

Brief Non-Technical Description of the Proposed Experiment

TIL (standing for tumor infiltrating lymphocyte) therapy is a new experimental treatment protocol for some patients who have advanced cancer. A portion of tumor is removed, grown in the laboratory under conditions which allow the cancer cells to die, but the invading immune cells (called lymphocytes) to multiply. These tumor infiltrating lymphocytes are then grown in the laboratory to very large numbers. The TIL, which are presumed to be the patient's own cancer-fighting cells, are infused back into a vein of the patient. The TIL are thought to circulate through the body, find the areas of cancer, and then invade and kill the cancer cells.

This TIL therapy has resulted in a substantial decrease in tumor size in about half of the patients treated thus far. Unfortunately, there has been no method up to now to follow and test the TIL that have been given back to a patient to determine why the TIL therapy works for some patients but not for others. The present protocol is designed to provide a means to "mark" TIL so that they can be isolated days or weeks later from the patient.

The proposed method for doing this is to mark or tag cells with a gene. The cell could then be recovered from the body for testing. The inserted gene would allow the marked cell to grow in a special culture solution in which unmarked cells die.

The procedure we are proposing would be to remove some of the TIL that are being grown in the laboratory, insert a marker gene (in this case, a gene called Neo^R that provides protection from a class of toxic antibiotics) using a technique termed retroviral-mediated gene therapy, and then combine these treated cells with the original TIL. The marked cells would act as a tracer. Furthermore, since the added gene becomes a permanent and stable part of the cell, the TIL and all its offspring would be marked in such a way that these cells could always, it is postulated, be identified and re-isolated even if they represented only a small fraction of the total cells present.

The addition of a marker into some of the TIL would, itself, be of no immediate benefit to the patient in which it is used. However, the information obtained should be of value in helping future patients and may be beneficial in later therapy of the same patient. The risks to the patient should be minimal, and there should be no risk to other patients or to health care personnel.