New Jersey State Commission on Cancer Research
LAY ABSTRACT OF RESEARCH PROJECT

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Project Title: **The Role of Inflammation in a Mouse Model of Prostate Cancer**

Description: **We will characterize the tumor infiltrating lymphocytes in a mouse model of prostate cancer that closely resembles the human disease and use genetic methods to evaluate their effect on the abnormal condition.**

All forms of cancer arise from early, pre-neoplastic conditions. This is especially important in prostate cancer because of its frequent occurrence. Research which reveals the nature of the pre-neoplastic conditions may lead to novel diagnostic tools. These tools can aid in the early detection of prostate cancer and theoretically can lead to its prevention.

Due to technological advances in the last decade, it is now possible to create mouse models of human cancer. These models are crucially important since many features of the human disease are replicated in the mouse. Mice have the distinct advantage of allowing researchers to control their genetic make-up, thus allowing mechanistic studies of the role that genes play in cancer initiation and progression.

Until relatively recently however, the research community lacked mouse models of prostate cancer which faithfully resemble the human disease. In particular, previous models did not utilize genes with established roles in normal prostate structure or function. The creation of mice with targeted removal of the homeobox transcription factor Nkx3.1 represented a significant step forward. Nkx3.1 plays an essential role in normal prostate development and significantly, mice lacking this gene develop prostate intraepithelilal neoplasia (PIN).

Studies of human prostatectomy samples have uncovered a pre-neoplastic condition termed proliferative inflammatory atrophy (PIA). In this condition, cells of the immune system infiltrate the prostate. Significantly, preliminary observations that we have generated demonstrate similar cells in the prostate of NKX3.1 deficient mice, suggesting that this may be a mouse analog of PIA. We propose to study these cells in order to understand their function. We will characterize the genes they express as a necessary first step to determining what kind of cells they are. Subsequently, we will reduce their presence by mating NKX3.1 mice to strains of mice which lack these lymphocytes. This will allow us to test the role they play on prostate growth *in vivo*. Based on published work in other forms of cancer, it is likely that the infiltrating lymphocytes affect the progression of prostate cancer. Finally, we propose to directly study the growth of these inflammatory regions by transplanting them into an accelerated growth environment. This allows a significant increase in the speed of data acquisition.

Our experiments will contribute to an understanding of the complex relationship between inflammation, the immune system and prostate cancer. In particular, since our investigation utilizes *in vivo* genetic methods, it is likely to be directly relevant to prostate carcinogenesis. We believe our results will suggest new avenues of experimentation to colleagues in the field, both to those using mouse models to dissect the human disease and to clinical scientists exploring immunotherapeutic treatments.