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Targeting brain tumor stem cells with oncolytic adenoviruses.

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Abstract

In 2004, brain tumor stem cells (BTSCs) were isolated from surgical human malignant gliomas. This cancer cell population has been identified as the root for tumor initiation and resistance to therapies. Thus, it is imperative to develop new therapies that can eradicate this subpopulation to improve the prognosis of patients with brain tumors. Our group previously reported the antiglioma effect of the tumor-selective oncolytic adenovirus Delta-24-RGD that is now being tested in a phase I clinical trial for patients with malignant gliomas. We also showed that Delta-24-RGD infects, replicates in, and induces cell death in BTSCs. Interestingly, we observed that adenoviral-infected cells undergo autophagy and that autophagy-related cytoplasmic vacuolization might be part of the lysis process. Here, we summarize the materials and methods used in our study as follows: establishment of neurosphere cultures from surgical samples of human glioblastoma multiformes; assessment of stem cell markers; examination of adenoviral receptors in BTSCs; evaluation of the cytotoxicity induced by oncolytic adenoviruses; and assessment of autophagy in oncolytic adenovirus-infected BTSCs in vitro, and finally we describe a method to detect upregulation of the autophagy-related protein Atg5 in tumors treated with Delta-24-RGD.

PMID: 21948473 [PubMed - in process]

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