



## **8. Prostate Cancer Stem Cell Biology and Treatment Research**

### **Statement of Problem**

Androgen blockade-resistant recurrent or advanced prostate can not be effectively treated with currently available medications. New therapeutic approaches need a better definition of the cells promoting tumor growth, and the specific molecular mechanisms that repopulate malignant lesions. Prostate cancer often shows variation in differentiation phenotype. Marker expression of either immature and mature cell types suggest that continued maturation from a basal or stem-like state or alternatively, de-differentiation from a more mature or luminal cell type could have occurred. Cell complexity and type(s) of origin and pathway(s) of malignant progression has not been determined for human prostate cancer. The physical and functional definition of normal tissue stem cell for human prostate or other species is incomplete. Further information about such cells is needed to define those cellular elements responsible for the creation of prostate cancer, its persistence or survival, and resistance to therapy.

### **Proposed Solution**

Focus on cancer stem cell biology identifies new therapeutic targets that to help solve therapy resistance. To achieve this goal we have identified the following potential areas of focus.

1. Define new methods to physically and functionally identify cell subpopulations responsible for the continued growth of prostate cancer despite conventional therapies. Such methods will be critical to define cellular signaling pathways and specific targets for therapeutics development. We need to use small molecules, bio-molecules, and cellular therapeutics. Studies will include human material and animal models for cross comparison and validation.
2. Define cell populations present in the normal prostate of man and animal models that are responsible for the normal growth and maintenance of the prostate gland. Provide an understanding of normal developmental control that is likely disrupted in cancer progression and treatment resistance.
3. Develop methodologies to directly assess stem cell populations in normal and cancerous prostate specimens. Focus on histological examination or other rapid laboratory methods to evaluate new therapeutic modalities in both animal models and human clinical trials.