Award ID: 
RP100768

Project Title: 
Mechanisms underlying delayed recurrence of ER positive breast cancer: a critical step in the development of effective biomarkers and therapies

Award Mechanism: 
Individual Investigator

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

Lay Summary: 
Delayed recurrence remains a major cause of morbidity and mortality in a subset of breast cancers. Indeed, ER positive (ER+) breast cancer has an unfortunate propensity to recur even after decades in contrast to other types of breast cancer that usually relapse within five years of diagnosis. The late relapse is most likely due to the phenomenon of ‘tumor dormancy’ which refers to a prolonged latent phase that occurs between treatment and evidence of disease progression. In the case of late recurrence, cells that escape the initial therapy survive in a dormant state and ‘hide’ for years or decades ultimately giving rise to incurable metastases. Although clinical evidence for tumor dormancy is growing, the mechanistic insights of this process that allow cells to enter a dormant phase, escape from therapy, ‘reawaken’ and become occult after many years of dormancy are poorly understood. One of the mechanisms that metastatic cancer cells can exploit to survive this dormant period in the body is autophagy, an evolutionarily conserved catabolic process wherein breakdown of components of the cancer cell generates energy. Therefore, this study will investigate whether the selective ability of ER+ cells to enter autophagy is a critical component of the process that leads to tumor dormancy, therapy resistance and delayed recurrence of ER+ breast cancer contributing to the poor outcome for ER+ breast cancer patients. Moreover, we will focus on genes modulating autophagy to explore whether manipulation of this process might be beneficial for breast cancer patients. In conclusion, understanding the mechanism underlying tumor cell dormancy and establishing a role for autophagy in this process would prompt development of molecular markers and manipulation of the autophagy process as a potential new effective therapy.