Spinal cord injury (SCI) continues to be a pressing health and social problem. The injury leads to neuronal and glial cell death accompanied by degeneration of nerve fibers. There are currently no particularly effective treatments. SCI causes profound disability of people affected and has attracted increased attention in the international field of neuroregeneration. For the past two decades, much hope has been placed in cell therapies for the restoration of both structure and function of the injured spinal cord. Embryonic and neural stem cells, olfactory ensheathing cells, microglia-like cells, Schwann cells, mesenchymal stem cells, human umbilical cord blood cells (UCBCs) and many other cell types have been investigated (Xu and Onifer, 2009; Ronaghi et al., 2010; Sabapathy et al., 2015). It has been shown that graft cells support tissue sparing, exert a trophic effect on neurons and glia, promote axonal growth, and participate in their remyelination.

The current literature suggests that after SCI, cell therapy is effective at promoting neuroregeneration. However, the optimal cell type for transplantation after neurotrauma has not been determined due to differences in experimental conditions, such as localization (cervical, thoracic, lumbar), injury type (contusion, compression, hemisection, complete transection, selective shutdown tracts, etc.), the severity of the injury, methods of cultivation and preparation of cells for transplantation, time of administration after SCI, site of cell injection (site of injury, intrathecal or intraventricular), the presence or absence of immunosuppression, and many other factors. It appears that researchers, SCI caused profound disability of people affected and has attracted increased attention in the international field of neuroregeneration. For the past two decades, much hope has been placed in cell therapies for the restoration of both structure and function of the injured spinal cord. Embryonic and neural stem cells, olfactory ensheathing cells, microglia-like cells, Schwann cells, mesenchymal stem cells, human umbilical cord blood cells (UCBCs) and many other cell types have been investigated (Xu and Onifer, 2009; Ronaghi et al., 2010; Sabapathy et al., 2015). It has been shown that graft cells support tissue sparing, exert a trophic effect on neurons and glia, promote axonal growth, and participate in their remyelination.

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vectors expressing VEGF and GDNF at the site of SCI induced behavioral recovery that correlated with tissue sparing. The efficiency of hUCB-MCs + Ad5-VEGF + Ad5-GDNF transplantation into the area of SCI was higher than transplanted hUCB-MCs transduced with adenoaviral vectors expressing a non-therapeutic gene (enhanced green fluorescent protein, EGFP) for both pathological cavitation and gray/white matter sparing. These results can be explained by the action of therapeutic gene products in targeting cells in the damaged tissue. An increase in the number of regenerating fibers in the white matter of the spinal cord as a result of gene therapy (unpublished data) could result from the direct effect of neurotrophic factors produced by the grafted cells on oligodendrocytes and myelination. Amplification of myelinated fiber regeneration may also be a consequence of reducing the volume of cavities and increased white matter sparing.

We have demonstrated that transplantation of hUCB-MCs transduced with adenoviral vectors expressing VEGF and GDNF genes into the site of SCI reduce glial scar formation and induce prominent axonal sparing/regeneration in comparison to the other constructs tested. Thirty days after SCI and transplantation of genetically modified VEGF and GDNF genes in hUCB-MCs, it was observed that growth associated protein 43 (GAP43+) fibers in the lesion zone had no detectable glial fibration acidic protein (GFAP) and grew through small and medium-sized cystic cavities (Figure 2A, 2A'). While in the group with transplanted hUCB-MCs transduced with adenoviral vectors expressing a non-therapeutic gene (hUCB-MCs + Ad5-EGFP), GAP43 expression was located in the islet of lesion zone and also distal to the lesion zone (Figure 2B, 2B'). Astrogial scars are known to inhibit the regeneration of nerve fibers. We hypothesize that decreased synthesis of chondroitin sulphate proteoglycans due to reductions in glial scar tissue contributed to sprouting nerve fibers after transplantation of the genetically modified hUCB-MCs.

Thus, the transplantation of hUCB-MCs transduced with adenoviral vectors expressing VEGF and GDNF genes after SCI supports functional tissue plasticity and its ability to regenerate. This approach permits the delivery into the damaged area of neurotrophic and angiogenic factors, which reduce the severity of retrograde axonal degeneration, support tissue reconstruction including remyelination, and elongation and collateral branching of axons to form synapses.

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