Introduction

- Osteosarcoma (OS) therapy has stagnated for nearly 40 years.
- There is a tremendous need for the development of novel therapeutic approaches such as immunotherapy.
- However, evaluation of immunotherapy for OS is challenging within current pre-clinical models, which generally utilize immunocompromised animals.
- A humanized model would more accurately recapitulate the human scenario and permit a more accurate assessment of novel therapies such as immunotherapy.

Purpose

A. To characterize OS growth within a humanized xenograft murine model
B. To create a cost-effective and reproducible process for scaling this model

Research Questions

1. Can human osteosarcoma grow within a humanized mouse model?
2. What is the lymphocyte infiltration pattern associated with tumor growth within this model?
3. What is the origin of vasculature within the tumor?

Methods

- NSG mice were irradiated with 250 cGy using a Cs137 source irradiator.
- CD34+ lymphocyte progenitor stem cells were isolated from human umbilical cord blood using density gradient centrifugation.
- CD34+ cells were purified using Magnetic-activated cell sorting (MACS®) and injected into mice.
- Peripheral blood was used to validate engraftment using a BD LSR II flow cytometer.
- Multiple standard and patient-derived xenograft tumors were cultured and implanted.
- Mice were euthanatized when tumors palpable.
- Tumor analysis radiographically and histologically.
- Tumor infiltrating lymphocytes identified using immunohistochemistry.

Results

Figure 1: 30% of Mice Humanized by Week 10

Figure 2: Human OS Grows in Humanized Mouse

Figure 3: Human Lymphocytes are Present in Medullary Cavity

Figure 4: Human Lymphocytes Infiltrate Both Primary and Metastatic Lesions

Figure 5: Lymphocytes include CD3+ and CD8+

Conclusions & Future Research

- Humanized model permits for reliable tumor implantation and growth.
- Human T-cells are the predominant tumor-infiltrating cells.
- Tumor vasculature appears to derive from both host and tumor origin.
- Infiltrating lymphocytes include CD3+ and CD8+ cells.
- Future work will focus on defining the humanization timeline, the infiltrative CD45+ leukocyte subpopulation, and the effect of various therapies on tumor within this model.