2-O-047 Oral Sessions

Pain inhibitory effect of macrophage / microglia function control using DREADD system on neuropathic pain model

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Chronic neuroinflammation plays an important role in the molecular basis of neuropathic pain. It has been widely accepted that the various immune cells contribute to the development of neuropathic pain. Among immune cells, the role of macrophages and microglia has been well demonstrated. In this study, we evaluated the effects of macrophages/microglia on neuropathic pain using mice that can induce Gi-Designer Receptors Exclusively Activated by Designer Drugs (Gi-DREADD) driven by macrophages/microglia-specific *cx3cr1* promoter (CX3CR1-hM4Di). Neuropathic pain model mice were generated by partial sciatic nerve ligation (PSL) or anti-cancer drugs, 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, attenuated mechanical allodynia in male CX3CR1-hM4Di mice after PSL or repeated administration of anticancer drugs. In addition, 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.