

II. Non-Technical Abstract

Neuroblastoma is a common type of malignancy arising in young children. The majority of children diagnosed with disseminated neuroblastoma have a high probability of succumbing to this disease despite the use of intensive chemotherapy, radiation, and surgery. Only 8% of children diagnosed with recurrent neuroblastoma are alive more than 36 months after this diagnosis is made. This Phase I protocol seeks to establish the safety of targeting neuroblastoma cells in children with relapsed or refractory disease with engineered immune cells. The ultimate goal of developing this new form of therapy is to combine it with current up-front therapies to decrease the incidence of relapse. Taking advantage of the high levels of expression of a cell-surface epitope recognized by the CE7 monoclonal antibody, a recombinant DNA molecule encoding an engineered T cell receptor having the specificity of CE7 has been constructed that, when expressed in cytolytic T lymphocytes, redirects their killing function to neuroblastoma cells. In the proposed study, children with relapsed/recurrent neuroblastoma will have T cells harvested. Genetically modified, and expanded to large cell numbers outside the body. Cytolytic T cell clones expressing the CE7R receptor and the selection/suicide fusion protein designated HyTK will be re-infused into each study participant in a series of three escalating cell doses and the safety of this procedure monitored. Additionally, patients will be studied to determine how long these cells remain in the circulation, and if administering the T cell growth factor Interleukin-2 will promote the persistence and anti-tumor activity of infused T cells. This study will provide the necessary safety data to justify larger Phase I/II protocols to study the ability of adoptively transferred neuroblastoma-specific T cells to prevent neuroblastoma relapse.