Mesenchymal stem cell exosomes as a cell-free therapy for nerve injury–induced pain in rats

Shiue, Sheng-Jie[a]; Rau, Ruey-Horng[b]; Shiue, Han-Shiang[c]; Hung, Yi-Wei[a]; Li, Zhi-Xiang[a]; Yang, Kuender D.[d,e,f]; Cheng, Jen-Kun[g,h,*]

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Nerve injury–induced neuropathic pain is difficult to treat. In this study, we used exosomes derived from human umbilical cord mesenchymal stem cell (UCMSC) as a cell-free therapy for nerve injury–induced pain in rats. Isolated UCMSC exosomes range in size from 30 to 160 nm and contain CD63, HSP60, and CD81 exosome markers. After L5/6 spinal nerve ligation surgery, single intrathecal injection of exosomes reversed nerve ligation–induced mechanical and thermal hypersensitivities of right hindpaw of rats at initial and well-developed pain stages. Moreover, continuous intrathecal infusion of exosomes achieved excellent preventive and reversal effects for nerve ligation–induced pain. In immunofluorescent study, lots of Exo-green-labelled exosomes could be found majorly in the ipsilateral L5 spinal dorsal horn, dorsal root ganglion, and peripheral axons, suggesting the homing ability of UCMSC exosomes. They also appeared in the central terminals or cell bodies of $IB4^+$, $CGRP^+$, and $NF200^+$ sensory neurons. In addition, exosome treatment suppressed nerve ligation–induced upregulation of c-Fos, CNPase, GFAP, and Iba1. All these data suggest that the analgesic effects of exosomes may involve their actions on neuron and glial cells. Exosomes also inhibited the level of TNF-α and IL-1β, while enhanced the level of IL-10, brain-derived neurotrophic factor, and glial cell line–derived neurotrophic factor in the ipsilateral L5/6 dorsal root ganglion of nerve-ligated rats, indicating anti-inflammatory and proneurotrophic abilities. Protein analysis revealed the content of vascular endothelial growth factor C, angiopoietin-2, and fibroblast growth factor-2 in the exosomes. In summary, intrathecal infusion of exosomes from UCMSCs may be considered as a novel therapeutic approach for nerve injury–induced pain.

Exosomes derived from human umbilical cord mesenchymal stem cells, given intrathecally, prevent and attenuate L5/6 spinal nerve ligation–induced pain, with anti-inflammatory and proneurotrophic effects.

[a]Department of Medical Research, Mackay Memorial Hospital, Taipei, Taiwan

[b]Department of Anesthesiology, Mackay Memorial Hospital, Hsinchu, Taiwan

[c]Institute of Neuroscience, National Yang-Ming University, Taipei, Taiwan

[d]Institute of Biomedical Science, Mackay Medical College, New Taipei City, Taiwan

[e]Department of Pediatrics, Mackay Memorial Hospital, Taipei, Taiwan

[f]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan

[g]Department of Anesthesiology, Mackay Memorial Hospital, Taipei, Taiwan

[h]Department of Medicine, Mackay Medical College, New Taipei City, Taiwan

Corresponding author. Address: Department of Anesthesiology, Mackay Memorial Hospital, No. 92, Sec 2, Zhongshan N Rd, Taipei 10449, Taiwan. Tel.: +886-2-2543-3535; fax: +886-2-2543-3642. E-mail address: jkcheng@usa.net (J.-K. Cheng).

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S.-J. Shiue and R.-H. Rau contributed equally to this work.

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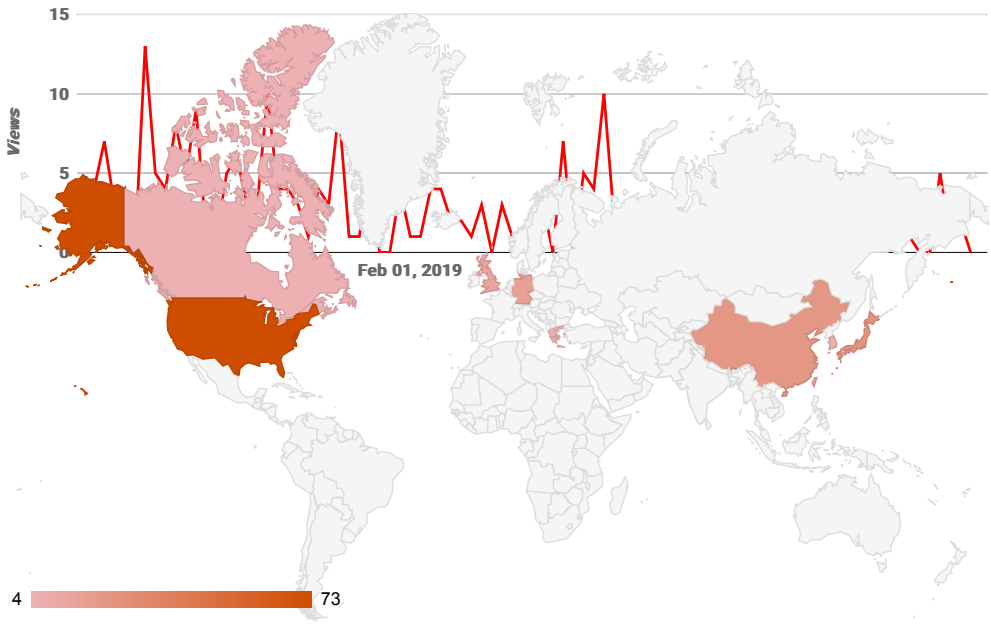

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