

PUBLIC ABSTRACT

Over 281,000 new cases of breast cancer are diagnosed annually within the United States. The majority are estrogen receptor- α positive (ER+) and these patients are often treated with adjuvant endocrine-targeted therapies to prevent tumor recurrence. These therapies include aromatase inhibitors (AIs; letrozole) or selective estrogen receptor modulators (SERM; tamoxifen). While initially effective, resistance can develop leading to tumor recurrence and the development of breast cancer metastases. ER+ breast cancer patients are more likely to develop bone metastases than other subtypes. However, the currently available preclinical models to study bone metastases are ER-negative. In collaboration, our group has developed several bone metastatic ER+ breast cancer models to test novel combinatorial strategies to treat metastatic ER+ breast cancer.

The human body contains more bacterial cells than human cells. Therefore, it is unsurprising that the gut microbiome plays a critical role in the development of disease. Menopause and breast cancer was shown to shift the gut microbiome. Literature also indicates that probiotic bacteria (such as *Lactobacillus* and *Bifidobacterium* species) often found in over-the-counter supplements, can reduce inflammation and preclinical breast tumor growth. Probiotic bacteria secrete numerous factors that can promote bone health. Therefore, probiotic bacterial supplements and probiotic-secreted metabolites could be a novel treatment factor to enhance current FDA-approved metastatic ER+ breast cancer therapies.

Our goal is to determine whether probiotic supplements in combination with Faslodex and Palbociclib reduce established ER+ breast cancer bone metastatic lesion growth, increases bone health, and improves overall survival. Throughout this project, we hope to impact women with stage IV bone metastatic ER+ breast cancer, uncovering new molecular mechanisms affecting therapy response. We also aim to develop implementable interventions modifying the microbiome to create a metabolically favorable microenvironment to reduce metastatic growth and progression in patients with bone metastatic ER+ breast cancer. Dietary supplements can be easily translated to the clinic; therefore, the transition to a phase I clinical trial in patients could be accomplished quickly, allowing for immediate benefit to women with stage IV metastatic ER+ breast cancer patients with bone lesions.