



## CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:  
RP180813

Project Title:  
BRCA Answers From Cancer Interactome Structures (BACIS)

Award Mechanism:  
Multi-Investigator Research Awards (Version 2)

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

### Lay Summary:

Patients with BRCA type breast cancer are often successfully treated with cisplatin and PARP inhibitor (PARPi). Unfortunately, after initial success, relapse is common and associates with resistance to further therapy. Thus, development of resistance is a fundamental problem facing BRCA patients. This BACIS Program aims to provide solutions from a molecular level understanding of the processes controlling the sensitivity and the resulting resistance. Efforts will focus on BRCA mechanisms underlying PARPi sensitivity and those with a significant probability of causing therapeutic resistance. Besides understanding the underlying mechanisms of resistance, we expect to find missing biological vulnerabilities that can be exploited with a treatment or combination of treatments to overcome resistance based upon biological knowledge.

Thus, this program will coordinate expert efforts from different disciplines and couple innovations that will synergize to generate key knowledge pertinent to the great challenge facing patients of resistance to chemotherapy. The proposed studies will improve our understanding directly relevant to the effectiveness of treatments for BRCA patients. It will furthermore define the biological science behind resistance, so that we can learn how to improve treatments and outcomes for patients. By defining BRCA mechanisms and employing chemical inhibitor tools on the one hand and incorporating clinical data on the other, we will gain missing molecular knowledge on the development of resistance to PARPi and chemotherapy. Basic scientists will therefore work closely with clinical scientists to focus their collective efforts to gain the biological knowledge critical to real patients' samples from an ongoing clinical trial.

From the integrated efforts on BRCA from all angles, clinical researchers will learn more about who is at risk for resistance and how to adjust treatment to overcome that risk. When we can predict who will not fully benefit from our effective standard chemotherapy treatments, we can better improve their therapy while furthermore focus our clinical trials on those who stand to benefit from a different treatment. Furthermore, when we know why a particular BRCA patient is likely to develop resistance to chemotherapy, and have worked out new treatment combinations that can overcome that resistance, then we will be able to improve patient care and outcomes. Overall, this program should lead to the foundational knowledge necessary to greater success in advancing and applying treatment options. This advance is expected to increase the probability of long-term survival for BRCA positive cancer patients as well as those with other aggressive forms of

BRCA-related cancer, who most urgently need more effective treatments to overcome resistance to chemotherapy.