Targeting rat brainstem glioma using human neural stem cells and human mesenchymal stem cells.


Division of Pediatric Neurosurgery, Seoul National University Children's Hospital, Seoul, Korea.

PURPOSE: Brainstem gliomas are usually inoperable and have a dismal prognosis. Based on the robust tropisms of neural stem cells (NSC) and mesenchymal stem cells (MSC) to brain tumors, we compared the tumor-tropic migratory capacities of these stem cells and evaluated the therapeutic potential of genetically engineered human NSCs encoding cytosine deaminase (CD) and IFNbeta against brainstem gliomas. EXPERIMENTAL DESIGN: The directed migratory capacities of NSCs and MSCs to brainstem glioma (F98) were evaluated both in vitro and in vivo. The human NSCs (HB1.F3) and various human MSCs, such as bone marrow-derived MSCs (HM3.B10), adipose tissue-derived MSCs, and umbilical cord blood-derived MSCs, were tested. Human fibroblast cells (HFF-1) were used as the negative control. As a proof of concept, the bioactivity of HB1.F3-CD-IFNbeta was analyzed with a cell viability assay, and animals with brainstem gliomas were injected with HB1.F3-CD-IFNbeta cells followed by systemic 5-fluorocytosine treatment. RESULTS: In an in vitro modified Transwell migration assay and in vivo stem cell injection into established brainstem gliomas in rats, all the stem cells showed a significant migratory capacity compared with that of the control (P < 0.01). Histologic analysis showed a 59% reduction in tumor volume in the HB1.F3-CD-IFNbeta-treated group (P < 0.05). Apoptotic cells were increased 2.33-fold in animals treated with HB1.F3-CD-IFNbeta compared with the respective control groups (P < 0.01). CONCLUSION: The brainstem glioma-tropic migratory capacities of MSCs from various sources were similar to those of NSCs. Genetically engineered NSCs show therapeutic efficacy against brainstem gliomas.

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