Engineered hNSCs for treating experimental spinal cord gliomas: a neurobiology based approach

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Introduction

Current treatment regimen of surgery, chemotherapy and radiation shows very limited efficacy for managing clinical spinal cord gliomas due to the malignant nature of the tumors and the vulnerability of spinal cord biology. Since neural stem cells (NSCs) demonstrate tumor tropic behavior, genetically engineered NSCs have been used to convert precursor compounds into oncolytic drugs to kill cancer cells locally.

Methods

We investigated cell interactions between Human Neural stem cells (hNSCs) carrying either cytosine deaminase (F3.CD) or CD-thymidine kinase double genes (F3.CD-TK) and G55 human glioblastoma cells in vitro. Per our protocol of establishing a rat model of spinal cord glioma, G55 cells were implanted into C6 spinal cord. Seven days later, DiI labeled F3.CD, F3.CD -TK or cell debris (n=6/group) was implanted at 1mm rostral and caudal to the tumor site, followed with repeated 5-FC and GCV administrations. Data collection included systematical evaluation of autonomic parameters such as respiratory function, blood pressure and body temperature in addition to locomotion performance. Post-glioma survival was defined by

Results

We determined that hNSCs per se did not stimulate tumor cell proliferation, and F3.CD-TK regimen had stronger tumor suppression effect than F3.CD treatment. F3.CD and F3.CD-TK eliminate tumor cells by metabolizing nontoxic 5-fluorocytosine (5-FC) and 5-FC+ganciclovir (GCV) into 5-FU and 5-FU+GCV-triphosphate, respectively. All rats developed spinal cord pathologic signs resulting from cervical glioma growth. Rats treated with F3.CD-TK plus 5-FC and GCV demonstrated significantly increased survival relative to controls receiving either F3.CD or cell debris, and significantly less respiratory deficits and better mean artery blood pressure maintenance. Pathologically, there was significantly increased G55 apoptosis around the infiltrated F3.CD-TK and F3.CD, relative to control group.

Conclusions

Our data suggest that F3.CD-TK cell therapy significantly improved autonomic function in rats with cervical glioma and markedly increased their survival post-tumor implantation.

Learning Objectives

Participants should learn: 1. Experimental modeling of Spinal cord tumor; 2. Stem cell biology-based chemotherapy; and 3. Neurobiology approach for treating spinal cord tumors.

References

N/A