Bioengineering technologies in the treatment of nervous system pathology

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Cell therapy using stem/progenitor cells (SPCs), regenerative biomaterials, tissue engineering technologies, and their combination is considered an effective strategy for the treatment of central nervous system (CNS) pathology. Bioengineering technologies are of particular importance in cases of CNS traumatic lesions, primarily for the purpose of filling traumatic cavities and providing adsorption loci for transplanted or endogenous cells; as well as to suppress the apoptosis, inflammation, glial scars formation and stimulation of neurogenesis, axons sprouting and angiogenesis. One of the most common severe injuries to the CNS is spinal cord injury (SCI). Regenerative biomaterials are designed to mimic the physiological extracellular matrix and reconstruct a favorable niche for spinal cord (SC) recovery, stimulating the growth and differentiation of SPCs inoculated into a biopolymer matrix (scaffold) and promoting axon regeneration of surviving neurons. Support matrices (cell carriers) made of natural, synthetic and combined materials are used; fibrin and hyaluronic acid are used among natural materials.

The aim was to study the effect of implantation of fibrin matrix (FM) associated with neural SPCs (NSPCs) on the rat spinal cord tissue after SCI.

Methods. SCI was modeled in rats by lateral hemisection in the lower thoracic-upper lumbar region and experimental groups were formed:

1) SCI (self-healing, $n = 7$);
2) SCI + implantation of a cell-free FM in the epicenter of the cavity ($n = 6$);
3) SCI + implantation of FM with incorporated rat neonatal brain cells (rNBCs, $1 \cdot 10^6/\mu l$, as NSPCs source) ($n = 9$).

In the distant period (8 months) after SCI, longitudinal serial SC slices ($5-7$ μm) were prepared and morphological study was performed.

Results. In the distant period after SCI in rats of group 1 the traumatic cavity is replaced by elements of glia and connective tissue. In rats of group 2 the defect zone with the implanted FM is incorporated by gliocytes and endogenous NSPCs undergoing differentiation; some of them undergo apoptosis and phagocytosis by microglia/macrophages; in the adjacent zone, there is reactive gliosis and increasing dystrophic changes in neurons. In rats of group 3, in the defect area with an implanted FM associated with rNBCs, an incorporated undifferentiated cells (rNBCs) and gliocytes ($GFAP^+$ astrocytes) and clusters of β-tubulin III^+ neurons are found; a small proportion of incorporated cells undergoes apoptosis; the gliofibrous ring around the defect zone is weakly expressed, the vast majority of neurons are preserved in the adjacent

zone.

Conclusion. Cell-free FM implanted in the traumatic area serves as a structural framework that creates a niche for cell migration and, possibly, endogenous regeneration of the defect due to its own NSPCs. FM, associated with rNBCs, implanted into the traumatic cavity, creates conditions for structural recovery of SC tissue (replacement by terminally differentiated astrocytes and neurons); incorporated rNBCs have a neuroprotective effect on neurons of the perifocal zone, which may be basis for SC functional recovery.