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Human Embryonic Stem Cell-derived Mesenchymal Stem Cells as Cellular Delivery Vehicles for Prodrug Gene Therapy of Glioblastoma.

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Abstract

Mesenchymal stem cells (MSCs) possess tumor-tropic properties and have been consequently utilized to deliver therapeutic agents for cancer treatment. Their potential in cancer therapy highlights the need for a consistent and renewable source for the production of uniform human MSCs suitable for clinical applications. In this study, we seek to investigate whether human embryonic stem cells can be used as a cell source to fulfill this goal. We generated MSC-like cells from two human embryonic stem cell lines, Hues9 and H1, and observed that MSC-like cells derived from human embryonic stem cells were able to migrate into human glioma intracranial xenografts after being injected into the cerebral hemisphere contralateral to the tumor inoculation site. We engineered these cells using baculoviral and lentiviral vectors respectively for transient and stable expression of the herpes simplex virus thymidine kinase gene. The engineered MSC-like cells were capable of inhibiting tumor growth and prolonging survival of tumor-bearing mice in the presence of ganciclovir after they were injected either directly into the xenografts or into the opposite hemisphere. Our findings suggest human embryonic stem cell-derived MSCs as a viable and attractive alternative for large scale derivation of targeting vehicles for cancer therapy.

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