Role of the CX3CR1/p38 MAPK pathway in spinal microglia for the development of neuropathic pain following nerve injury-induced cleavage of fractalkine.

溫永銳

Zhuang ZY;Kawasaki Y;Tan PH;Wen YR;Huang J;Ji RR

摘要

Abstract

Accumulating evidence suggests that microglial cells in the spinal cord play an important role in the development of neuropathic pain. However, it remains largely unknown how glia interact with neurons in the spinal cord after peripheral nerve injury. Recent studies suggest that the chemokine fractalkine may mediate neural/microglial interaction via its sole receptor CX3CR1. We have examined how fractalkine activates microglia in a neuropathic pain condition produced by spinal nerve ligation (SNL). SNL induced an upregulation of CX3CR1 in spinal microglia that began on day 1, peaked on day 3, and maintained on day 10. Intrathecal injection of a neutralizing antibody against CX3CR1 suppressed not only mechanical allodynia but also the activation of p38 MAPK in spinal microglia following SNL. Conversely, intrathecal infusion of fractalkine produced a marked p38 activation and mechanical allodynia. SNL also induced a dramatic reduction of the membrane-bound fractalkine in the dorsal root ganglion, suggesting a cleavage and release of this chemokine after nerve injury. Finally, application of fractalkine to spinal slices did not produce acute facilitation of excitatory synaptic transmission in lamina II dorsal horn neurons, arguing against a direct action of fractalkine on spinal neurons. Collectively, our data suggest that (a) fractalkine cleavage (release) after nerve injury may play an important role in neural-glial interaction, and (b) microglial CX3CR1/p38 MAPK pathway is critical for the development of neuropathic pain.