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**Cellular and molecular mechanisms of breast cancer invasion**

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**Public Abstract:**

For breast cancer patients, the dissemination of the tumor through the body, a process called metastasis, marks the transition away from curable disease. Unfortunately, the biological mechanisms that initiate tumor metastasis are poorly understood, and most cancer therapies do not target metastasis. My objective is to identify which tumor cells initiate breast cancer metastasis, which of these cells’ genes drive them to metastasize, and what novel drugs we can use to specifically target these genes. I have strong advocate/survivor support for the high potential impact of my research aims on breast cancer patient.

The gene Twist1 is frequently active in several types of breast cancers, and its presence is associated with increased tumor invasion and poorer survival for patients. In the breast tumor, Twist1 is known for initiating the dissemination of tumor cells. However, as tumors are composed of different types of cells but not all of which metastasize, my first aim is to use identify the cell type that is the most ‘corruptible’ into disseminating by Twist1. Starting from a controllable genetically engineered mouse model, I will culture breast tissue, switch on Twist1 in the different cell types, and use the microscope to observe which cells disseminate. I will then validate the dissemination of these cell types in cultured human tumors sampled from patients. The presence of such disseminative cells in human tumors could
ultimately be applied to predict if a certain type of cancer will metastasize and how overall survival of the patient will be affected.

My second aim is to develop new therapies against Twist1-driven metastasis. Despite the fact that there are no drugs that can directly target Twist1, we know that Twist1 functions inside tumor cells by activating a multitude of their genes. By combining mouse tissue culture, genetic engineering and methods for monitoring gene activation in the presence of Twist1, our lab has recently identified these Twist1-activated genes in the tissue from which breast cancers arise. Since found that the targeting of at least three of these genes with specific chemical compounds can block dissemination of cultured mouse tissue. We have also developed state-of-the-art techniques that allow us to culture individual patient-derived breast tumors and capture their invasion as it occurs in real time. As there are different types of breast cancers, I will validate chemical compounds successful in stopping tumor invasion for each major cancer type. By finding the tumor type which is most susceptible to a certain drug, we will be able to design more accurate and efficient preclinical and clinical studies to develop therapies with maximal potential benefit to patients diagnosed with that same tumor type.