CDB SEMINAR

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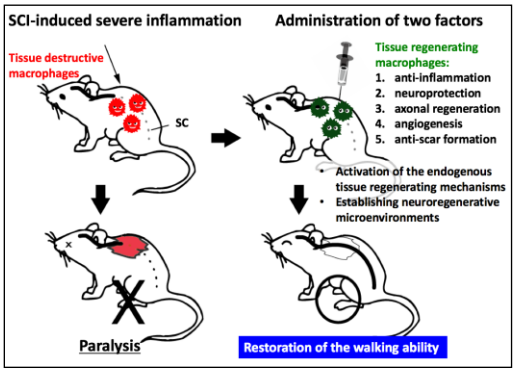
Thursday, April 28, 2016

16:00~17:00 A7F Seminar Room

## Development of new cell-free regeneration therapies based on the novel protein complex inducing tissue-regenerating microenvironment


### Summary

Neuroregenerative therapy based on stem-cell transplantation holds great promise for treating spinal cord injury (SCI). In the last decade, a variety of stem cell types have been transplanted into the injured spinal cord of model animals. In these preclinical studies, the engrafted stem cells promote functional recovery. However, most of these studies report poor survival of the cell graft, and suggest that neurological deficits were recovered primarily through paracrine/trophic mechanisms. The goal of our study is to identify a major therapeutic factors derived from stem cells and develop a new cell-free neuroregenerative therapy activating endogenous tissue-repairing mechanisms.




We have identified a previously unrecognized set of neuroregenerative factors, monocyte chemoattractant protein-1 (MCP-1) and the secreted ectodomain of sialic acid-binding Ig-like lectin-9 (ED-Siglec-9), in serum free conditioned medium (CM) from mesenchymal stem cells (MSC) of human dental pulp. Notably, intrathecal administration of MCP-1 and ED-Siglec-9 into the severely injured rat spinal cord leads to a marked recovery of hindlimb locomotor function through the induction of anti-inflammatory/tissue-regenerating macrophages, which produce various tissue-repairing trophic factors, suppress SCI-induced tissue-destructive pro-inflammatory response and massive cell death, and promote axonal regeneration against anti-neuroregenerative substances of injured CNS, Chondroitin sulfate proteoglycan. This study strengthens the idea that the tissue-regenerating macrophages activate endogenous tissue-regenerating mechanisms, by which the locomotor function of SCI rats was substantially restored.

Macrophages are central player of the innate immune response, which play crucial roles in early host defense against invading pathogens. However, in various intractable diseases, the prolonged activation of the pro-inflammatory macrophages accelerates tissue destruction, fibrosis and subsequent organ failure. The application of MCP-1/ED-Siglec-9 would provide a novel strategy to develop a novel cell-free regenerative therapy for various types of intractable diseases.


**References**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2. Yamagata M, Yamamoto A, et al. Human dental pulp-derived stem cells protect against hypoxic-ischemic brain injury in neonatal mice. ***Stroke*** 2013;44:551-554.
3. Yamamoto A, et al. Multifaceted neuro-regenerative activities of human dental pulp stem cells for functional recovery after spinal cord injury. ***Neurosci. Res.*** 2014;78:16-20.
4. Matsubara K, Yamamoto A, et al. Secreted ectodomain of sialic Acid-binding Ig-like lectin-9 and monocyte chemoattractant protein-1 promote recovery after rat spinal cord injury by altering macrophage polarity. ***J. Neurosci.*** 2015;35:2452-2464.


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