

Original Article

Gene Therapy **18**, 394-402 (April 2011) | doi:10.1038/gt.2010.152

VEGF-expressing human umbilical cord mesenchymal stem cells, an improved therapy strategy for Parkinson's disease

N Xiong, Z Zhang, J Huang, C Chen, Z Zhang, M Jia, J Xiong, X Liu, F Wang, X Cao, Z Liang, S Sun, Z Lin and T Wang

Abstract

The umbilical cord provides a rich source of primitive mesenchymal stem cells (human umbilical cord mesenchymal stem cells (HUMSCs)), which have the potential for transplantation-based treatments of Parkinson's Disease (PD). Our previous study indicated that adenovirus-associated virus-mediated intrastriatal delivery of human vascular endothelial growth factor 165 (VEGF 165) conferred molecular protection to the dopaminergic system. As both VEGF and HUMSCs displayed limited neuroprotection, in this study we investigated whether HUMSCs combined with VEGF expression could offer enhanced neuroprotection. HUMSCs were modified by adenovirus-mediated VEGF gene transfer, and subsequently transplanted into rotenone-lesioned striatum of hemiparkinsonian rats. As a result, HUMSCs differentiated into dopaminergic neuron-like cells on the basis of neuron-specific enolase (NSE) (neuronal marker), glial fibrillary acidic protein (GFAP) (astrocyte marker), nestin (neural stem cell marker) and tyrosine hydroxylase (TH) (dopaminergic marker) expression. Further, VEGF expression significantly enhanced the dopaminergic differentiation of HUMSCs in vivo. HUMSC transplantation ameliorated apomorphine-evoked rotations and reduced the loss of dopaminergic neurons in the lesioned substantia nigra (SNc), which was enhanced significantly by VEGF expression in HUMSCs. These findings present the suitability of HUMSC as a vector for gene therapy and suggest that stem cell engineering with VEGF may improve the transplantation strategy for the treatment of PD.