

Bankhead-Coley Cancer Research Program

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*Interdisciplinary Oncology
H. Lee Moffitt Cancer Center & Research Institute*

*2008 Program
Bridge (1-year project)*

Project Title: PD-1 Abrogation and Immunity in Melanoma

Project Summary: We will treat ten patients with stage IV distant melanoma in a clinical trial; we will give increasing doses of an antibody against a molecule on immune T cells, called Programmed Death-1 (PD-1). PD-1 is found on the surface of immune T cells that have been activated or turned on. It causes immune cells to decrease their function. Decreasing the function of PD-1 on immune T cells by the use of antibodies in animals that have tumors has resulted in increased immunity to those tumors but also caused a reaction against normal tissues called auto-immunity. Early testing of an anti-PD-1 antibody in animals as well as with human immune T cells in the test tube has shown that decreasing the function of PD-1 results in shrinkage of tumors in mice and causes the rapid growth of potent tumor-killing immune T cells. Ten patients with widespread stage IV melanoma that have the blood type HLA A0201 will receive increasing amounts of the anti-PD-1 antibody with a vaccine to measure the side effects of the combination and find out how well tolerated it is. We also wish to find out how long the injected anti-PD-1 antibody can be detected in the blood and how it affects the immune system with particular attention to the development of increased immunity against the body's own normal tissues. Anti-PD-1 antibody will be given every two weeks, six times with a vaccine. In this trial, we will ask whether anti-PD-1 antibody will have the same effects predicted from the mouse experiments such as increased growth of immune anti-tumor T cells. We will also find out if the presence of certain variants of the gene for PD-1 found in the population can predict whether increased immune reactions against normal tissues will occur in patients in the group receiving the anti-PD-1 antibody with vaccine as well as whether the variants seem promising to be able to predict the effects of the PD-1 antibody at that dose on the immune system.