
II. NON-TECHNICAL ABSTRACT

Gene Therapy of Malignant Mesothelioma

This protocol is designed to develop a new approach for the treatment of a type of chest tumor called pleural mesothelioma. This is a malignant tumor of the lining cells of the lungs that is strongly linked to prior asbestos exposure. At present, the disease is uniformly fatal- with a life-expectancy at time of diagnosis of about one to one and a half years. 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 which can be used to help destroy the cancer.

Our approach to gene therapy is to place a "suicide" gene 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 makes them sensitive to an anti-viral drug (called ganciclovir) that does not harm humans or animals.

We have developed animal models of mesothelioma by injecting tumor cells into mice and rats. In these animals, the tumors grow rapidly causing death within 4-6 weeks. In animals with growing tumors, injection of the modified virus followed by treatment with the drug ganciclovir, has cured 80% 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 mesothelioma by injecting the modified virus directly into the chest cavity (near the tumors) and then treating the patients with the drug ganciclovir. 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.