Treatment of Spinal Cord Injury Using Transplantation of Adipose Mesenchymal Stem Cells Transfected with Poly-L-Lysine/ DNA (GDNF) - Super Paramagnetic Iron Oxide Nanoparticles

Marzieh Darvishi1,2, Taghi Tiraihi1,2*, Taher Taheri1

1Shefa Neuroscience Research Center, Khatam Alanbia Hospital, Tehran, Iran.
2Department of Anatomy, Tarbiat Modares University, Tehran, Iran.

Abstract

For repair of injured nerve fibers after spinal cord injury (SCI), the environment must be appropriate for axonal growth. The delivery of a therapeutic gene, beneficial for axonal regeneration and promote survival neurons, into the central nervous system for repair can be accomplished in many ways. The use of gene therapy to improve of the injured nervous system is a new strategy of treatment. It is based on delivering therapeutic genes to neurons. Direct in vivo gene transfer or gene transfer in combination with transplantation (ex vivo gene transfer) cause promote neuronal survival and axonal re-growth following traumatic injury to the central nervous system. Gene therapy has great potential to treating various diseases and disorders, but the efficient delivery of genes to injury site with the lowest side effects remains a challenge. Moreover, after gene delivery to stem cells, it is also highly desirable to provide screening and post-therapy monitoring. In this study used from Poly-L-lysine coated with super paramagnetic iron oxide nanoparticles (SPIONs) that can deliver nucleic acid-based therapeutic agents (GDNF) and also provide magnetic resonance imaging (MRI). Adipose tissue from rat perinephric fat was digested with collagenase type I, followed by filter and centrifugation; the isolated adipose stromal cells were cultured and then mesencymal stem cells (MSCs) markers were evaluated by RT-PCR and immunocytochemistry; 2 to 5 passage cells were used for ex vivo gene delivery. Poly-L-lysine and Lipofectamine 2000 were compared as transfection vehicles of SPIONs. Labeled adipose MSCs were examined for iron content with Prussian blue staining that was used after differentiation to determine SPIONs localization. Poly-L-lysine transfected up to 20 times more SPIONs into adipose MSCs. SPIONs were disseminated in both the soma and neuritis. Result of real time RT-PCR and SDS page and western blotting techniques showed that transfected cells secrete human GDNF at high level. These findings indicate that Poly-L-lysine is an effective vehicle for SPIONs transfeciton of adipose MSCs. The intracellular localization of SPIONs distinguished cell migration from axonal or dendritic growth in vivo. The transfected cells with GDNF can be used in clinical applications and treatment of CNS disorders.

Keywords: Nanoparticle, Gene Therapy, Mesenchymal Stem Cells, Spinal Cord Injury.

*Corresponding Author: Taghi Tiraihi
E-mail: ttiraihi@yahoo.com