Protective effect of genetically modified cord blood on spinal cord injury in rats

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Transplantation of genetically modified cells carrying a transgene has a greater stimulating effect on the central nervous system after traumatic injury. During spinal cord injury, the extensive area adjacent to the epicenter of the injury is involved in the pathological process. In order to achieve complete therapeutic action, the transgene must be delivered not only to the epicenter of traumatic injury but also to those surrounding areas.

Two transgenes such as vascular endothelial growth factor (VEGF) and glial cell-derived neurotrophic factor (GDNF) proved to be beneficial for the maintenance of viability of a number of cell populations in the spinal cord, including the motor neurons.

VEGF stimulates neurogenesis and axonal growth as well as the rapid reproduction of astrocytes, neural stem, and Schwann cells. GDNF reduces apoptosis and tissue degeneration, supports expression of neurofilament protein, calcitonin gene-related peptide (CGRP) and growth associated protein 43.

For this study, researchers of Kazan Federal University and Kazan State Medical University chose human umbilical cord blood mononuclear cells (UCB-MCs), which are easy to produce and safe, and have low immunogenicity and the potential to increase neuroregeneration. Cord blood cells were transduced with genes VEGF and GDNF.

"Considering the action of VEGF and GDNF through different receptors

and pathways, we hypothesized that the simultaneous delivery of these two therapeutic genes would promote synergistic neuroprotective effects.

Thus, using a rat contusion spinal cord injury model, we examined the efficacy of the construct on tissue sparing, glial scar severity, the extent of axonal regeneration, recovery of motor function, and analyzed the expression of the recombinant genes VEGF and GNDF in vitro and in vivo," says co-author Yana Mukhamedshina.

The results show that the adenoviral vectors encoding VEGF and GDNF, used to transduce UCB-MCs, are effective and stable in these cells following transplantation.

The construct managed to increase tissue sparing and numbers of spared/regenerated axons, reduce glial scar formation and promote behavioral recovery when transplanted immediately after a rat contusion spinal cord injury. Researchers conclude that genetically modified human umbilical cord blood cells are a promising strategy for enhancing post-traumatic spinal cord regeneration.

More information: Yana O. Mukhamedshina et al. Assessment of Glial Scar, Tissue Sparing, Behavioral Recovery and Axonal Regeneration following Acute Transplantation of Genetically Modified Human Umbilical Cord Blood Cells in a Rat Model of Spinal Cord Contusion, *PLOS ONE* (2016). DOI: 10.1371/journal.pone.0151745

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