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Background and Aims Neuroinflammation is regarded as a leading cause of neuropathic pain. Mincle (macrophage-inducible C-type lectin), an innate immune receptor has shown to be involved in neuroinflammation in central nervous system. In contrast with toll-like receptor (TLR), much less is known about the role of C-type lectin or Mincle in initiation and maintenance of neuropathic pain. Spinal administration of Mincle ligand induced microglial activation and pain behavior of neuropathic pain in rat. This study evaluated the effects of Mincle antibodies in spinal nerve ligation (SNL) model and compared the binding site using epitope mapping.

Methods With approval of IACUC, Male Sprague-Dawley rats underwent surgery for L5/L6 spinal nerve ligation (SNL) and intrathecal catheter implantation. Using von Frey test, anti-allodynic effect of three commercially available Mincle antibodies (Santa cruz, Invitrogen, Novus Biological) was examined after single intrathecal administration of antibodies. In addition, epitope mapping was performed to determine the antigen-binding site for each antibody. Interaction between Mincle antibody and TLR4 antagonist for reducing mechanical allodynia was also investigated using isobolographic analysis.

Results Mincle antibodies significantly inhibited the mechanical allodynia and the strength of maximum inhibitory effects were in order of SantaCruz > Invitrogen > Novus Biological. All the antibodies bind to extracellular domain of Mincle with no overlapping epitope. In addition, synergistic anti-allodynic effect was shown by co-administration of Mincle antibody and TLR4 antagonist.

Conclusions Blockade of Mincle by intrathecal antibodies has a strong anti-allodynic effect and produces a synergistic anti-allodynic effect with TLR4 antagonist in SNL model, suggesting Mincle as a potential target for therapeutic strategies for neuropathic pain.

Involvement of the Spinal γ-Aminobutyric Acid Receptor in the Analgesic Effects of Intrathecally Injected Hypertonic Saline in Spinal Nerve-Ligated Rats

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Background and Aims Hypertonic saline is used for treating chronic pain, but clinical studies with optimal therapy protocols are lacking. This study aimed to determine the concentration at which the effect reaches its peak and the antinociceptive mechanism of Hypertonic saline.
**Methods**

A spinal nerve ligation (SNL, left L5, and L6) model was used to induce neuropathic pain in rats weighing 250–300 g. One week after implantation of the intrathecal catheter, different concentrations of NaCl were injected intrathecally into the rats. Behavioral tests (von Frey filaments, hot-plate, and cold-plate tests) were used to derive the results at baseline, 30 minutes, 2 hour, 1 day, and 1 week. After the same preparation, the rats were randomly divided into four groups of 10: the control group, hypertonic group, bicuculline group, and phaclofen group. Behavioral tests were then performed at weeks 1 and 3 after each drug administration, which followed the administration of intrathecal 5% NaCl. This study was reviewed and approved by the Institutional Animal Care and Use Committee Asan Institute for Life Sciences.

**Results**

Using more than 5% NaCl in the rats induced mechanical allodynia and thermal hyperalgesia has a significant therapeutic effect. Moreover, more than 5% NaCl showed a partial time- and dose-dependent antinociceptive effect on cold hyperalgesia. Pretreatment of the $gamma$-Aminobutyric Acid (GABA) receptor antagonist inhibited the antinociceptive effect of hypertonic saline in the SNL rats.

**Conclusions**

Intrathecally injected hypertonic saline is effective at concentrations greater than 5% for treating neuropathic pain, and its effects may be associated with the GABAA and GABAB receptors.