New Jersey State Commission on Cancer Research
LAY ABSTRACT OF RESEARCH PROJECT

NAME OF PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR: **Raymond B Birge**

Project Title: **A Novel Strategy to Target Dendritic Cells**

Description: **We propose a new strategy for cancer vaccines**

Breast cancer, an epidemic in women with a predicted 190,000 cases in 2003, is a disease in which maligancies are found in the ducts and lobules of the breast. Surgery, radiation therapy, chemotherapy, and biological therapy are among standard treatment modalities, although there are serious side effects and limitations to the aforementioned strategies. Biological therapies include a number of new therapies such as monoclonal antibodies against tumor antigens, hormone treatments, smart medicines directed against receptors and signaling molecules, as well as immunotherapy. Immunotherapies are defined as technologies that harness the power of the immune system to provide cell and antibody-based treatments to treat cancer. There is a great hope and anticipation that immunotherapy, when applied in optimal strategies, will have a significant impact on the cancer problem. In this application, we propose a new approach for vaccine development applicable to human breast cancer. The project is based on the observations that dendritic cells (potent antigen-presenting cells that display antigens to cytotoxic T lymphocytes) can engulf or phagocytose apoptotic tumor cells (including breast cancer cells) and in turn process antigens to activate tumor-specific CTLs. This process is called cross-presentation of cross-presenting antigen to T cells. Remarkably, in this way, the DCs in the peripherial tissue sample and survey recently killed cells for genetic abnormalities (tumor cells) by performing a molecular autopsy on the engulfed cellular material, and in turn relay this information to induce an immune response against the native tumor. Interestingly, DCs appear to be unique in this manner and other phagocytic cells, such as macrophages and amateur phagocytes, digest apoptotic material in phagolysosomes without presenting antigen. We have recently identified a receptor on DCs, called the alphav-beta5 ($\alpha v\beta 5$) integrin, that is involved in the recognition, internalization, and trafficking of apopototic material in a manner that permits the activation of tumor-specific T cells. In the present application, we will exploit this biology and attempt to develop novel DC targeting vectors that promote DC/apoptotic interactions, and potentiate phagocytosis and antigen cross-priming. Towards this goal, we will generate novel soluble molecules that will serve as a platform technology for a new class of anti-tumor modulators that target DCs and stimulate an anti-tumor cellular response. Ultimately, we anticipate these reagents will be used in combination with other anti-breast cancer therapeutics, particularly to cooperate with strategies in which selective tumor cell killing is achieved.