TRP Ion Channels and Temperature Sensation

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First published online as a Review in Advance on March 15, 2006

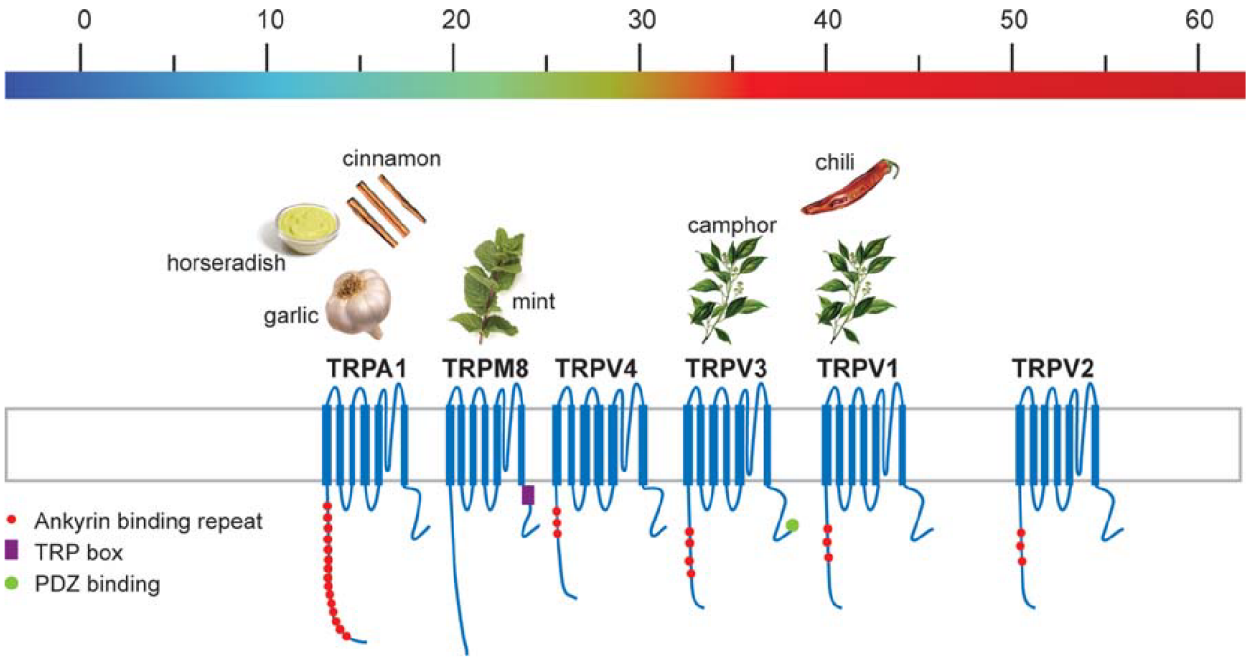


Figure 1

Schematic representation of the thermoTRPs that function in temperatures ranging from noxious heat to noxious cold. Proposed membrane topology and functionally important domains are represented. They include six putative transmembrane units with a proposed pore region between transmembrane domains 5 and 6. The amino and carboxy termini are cytoplasmic and contain various interaction domains like variable number of ankyrin repeats, TRP box or PDZ binding domains. Various botanical compounds activate the thermoTRPs. TRPV1 is activated by capsaicin, the pungent ingredient in chilly peppers, whereas TRPM8 is activated by menthol, the cooling compound from mint. TRPA1 is activated by various pungent compounds like allicin, the active ingredient in garlic, cinnamaldehyde, the pungent component of cinnamon, and isothiocyanates, the pungent ingredients found in wasabe.

?

Mammalian thermal-sensitive channels

Channel	Threshold	Chemicals that evoke thermal-like response
TRPV1	≥43	Capsaicin
TRPV2	≥52	–
TRPV3	≥30-39	–
TRPV4	≥27	–
TRPM8	23-28	Menthol, icilin
TRPA1	17	Icilin, mustard oil

***Drosophila* thermal-sensitive channels**

Painless (TRPA subfamily)	≥39	–
TRPA1	≥27	–

Table 5. Mammalian and fly thermosensitive TRPs. Those that respond to warm temperatures are red and those that respond to cold are blue.

- TRPA1 is an ancient molecule expressed in nematodes (Caenorhabditis elegans) and in Drosophila (activated by hot and not by cold as in mammals…)

- TRPM8 is only present in tetrapodes:

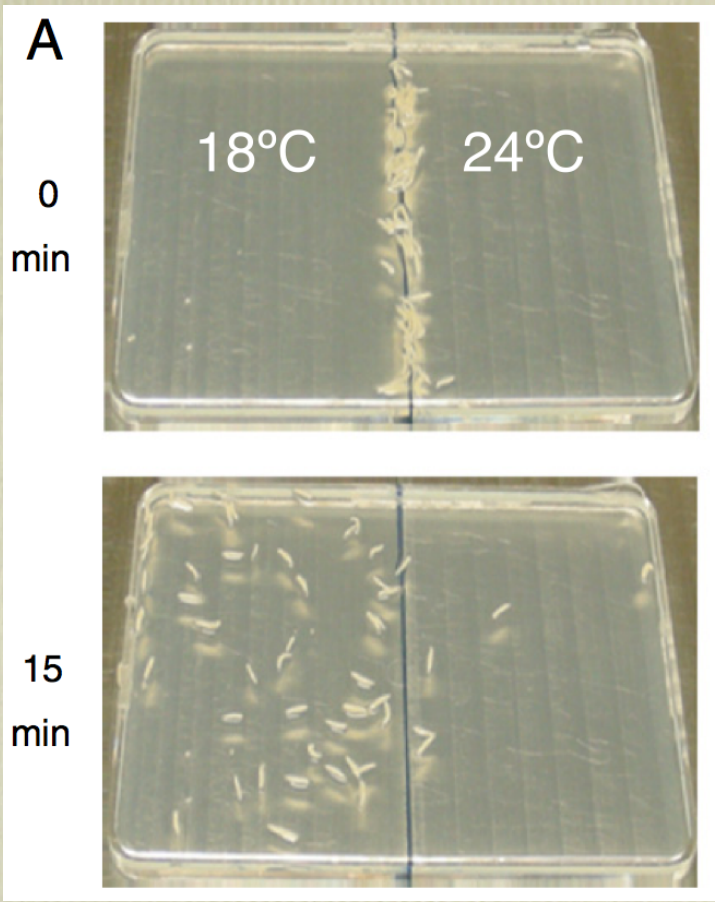
The development of a thermosensor with a new range of sensitivity seems to be associated with the transition from water to land and larger temperature fluctuations…

Termoception

- **Drosophila larvae** : TRPA and behaviour

Painless: avoidance of noxious heat

dTRPA1: activated by comfortable warm (threshold 27°C)



- **mammals**: TRPV1-4, TRPM8, TRPA1 (?)

Skin thermosensors transduce information on:

- what an object is made of
  * wood, metal, plastic, stone, glass
  * dry or wet

- pain
  * very cold/very hot surfaces…

- behavioural thermoregulation

Anatomical distribution drives the selectivity (and sensitivity) of the receptor

Table 1 Properties of TRP channels involved in thermal transduction[1]

Channel	Temperature sensitivity	Nonthermal agonists	Blockers	Tissue distribution	Null mutants
TRPV1	≥42°C	capsaicin, lipoxygenase acidic pH, resiniferatoxin, NADA, anandamide, ETOH allicin, camphor	ruthenium red capsazepine	PNS, brain, spinal cord, skin, tongue, bladder	impaired thermal avoidanceand hyperalgesia
TRPV2	≥52°C	growth factors (mouse)	ruthenium red	PNS, brain, spinal cord, widely expressed	not reported
TRPV3	≥33°C	camphor, 2-APB	ruthenium red	PNS (human)?, skin	impaired thermotaxis and thermal avoidance
TRPV4	~27 °C –42°C	hypotonic, phorbol esters	ruthenium red gadolinium	kidney, PNS, skin, inner ear, brain, liver, trachea, heart, skin, hypothalamus, fat	impaired thermotaxis, thermal avoidance, and hyperalgesia osmotic regulation pressure sensation
TRPM8	≤25°C	menthol, icilin, eucalyptol		PNS, prostate (human)	not reported
TRPA1	≤17°C	cinnamaldehyde, mustard oil allicin, icilin, etc. (see Bandell et al. 2004)	ruthenium red, camphor	PNS, hair cells	not reported
Non-TRP proteins that may be involved in thermosensation					
TREK-1	cold	membrane stretch, polyunsaturated fatty acids intracellular pH		PNS, brain	not reported
P2X3	warmth	ATP		PNS	enhanced thermal avoidance
Na/K ATPase	cold?		Ouabain	PNS?	not reported
BNC1, ASIC DRASIC	cold (potentiated)	acidic pH	amiloride	PNS	not reported