Exosomes Derived from Human Neural Stem Cells Mediate Cellular Stress Ability and Promote Neurological Function Recovery of Cerebral Ischemic Rats

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Abstract

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 cells, and whether human NSCs-derived exosomes can repair the functions of ischemic stroke rats. This study finds that IFN-γ stimulating managed the abilities of human NSCs-derived exosomes (hNSCs-Exo), including alleviated the level of oxidative stress of NSCs following H2O2 stimulating, augmented the NSC survival, and promoted the neuronal differentiation of NSCs. Furthermore, in rats ischemic stroke model, IFN-γ-hNSCs-Exo further facilitated the neurological functional recovery (such as modified Neurological Severity Score, Rotarod test, etc.) compared to hNSCs-Exo group, enhanced nerve cell survival and promoted neovascularization (microvessel density, MVD). Importantly, exosomes can be internalized or endocytosed by cells, after labeled with PKH67, it showed that exosomes migrated to the infarct regions together with cells, as interestingly, many exosomes entry into the nucleus. Next generation sequencing (NGS) revealed 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 was to deliver specific exosomal microRNAs to cells for increasing cell survival and proliferation. In summary, hNSCs-derived exosomes possess the ability of neural regeneration and modulate neurological functional recovery, and play more positive roles by stimulating with IFN-γ (IFN-γ-hNSCs Exo). Exosomes provide a novel and promising strategy in modulating disease treatment and tissue regeneration, avoiding the risk of teratomas associated with cells.

Keywords—*Exosomes, Neural stem cells, Cellular stress, Cerebral ischemia*

Some figure of this study

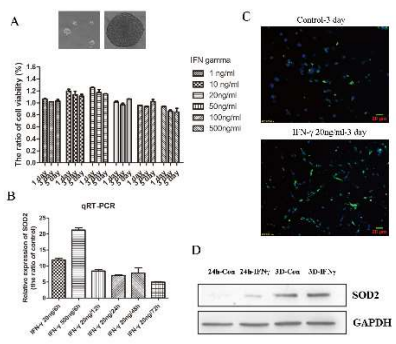


Fig.1 The role of IFN-γ on NSCs

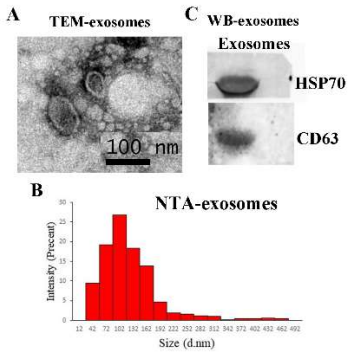


Fig.2 The identify of exosomes

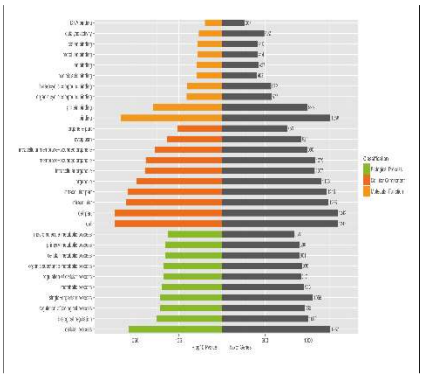


Fig.3 The GO categories of NGS

Professional Biography

Guilong Zhang is a PhD candidate at the School of Medicine, Southeast University, Nanjing, China. His major is Neurosurgery, and will graduate at 2018/2019. His research field is stem cells therapy and clinical translational research. He has published about 10 papers in molecular and biomedical journals.



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