Commentary

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Thermo-TRPs Contribution to Thermosensation: A Commentary

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Description

The somatic thermosensing ability of homeothermic animals is indispensable for the maintenance of body temperature within an optimal range and the avoidance of harmful temperatures that could damage tissues. Changes in ambient and peripheral skin/abdominal temperatures are detected by peripheral terminals of somatic sensory neurons. The thermo-sensitive machinery transforms alterations in temperature to membrane potential changes, thereby regulating action potentials that travel to the central nervous system. Peripheral thermosensory signals for thermoregulation are transmitted to the preoptic area (POA) of the hypothalamus *via* the spino-parabrachial pathway regulating the autonomic nervous system, whereas spino-thalamocortical pathways mediate temperature discrimination. Moreover, core brain temperatures are monitored by temperature-sensitive structures in the brain. The POA of the hypothalamus has clear intrinsic temperature sensitivity and the neural activity is elevated by slight increases in local brain temperature [1]. Recent research has gradually revealed the molecules and mechanisms underlying thermosensation in sensory neurons, non-neuronal cells and POA neurons, permitting thermoregulation and temperature-induced avoidance/preference behaviours. We have recently reviewed the field's current understanding of thermo-sensitive Transient Receptor Potential Channels (thermo-TRPs) involved in somatic thermosensation and temperature sensing in the brain [2].TRP Vanilloid member 1 (TRPV1) is the founding member of the mammalian thermo-TRP family [3]. Cloning of TRPV1 prompted the discovery and characterization of other TRP channels, and 11 members of the TRP channel family are now considered to be thermo-TRPs. Noxious high/low temperatures initiate avoidance behaviours whereas innocuous warm/cool temperatures are not accompanied by acute behavioural responses. However, detection of temperatures in innocuous range is involved in adaptive body temperature regulation. Noxious heat seems to be detected by a trio of thermo-TRPs: TRPV1 and TRPM3 (M; melastatin). TRPA1 (A; ankyrin) is highly colocalized in the same sensory neurons in order to establish a robust system to sense harmful high temperatures [4]. Mice that lack all sensors (TRPV1/TRPM3/TRPA1) do not respond to noxious high temperatures, whereas single gene knock-outs retain reactivity to noxious heat. In contrast, the identification of somatic noxious cold sensors is incomplete. However, the involvement of TRPA1 and TRPM8 are suggested. Somatic innocuous warmth sensation is reportedly mediated by the activation of a warmth sensor TRPM2 and the inhibition of a cool sensor TRPM8 [5,6]. Activation of TRPM8 in sensory neurons is involved in innocuous cool temperature sensation. For example, TRPM8 activation by the super-cooling agent icilin evokes avoidance behaviors in WT mice but not in TRPM8KO mice [7]. Cool temperature sensation by TRPM8 is likely involved in temperature avoidance to maintain body temperature. Indeed, TRPM8KO mice show impaired thermoregulation and enhanced hypothermia during cold exposure [8]. Non-neuronal skin keratinocytes are also involved in somatic thermosensation. Skin keratinocytes express a warmth sensor TRPV3, which sends temperature information to sensory neurons by release of transmitters such as ATP [9]. Moreover, we have recently discovered that TMEM79 negatively regulates TRPV3 function in skin keratinocytes to modulate the temperature preference in the range of warm temperatures [10]. Non-neuronal odontoblasts were shown to detect cold temperatures f TRPC5 and TRPA1, causing cold-induced tooth pain [11]. Moreover, thermo-TRP is reportedly involved in brain temperature sensing. TRPM2 was shown to be involved in warmth sensitivity of POA neurons and possibly involved in body temperature regulation [12,13]. Thermo-TRPs are broadly expressed not only in sensory neurons exposed to substantial temperature changes but also deep in the brain, sensing core body temperature. Thermo-TRPs localized at each level seem to work as thermosensors to achieve optimal responses to a wide range of temperatures from noxious cold to noxious hot, promoting animal's survival.

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