Evaluating Macrophage Metabolism and Polarization in Lean and Obese Mice Following Radiation Therapy

Cancers are a class of diseases characterized by abnormal cells that develop and spread uncontrollably, and triple negative breast cancer (TNBC) is a particularly aggressive disease whose treatment typically includes radiation therapy. Excessive macrophage infiltration has been shown to promote TNBC recurrence following radiation therapy in certain patients. In the irradiated microenvironment, adipocytes make up a large portion of the normal tissue cells that will interact with post-radiotherapy recruited macrophages. To begin this analysis, we are characterizing macrophages from lean and obese mice in addition to their interactions with adipocyte spheroids that will help predict differences *in vivo*. As innate immune system cells, macrophages play a crucial role in the initial line of defense against infections and cancerous cells. Stem cells that can develop into myeloid precursor cells are found in the bone marrow. These cells can then exit the bone marrow and move throughout the bloodstream where they are recruited to tissues following radiation damage. It is known that M1 macrophages, which are significant components of the first line of defense against bacterial infections and are considered "anti-tumorigenic", get their energy from glycolysis. Oxidative metabolism is necessary for M2 macrophages' long-term functions, which include wound healing and tissue regeneration, but are considered "pro-tumorigenic". We are currently evaluating how macrophages in obese and lean subjects respond to irradiated adipocytes and influence TNBC recurrence. We hypothesize that macrophages isolated from the bone marrow of lean and obese mice will inherently have different metabolic profiles and M1/M2 polarization abilities, which will affect their interactions with irradiated adipocytes and ultimately, impact TNBC recurrence. Macrophages were isolated from three lean mice and three obese mice and MitoTracker intensity, a measure of

mitochondrial respiration, was evaluated. Macrophages from obese mice displayed evidence of high mitotracker intensity. Lean mice displayed evidence of low mitotracker intensity. These results suggest a baseline difference in macrophage polarization. We are currently evaluating metabolic activation markers such as CD36 and Perilipin-2, and M2 markers CD206, CD163, and arginase-1. These studies will help understand how macrophages may interact with irradiated adipocytes and ultimately influence TNBC recurrence mechanisms.