Scientific Abstract

The goal of immunotherapy is to stimulate the immune system by modification of tumor cells or expansion of lymphocytes which respond specifically to tumor antigens. In this study, we will apply techniques of direct gene transfer to enhance immune response against tumors *in vivo*. Patients with advanced cancer who have failed all effective therapy will be treated by injection of a DNA/lipid complex directly within the tumor. DNA will be used which encodes a heterodimeric cell surface protein recognized in the transplantation response. These genes include the HLA-B7 histocompatibility antigen and β-2 microglobulin gene in a non-viral plasmid eukaryotic expression vector. For this vector, a safe and effective dose to introduce this recombinant gene in HLA-B7 negative patients will be established. HLA-B7 expression will be confirmed *in vivo*, and the immune response stimulated by the expression of this antigen will be characterized. We will also determine whether this treatment facilitates tumor regression. This study employs the same study drug as Dr. Gary Nabel of the University of Michigan, previously proposed gene therapy protocol, but expands the study to two other clinical sites, the Mayo Clinic and the Arizona Cancer Center. These studies will facilitate the development of other approaches, using different recombinant genes or in combination with cytokines or adoptive T-cell therapy, to augment tumor immunity, and allow for greater potential efficacy. This method will also establish the safety on this non-viral approach to gene therapy, which could potentially be extended to treat a variety of other human diseases.