CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP150179

Project Title:
Regulation of dormancy of metastatic prostate cancer cells by bone microenvironment

Award Mechanism:
Individual Investigator

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

Lay Summary:

The majority of men who succumb to prostate cancer die of bone metastasis. Bone metastasis can occur years or decades after prostectomy, due to reactivation of disseminated tumor cells that had been dormant at the metastatic site in bone. The mechanisms that lead to tumor dormancy and reactivation are poorly understood. Identification of factors that cause tumor dormancy and the mechanisms by which tumors exit dormancy will lead to new strategies that prevent dormant disseminated tumor cells from reactivation in bone.

Metastasis is attributed to properties of the tumor cells (seed) and their interaction with the microenvironment of the metastasized organs (soil). It is possible that microenvironment signaling in bone regulates the switch between proliferation and dormancy. We hypothesize that bone secretes factors, we termed “dormancy osteocrines”, which activate dormancy signaling pathways, resulting in transcriptional reprogramming and induction of tumor cell dormancy in bone.

The objective of this study is to identify the mechanisms that lead to tumor dormancy. We will identify dormancy osteocrines that are secreted by bone, delineate the signaling pathway(s) by
which dormancy osteocrines lead to cell dormancy, elucidate their function in dormancy induction in vivo, and confirm their clinical relevance in human prostate cancer patient bone marrow samples. We will also use proteomics approach to identify the specific protein profile (“dormancy signature”) in the bone marrow aspirates of patients before and after they develop clinically evident bone metastasis. The “dormancy signature” may be used to guide diagnosis and for therapy selection.

Our proposed studies will open up the possibility of developing therapy strategies to prevent disseminated tumor cells from exiting dormancy. Maintaining tumor dormancy will be a novel therapy approach and will be of significance for patients with a high risk of developing bone metastasis.