CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP170172

Project Title:
Targeting Therapy Resistance using Epithelial to Mesenchymal Transition (EMT) Pathways in Preclinical Claudin Low Breast Cancer Models

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
Baylor College of Medicine

Lay Summary:

Targeted drug treatments have been used to treat some breast cancer subtypes, but there are no effective treatment options for patients with triple-negative breast cancer (TNBC). TNBC patients often tend to develop resistance to chemotherapy and metastasis. In fact, 1/3 of these TNBC patients live less than 3 years following diagnosis. It is now evident that breast cancer cells with stem cell properties are often present as a subpopulation of most breast cancers and are thought to be responsible for initiating tumor growth, resistance to chemotherapy as well as metastasis. Our laboratories have focused on understanding the properties and origins of these cells as well as defining the molecular pathways essential for their function. We found that cancer cells acquire therapy resistance by activating a latent embryonic program known as epithelial-mesenchymal transition (EMT). Due to its complex nature and the lack of markers specific to EMT, it has been difficult to identify these cells within a tumor. Using novel fluorescence reporter based approach, we have developed a dual sensor, which can tell whether the cancer cells are in chemo-sensitive state (Red) or chemo-resistant state (Green). Using this novel reporter in vivo, we can identify and develop drugs, which either specifically eliminate the resistant green cells or convert them to sensitive red cells. In fact, we have identified several such new agents capable of converting the resistant cells to sensitive cells. We will combine these new agents with existing therapies and test, whether together they can eliminate resistant cells with a focus on established metastases. We hope to translate our findings to address the unmet clinical need to treat or sensitize the chemotherapy resistant breast cancer cells, thereby helping to decrease overall mortality due to metastatic breast cancer. Our unique mouse models with an intact immune system will help rapidly translate these findings for the benefit of patients.