CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP140482

Project Title:
Preclinical Intravital Microscopy of Prostate Cancer Lesions in Bone: Identification and Eradication of Survival Niches by Combination Therapy

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
The University of Texas M.D. Anderson Cancer Center

Lay Summary:

Bone metastases are a major complication in patients with advanced prostate cancer (PCa). After colonizing bone, PCa cells lead to its remodelling, followed by symptoms and detrimental consumption of the organism. At this stage, PCa disease is usually incurable. Despite recent encouraging results obtained with innovative cures, including radiation and molecular therapy, the benefit for patients is often incomplete and limited in duration. Such therapy resistance occurs when tumor cells adapt to anticancer treatments and escape from death, re-initiating tumor growth. With this project we establish a bone-window mouse model suited for monitoring by microscopy to investigate (i) how PCa cells grow within bone and resist to therapy and (ii) how we can disrupt such resistance mechanisms by new combination treatments. Our original mouse model approximates the biology of human bone and contains a glass window through which the disease can be directly inspected by a last generation multiphoton microscope (MPM). MPM allows relatively deep imaging (0.5 mm) into living tissues with single-cell resolution, so that several layers of PCa cells can be visualized in the tissue context, in real time and in three dimensions. Monitoring bone lesions by MPM will extract medically important information, including tumor cell division and growth, and (therapy-induced) tumor cell death. Using this imaging approach, we will first test how PCa cells respond to radiation treatment, the current standard of care, and identify if and where small cell groups (niches) resist therapy. Such survival niches may support PCa cells re-growth during or after therapy. By combining radiation with molecular targeted therapy, here an inhibitor of proteins that mediate PCa cell adhesion to bone tissue, we aim to specifically eradicate resistance niches. Our mouse model and imaging technology will improve clinical practice by delineating innovative combination regimen to break tumor cell resistance in bone.