Abstract:

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease caused by degradation of motoneurons (MN). No effective treatment is currently available. Cellular therapy is considered to be a promising experimental treatment that could target the pathology of complex disease through many potential mechanisms. We compared the effect of three types of repeated applications of human mesenchymal stem cells (hMSC): intrathecal administrations, intramuscular administrations and the combination of these applications. Best results were obtained after combined repeated hMSC administrations. We observed the rescue of MN, neuromuscular junctions and decreasing levels of proteins involved in the signaling of necroptosis (Rip1, cl-casp 8), apoptosis (cl-casp 9) and autophagy (beclin 1), decreasing astrogliosis and the level of astrocytic connexin 43. Neural precursors derived from induced pluripotent stem cells (NP-iPS) are considered as other promising candidates for ALS therapy. Intraspinal administration of NP-iPS increased mRNA expression of *BDNF* and *IGF-1*, on the other hand decreased expression of proapoptotic *casp 3*. We also observed their effect on expression of components of perineural nets (PNN).

Human embryonic stem cells (hESC) are the other cell candidates for the treatment of neurodegenerative diseases. However it is necessary for their future safe use to clarify the mechanisms involved in the accumulation of mutations in those cells during *in vitro* cultivation. Better understanding will allow us to modulate these mechanisms to prevent mutations. We have found that double-strand breaks are repaired by Ligase 3- mediated- EJ quickly and efficiently and Ligase 3 contributes to maintaining the genome stability of hESC.

Another aim of the work was to test the safety and efficiency of two types of magnetic nanoparticles (CZF and PLL-γ-Fe_2O_3) to monitor their influence on proliferation and differentiation of NP-iPS into dopaminergic neurons. Our results show that PLL-γ-Fe_2O_3 nanoparticles are suitable for detection by magnetic resonance, because they did not affect the proliferation and differentiation potential of NP-iPS.

Klíčová slova: Amyotrophic lateral sclerosis, cell therapy, stem cells, repair mechanisms, magnetic nanoparticles, magnetic resonance