The Role of Advillin in Axon Regeneration and Neuropathic Pain

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Neuropathic pain, characterized as a hypersensitive response to noxious and innocuous stimuli, is caused by a disease or lesion of the somatosensory nervous system. There are estimated more than 385.0 million people worldwide suffered from chronic neuropathic pain, which greatly impairs their life quality, but current analgesics are either nonspecific or insufficiently effective. Thus the proper diagnosis of cause and specific treatment of pain is necessary and important. Here we report a vital actin-binding protein called advillin could serve as a biomarker for diagnosing the cause of lesion, as well as a target to promote nerve regeneration and aid recovery in patients with neuropathic pain.

Advillin is a sensory neuron-specific protein that modulates axonal outgrowth. In adult mice, advillin is expressed in a specific subset of pain-sensing afferent neurons (nociceptors) that binds with isolectin B4 (IB4) and coordinates with focal adhesion components to fine-tune the axon regeneration. Lack of advillin in pain-sensing neurons causes the disturbed axon outgrowth with decrease in outgrowth velocity, branch number, and projection dynamics. The causal effect of advillin-mediated axon regeneration and neuropathic pain has been demonstrated in mouse models of multiple sclerosis, nerve damage caused by the chemotherapy drug oxaliplatin, and sciatic nerve injury. Eliminating or diminishing the expression of advillin in mouse models demonstrates the proper and accurate nerve regeneration is crucial for the recovery of neuropathic pain. Also, advillin-containing protein complex is often shed from the axon terminals during axon retraction in the context of axonal regeneration, and thus detected in the cerebrospinal fluid in mice with painful peripheral neuropathy.

Together, advillin plays an important role in recovering from diverse nerve damages, which is essential for resolving neuropathic pain. Advillin is thus a therapeutic target to promote precise axon regeneration and resolve neuropathic pain, as well as a potential biomarker to diagnose peripheral painful neuropathy.