

5th International Conference on

BRAIN DISORDERS AND THERAPEUTICS

November 29-30, 2017 | Madrid, Spain

Transplantation of human embryonic stem cell - derived neural stem with an injectable hyaluronic acid-gelatin hydrogel into contusion model of rat spinal cord injury

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Introduction: Transplantation of neural stem/progenitor cells (NSPCs) and their differentiation potency are promising to preserve or regenerate functional pathways after central nervous system injury. However, reconstruct material that can bridge the injury gap and regenerating axons remain a challenge in spinal cord injury (SCI). Simple and effective biocompatible materials that mimic the natural extracellular matrix (ECM) have been applied in regenerative medicine and there are loads of previously published data that establish benefit of these materials for cell growth and differentiation. Injectable biocompatible hydrogels would be desirable in regenerative medicine in order to promote not only cell survival and differentiation, but also the regeneration of descending or ascending nerve fibers. The purpose of this study initially is to increase viability of transplanted cells in injured site to efficiently support and guide axonal regeneration, secondly to reduce glial scar formation and cavity size as well.

Methods: Moderate to severe contusive spinal cord injury was performed at T10-T11 level of spinal cord using NYU-impactor (10g, 25mm) and rats (Wistar, male, 250-280 g) were given a daily extensive post-surgery care and were kept for seven weeks. Three transplantation groups contain GFP labeled human embryonic stem cell derived neural stem cells (hESC-NSC). The hESC-NSC encapsulated in the hyaluronic acid gelatin hydrogel and hydrogel was injected directly to the cavity sub-acute to the injury and control group just receiving needle stress at one week post SCI. For motor function assessment Basso, Beattie and Bresnahan (BBB) scores were given to each rat hind limb function from 0 to 21 once a week during the experiment. One week prior to spinal cord injury surgery, rats underwent stereotaxic screws implantation in somatosensory motor cortex area that allow stimulation and recording of motor and somatosensory evoked potentials (MEPs, SEPs) and control recording was performed and then it was repeated at 7 days after spinal cord injury and also at the end of the experiment.

Results: After 7 weeks GFP labeled were easily detectable around injured site for cell group and also showed rostrocaudal immigration in cell + hydrogel group. We observed differentiation capacity of hESC-NSC mostly to glial fate and less into neural fate, with expression of platelet derived growth factor receptor alpha (PDGFR α) and Glial fibrillary acidic protein (GFAP) for glial and Tuj for neural cells. BBB scores in hydrogel + hESC-NSC group shows significantly better improvement in motor functions.

Conclusion: We use human embryonic stem cell-derived neural stem cells with a hyaluronic acid gelatin hydrogel in rat model of spinal cord injury and our results demonstrate that combinational transplantation of cells plus hydrogel could increase cell survival, differentiation and also migration of transplanted cells and BBB scores in combinational therapy group shows functional recovery compared to control group.

Biography

Hoda Sadrosadat has finished Master thesis from Tarbiat Modares University under the supervision of Dr. Sahar Kiani and Dr. Hossein Baharvand and now working at Royan institute as a research student to publish articles.

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