

Summary

The molecular mechanisms regulating the sensitivity of sensory circuits to environmental stimuli are still poorly understood. In this study a central role for SCF (stem cell factor) and its receptor c-Kit, in tuning the responsiveness of sensory neurons to natural stimuli is demonstrated.

Mice lacking a functional SCF/c-Kit signaling system displayed profound thermal hypoalgesia, attributable to a marked elevation in the thermal threshold and reduction in spiking rate of polymodal heat-sensitive C-fiber nociceptors.

Acute activation of c-Kit by its ligand, SCF, resulted in a reduced thermal threshold and profound potentiation of heat-activated currents in isolated small diameter neurons. In mice acute activation of c-Kit induced thermal hyperalgesia. This SCF induced thermal hyperalgesia required the TRP-family cation channel TRPV1.

In addition the c-Kit receptor is needed for the normal functional development of some mechanoreceptors. Lack of c-Kit signaling during development results in hypersensitivity of discrete neuronal subtypes in response to mechanical stimuli. Thus c-Kit, can now be grouped into a small family of receptor tyrosine kinases, including c-Ret and TrkA, that control the transduction properties of distinct types of sensory neuron to thermal and mechanical stimuli. However the c-Kit/SCF signaling system plays, in contrast to other receptor tyrosine kinases expressed in the dorsal root ganglion, no role for the survival of sensory neurons.