

We have shown that patients aged <45 who are within 5 years of last childbirth at diagnosis, or postpartum breast cancer patients, have high rates of metastatic recurrence. Specifically, our comparison of risk for metastasis and death between postpartum and age-matched nulliparous patients revealed that risk of metastasis and death from breast cancer is ~2.7 times higher in the postpartum group. This alarming data has driven our research focused on how to treat metastasis in postpartum patients. Using pre-clinical models, we identified a molecule, SEMA7A, as important for metastasis in the postpartum setting and in general models of ER+ and ER- breast cancer. Importantly, we demonstrated that overexpression of SEMA7A in breast tumor cells results in more metastasis, even under conditions that would normally be used to treat metastatic breast cancer. Consistent with this observation, we observe increased expression in both primary tumors and metastases in patient datasets. These results suggest that Sem7a mediates metastasis in a large number of patients, not just those who are postpartum. Furthermore, high Sem7a expression was associated with early metastasis and death from breast cancer in 3 independent patient datasets. The studies we propose will address whether there are specific therapeutic vulnerabilities that could be targeted for SEMA7A+ metastasis to result in achieving a durable *No Evidence of Disease* clinical state for women with Stage IV metastatic breast cancer, creating a chronic, survivable, "*meta-thrivable*" disease state.