TRPC3

TRPC3 is highly expressed in primary sensory neurons and has been implicated in peripheral sensitization induced by proinflammatory mediators. Yet, the role of TRPC3 in acute and chronic itch is still not well defined. Here, we show that, among mouse trigeminal ganglion (TG) neurons, Trpc3 mRNA is predominantly expressed in nonpeptidergic small diameter TG neurons of mice. Moreover, Trpc3 mRNA signal was present in the majority of presumptively itch sensing neurons. TRPC3 agonism induced TG neuronal activation and acute nonhistaminergic itch- and pain-like behaviors in naïve mice. In addition, genetic deletion of Trpc3 attenuated acute itch evoked by certain common nonhistaminergic pruritogens, including endothelin-1 and SLIGRL-NH2. In a murine model of contact hypersensitivity (CHS), Trpc3 mRNA expression level and function were upregulated in the TG following CHS. Pharmacological inhibition and global knockout of Trpc3 significantly alleviated spontaneous scratching behaviors without affecting concurrent cutaneous inflammation in the CHS model. Furthermore, conditional deletion of Trpc3 in primary sensory neurons but not in keratinocytes produced similar antipruritic effects in this model. These findings suggest that TRPC3 expressed in primary sensory neurons may contribute to acute and chronic itch via a histamine independent mechanism and that targeting neuronal TRPC3 might benefit the treatment of chronic itch associated with ACD and other inflammatory skin disorders [1)].

1)
Liu Y, Liu Y, Limjunyawong N, Narang C, Jamaldeen H, Yu S, Patiram S, Nie H, Caterina MJ, Dong X, Qu L. Sensory neuron expressed TRPC3 mediates acute and chronic itch. Pain. 2022 May 4. doi: 10.1097/j.pain.0000000000002668. Epub ahead of print. PMID: 35507377.