

## Non-Technical Abstract

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Neuroblastoma is the most common solid tumor (cancer) to occur outside of the brain in children. Although high doses of chemotherapy followed by bone marrow transplantation can achieve a complete remission in a large percentage of patients, most (60%) of high risk patients will subsequently relapse and die of progressive disease. We wish to use a novel gene therapy approach to try to eradicate the relatively small number of cancer cells that survive maximal chemotherapy, or to treat progressive disease in patients that have failed therapy. To accomplish this we will "insert" genetic material (DNA) designed to express human gamma interferon ( $\gamma$ -IFN), using a DNA delivery system known as a retroviral vector, into tumor cells obtained from the patient or cells from neuroblastoma patients with a shared tissue type (HLA type). We will then inject  $\gamma$ -interferon producing neuroblastoma cells ( $\gamma$ -IFN) in an effort to provoke an "immune" response against the cancer cells. The purpose of this study is to determine the maximal tolerated dose of such genetically engineered cells, and to obtain preliminary information regarding efficacy. Injection of  $\gamma$ -IFN producing tumor cells has resulted in protective immunity against "non-engineered" parental tumor cells in some animal models.

Tumor cell lines will be derived from clinical specimens, obtained at the time of surgical resection of tumor, from diagnostic bone marrow aspirations, or from peripheral blood. These tumor cell lines will be infected with a  $\gamma$ -IFN producing retroviral vector prepared by Viagene Inc. (San Diego). Following this, we will select for "engineered" tumor using the antibiotic G418 (which kills cells that do not carry the vector) and measure levels of  $\gamma$ -IFN production. We will test for sterility of the engineered cells, and freeze them for storage until needed. Just prior to use, they will be thawed, irradiated (with X-rays) to make sure they cannot grow in the patient. We will then inject various doses of tumor cells into the patient under the skin, according to a schedule outlined in the protocol, at 2 week intervals. We will determine whether this approach is safe, whether it increases the number of patients who remain disease free, whether it can decrease the size of tumor which is already present, and finally, whether a specific immune response can be measured in the laboratory following vaccination with genetically engineered neuroblastoma cells.