CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP180313

Project Title:
A somatic mutant p53 mouse model of metastatic triple negative breast cancer

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
The University of Texas M.D. Anderson Cancer Center

Lay Summary:

Cancers arise from an accumulation of changes to normal cells that allow those cells to grow uncontrollably. To accomplish this feat, most tumor cells disable the function of an important tumor suppressor, p53. When deletion or mutation of p53 occurs, cells no longer listen to internal signals that say ‘stop dividing’. As cells continue to divide, they acquire additional changes that fuel tumor growth. Ultimately, these changes contribute to cells leaving the organ they live in and disseminating to other organs such as the lung, liver, bone and brain, a process called metastasis. The great majority of triple negative breast cancers have lost p53 function and these tumors are the most aggressive kind of breast cancer. In this study, we developed a novel mouse model whereby we can make a p53 mutation in a single normal breast cell. These mice develop highly aggressive and metastatic triple negative breast cancers. We aim to understand the changes that cooperate with p53 mutations to yield these aggressive breast tumors. We have observed metastases to the lung and liver thus far and will determine what additional changes these cells have that drove metastatic behavior. By understanding how mutant p53 proteins promote tumor development, we hope to identify pathways and mechanisms that can be therapeutically targeted in the clinic to treat patients. Understanding these mechanisms is essential for developing new strategies to specifically and effectively treat breast cancers with mutant p53.