Exosomes derived from human neural stem cells-stimulated by interferon-gamma improve therapeutical ability via exosomal microRNAs

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Abstract

Transplanted neural stem cells promote neural tissue regeneration and functional recovery mainly via the release of paracrine factors. Exosomes as an important secreted molecules of paracrine deliver therapeutic agents to involve in cellular functions. Here, we focused on the role of exosomes derived from hNSCs (hNSCs-Exo), utilized IFN-γ to induce hNSCs exosomes generation (IFN-γ-hNSCs-Exo), compared their roles with original exosomes and explored the potential mechanism. Importantly, IFN-γ preconditioning significantly augmented the yield of exosomes derived from hNSCs. And the ability of IFN-γ-hNSCs-Exo was superior to hNSCs-Exo, further increased cell proliferation, cell survival and decreased cell apoptosis in vitro. Furthermore, IFN-γ-hNSCs-Exo further exerted the therapeutical effects (improved more both behavioral and

structural outcomes) compared to the hNSCs-Exo in vivo ischemic stroke model of rats. Next-generation sequencing (NGS) revealed different exosomal miRNAs expression between them. Special exosomal miRNAs in IFN-γ-hNSCs-Exo presented more therapeutical roles than hNSCs-Exo. And the functional enrichment and signal pathways were correlated with stem cell survival and exosomal transportation. Thus, our findings demonstrate that IFN-γ as an inflammatory factor can regulate the functions of exosomes, highlights a surprising role for regulating stem cell-derived exosomes in the treatment application. In conclusion, exosomes as cell-derived bioactive molecules and next-generation cell-free therapeutic candidates have numerous practical and conceptual advantages in the future.