



**SU2C–Prostate Cancer Foundation Prostate Dream Team:
“Targeting Adaptive Pathways in Metastatic Castration-Resistant Prostate Cancer”**

Prostate cancer is the most commonly diagnosed cancer in American men and is the second leading cause of cancer-related death among males in this country. There have been a number of recent treatment breakthroughs in the field that have resulted in decreased suffering and prolonged survival for men with prostate cancer that has spread to other sites in the body ("metastatic") and is no longer responding to initial hormonal therapy ("castration resistant").

These advances include drugs capable of blocking minute amounts of residual testosterone that tumors use to grow and progress (abiraterone acetate (Zytiga®)) and new chemotherapies (cabazitaxel (Jevtana®)). However, even with these important new therapies, prostate cancer become resistant, often over a period of only months, resulting in significant pain and suffering. Our Team is focused on understanding the cause of this rapid resistance and developing more effective combination treatments that can immediately impact most men with metastatic, castration-resistant prostate cancer in the near term.

Our hypothesis is that prostate cancer cells use common cellular responses (termed "adaptive pathways") to become resistant to the newest prostate cancer therapies, and by identifying and inhibiting these processes we will be able to profoundly improve the care of men with this fatal disease.

We will test this hypothesis by integrating the intellectual and investigational resources available among the top prostate cancer researchers on the West Coast. Working together, our Team clinicians, scientists, and computational biologists will ACCESS drug resistant metastatic tumors through image-guided biopsy procedures, ASSESS these patient samples using established and emerging technologies to identify adaptive pathways active in resistant prostate cancer, and ACT on the findings by testing combinations of established and emerging therapies in pre-clinical and clinical settings.

Our Dream Team has been carefully assembled in order to bring the human capital and physical resources needed to bear on the problem of treatment resistance. By bringing together laboratory, computational, and clinical investigators, we have the potential to identify, functionally validate, and clinically test novel combinations of therapy targeting adaptive pathways.

The ultimate proof of our hypothesis will result from the study of how patients with different tumor profiles will respond following enrollment into established clinical trials, and the subsequent development of trials that will guide therapy based upon adaptive pathways identified in individual patient samples.



Scientific Abstract

If our hypothesis is true, we believe that combining established therapies with new treatments that co-target adaptive pathways causing resistance will dramatically improve the outcome for men with advanced prostate cancer.