CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP160054

Project Title:
The CTC Circulator Phenotype: Insights into Mechanisms of Breast Cancer Dormancy

Award Mechanism:
Individual Investigator

Principal Investigator:
Marchetti, Dario

Entity:
Baylor College of Medicine

Lay Summary:

Breast cancer brain metastasis (BCBM) is the most feared consequence of breast cancer with Circulating Tumor Cells (CTCs) being the essential pre-condition for BCBM to occur. CTCs are shed into the vasculature, circulate and survive in the blood, arrest/adhere at distant organ sites, and extravasate at the target organs to generate metastasis. Importantly, higher than 67% of deaths in breast cancer patients occur after a 5-year survival mark and residual disease can be dormant for periods longer than 20 years. The patients are asymptomatic because CTCs appear to become dormant and are undetectable by clinical tools. Further, rates of CTC survival can be highly variable, lasting less few hours in some patients but in the order of decades in others. This proposal is designed to reveal fundamental characteristics of CTCs in their abilities to survive while in the circulation, and possessing the potential to generate BCBM. We put forward the notion of "The CTC Circulator Phenotype", a combination of markers and properties in specific CTC sub-populations allowing them to avoid organ arrest with extreme efficiency, yet being able to survive for long periods of time as "timing bombs"; and to promote BCBM when triggered by microenvironmental cues. Our proposal is paradigm-shifting as first-time attempt to elucidate mechanisms underlying tumor dormancy by characterizing sub-populations of CTCs directly isolated from cancer patients. The implementation of studies proposed will help stratifying patients at high-risk of developing BCBM. Therefore, project outcomes have the potential for a high payoff. They will represent a game-changer towards combating brain metastasis more effectively by attacking the very source of it: CTCs. Employing CTCs directly isolated from patients will improve the prediction and prognosis of BCBM and represent a prime example of precision medicine to achieve clinical excellence. We are much dedicated to this goal.