II. NON-TECHNICAL ABSTRACT

Lymphoma is the most common blood cancer and the third most common cancer of childhood. Furthermore, since the early 1970's, incidence rates for non-Hodgkin's lymphoma (NHL) have nearly doubled. NHL is broadly divided into two groups: B-cell lymphoma, the most common, which develops from abnormal B-lymphocytes (specialized cells of the immune system), and T-cell lymphoma, which is relatively rare. NHL can also be broadly divided in indolent and aggressive. While the indolent type can be watched for months or years without requiring treatment, but can virtually never be eradicated, 30% to 80% of patients with aggressive NHL can be cured. Many people treated for NHL will receive some form of chemotherapy, radiation therapy, biologic therapy, or a combination of these. New antibody treatments are used usually in combination with chemotherapy. The most widely used antibody is called rituximab and attacks and destroys B-lymphocytes that carry on their surface a protein called CD20. Unfortunately, despite of all the recent advances in therapy of lymphoma, between 20 and 70% of patients with this disease (depending on the "aggressiveness" of their particular type of lymphoma) eventually succumb.

The overall goal of this study is to develop ways to vaccinate against lymphoma. Specifically, we are proposing a clinical trial to test if vaccination of patients with NHL against the CD20 protein can induce their immune system to produce not only antibodies against CD20 but also a special type of killer cells, called T cells, induced to attack only cells with CD20 on their surface. The vaccination process consists of five injections of DNA purified from bacteria, which contains the gene for CD20. DNA is the blueprint that cells use to produce all the substances necessary for their own existence. The DNA blueprint for CD20 is normally only used by the normal B cells. In patients with B-cell NHL, their cancer cells, which are B cells, make CD20 as well. Because it is found in normal cells in the body, CD20 is also called a self-protein. The immune system does not under normal circumstances recognize CD20 as foreign, and therefore does not produce antibodies (or T cells) against it. We propose that a patient's immune system can be taught to recognize CD20 if it is exposed to the same protein derived from a different species, for instance mouse. Mouse CD20 is very similar, but not identical, to the human CD20 and is considered foreign by our immune system. We know from laboratory experiments that once the immune system is educated to attack the foreign protein, it can also produce antibodies and T cells against the equivalent own protein, in this case CD20.

All patients in this study will receive vaccination of purified DNA into the skin, given by a needless device called Bioject2000. Three different doses of DNA are being studied, based on previous experience with DNA vaccination at our center. Because the primary goal of the study is to check if we were indeed able to stimulate an immune response against CD20, blood will be drawn before and at regular interval during the study to look for antibodies and T cell against CD20 at each time point. This study will be offered to patients who have not had a good outcome after conventional therapy. We will look at CAT scans to determine if any activity against the tumor itself was achieved with the vaccination, although this is a secondary objective of the study.