

Gene Therapy of Pleural Malignancies Non-Technical Abstract

This protocol is designed to develop a new approach for the treatment of a group of chest tumors involving the pleural space. These are malignant tumors of the lining of the lungs and rib cage that carry an extremely poor prognosis. At present, these cancers are uniformly fatal with a life-expectancy at time of diagnosis of one to one and a half years at best. Although trials of radical surgery and chemotherapy have been conducted, none have shown much promise or efficacy. Clearly there is a need for new treatment approaches.

One of the most exciting new approaches to cancer treatment is gene therapy. This strategy involves inserting a specially designed "gene" into cancer cells. Once inside the cancer cell, this gene becomes the blueprint for the production of a new protein that can be used to help destroy the cancer.

Our approach to gene therapy is to place a gene activating the body's immune system into a type of common-cold virus (the adenovirus) and infect tumors with the modified virus. In preliminary experiments, we have found that this virus efficiently infects tumor cells and can stimulate the body's immune system to destroy the cancer cells with minimal injury to neighboring normal cells.

We have developed animal models of pleural tumors by injecting cancer cells into mice. In these animals, the tumors grow rapidly causing death within 4-6 weeks. In mice with growing tumors, a single injection of the modified virus has cured over 90% of the animals and markedly reduced the tumor burden in the remainder.

Based on these observations, we propose to use this gene therapy strategy in patients with pleural cancers by injecting the modified virus directly into the chest cavity (near the tumors) through a small, flexible catheter. In the first trial, the safety of using this system will be determined. Each subject will be carefully observed for any signs of infection, irritation, or other adverse effects. Successful completion of this project would pave the way for additional studies aimed at effectively treating, and hopefully curing, patients with this form of cancer.