CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP110327

Project Title:
Prostate Cancer Bone Metastasis Secretome

Award Mechanism:
Individual Investigator

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

Lay Summary:

Prostate cancer (PCa) is dominated by complications arising from bone metastasis. Besides causing suffering and pain, bone metastasis often has a lethal outcome in PCa. Effective therapies that can prevent or reduce bone metastasis are urgently needed. A distinct feature of human PCa with lethal potential is the ability of tumor cells to survive in a castrated environment and develop metastases in bone with a bone-forming phenotype. The preferential metastasis of PCa to bone and the induction of new bone formation suggest that PCa cells have unique interactions with bone environment, especially osteoblasts, and these interactions lead to survival, growth, and resistance to therapy of PCa bone metastasis. It is likely that deciphering these interactions will lead to development of strategies to block such interactions. We hypothesize that factors secreted by the metastatic PCa cells induce new bone formation that alter the balance between osteoblastic and osteolytic activities in the bone. The newly formed bone provides factors that permit PCa cell invasion, survival, or proliferation in bone. The objective of this study is to identify these secreted factors (we name them bone metastasis secretome) and characterize for their roles in PCa bone metastasis. We will identify these factors in two unique PCa xenografts that were generated from bone lesions from PCa patients. Identification and characterization of these factors will define a bone metastasis secretome, a profile of proteins collected from the tumor microenvironment. The secretome will be used as a template to dissect the functional roles of select factors in enhancing PCa progression in bone. We will validate the clinical relevance of these factors using human PCa specimens. A multiplex assay will be developed to use this panel of validated secreted factors for monitoring PCa progression in bone. Therapeutically, they could serve as targets for individualized therapy among PCa patients.