Metavivor Lay Abstract:

Despite improvements in survival in breast cancer patients diagnosed with non-invasive disease, breast cancer remains a leading cause of death. This is largely due to the ability of breast cancer cells to spread (metastasize) to distant sites including lung, brain, and bone. Over 70% of breast cancer patients who die from the disease have tumors in the bone, which can develop after decades of disease-free survival and can be the only metastatic site or in combination with other metastases. Once tumors establish in bone, they are incurable and lead to the disruption of normal bone repair resulting in bone pain and fractures, which impair quality of life and overall survival. Bone metastases are resistant to standard chemotherapies and immunotherapies, and the identification of therapies to treat patients with bone metastatic disease remains a critical gap in cancer treatment. Our previous studies have demonstrated that tumor cells interact with the bone and bone marrow microenvironment to improve survival by altering the immune responses to allow tumors to escape immune surveillance and increase the drug resistance of tumors. In this grant, we investigate the Eph receptor signaling pathway, which helps tumor-promoting interactions between tumor cells and immune cells. We hypothesized that inhibition of Eph signaling would reduce this interaction and block tumor-cell reprogramming of macrophages (an immune cell) to reduce tumor growth in the bone and restore immune killing of tumor cells. We proposed to investigate the Eph signaling pathway to better understand how Ephs contribute to bone metastatic disease and test Eph-targeted drugs as potential therapies to reduce tumor burden and bone destruction, which will improve patient quality of life and survival.