

Exosomes Derived From Human Neural Stem Cells Mediate Cellular Stress Ability And Promote Neurological Function Recovery Of Cerebral Ischemic Rats

Lukui Chen, Guilong Zhang, Hong Wang, Bingqian Li, Wanghao Chen, Yongbo Yu, Zhihan Zhu¹

¹Neurosurgery/ Zhongda Hospital Southeast University/ China

Purpose:

Ischemic stroke recovery is associated with neural stem cells (NSCs) development and neurovascular unit reconstruction. Exosomes, as important intercellular players in cellular communication, mediate neuro-restorative events, however, their effects / mechanisms in the injured brain is unknown. The objective of this study is to determine the effect of human NSCs-derived exosomes on the potential abilities of neural cells, and whether human NSCs-derived exosomes can repair the functions of ischemic stroke rats.

Methods and results:

Our study found that IFN- γ stimulation affected the abilities of human NSCs-derived exosomes (hNSCs-Exo), which included alleviating the level of oxidative stress of NSCs following H₂O₂ stimulating, augmenting the NSC survival, and promoting the neuronal differentiation of NSCs. Furthermore, in rats ischemic stroke model, IFN- γ -hNSCs-Exo further facilitated the neurological functional recovery (assessed by the modified Neurological Severity Score, Rotarod test, etc.) compared to hNSCs-Exo group, enhanced neural cell survival and promoted neovascularization (assessed by microvessel density, MVD). Importantly, exosomes can be internalized or endocytosed by cells, after labeled with PKH67, which showed that exosomes migrated to the infarct regions together with neural cells, as interestingly, many exosomes entered into the nucleus. Next generation sequencing (NGS) revealed a significant enrichment of hsa-miR-206 and hsa-miR-133a-3p in IFN- γ -hNSCs exosomes compared with hNSCs exosomes. The mechanisms or effects of exosomes were delivering specific exosomal microRNAs to cells for increasing cell survival and proliferation.

Conclusion:

hNSCs-derived exosomes possess the ability of neural regeneration, modulate neurological functional recovery, and play more positive roles by stimulating with IFN- γ (IFN- γ -hNSCs Exo). Exosomes provide