**Lay Report of Important Outcomes**

The invasive lobular histological subtype of breast cancer (ILC) displays a unique pattern of metastasis relative to the more frequently studied subtype, invasive ductal breast cancer (IDC). ILC tumors more frequently metastasize to the ovaries, gastrointestinal tract, peritoneum, and leptomeninges whereas IDC tumors more

frequently metastasize to the liver and lungs. Mesothelial cells are normal cells that line all organs of the body. Ovarian cancer displays a metastatic pattern similar to that of ILC, and this is largely due to their interactions with mesothelial cells. We are investigating the hypothesis that ILC cells have a unique ability to adhere to and invade through mesothelial cells, which explains their unique metastatic pattern. Importantly, the interaction

between breast cancer and mesothelial cells has never been studied. We found a trend for ILC cells having a greater ability to adhere to mesothelial cells, whereas IDC cells have a greater ability to invade through a mesothelial cell layer. These results may reflect the clinical observation that ILC tumors “cake” the surface of their metastatic site whereas IDC tumors form large nodules at the metastatic site. The results were not statistically significant, though we plan to employ increasingly clinically relevant models using cells directly isolated from humans and mice in the next funding period to confirm these results. We have also identified a protein that may promote mesothelial adhesion that is highly abundant on ILC cells called TSPAN7. TSPAN7 is a member of the tetraspanin family of proteins which can interact with other proteins that can be targeted therapeutically. We will deplete TSPAN7 expression in ILC cells, test whether mesothelial adhesion is

prevented.