No. 2330

Role of K^+ Channel Regulator NCS-1 in Pain Relief during Neuropathy and Related Signals during Neuropathy

Tomoe Nishitani[1], Norikazu Kiguchi[2], Takuya Notomi[1], Chen I-Shan[1],Jumpei Yasuda[1]

[1] Department of Pharmacology, Faculty of Medicine, Wakayama Medical University,
[2] Department of Physiological Sciences, School of Pharmaceutical Sciences, Wakayama Medical University

Summary

"Pain" serves as a defense mechanism for living organisms, but severe pain is a source of suffering, making its alleviation extremely important. Many ion channels are involved in the mechanisms of pain perception. On the other hand, pain relief pathways also exist within the body, with the voltage-dependent Kv4 K^+ channels, which constitute the I_{SA} current. In fact, it has been reported that reducing Kv4 channels results in hypersensitivity to painful stimuli. We previously identified NCS-1 (Neuronal Ca^{2+} sensor-1) as a regulatory subunit of Kv4 channels. NCS-1 binds to and co-localizes with Kv4 channels in the brain, increasing Kv4 channel currents. However, it is unknown whether NCS-1 contributes to pain relief through Kv4 channel currents under normal and neuropathic conditions. The aim of this study was to elucidate whether NCS-1 contributes to pain relief under normal and neuropathic conditions and to determine whether its effects vary depending on the type of pain.

Immunofluorescence analysis confirmed the expression of Kv4.3 and NCS-1 in the dorsal root ganglion (DRG) of mouse spinal cords, revealing high expression and co-localization of both proteins. Using NCS-1 knockout (KO) mice, we compared pain sensitivity to that of wild-type (WT) mice. The results showed that KO mice of both sexes exhibited increased sensitivity to mechanical stimuli compared to WT mice. However, no difference was observed in sensitivity to thermal stimuli. Currently, we are investigating whether NCS-1 has an analgesic effect on neuropathic pain by creating a neuropathic pain model through partial sciatic nerve ligation. Additionally, due to the high expression of NCS-1 in the central nervous system, we created NCS-1 flox mice using the Crispr/Cas9 system to produce site-specific KO mice.

The above results indicate that NCS-1 contributes to pain relief. Furthermore, we plan to generate mice with nociceptive cell-specific KO of NCS-1 by crossing NCS-1 floxed mice with Nav1.8 Cre mice to confirm the same effect.