

“Bromodomain Inhibition For The Treatment Of Lethal Prostate Cancer”

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Prostate cancer is the second leading cause of cancer-related death among American men. Nearly all of these deaths are due to metastatic, advanced prostate cancers that are progressing despite male hormone-lowering therapies – the principal treatment for this disease. This underscores the urgent need to develop more effective treatments for men with advanced prostate cancer.

Recently, we demonstrated that the bromodomain inhibitor JQ1 shuts down many genes that are critical for survival of cells from advanced prostate cancer patients. This drug also causes these advanced prostate cancer cells to die. However, several important questions must be addressed before developing optimal clinical trials with bromodomain inhibitors in men with advanced prostate cancer.

In this proposal, we will: 1) Test JQ1 in vitro and in vivo using advanced prostate cancer models and quantify the cellular changes that contribute to the tumor-suppressive effect and 2) Identify a gene signature of response using RNA-sequencing of advanced prostate cancer models after JQ1 treatment. We will then apply these results to a large cohort of patients with advanced prostate cancer under our care whose tumors have already undergone RNA-sequencing.

Completion of the proposed work will: 1) Identify specific subsets of patients with advanced prostate cancer that may be ideal candidates for treatment with bromodomain inhibitors like JQ1 and 2) Identify markers indicating that JQ1 has hit its target. In the future, we will apply these results to a phase I clinical trial testing bromodomain inhibition in men with advanced prostate cancer in the near-term.