are coupled to subunits of G proteins such as α-gustducin, $G\beta_3$, and $G\gamma_{13}$, which further lead to changes in cyclic nucleotide concentrations, production of IP_3/DAG through PLCβ2 and activation of the inositol trisphosphate receptor subtype III (reviewed in Margolskee, 2002). The subsequent steps in the signal transduction cascade are uncertain, but may include store depletion and activation of (store-dependent) plasma membrane Ca^{2+}-permeable channels. Recently, a TRP-like channel that is preferentially expressed in α-gustducin-positive taste receptor cells has been identified and termed TRP-T (TRP-taste) (Perez et al., 2002b). It has been hypothesized that this channel mediates Ca^{2+} entry into the taste receptor cells, possibly secondary to store-depletion, but further research is needed to substantiate this.

Recently, it has been shown that TRP-T is TRPM5, which is expressed in taste cells together with taste-signaling molecules (alpha-gustducin, Gγ-13, phospholipase C-β2 (PLC-β2) and the inositol 1,4,5-trisphosphate receptor type III (IP3R3). TRPM5 may be responsible for the response of taste receptor cells to bitter and/or sweet compounds (Perez et al., 2002a).

TRPs and Pain

Noxious stimuli, such as burning heat, noxious cold, intense pressure or irritant chemicals, result in the unpleasant sensation of pain. This pain is meant to warn us of real or potential injury to our body, al-

Table 1. Sensory functions of TRP channels

Subfamily	Channel	Potential function
TRPC	dTRP, dTRPL, dTRPg	Light
	TRPC2	Pheromones, smell
TRPV	TRPV1	Heat (>43°C), pain
	TRPV2	Heat (noxious), pain
	TRPV3	Heat (>33°C), Mechanosensation
	TRPV4	Heat (25–45°C), Mechanosensation, sound
TRPM	TRPM5 (TRP-T)	Bitter/sweet taste
	TRPM8	Cold (<25°C), pain
TRP-like	NOMPC	Sound

though sometimes pain can become chronic and lose its warning function (Julius & Basbaum, 2001). It was proposed about 100 years ago that sensation of pain depends on a special set of primary sensory neurons, the nociceptors, which are relatively insensitive to innocuous stimuli but become activated by stimuli capable of causing tissue damage (Sherrington, 1906). The fibers arising from cell bodies in the trigeminal and dorsal root ganglia that innervate our head and body can be subdivided into three groups based on their anatomical and functional (nociceptive) properties: the large-diameter, myelinated, very rapidly conducting Aα and Aβ fibers mainly detect innocuous stimuli, whereas the medium-diameter, myelinated, rapidly conducting Aδ fibers and the small-diameter, unmyelinated, slowly conducting C fibers are responsible for, respectively, the rapid and the more delayed pain evoked by noxious stimuli (Julius & Basbaum, 2001).

The molecular nature of the detection of the different noxious stimuli is not yet fully understood, but several of the above-described sensory channels are likely to be involved. At least three of the temperature-sensitive TRP channels (TRPV1, TRPV2 and TRPM8) are expressed in Aδ and/or C fibers, making them excellent candidates for the detection of painful thermal (and chemical) stimuli, but this has only been unequivocally proven for TRPV1. TRPV1$^{-/-}$ mice are impaired (but not defect) in the detection of painful heat, are insensitive to painful chemicals such as the vanilloids, capsaicin and resiniferatoxin but show normal reactions to mechanical stimuli. Moreover, factors that are formed at sites of inflammation or ischemia, including protons, bradykinin, growth factors, ethanol and lipid metabolites such as anandamide, directly alter the temperature sensitivity of TRPV1 (Tominaga et al., 1998; Chuang et al., 2001; Trevisani et al., 2002), which explains the pain sensation of injured tissue. Doubtlessly, TRPV1 and other (TRP) channels involved in nociception are amongst the most promising new targets for the development of new analgesic drugs.

Conclusion

TRP channels form a novel superfamily of cation channels. Their ability to respond to a large variety of physical and chemical stimuli predestines TRP channels to fulfill the role of sensor proteins. Table 1 summarizes the sensory functions of TRP channels that where highlighted in this review. Our relatively weak knowledge of the functional properties and physiological implications of many TRP channels holds the promise that even more novel and exciting functional properties of new or already known members of the TRP superfamily are to be expected.

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