***Cite this as*:** Li-na YU, Li-hong SUN, Min WANG, Min YAN, 2016. Research progress of the role and mechanism of extracellular signal-regulated protein kinase 5 (ERK5) pathway in pathological pain. *Journal of Zhejiang University-Science B (Biomedicine & Biotechnology).* **17**(10):733-741. http://dx.doi.org/10.1631/jzus.B1600188

Research progress of the role and mechanism of extracellular signal-regulated protein kinase 5 (ERK5) pathway in pathological pain

Key words: Extracellular signal-regulated protein kinase 5 (ERK5), pain, cAMP-response element-binding protein (CREB), *N*-methyl-D-aspartate (NMDA), nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF)

Summary

This review mainly focused on elaborating ERK5-associated pathway in pathological pain, in which the ERK5/CREB pathway plays a crucial role in the transduction of pain signal and contributes to pain hypersensitivity.

Highlights

- **ERK5/CREB pathway plays a crucial role in the transduction of pain signal**
- **ERK5 activation in the spinal dorsal horn occurs mainly in microglia.**
- **The activation of ERK5 can be mediated by *N*-methyl-D-aspartate (NMDA) receptors.**
- **The relationship between ERK5 activation and NGF-TrkA, and BDNF in pathological.**

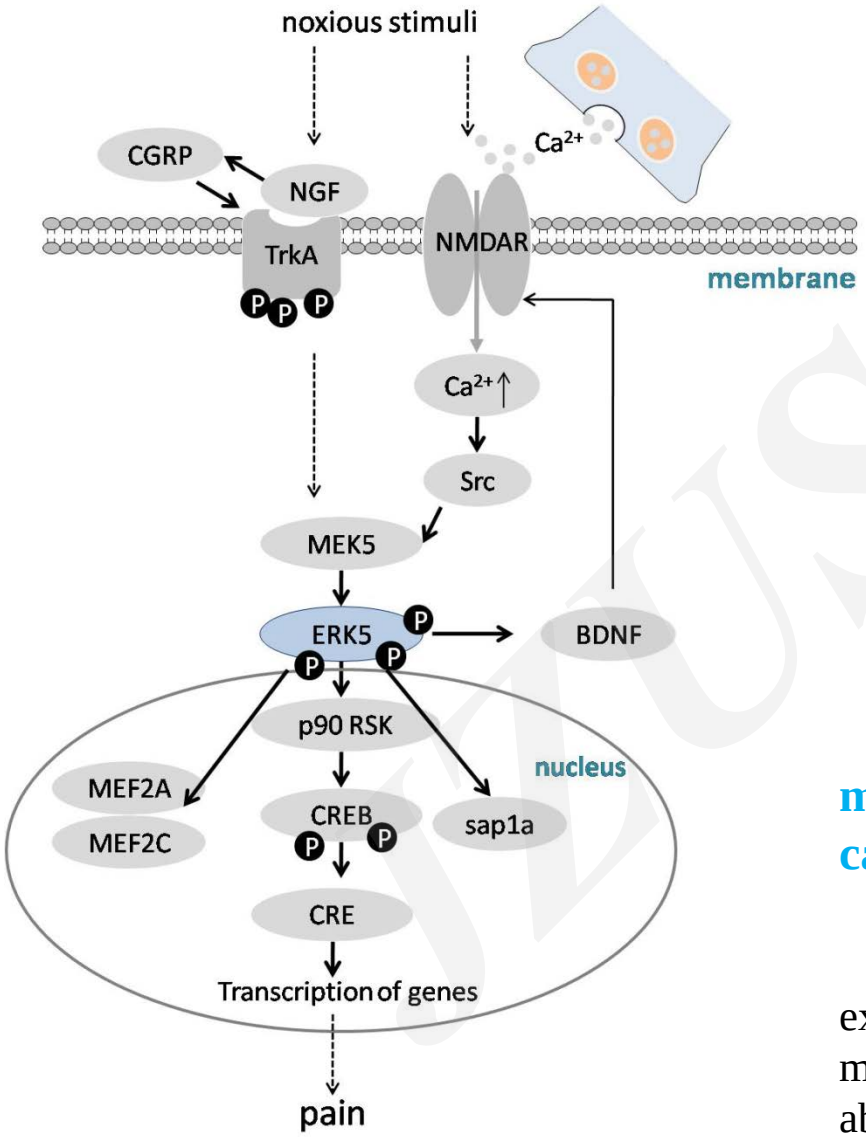

Figure 1. Upstream and downstream mechanisms of the ERK5 signaling cascade in DRG neurons.

Dashed lines indicate the need for further examination of possible signaling or the mechanism, which is complicated and abbreviated in this text. See text for details.

Conclusions

In this review, we summarized the ERK5 pathway and described the role of ERK5 in pain signal transduction in pathological pain.

Noxious stimuli can induce ERK5 activation in the DRG neurons and the spinal cord. The activation of the ERK5 pathway contributes to pain hypersensitivity and is involved in the formation of central sensitization in pathological pain.

Figure 4

Perspectives

More studies are needed to examine the role of the ERK5 pathway in the supraspinal structures in modulating neuropathic pain.

Better and deeper investigation of the ERK5 transduction pathway may provide further insights into the potential mechanisms underlying pathological pain and will help us exploit new therapeutic opportunities targeted specifically at inhibiting the pain signal transduction.

Figure 4