S19-4 In situ gene therapy with vector-producing MSCs

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Suicide cancer gene therapy with retroviral vector-producing cells was feasible as an adjuvant to the surgical resection of recurrent glioblastoma, although any benefit appeared to be marginal. Further evaluation of the cancer gene therapy strategy with the vector-producing cells must incorporate improved delivery of vectors and transgenes to the tumor cells. We have previously demonstrated the ability of vector-producing tumor cells engineered by the adenovirus-retrovirus hybrid vector to destroy satellite tumor cells, although therapeutic efficacy for aggressive tumor has to be further evaluated by the systemic delivery of the vector-producing cells.

Mesenchymal stem cells (MSCs) appear to be effective delivery vehicle to seek out tumor cells *in vivo* and transport cancer-killing gene or immune products with minimal rejection reaction by the host. In this study, we developed vector-producing tumor-tracking cells to improve suicide cancer gene therapy. Nucleofection was attempted to deliver retrovirus vector components into rodent MSCs. Athymic nude mice with subcutaneous 9L glioma were received vector-producing MSCs through the left ventricular cavity. Optical bioluminescence imaging *in vivo* revealed accumulation of the MSCs into the subcutaneous 9L tumors but not Rat-1 transplants. Consequently, the vector-producing MSCs significantly enhanced pro-drug killing of glioma cells compared to MSCs without ability to generate progeny virus. Our study demonstrated the effective MSCs-mediated tumor transduction with progeny vector production to improve suicide gene therapy. Although therapeutic benefit in the various orthotopic or metastatic tumor models has to be further validated, this transduction strategy would realize systemic administration of the labeling vehicles to detect and eradicate evasive tumors *in situ*.