

**UPCI # 09-021: A Phase II Trial Testing Multiple Antigen-Engineered DC Followed by IFN $\alpha$ 2b Boost for Immunization of HLA-Unrestricted Melanoma Patients.**

**Technical Abstract**

This clinical protocol will test a new multiple tumor antigen-engineered dendritic cell (DC)-based vaccine which is designed to activate multiple CD8<sup>+</sup> and CD4<sup>+</sup> T cells specific to three different melanoma antigens. We will test melanoma lineage antigens MART-1, tyrosinase, and the cancer-testes antigen MAGE-A6, all encoded by a novel adenovirus (AdV), “AdVTMM2”. This vaccine is also designed to promote NK cell activation via AdV-activated DC-NK cell cross-talk. We will employ thorough immunological monitoring to study antigen-specific CD8<sup>+</sup> and CD4<sup>+</sup> T cell responses to the antigens delivered with the vaccine, as well as NK cell activation. We will also test the importance of determinant spreading for clinical response. We hypothesize that vaccination with multiple, full length tumor antigens, expressed in a matured dendritic cell, will activate a broad range of CD4<sup>+</sup> and CD8<sup>+</sup> T cells, and, that in the subset of patients who further activate and diversify their T cell response to include other antigens expressed by their tumor (or undergo “determinant spreading”), objective clinical response will be observed. Because many vaccine trials have had limited clinical impact as stand-alone interventions, we will also test for a boosting effects from IFN $\alpha$ . We hypothesize that systemic IFN $\alpha$  delivered after the vaccine will boost the vaccine-specific T cell and NK cell responses.