

Laboratory Study Supported by Ann's Hope Melanoma Research Fund at the University of Wisconsin Carbone Cancer Center

Human malignant melanoma is a cancer responsible for considerable suffering and death. While cure is often possible by surgical removal of a localized primary tumor, therapy is usually ineffective after spread (metastasis). Findings from laboratory and clinical research indicate that melanoma patients have special white blood cells (T cells) that can attack the tumor and limit its growth. These special T cells have molecular structures on their surfaces called T cell receptors (TCRs) by which they recognize anything foreign to the body. One feature of T cells activated to attack anything "foreign" is that they multiply by rapid cell division to develop large numbers. Rapid cell division has a "side effect" in that mutations, which are mistakes made when a cell replicates its genetic material, tend to occur more frequently in rapidly dividing as compared to non-dividing cells. Focusing on T cells that have a specific mutation, which has no effect on the cell's well being, allows identification of T cells enriched for rapidly dividing and thus immunologically relevant cells. Dr. Albertini's strategy is to study T cells with certain indicator mutations in order to identify melanoma-reactive T cells in melanoma patients. This selection strategy is called "surrogate selection", and the studies have focused on one particular reporter mutation (the hypoxanthine guanine phosphoribosyltransferase (*HPRT*) system). The support from Ann's Hope provides valuable flexible funding for these detailed laboratory studies.

The research is designed to identify the T cells in melanoma patients that are able to recognize and destroy melanoma cells. If successful, this approach will allow us to identify the subset of T cells that need to be manipulated in order to activate immune rejection responses against melanoma. This approach could also allow us to monitor the effectiveness of new cancer treatments such as cancer vaccines. While the potential therapeutic uses are not all known at this time, one could certainly envision approaches to amplify specific T cell subsets that have the potential to mediate anti-melanoma activity but normally exist in the patient at insufficient numbers to be effective. We hypothesize that the anti-melanoma T cell responses identified by surrogate selection will be protective in controlling tumor growth and/or involved in regulating the immune response to melanoma. Findings from this study could therefore provide direction for novel immune treatments for melanoma patients.