**Summary of the work accomplished (lay report):**

Despite decades of breast cancer research into fundamental mechanisms, drug

development, and early detection, breast cancer remains the second deadliest cancer for

women. Rather than targeting the cancer cells, therapeutics that seek to re-activate the

immune system as living drugs against breast cancer cells offers the best hope for a cure

to metastatic breast cancer, as has been witnessed with immunotherapies such as

Keytruda™ in metastatic melanoma and lung cancers. Recent research has

demonstrated that breast cancer cells subvert the immune system in their local

environment to dampen the anti-tumor immune response, making immunotherapies such

as Keytruda™ ineffective. In this study, we focus on an enzyme called ALDH1a2 that is

expressed in immune cells and use retinoid acid signaling to generate an immune-

suppressive environment in cancer. By removing this enzyme either genetically or

pharmacologically using a compound developed in our laboratory, anti-tumor T cell

proliferation is increased, leading to more robust tumor killing effects. We believe that

findings from this research will lead to the development of a new curative therapy for

stage IV breast cancer patients.