A Novel Cell-Based Therapy for Contusion Spinal Cord Injury Using GDNF-Delivering NIH3T3 Cells with Dual Reporter Genes Monitored by Molecular Imaging.

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摘要

Abstract

This aim of our study was to evaluate a novel cell-based therapy for contusion spinal cord injury (SCI) using embryonic-derived NIH3T3 cells, which endogenously express glial cell line – derived neurotrophic factor (GDNF). Methods: Proliferation and differentiation of transplanted NIH3T3 cells and their anti-apoptotic effects were examined after their engraftment into the spinal cords of Long-Evans rats subjected to acute SCI at the T10 vertebral level by a New York University impactor device. NIH3T3 cells were initially engineered to contain dual reporter genes, namely thymidine kinase (T) and enhanced green fluorescence protein (G), for in vivo cell tracking by both nuclear and fluorescence imaging modalities. Results: Planar and fluorescence imaging demonstrated that transplanted NIH3T3-TG cells at the L1 vertebral level migrated 2 cm distal to the injury site as early as 2 h, and the signals persisted for 48 h after SCI. The expression of GDNF by NIH3T3-TG cells was then confirmed by immunohistochemical analysis both in vitro and in vivo. GDNF-secreting NIH3T3-TG transplant provided anti-apoptotic effects in the injured cord over the period of 3 wk. Finally, NIH3T3-TG cells cultured under neuronal differentiation medium exhibited both morphologic and genetic resemblance to neuronal cells. Conclusion: GDNF-secreting NIH3T3-TG cells in combination with molecular imaging could be a platform for developing therapeutic tools for acute SCI.