Gene therapy using a somatostatin receptor for malignant brain tumors

Verwijnen SM, Sillevis Smitt PAE*, Hoeben RC**, Krenning EP, De Jong M
Department of Nuclear Medicine and *Department of Neuro-Oncology, Erasmus University Medical Center, Rotterdam, **Department of Molecular Cell Biology, Leiden University Medical Center, Leiden

Aim: The prognosis of malignant brain tumor patients is very poor, the median survival is less than a year, despite surgery, radiation therapy and chemotherapy. Therefore new therapy approaches are necessary. Nowadays, somatostatin analogues are widely used for imaging and radionuclide therapy of neuroendocrine tumors. However, these peptides cannot be used for malignant brain tumors, which do not express somatostatin receptors. Local gene therapy is an attractive strategy because brain tumors are localized in the skull with hardly any distant metastases. We performed gene therapy by using an adenoviral vector with two new genes in its genome, the Ad5.tk.sst_2 virus. The two new genes are thymidine kinase enzyme (tk) and somatostatin subtype 2 receptor (sst_2) and can both be detected with radiolabeled tracers. For tk, a substrate was used (^{125}I-FIRU) and for sst_2, the somatostatin analogue ^{111}In-octreotate was used.
Material and Methods: We tested the possibilities of this new therapy modality by *in vitro* infection of rat and human brain tumor cells with increasing concentrations of Ad5.tk.sst_2. Two days after infection, ^{125}I-FIRU and ^{111}In-octreotate were incubated on these cells for one hour. After incubation a gamma counter counted the uptake of the tracers.
Results: In all brain tumor cell lines, the uptake of ^{125}I-FIRU and ^{111}In-octreotate increased with increasing concentration of Ad5.tk.sst_2. In control cells, which were not infected with Ad5.tk.sst_2, no uptake of these tracers was measured. Results show that the uptake of ^{111}In-octreotate was higher in these cell lines that of ^{125}I-FIRU and that the uptake of ^{111}In-octreotate was also sst_2 -specific.
Conclusions: These results show that after infection with the Ad5.tk.sst2 virus, the tk and sst_2 genes are expressed in brain tumor cell lines *in vitro*. These two genes with their tracers might therefore be useful *in vivo* for diagnosis and therapy of malignant brain tumors.

Suzanne M. Verwijnen, Department of Nuclear Medicine, Erasmus MC, University Medical Center Rotterdam, Dr. Molewaterplein 40, 3015 GD Rotterdam, t 010-4087636, e-mail suzanneverwijnen@hotmail.com

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