

## NON-TECHNICAL ABSTRACT

This study involves the use of novel methods to treat patients with advanced cancer by manipulation of their immune system. Based on extensive animal studies, we know that the immune system has the potential to recognize tumor cells as being foreign to the body and destroy them. The critical component of the immune system which appears to be involved in the rejection of tumors are lymphocytes. The ability to generate these lymphocytes in the laboratory would be useful for potential therapy of cancer. This approach has been called adoptive immunotherapy and involves the infusion of cancer reactive lymphocytes into patients in order to cause tumor shrinkage.

Unfortunately, the generation of immune lymphocytes which can reject human cancers has been extremely difficult. One possible reason why this problem exists is that the foreign proteins present on human tumor cells are very weak in their ability to stimulate the immune system to react against them. Based on our animal studies, we have devised an approach to artificially stimulate immune cells that may be used for the treatment of human tumors that under normal circumstances would not occur. This involves a two-step process. The first step requires vaccination of the patient with their own tumor cells which have previously been removed and genetically engineered to secrete an immune factor called GM-CSF. The tumor cells are irradiated prior to injection into the skin in order to prevent outgrowth of tumor at the site. It has been found in animal studies that the production of GM-CSF by the gene-modified tumor cells promotes an immune response in lymph nodes near the vaccination site. Lymph nodes are small glands of the immune system where lymphocytes congregate. The lymph nodes adjacent to the vaccination sites will be surgically removed approximately 7 to 10 days later and taken to the laboratory for further processing. In the laboratory, cells from the lymph nodes will be stimulated and grown in special flasks by methods we have previously described for a 2 to 3 week period in order to generate a large number of immune lymphocytes. These lymphocytes will be collected and infused back into the patient along with the administration of interleukin-2, another immune protein. The interleukin-2 has been found to promote the antitumor effect of the immune lymphocytes in cancer patients.

This clinical study proposes to address several important questions. These questions include: 1) Can this clinical treatment program be performed as described and what are its side-effects, 2) What antitumor response can be seen with this treatment, and 3) What is the immunological function of the immune lymphocytes, as assessed by laboratory tests.