Perineural treatment with anti-HMGB1 antibody alleviates nociceptive-like behaviors in mice with chronic constriction injury of distal infraorbital nerve

Kochi Takahiro[1,2], Yoki Nakamura[1], Kazue Nakashima[1], Keyue Liu[3], Hidenori Waki[3], Masahiro Nishibori[3], Masahiro Irifune[2], Norimitu Morioka[2]

[1]Dept. Pharmacol., Grad. Sch. Biomed. & Health Sci., Hiroshima Univ., [2]Dept. Dental Anesthesiology, Grad. Sch. Bio. & Health Sciences, Hiroshima Univ., [3]Dept. Pharm., Grad. Sch. Med., Dentistry and Pharmaceutical Sciences, Okayama Univ.

Trigeminal neuropathy, caused by injury to trigeminal nerve, manifests as orofacial numbness, paresthesias, or/and pain and are refractory to treatment with commonly used analgesics. In this study, we employed distal infraorbital nerve chronic constriction injury (dIoN-CCI) model, which mimic pathology of trigeminal neuropathy, to investigate whether high mobility group box 1 (HMGB1), a kind of damage-associated molecular patterns, is involved in trigeminal neuropathy.

Under anesthesia, silk sutures were tied loosely around the dIoN of ddY male mice. Nociceptive-like behaviors were evaluated by measurement of face grooming episodes and conditioned place preference test. Microglial activity in spinal trigeminal nucleus caudalis (Sp5c) was determined by immunohistochemistry. Anti-HMGB1 neutralizing antibody (nAb) was perineurally injected right after surgery.

In dIoN-CCI mice, the mouse face grooming time was increased compared with sham mice. In addition, dIoN-CCI evoked activation of microglia in Sp5c and preference to mirogabalin-paired chamber. Moreover, the perineural treatment with anti-HMGB1 nAb blocked the dIoN-CCI-induced face grooming, microglia activation, and preference to mirogabalin. The anti-HMGB1 nAb could be a novel therapeutic reagent for inhibiting the induction of trigeminal neuropathy.