

Analysis of recombinant VEGF gene expression by genetically modified umbilical cord blood mononuclear cells in experiment in vivo

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Abstract

To obtain a significant therapeutic effect transplanted genetically modified cells should have an enhanced ability to survive and active expression of the therapeutic gene. In this paper, by using immunofluorescent staining we investigated the functional activity of the gene-cell formulation designed to deliver a therapeutic gene into the area of regeneration. As a model we used transgenic SOD1-G93A mice with amyotrophic lateral sclerosis phenotype which received xenotransplantation of human umbilical cord blood mononuclear cells, genetically modified with adenoviral expression vector encoding vascular endothelial growth factor (VEGF) and the reporter green fluorescent protein (EGFP). Results of the study allowed to establish not only the duration of survival of transplanted cells, but also the efficiency of expression of recombinant genes in genetically modified cells in vivo. Double immunofluorescent staining with antibodies against human nuclear antigen HNA and VEGF detected HNA+/VEGF+ cells in the terminal stage of disease 15 weeks after transplantation. These data suggest that genetically modified umbilical cord blood mononuclear cells, transplanted into SOD1-G93A transgenic mice, are able to penetrate the blood-brain barrier and migrate into the area of degeneration of nerve tissue and survive from the time of transplantation until the death of animals at the terminal stage of disease. At that time adenoviral expression vector encoding therapeutic gene is functionally active in transplanted cells, and secretory products of recombinant gene act on target cells by a paracrine mechanism.

Keywords

Amyotrophic lateral sclerosis, Gene-cell therapy, Green fluorescent protein, Umbilical cord blood mononuclear cells, Vascular endothelial growth factor