Poster Session 3

Balcony, Easel 113

2:30 PM to 4:00 PM

Immune Response to Cancer Cell Death

Kristy Chiang, Junior, Biology (Molecular, Cellular & Developmental)
Mentor: Andrew Oberst, Immunology
Mentor: Annelise Snyder, Immunology

Necroptosis is a lytic and immunogenic form of programmed cell death (PCD), characterized by pro-inflammatory cytokine production and the release of intracellular molecules, including cell-associated antigens. In the context of tumor immunology, tumor cell death is a necessary step in causing the release of tumor antigens, allowing for antigen-specific tumor recognition by the immune system. However, how distinct forms of PCD within tumor cells could differentially instruct immune recognition of tumor-associated antigens remains poorly understood. Our research question addresses how the immune system responds to cancer cell death, and will help determine whether necroptosis can promote tumor immunity. We propose that induction of necroptosis within tumor cells could promote anti-tumor immune responses by releasing tumor antigens accompanied by pro-inflammatory signals, resulting in potent immune recognition of cancerous cells. To study the immune responses to cell death in tumors, we have modeled the effects of various cancer cell death programs using flank tumors implanted in B6/J mice. Using flank tumors engineered to express versions of various pro-death signaling proteins that can be activated, we show that induction of necroptosis within the tumor microenvironment leads to robust tumor control. Measuring serum cytokine levels, in addition to analyzing the identity and activation status of immune cells isolated from the tumor tissue following treatment, will yield critical insights towards the immune cell subsets and signaling axes responsible for the observed response to necroptosis. These experiments provide us with a comprehensive understanding of whether cell death in a solid tumor has a therapeutic benefit as well as the underlying mechanism of the immune response to dying cells within a solid tumor. Considering the pro-inflammatory nature of necroptosis, it represents a promising therapeutic target in the context of cancer immunology.

Poster Session 4

Balcony, Easel 108

4:00 PM to 6:00 PM

Tamoxifen-Inducible Cre System in Immunotherapy Against Lung Cancer

Oanh Tran, Senior, Biochemistry
Mentor: Philip Greenberg, Medicine and Immunology
Mentor: Leah Schmidt, Medicine

Immunotherapy has yielded exciting results in the clinic, primarily against blood cancers. Moving toward applying immunotherapy to solid cancers, the field has seen success in treating certain cancers, such as lung cancer, with immunotherapy. However, only a fraction of patients respond to treatment, highlighting a need for continued research in this area. The ‘KP’ model is a genetically engineered mouse model of lung cancer, relying on Cre-recombinase inducible activation of oncogenic Kras and inactivation of the tumor suppressor p53, the two most frequently mutated genes in human lung adenocarcinoma. Tumors are initiated by delivery of Cre into lung alveolar cells by the administration of Cre-expressing viruses. Using this virally-induced model, we can control the timing of tumor induction and tumor burden, and introduce additional genetic modifications into tumors. However, the use of viruses can cause inflammation, potentially impacting the immune responses that we are studying. Improving this model will make the study of lung cancer more physiologically relevant. Therefore, we are developing a system for separating viral infection from tumor initiation, dependent on a tamoxifen-inducible Cre-ER allele. By developing viruses that express Cre-ER, mice can be infected and the induction of tumors can be delayed until a timepoint when virus-related inflammation has subsided. Then, Cre activity can be induced by administration of tamoxifen. Additionally, this system allows us to control the number tumors that form, by titrating the doses of tamoxifen, to better recapitulate human disease. To date, we have cloned DNA fragments and performed Gibson Assembly, and are currently validating clones. We have produced lentiviruses and titered the viruses using GreenGO cells, a cell line carrying a Green Fluorescent Protein reporter of Cre activity. To test Cre-ER functionality and sensitivity, we will use GreenGO cells to assay differences in Cre–ER activity, using different concentrations of tamoxifen *in vitro*.