Dorsal Root Ganglia Homeobox (DRGX) in the DRG neurons is involved in neuropathic pain

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Neuropathic pain is caused by lesions or diseases of the somatosensory system and is less responsive to pain medications. Transcriptomic changes in dorsal root ganglion (DRG) neurons are involved in initiation and maintenance of neuropathic pain. Dorsal Root Ganglia Homeobox (DRGX) is a paired-like homeodomain transcription factor crucial for the development of nociceptive DRG neurons. However, roles for DRGX after development are almost unclarified. Here, we report that DRGX downregulation in DRG neurons due to nerve injury in the post-developmental stage is involved in neuropathic pain in rats. DRGX expression was persistently decreased in DRG neurons in neuropathic pain model rats produced by spinal nerve ligation. DRGX protein was mainly downregulated in nuclei of small-to-medium DRG neurons after the nerve injury. Additionally, DRGX downregulation using an adeno-associated viral vector expressing short hairpin RNA induced mechanical allodynia and thermal hyperalgesia in intact rats, while DRGX overexpression suppressed neuropathic pain. DRGX regulated mRNA expression of matrix metalloproteinase-9 and prostaglandin E receptor 2 in the DRG. These results suggest that DRGX downregulation after development contributes to neuropathic pain through transcriptional modulation of pain-related genes in DRG neurons.

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