CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP150093

Project Title:
Targeting 17q23 amplicon in HER2-positive Breast Cancer

Award Mechanism:
Individual Investigator

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

Lay Summary:

In about 1 of every 5 breast cancers, the cancer cells make an excess of HER2 (human epidermal growth factor receptor 2) due to the gene amplification and overexpression. HER2-positive breast cancers tend to be more aggressive than other types of breast cancer. They are also less responsive to hormone treatment. The HER2 antibody trastuzumab and the tyrosine kinase inhibitor lapatinib are currently the two FDA-approved drugs for the treatment of HER2-positive breast cancer. Although clinically effective, many patients with HER2-positive breast cancer either do not respond or eventually develop resistance to trastuzumab and lapatinib, suggesting the presence of de novo and acquired mechanisms of drug resistance. The research proposed in this application aims at discovering those mechanisms of resistance to anti-HER2 drugs which, in turn, will contribute to the eventual elimination of HER2-positive breast cancer. Clinical doctors envision the day when each breast cancer patient will have therapy precisely matched to the genetic information of their own cancers. The holdup has been that breast cancer has proven to be more crafty than researchers once imagined. In anti-HER2 therapies, a breast tumor may employ its undiscovered genetic tricks to keep itself alive. Instead of a magic bullet like trastuzumab, we need to know those ‘genetic tricks” and attack the precise vulnerability of breast cancer. The proposed studies are based on our novel discovery that two cancer genes, Wip1 and miR-21 in the chromosomal region 17q23, are amplified in 65.8% of human HER2-positive breast tumors. Errant overexpression of these two genes contributes to drug resistance in anti-HER2 therapies. The research question we address in this proposal is directly relevant to clinical therapy. Our approach simultaneously reduces major bottlenecks that have up to now impeded the translation of discoveries to therapeutic settings.