

II. Non-Technical Abstract

There are presently more than 40,000 new cases of melanoma in the U.S. per year with 7,300 melanoma-related deaths. Patients with stage III disease have at least a 50% chance of recurrence after surgical resection; patients with stage IV melanoma have a median survival of less than 1 year and most of these patients eventually die of melanoma. Standard therapy is dacarbazine chemotherapy, and while response rates range from 8-25%, there is little evidence that treatment improves survival. Combination chemotherapy and biochemotherapy regimens have been reported to induce higher response rates with the disadvantage of greater toxicity and, to date, there is no evidence that they result in improved survival. New approaches to the treatment of this disease are needed.

The overall goal of this study is to develop ways to vaccinate against melanoma. In particular, we are trying to immunize against TYRP2, which is a substance found in melanoma cells that helps produce its black color. This study is designed to establish a safe and effective dose of DNA vaccine for TYRP2. The vaccine is a piece of DNA purified from bacteria, which contains the gene for TYRP2 from mouse. DNA is the blueprint used by cells to produce the substances that make up the body. We are testing a type of DNA vaccine against TYRP2, which is made from a piece of DNA that contains the blueprint for TYRP2 from mice. The mouse gene is very similar, but not identical to human TYRP2 DNA. We expect 9-18 patients to participate in this study.

The purpose of this study is to see if we can immunize against melanoma and study whether the vaccine causes any side effects. All of the patients on this study will receive vaccine, but groups of patients will receive increasing doses. Because of this, the first patients to be treated in this study will receive lower doses of the vaccine than the later patients, watching for side-effects to be sure that it is safe to give the higher doses. We believe, based on laboratory experiments that the use of DNA vaccines could result in the production of immune substances (antibodies and T-cells) which recognize melanoma cells.

Patients will be treated in the outpatient Clinical Immunology unit and will receive vaccinations into the skin and into a muscle approximately every three weeks for the first 18 weeks of the study. The injections are given intramuscularly by a needleless device called a Bioject2000. This device is held in the hand and shoots the vaccine into the muscle. Blood will be drawn at regular intervals for analysis of antibodies and T-cells. We will also be monitoring patients for any evidence of an effect on tumors.