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INTRATHECAL ADMINISTRATION OF RECOMBINANT HUMAN HEPATOCYTE GROWTH FACTOR FOR ACUTE SPINAL CORD INJURY: ROAD FROM BENCH TO BEDSIDE AND FUTURE PERSPECTIVE

Introduction: We have reported efficacy of intrathecal infusion of recombinant human HGF (intrathecal rhHGF) in cervical spinal cord injury (SCI) model of marmosets. The purpose of this study is to investigate therapeutic time window, confirm efficacy in clinically-relevant severe cervical SCI model of marmosets and establish novel treatment by conducting clinical trial.

Methods: 1) To investigate therapeutic time window of intrathecal rhHGF, rhHGF was infused intrathecally for 2 weeks from right after, 4 days, 2 or 6 weeks after thoracic SCI in rat. 2) To examine efficacy of intrathecal rhHGF in clinically-relevant severe cervical SCI model as preclinical trial, contusive SCI was induced at C5 level followed by intrathecal rhHGF for 4 weeks in marmosets and marmosets without any recovery of forelimbs until 3 days after SCI were included.

Results: 1) Significant motor recovery of hindlimbs was observed when intrathecal rhHGF started from right after or 4 days after SCI, whereas no effects were observed when intrathecal rhHGF started from 2 or 6 weeks after SCI. 2) Original scoring scale that focuses on hand function in walking and grasp performance revealed that more than one key muscle of forelimbs became useful in marmosets with intrathecal rhHGF, whereas all key muscles remained useless thereafter in control marmosets.

Discussion and Conclusion: Present study suggests the evidence of efficacy and therapeutic time window of intrathecal rhHGF in SCI. We have recently launched phase I/II clinical trial (randomized, double-blinded, placebo-controlled) for people with cervical SCI who show modified-Frankel A/B1/B2 at 72 hours after onset.