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# Embryonic stem cell (ESC)-mediated transgene delivery induces growth suppression, apoptosis and radiosensitization, and overcomes temozolomide resistance in malignant gliomas.

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### Abstract

High-grade gliomas are among the most lethal of all cancers. Despite considerable advances in multimodality treatment, including surgery, radiotherapy and chemotherapy, the overall prognosis for patients with this disease remains dismal. Currently available treatments necessitate the development of more effective tumor-selective therapies. The use of gene therapy for malignant gliomas is promising, as it allows in situ delivery and selectively targets brain tumor cells while sparing the adjacent normal brain tissue. Viral vectors that deliver proapoptotic genes to malignant glioma cells have been investigated. Although tangible results on patients' survival remain to be further documented, significant advances in therapeutic gene transfer strategies have been made. Recently, cell-based gene delivery has been sought as an alternative method. In this paper, we report the proapoptotic effects of embryonic stem cell (ESC)-mediated mda-7/IL-24 delivery to malignant glioma cell lines. Our data show that these are similar to those observed using a viral vector. In addition, acknowledging the heterogeneity of malignant glioma cells and their signaling pathways, we assessed the effects of conventional treatment for high-grade gliomas, ionizing radiation and temozolomide, when combined with ESC-mediated transgene delivery. This combination resulted in synergistic effects on tumor cell death. The mechanisms involved in this beneficial effect included activation of both apoptosis and autophagy. Our in vitro data support the concept that ESC-mediated gene delivery might offer therapeutic advantages over standard approaches to malignant gliomas. Our results corroborate the theory that combined treatments exploiting different signaling pathways are needed to succeed in the treatment of malignant gliomas. *Cancer Gene Therapy* advance online publication, 4 June 2010; doi:10.1038/cgt.2010.31.

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