CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP150696

Project Title:
Inhibition of Breast Cancer Metastasis to the Bone by microRNA Transmission through Gap Junctions

Award Mechanism:
High Impact/High Risk

Principal Investigator:
Nicholson, Bruce

Entity:
The University of Texas Health Science Center at San Antonio

Lay Summary:

1 in 8 women will be diagnosed with breast cancer, with the disease claiming 40,000 lives in the US in 2013, and 10 fold more world-wide. These deaths result mostly from metastasis rather than the primary tumor, with a median survival time under 3 years after first diagnosis of metastatic spread. No effective cure currently exists for the metastatic phase of the disease, leading some high risk women to even contemplate preventative mastectomy! Yet we know that the body does have defenses against the metastatic process, as there are often long latent periods between initial breast cancer diagnosis and manifestation of bone metastases. This is the equivalent of the “soil” trying to reject the "seed", and suggests that rather than focus solely on how to treat the "seed" (cancer cells), we should identify what defensive tools the "soil" (target tissue) makes.

Defensive tools that have gained recent attention are microRNAs, small versions of the protein coding machinery, which regulate many cell behaviors, including the suppression of tumor growth and invasiveness. Recently, they have been shown to pass from bone marrow cells to breast cancer cells grown in the lab, causing the cancer cells to stop growing. We have now shown that these microRNAs pass through gap junctions, small pores that directly connect the insides of cells in contact. Furthermore, genetic deletion of gap junctions from the major bone cell type results in dramatic increases in bone metastasis of breast cancer cells in mice. In this proposal, we will expand the use of these genetically engineered mice, along with similarly manipulated breast cancer cells, to directly measure if microRNAs transfer through the gap junctions that form between invading tumor cells and the bone. By identifying specific bone microRNAs that suppress metastasis, we may be able to harness the body’s own tools to combat breast cancer spread to the bone, and extend survival time of breast cancer patients.