ABSTRACT

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Potent bystander effect and tumor tropism in suicide gene therapy using stem cells from human exfoliated deciduous teeth.

Horikawa M(1), Koizumi S(1), Oishi T(1), Yamamoto T(1), Ikeno M(2), Ito M(3), Yamasaki T(1), Amano S(4), Sameshima T(1), Mitani Y(5), Otani Y(6), Yan Y(7), Suzuki T(3), Namba H(8), Kurozumi K(9).

Author information:
(1)Department of Neurosurgery, Hamamatsu University School of Medicine, Hamamatsu, Shizuoka, Japan.
(2)Department of Biology, Aichi Medical University, Nagakute, Aichi, Japan.
(3)Department of Virology and Parasitology, Hamamatsu University School of Medicine, Hamamatsu, Shizuoka, Japan.
(4)Department of Neurosurgery, Iwata City Hospital, Iwata, Shizuoka, Japan.
(5)Kidswell Bio Corporation, Tokyo, Japan.
(6)Department of Neurological Surgery, Okayama University Faculty of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan.
(7)Department of Surgery, Northwestern University, Chicago, IL, USA.
(8)Department of Neurosurgery, Enshu Hospital, Hamamatsu, Shizuoka, Japan.
(9)Department of Neurosurgery, Hamamatsu University School of Medicine, Hamamatsu, Shizuoka, Japan. kurozu20@hama-med.ac.jp.

Herpes simplex virus thymidine kinase (HSVTK)/ganciclovir (GCV) suicide gene therapy has a long history of treating malignant gliomas. Recently, stem cells from human exfoliated deciduous teeth (SHED), which are collected from deciduous teeth and have excellent harvestability, ethical aspects, and self-renewal, have been attracting attention mainly in the field of gene therapy. In the present study, we assessed SHED as a novel cellular vehicle for suicide gene therapy in malignant gliomas, as we have previously demonstrated with various cell types. SHED was transduced with the HSVTK gene (SHEDTK). In vitro experiments showed a significant bystander effect between SHEDTK and glioma cell lines in coculture. Furthermore, apoptotic changes caused by caspase 3/7 activation were simultaneously observed in SHEDTK and glioma cells. Mice implanted with a mixture of U87 and SHEDTK and treated with intraperitoneal GCV survived for longer than 100 days. Additionally, tumors in treatment model mice were significantly reduced in size during the treatment period. SHEDTK implanted at the contralateral hemisphere migrated toward the tumor crossing the corpus callosum. These results suggested that SHEDTK-based suicide gene therapy has potent tumor tropism and a bystander-killing effect, potentially offering a new promising therapeutic modality for malignant gliomas.

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