



## CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:  
RP180047

Project Title:  
A Novel Dual Suppressor of Cancer Bone Metastasis

Award Mechanism:  
Individual Investigator

Principal Investigator:  
Wan, Yihong

Entity:  
The University of Texas Southwestern Medical Center

### Lay Summary:

Current cancer research often focuses on the primary tumors alone. However, most cancer mortality relates to metastasis, a complex process involving not only cancer cells but also their microenvironment in the host tissues. Bone metastasis is a frequent, debilitating and deadly consequence of many cancers. It affects >70% of patients with advanced breast cancer. This leads to bone pain, fractures, life-threatening hypercalcemia, limited mobility and increased mortality. Current bone-met drugs cannot improve patient survival, and thus bone met remains incurable. Since late 2014, three PARP inhibitors have been approved by the FDA for treating ovarian cancer. Several PARP inhibitors are also in clinical trials for breast cancer. Despite the clinical efforts on PARP inhibitors, little is known about whether and how PARP impacts cancer metastasis. Surprisingly, we have recently discovered that PARP2, but not PARP1, suppresses bone met by acting in both bone environment and tumor cells. Thus, we hypothesize that PARP2 activators can effectively block bone met, thereby conferring a synergistic cancer-fighting power to better reduce cancer mortality. Here we will test this hypothesis using integrated approaches and state-of-the-art technologies. This study is highly significant, timely and clinically relevant because it will 1) reveal the remarkable therapeutic potential of PARP2 as a novel dual suppressor of breast cancer bone metastasis, 2) uncover possible deleterious effects of current PARP1/2 inhibitor drugs to exacerbate bone met, and 3) suggest PARP1-specific inhibitors as safer options. The outcome of this investigation will help all cancer patients, especially patients with advanced and metastatic diseases, and patients treated with PARP inhibitors. We envision that a major breakthrough will be achieved for the effective prevention and treatment of metastatic complications, which will ultimately alleviate breast cancer mortality.