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Neurogenin-2–transduced human neural progenitor cells attenuate neonatal hypoxic-ischemic brain injury

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Neonatal hypoxic-ischemic (HI) brain injury leads to high mortality and neuro-developmental disorders. Multipotent neural progenitor cells (NPCs) with self-renewing capacity, have the potential to reduce neuronal loss and improve the compromised environment in the HI brain injury. However, the therapeutic efficacy of neuronal committed progenitor cells and the underlying mechanisms of recovery are not fully understood yet. Therefore, this study investigated the regenerative ability and action mechanisms of neuronally committed human NPCs (hNPCs) transduced with neurogenin-2 (NEUROG2) in neonatal HI brain injury. NEUROG2- or green fluorescent protein (GFP)–encoding adenoviral vector–transduced hNPCs (NEUROG2- or GFP-NPCs) were transplanted into neonatal mouse brains with HI injury. Grafted NEUROG2-NPCs showed robust dispersion and engraftment, prolonged survival, and neuronal differentiation in HI brain injury. NEUROG2-NPCs significantly improved neurological behaviors, decreased cellular apoptosis, and increased the neurite outgrowth and axonal sprouting in HI brain injury. In contrast, GFP-NPC grafts moderately enhanced axonal extension with limited behavioral recovery. Notably, NEUROG2-NPCs showed increased secretion of multiple factors, such as nerve growth factor, brain-derived neurotrophic factor, neurotrophin-3 (NTF3), fibroblast growth factor 9 (FGF9), ciliary neurotrophic factor (CNTF), and thrombospondins 1 and 2 (THBS 1/2), which promoted SH-SY5Y neuroblastoma cell survival and neurite outgrowth. Thus, we postulate that NEUROG2-expressing human NPCs facilitate functional recovery after neonatal HI brain injury via their ability to secrete multiple factors that enhance neuronal survival and neuroplasticity.

Biography

Kook In Park has completed his MD and PhD from Yonsei University College of Medicine (YUMC) and Post-doctoral studies from Harvard Medical School, Boston. He is a Professor in the Department of Pediatrics and a Chief of Neonatology in Severance Children's Hospital, YUMC. He has published more than 200 papers in reputed clinical and basic biology journals and has been serving as an Editorial Board Member of repute.

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