

(2) Non-technical Abstract

Gene therapy is being developed to treat a number of diseases that currently have no acceptable standard therapy. Ovarian cancer is an example of a devastating disease that often subjects patients to multiple rounds of toxic treatment. Although standard therapies may be curative for many cases, over 70% of patients eventually relapse. Once the patients are in relapse, none of the available therapies prolong survival. Relapse occurs because the cancer cells have become resistant to radiation and chemotherapy, and surgical removal could not be complete.

We have developed an experimental gene therapy approach for the treatment of cancers that are resistant to standard therapeutic agents. In this protocol, tumor cells are modified with a gene from the Herpes Simplex Virus. One gene is isolated from the virus to be used in the protocol so that no risk of infection with the Herpes virus is present. Expression of the isolated gene, known as the thymidine kinase gene, causes cells to be killed when exposed to the anti-viral agent ganciclovir. This killing of cells is caused by a separate mechanism than the one responsible for killing by radiation and chemical agents, thus this approach successfully eliminates cells that have escaped standard therapies. We have used this technology to treat patients in relapse by delivering the thymidine kinase gene into the area in which the ovarian tumor is growing. Although it is still too early to fully evaluate the effect of therapy, two of fourteen treated patients have achieved complete remission of their disease for 7 and 16 months. The main side effects have been fever and nausea. Overall patient survival has been slightly better trend (approx. 9 months) than expected when compared to patients treated with other forms of therapy (6-8 months).

Studies in mice have shown that this therapy is enhanced if the mice are immunized to their tumor prior to therapy. We propose to initiate a therapy which first immunizes the patients to their tumor prior to treatment with the Herpes thymidine kinase expressing tumor cells.