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Construction of recombinant adenovirus containing picorna-viral 2A-peptide sequence for the co-expression of neuro-protective growth factors in human umbilical cord blood cells

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Abstract

© 2015 International Spinal Cord Society Study design:Experimental study.Objective:Several neuro-degenerative disorders such as Alzheimer's dementia, Parkinson's disease and amyotrophic lateral sclerosis (ALS) are associated with genetic mutations, and replacing or disrupting defective sequences might offer therapeutic benefits. Single gene delivery has so far failed to achieve significant clinical improvements in humans, leading to the advent of co-expression of multiple therapeutic genes. Co-transfection using two or more individual constructs might inadvertently result in disproportionate delivery of the products into the cells. To prevent this, and in order to rule out interference among the many promoters with varying strength, expressing multiple proteins in equimolar amounts can be achieved by linking open reading frames under the control of only one promoter.Setting:Kazan, Russian Federation.Methods:Here we describe a strategy for adeno-viral co-expression of vascular endothelial growth factor (VEGF) and fibroblast growth factor 2 (FGF2) interconnected through picorna-viral 2A-amino-acid sequence in transfected human umbilical cord blood mono-nuclear cells (hUCB-MCs).Results:Presence of both growth factors, as well as absence of immune response to 2A-antigen, was demonstrated after 28–52 days. Following injection of hUCB-MCs into ALS transgenic mice, co-expression of VEGF and FGF2, as well as viable xeno-transplanted cells, were observed in the spinal cord after 1 month.Conclusion:These results suggest that recombinant adeno-virus containing 2A-sequences could serve as a promising alternative in regenerative medicine for the delivery of therapeutic molecules to treat neurodegenerative diseases, such as ALS.Spinal Cord advance online publication, 6 October 2015; doi:10.1038/sc.2015.162.

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