INVESTIGATING TUMOR MICROENVIRONMENT AND BONE METASTASIS IN PROSTATE CANCER

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ABSTRACT

Interning at the Van Andel Institute provided me with experience I would not obtain in a classroom setting. This component of the PSM program provides a great networking environment and fast-paced learning opportunity that only comes from working in a laboratory setting. Without having much research background, I had a lot to learn about how a laboratory runs as well as various techniques I had never used before. One of my goals was to examine the role of the lab manager to prepare myself for this potential career path. The first few weeks of my internship involved learning many new techniques and becoming familiar with the flow of the lab. My PI and other lab mates were very helpful throughout the process and after I caught on to most of the new techniques, I began helping with existing projects as well as working on projects of my own. I was able to work with mouse models and learn how to perform x-rays and collect various tissue types and culture them. My cell culture skills were enhanced throughout the experience as this was vital for most experiments, and I was able to observe the lab manager and determine the various components involved in running and managing a lab. I learned many new techniques and skills that I will be able to apply to my work in the future. I also made connections that will hopefully help my future employment as well as future PSM internship candidates.

BACKGROUND

The Li lab focuses on the study of tumor microenvironment influences on bone metastasis in prostate cancer. TGF-β in the bone microenvironment has shown involvement in both tumor suppression and promotion at different stages of cancer progression. We induce a loss of TGF-β type II receptor in the mice using a Cre-lox system induced by Tamoxifen injections. After the TGβRII receptor is knocked out, we perform intratibial injections with cancer cells to study the effects on lesion development and examine the tissue after tumor growth is established.

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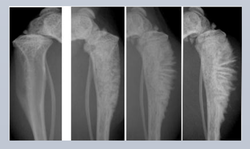
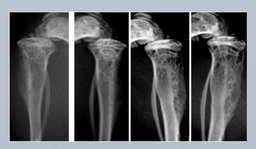
Different cancer cell lines present varying tumor characteristics upon injection. LUCap cells generally create osteoblastic lesions, but have a low take rate so they are difficult to use. C4-2B cells create mixed lytic and blastic lesions and have a much higher take rate. This cell line is currently the best model used for prostate caner bone lesion development.



PBS LUCaP

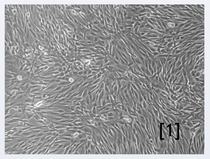


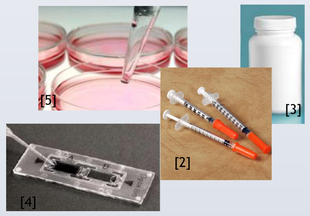
PBS C4-2B

RESPONSIBILITIES

❖Cell culture of prostate fibroblasts was done for freezer stock and injection.

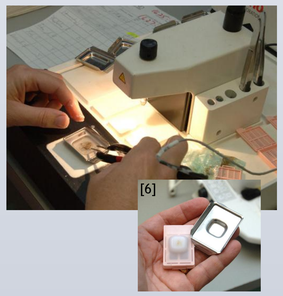
❖Cultures of prostate cancer cell lines was done for injection, qPCR analysis, and Von Kossa staining.





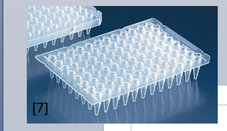
❖Tamoxifen injections were used to induce the Cre-lox system in the mice.

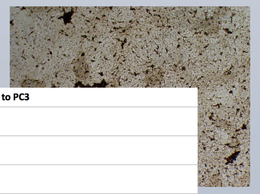
❖ Cancer cells were counted to obtain specific concentrations prior to injection.

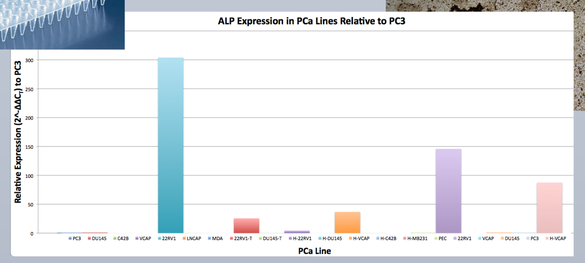


❖After tissues were harvested from the mice, they were either fixed for paraffin embedding or cryosectioning, flash frozen, or used for microCT analysis.

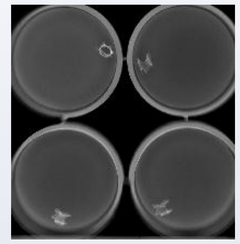
Line	ALP Activity	Bone Lesion Type
VCaP n=1	+	Osteoblastic
22Rv1 n=2	+	Osteoblastic
DU-145 n=3	+	Osteoblastic
C4-2B n=3	–	mixed
PC3 n=1	–	Osteolytic
LNCaP n=2	–	N/A







❖Various tissues were harvested from the mice for further analysis. I had the opportunity to harvest tibia, vertebrae, and prostates.



❖Mouse x-rays were done weekly to monitor tumor growth following intra-tibial injections.

❖Previous interns performed a differentiation assay with ALP staining to investigate the presence of osteoblastic markers in various cancer types

❖I followed up their experiment using qPCR and Von Kossa staining using various cell lines.

OVERALL EXPERIENCE

I had a very enjoyable experience during my internship and learned a lot of useful tips and techniques that I will use in the future. Working with mouse models for the first time was a unique experience that I would not have had in any of my courses. Tissue harvesting was a major part of my responsibilities and was also something I had never had the opportunity to do before. My PI and her research technician were very helpful in teaching me what it takes to manage a lab and I feel much more prepared for my future career after having this experience.

ACKNOWLEDGEMENTS

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❖Center for Skeletal Disease and Tumor Metastasis- Jackie Peacock (for help with qPCR machine)

❖Grand Valley State University, CMB Department

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