

Public/Lay Abstract

Bone metastasis is the leading cause of death from breast cancer. About 6% of breast cancer patients are positive with metastasis when they are first diagnosed cancer. Recent preclinical studies reported that tumor cell dissemination occurs even before a primary tumor established, suggesting that a significantly more patients may carry disseminated tumor cells in their bone marrow when the tumor is first diagnosed. Successfully disseminated tumor cells (DTCs) in the bone marrow lie dormant for years and decades. Exact mechanisms by which dormant DTCs awake and develop lethal metastasis remain uncertain but the advanced age is an important risk factor.

Chemotherapy is the standard treatment for stage IV (metastatic) breast cancer patients, but this therapy is known to accelerate patients aging. For example, survivors experience osteoporosis much earlier than an age-matched demographic group. Many investigators believe that therapy-induced bone aging is functionally linked to awakening of disseminated tumor cells. However, the mechanism behind remains unclear due to intrinsic challenge to investigate bone metastasis in the context of aging; inner bone cavity is anatomically difficult to access, and bone aging and metastasis are lengthy processes. We have developed a tissue-engineered bone model that faithfully recapitulates surface and subsurface of bone tissue complexity in a controlled and analytical manner. The goal of this proposal is to apply a tissue-engineered bone model developed in our lab to determine functional connections between therapy-induced bone aging and metastatic disease progression. If successful, our tissue-engineered bone model will allow to ask experimental questions regarding the impact of cancer therapy in bone aging and associated tumor cell biology. Our research will be the foundation to develop better therapeutic strategies to prevent or delay lethal metastasis for breast cancer survivors.