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Involvement of phosphatase and tensin homolog deleted from chromosome 10 in rodent model of neuropathic pain

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Abstract

Background: Many cancer research studies have extensively examined the phosphatase and tensin homolog deleted from chromosome 10 (PTEN) pathway. There are only few reports that suggest that PTEN might affect pain; however, there is still a lack of evidence to show the role of PTEN for modulating pain. Here, we report a role for PTEN in a rodent model of neuropathic pain.

Results: We found that chronic constriction injury (CCI) surgery in rats could elicit downregulation of spinal PTEN as well as upregulation of phosphorylated PTEN (phospho-PTEN) and phosphorylated mammalian target of rapamycin (phospho-mTOR). After examining such changes in endogenous PTEN in neuropathic rats, we explored the effects of modulating the spinal PTEN pathway on nociceptive behaviors. The normal rats exhibited mechanical allodynia after intrathecal (i.t.) injection of adenovirus-mediated PTEN antisense oligonucleotide (Ad-antisense PTEN). These data indicate the importance of downregulation of spinal PTEN for nociception. Moreover, upregulation of spinal PTEN by i.t. adenovirus-mediated PTEN (Ad-PTEN) significantly prevented CCI-induced development of nociceptive sensitization, thermal hyperalgesia, mechanical allodynia, cold allodynia, and weight-bearing deficits in neuropathic rats. Furthermore, upregulation of spinal PTEN by i.t. Ad-PTEN significantly attenuated CCI-induced microglia and astrocyte activation, upregulation of tumor necrosis factor-α (TNF-α) and phospho-mTOR, and downregulation of PTEN in neuropathic rats 14 days post injury.

Conclusions: These findings demonstrate that PTEN plays a key, beneficial role in a rodent model of neuropathic pain.

Keywords: Chronic constriction injury, Intrathecal, Astrocyte, Neuroinflammation

Background

Pain affects 1.5 billion people globally, including 116 million people in the USA and 164 million people in Europe and Israel combined [1]. The 2009 global pain market was estimated to be over US $50 billion [2]. Previous studies indicated that chronic pain occurs in about 20% of the general population [3,4], and the prevalence of neuropathic pain is 6.9% [4]. In a review of 174 trials published, Finnerup *et al.* [5] reported that there are no drug treatments available that can relieve all neuropathic pain conditions. Moreover, the detailed mechanisms underlying neuropathic pain still remain unclear.

The phosphatase and tensin homolog deleted from chromosome 10 (PTEN) is a tumor suppressor of phosphatased activity [6]. PTEN has been studied extensively through cancer research [7,8]; however, there are only few reports that suggest that PTEN might affect pain [9]. Goebbels *et al.* have demonstrated that by targeted disruption of *Pten* in Schwann cells that causes focal hypermyelination in the PNS and is associated with progressive peripheral neuropathy in mice [9]. However, there is still a lack of evidence to show the role of PTEN

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