Endostatin Gene Therapy for Metastatic Renal Cell Carcinoma

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Inhibiting tumor angiogenesis is a promising new strategy for treating cancer. The aim of this study was to investigated whether transfer of the gene encoding the angiogenesis inhibitor endostatin into the NIH/3T3LendSN fibroblast cell line could inhibit metastatic renal cell carcinoma. NIH/3T3 cells were transduced with retroviral vectors containing the murine endostatin gene. Endostatin in transduced cell supernatants and animals plasma were measure by ELISA. Two biological assays were performed: efficacy and survival. In both Balb/C mice were inoculated with $5x10^5$ murine renal cell carcinoma in tail vein and after 24h was divided into two groups: Control and treated, the second received treatment with $3,6x10^6$ producing endostatin cells. In the efficacy assay mice were treated for 2 weeks and than killed. Blood samples were collected and lungs were resected, weighed and fixed with formaldehyde. In survival studies, mice were monitorated until they died. Quantification of lung infiltration with metastasis was done by Immunohistochemical for lymphocytes CD4, CD8 and natural killer (NK) cells. *In vitro* endostatin production of NIH/3T3-LendSN was 135.3ng/mL. Endostatin plasma levels of animals on day 0 was 60±2.1ng/mL and at the end of efficacy assay the control group 75±3.3ng/mL and NIH/3T3LendSN injected animals 173±3.8ng/mL. The medium lung weight was 1.32±0.11g for control mice and 0.53±0.04g for NIH/3T3LendSN injected animals. Was revealed that ES treatment caused significantly rise in NK infiltrated. Retroviral endostatin gene transfer led to secretion of functional endostatin that was sufficiently active to inhibit metastatic renal. Our results indicated that besides its antiangiogenic properties, endostatin may be a promising adjuvant to immunotherapy.