

## **I. Scientific Abstract**

This is a phase I trial to evaluate DNA vaccination in patients with renal cell carcinoma. The objective of this study is to determine the safety and immunogenicity of vaccination with the genes coding for mouse and human prostate specific membrane antigen (PSMA) in patients with renal cell carcinoma who have a limited burden of disease. PSMA has previously been used by other groups as an antigen using autologous dendritic cells pulsed with PSMA peptides. PSMA is known to be expressed on the vasculature of many solid tumors, including renal cell carcinoma. We will assess whether DNA vaccination is safe and generates an immune response to an otherwise poorly immunogenic surface antigen.

The hypothesis that xenogeneic DNA encoding a homologous antigen is more potent than syngeneic DNA encoding a tumor antigen will be tested. A randomized crossover design of a phase I study will be used to assess this hypothesis. We will assess two closely related DNA vaccines against PSMA. Studies in animal models have demonstrated that xenogeneic DNA (i.e., homologous DNA from a different species) can be more potent in inducing antibody and T cell responses against differentiation antigens than vaccination with self DNA. Patients will be randomly assigned to vaccination with either xenogeneic (mouse) or human PSMA DNA delivered intramuscularly at three different dose levels (500, 1500, or 3000  $\mu\text{g}$  in divided doses) every three weeks for six immunizations. Following this initial vaccination period, those patients previously randomized to receive mouse PSMA DNA will receive three immunizations with human PSMA DNA at three week intervals. Likewise, those patients initially randomized to receive human PSMA DNA will then receive three immunizations with mouse PSMA DNA at three week intervals. If patients have stable or clinically responding disease, additional vaccinations will be administered bimonthly for up to four additional vaccinations. Patients' sera will be collected in order to measure the antibody responses induced by the vaccines. Specifically, titers of IgM and IgG antibodies against human and mouse PSMA will be measured for serological response.