Chemogenetic inhibition of macrophages and microglia exerts anti-allodynic effects on different types of neuropathic pain in male mice

Yuya Ideguchi, Fumihiro Saika, Norikazu Kiguchi, Daichi Kobayashi, Shinsuke Matsuzaki, Shiroh Kishioka

Dept. Pharm., Wakayama Med Univ

Chronic neuroinflammation in the peripheral/central nervous system is important for the molecular basis of neuropathic pain. In particular, roles of macrophage and microglia have been well demonstrated. In this study, we evaluated the region, time, and sex-dependent effects of macrophages/microglia on neuropathic pain using mice that can induce Gi-DREADD driven by macrophages/microglia-specific *cx3cr1* promoter (CX3CR1-hM4Di). Neuropathic pain model mice were generated by partial sciatic nerve ligation (PSL) or paclitaxel treatment, and mechanical allodynia was evaluated using von Frey test.

In CX3CR1-hM4Di mice after PSL, expression of hM4Di was localized in both F4/80 positive macrophages and Iba1 positive microglia. Intraperitoneal or intrathecal administration of clozapine-N-oxide (CNO), a ligand for hM4Di, improved mechanical allodynia in male CX3CR1-hM4Di mice after PSL or paclitaxel treatment. These anti-allodynic effects was observed in male, but not in female mice. These results support the notion that sex-dependent roles of macrophage/microglia in neuropathic pain and the pharmacological inhibition of these cells might be effective therapeutics for neuropathic pain.