

SECTION 2 NON-TECHNICAL ABSTRACT

Prostate cancer is the most commonly diagnosed malignancy in men. Although conventional therapies (surgery and radiation therapy) produce high cure rates of early stage prostate cancer, many of these tumors recur and metastasize. Unfortunately, effective therapies are still lacking for recurrent and advanced stages of this disease.

In light of this, we have developed a novel, multi-faceted gene therapy approach for the treatment of prostate cancer. Our approach utilizes a modified cold virus, called an adenovirus, to selectively and efficiently deliver a pair of therapeutic genes to prostate tumors. The virus itself generates a potent anti-tumor effect by preferentially replicating in and destroying prostate tumor cells. The tumor-specific killing effect of the virus can be enhanced by combining it with a form of tumor-targeted chemotherapy called suicide gene therapy. Activation of the suicide genes renders malignant cells sensitive to specific pharmacological agents (prodrugs) and sensitizes them to the therapeutic effects of radiation. Importantly, the suicide gene systems can be used to control viral replication, providing a safeguard against excessive viral spread.

In this study, the safety and efficiency of delivering the suicide genes via a replication-competent adenovirus will be evaluated in patients with organ-confined prostate cancer prior to surgery. The adenovirus, prepared three different ways, will be injected into the prostate gland under ultrasound guidance. Two days after injection of the virus, patients will undergo surgery to remove the prostate and the efficiency of gene delivery will be determined. The primary objective of this study is to determine whether the treatment is safe for use in humans. A second objective is to develop more efficient ways of delivering the therapeutic genes.