PAIN

Keeping Trk of pain

A new study by Fang *et al.* describes the sensory properties of nociceptors that express TrkA in the dorsal root ganglion (DRG), and provides important evidence that links TrkA expression to the electrophysiological properties of certain nociceptors.

Combining immunocytochemical and electrophysiological techniques, the authors showed that in the rat DRG, TrkA was highly expressed only in nociceptive neurons, although there was weak TrkA expression in some low-threshold mechanoreceptors. Moreover, this high intensity of expression was present in the often-overlooked fast-conducting (Aα/β), as well as slow-conducting (C and Aδ), types of nociceptor. These researchers therefore investigated whether the high levels of TrkA expression in nociceptors of the DRG might explain the strong effect of nerve growth factor (NGF) on these neurons.

Their studies revealed that the level of TrkA expression in individual Aα/β nociceptors correlated with electrophysiological properties that are characteristic of nociceptors, including slow conduction velocity, long action potential and after-hyperpolarization durations and large action potential amplitudes. This correlation did not hold for C and Aδ nociceptors, in which TrkA is also highly expressed.

Previous studies have reported that NGF influences the expression of the sodium channel Nav1.8 in DRG neurons. This raises the interesting possibility that the link between TrkA expression and electrophysiological properties is mediated through TrkA regulation of NGF uptake and its effect on Nav1.8. In support of this idea, Fang *et al.* showed that in Aα/β nociceptors, the relationship between the intensity of the expression of Nav1.8 and electrophysiological properties resembled that between TrkA expression and electrophysiological properties. A similar relationship was not found for another type of sodium channel, Nav1.9, which is also expressed in nociceptors but is not regulated by NGF.

To confirm this potential functional link between TrkA and Nav1.8, the authors went on to show that TrkA expression was correlated with Nav1.8, but not Nav1.9, expression in Aα/β nociceptors. Although this does not exclude the influence of other NGF-regulated sodium channels, it does indicate an important role for Nav1.8 in these nociceptors.

The finding that high TrkA expression is specific to nociceptive neurons in the DRG provides a useful tool for the future identification of pain-receptive neurons. Moreover, these results highlight an important association between TrkA and functional properties, mediated through NGF and Nav1.8 expression in fast-conducting DRG nociceptive neurons. The authors suggest that the effects of TrkA and Nav1.8 on slow-conducting nociceptors could be present but not apparent owing to a greater complexity of influences. Future work might shed light on the extent to which the nociceptive phenotype is altered by changes in the NGF/TrkA pathway in disease states.

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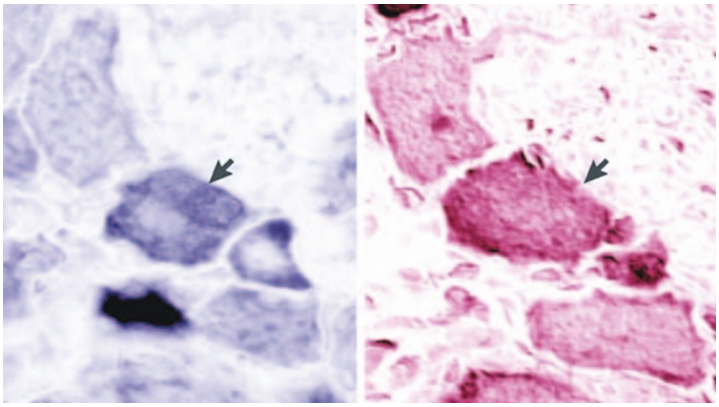
References and links

ORIGINAL RESEARCH PAPER Fang, X. *et al.* trkA is expressed in nociceptive neurons and influences electrophysiological properties via Nav1.8 expression in rapidly conducting nociceptors. *J. Neurosci.* **25**, 4868–4878 (2005)



Sections through the same Aβ nociceptor, stained for TrkA (left) and Nav1.8 (right). Image courtesy of S. Lawson, University of Bristol, UK.