Metastatic breast cancer is a difficult to treat disease with a grim prognosis for many patients, therefore it is essential to develop new effective strategies to reduce disease morbidity and mortality. One reason that tumors spread is due to escaping recognition by the immune system. Tumors release factors that render immune cells exhausted and unable to activate an immune response to clear cancer cells. Previous studies show that a molecule known as CD47 is abnormally expressed in invasive breast cancer cells and on immune cells. This high expression of the CD47 molecule is associated with poor survival outcomes in cancer patients. Our previous studies show that drugs that block the CD47 molecule inhibit tumor growth in animal cancer models alone or in combination with radiotherapy. Moreover our new data shows that targeting CD47 reduces breast cancer growth and metastasis. We have discovered that blocking CD47 activates immune cells known as T cells that can recognize the tumors and kill cancer cells. Data presented in this proposal shows that blocking CD47 is associated with the release of growth factors that can activate an immune response. Therefore we predict that by inhibiting CD47 we can harness the potential of our immune system to activate T cells to clear metastatic lesions.