

## Review

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## Stem and progenitor cell-mediated tumor selective gene therapy

K S Aboody<sup>1,2</sup>, J Najbauer<sup>1</sup> and M K Danks<sup>3</sup>

<sup>1</sup>Division of Hematology/Hematopoietic Cell Transplantation, City of Hope National Medical Center and Beckman Research Institute, Duarte, CA, USA

<sup>2</sup>Division of Neurosciences, City of Hope National Medical Center and Beckman Research Institute, Duarte, CA, USA

<sup>3</sup>Department of Molecular Pharmacology, St Jude Children's Research Hospital, Memphis, TN, USA

Correspondence: Dr KS Aboody, Divisions of Hematology/Hematopoietic Cell Transplantation, City of Hope National Medical Center and Beckman Research Institute, 1500 E Duarte Road, Duarte CA 91010, USA. E-mail: [kaboody@coh.org](mailto:kaboody@coh.org); Dr MK Danks, Department of Molecular Pharmacology, St Jude Children's Research Hospital, 332 N Lauderdale, Memphis, TN 38105, USA. E-mail: [mary.danks@stjude.org](mailto:mary.danks@stjude.org)

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## Abstract

**The poor prognosis for patients with aggressive or metastatic tumors and the toxic side effects of currently available treatments necessitate the development of more effective tumor-selective therapies. Stem/progenitor cells display inherent tumor-tropic properties that can be exploited for targeted delivery of anticancer genes to invasive and metastatic tumors. Therapeutic genes that have been inserted into stem cells and delivered to tumors with high selectivity include prodrug-activating enzymes (cytosine deaminase, carboxylesterase, thymidine kinase), interleukins (IL-2, IL-4, IL-12, IL-23), interferon- $\beta$ , apoptosis-promoting genes (tumor necrosis factor-related apoptosis-inducing ligand) and metalloproteinases (PEX). We and others have demonstrated that neural and mesenchymal stem cells can deliver therapeutic genes to elicit a significant antitumor response in animal models of intracranial glioma, medulloblastoma, melanoma brain metastasis, disseminated neuroblastoma and breast cancer lung metastasis. Most studies reported reduction in tumor volume (up to 90%) and increased survival of tumor-bearing animals. Complete cures have also been achieved (90% disease-free survival for >1 year of mice bearing disseminated neuroblastoma tumors). As we learn more about the biology of stem cells and the molecular mechanisms that mediate their tumor-tropism and we identify efficacious gene products for specific tumor types, the clinical utility of cell-based delivery strategies becomes increasingly evident.**

**Keywords:** neural stem cells, mesenchymal stem cells, targeted tumor therapy, enzyme/prodrug therapy, malignant tumors, cancer treatment