

Non-Technical Abstract:

This protocol is designed to develop a new approach for the treatment of refractory colorectal carcinoma with liver metastases. This disease has an extremely poor prognosis. Although trials of chemotherapy and other treatments have been conducted, none have shown much promise or efficacy. Clearly there is a need for new treatment approaches.

Gene therapy provides a novel strategy that involves inserting a specially designed "gene" into cells. Once inside a 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 and other cells 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 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 refractory colorectal carcinoma with liver metastases by injecting the modified virus intravenously. In the first trial, the safety of using this method will be determined. Each subject will be carefully observed for any sign of infection, irritation, or other adverse effects. Successful completion of this project would pave the way for additional studies aimed at effective treating patients with this form of cancer.