

Scientific Abstract

Although murine retroviral vectors can infect diverse types of proliferating cells, inclusion of tissue-specific or inducible promoters within retroviral vectors should theoretically target expression to allow selective expression within tumor cells. The mouse mammary tumor virus (MMTV) long terminal repeat (LTR) is expressed at high levels in only certain tissues in vivo: breast, prostate, salivary gland. We have constructed retroviral vectors which express antisense RNA under the control of the MMTV promoter and have employed these vectors to infect MCF-7 human breast cancer cells. Infection of cultured cells by supernatants from cloned producer cells expressing either antisense c-fos RNA or antisense c-myc RNA (titer 4×10^6 virions/ml) produces a greater than 90% reduction in the tumor size when cells are injected into an estrogen-dependent nude mouse model (compared with control MMTV-based viral vectors). Studies of viral supernatant efficacy on established peritoneal, MCF-7 breast tumors in nude mice are in progress.

Based upon these findings, we have proposed a clinical trial to determine if injection of either antisense c-fos or antisense c-myc viral vectors will induce regression of metastatic breast cancer in the meninges (carcinomatous meningitis), peritoneum (malignant ascites) or pleura (malignant pleuritis). The patient population will consist of women who have failed standard therapy and have extensive, biopsy or cytology-proven metastatic breast cancer involving the meninges, peritoneum, or pleura which result in malignant effusions. In this protocol, patient effusions will be drained and the fluid replaced with retroviral vector, followed by periodic drainage of fluid to follow disease extent and assess gene transfer. These are patients who have failed standard therapy for their cancer and are expected to survive for a few months.