Validation of a New Mouse Model System for Castration Resistant Metastatic Prostate Cancer

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Abstract: Each year in the United States, approximately 30,000 men die of castration resistant prostate cancer. Human prostate cancer (PC) is characterized by large variability in disease outcomes. We hypothesize that spontaneous genetic changes are behind much, if not most of this variability. Yet, there is a lack of molecular/ genetic features that predict these different outcomes better than histology. Our newly developed RapidCaP mouse system for endogenous metastatic prostate cancer analysis and therapy recreates this variability. We see variable latency to metastasis and castration response/relapse patterns, in spite of disease initiation through a common genetic insult. We hypothesize that also in mouse, spontaneous genetic changes are behind most of this variability. Therefore, we will test if the RapidCaP system can point to biomarkers or therapeutic targets that help clinicians combat castration resistant prostate cancer (CRPC).

Aim1: To determine if CRPC in the RapidCaP mouse shares molecular/genetic features with human.

Aim2: To perform RapidCaP-based functional validation of candidate genes as CRPC drivers.

We are forming a team of basic researchers from CSHL, clinicians and a genome analyst from MSKCC to tackle the challenge of defining CRPC genes, testing them in mouse, and finally, to ask if genes that we identify have prognostic potential in human.

Based on our preliminary success, we expect to 1) define RapidCaP as a novel type of human-mimicking GEM model system for therapy of CRPC, and 2) define gene or protein markers with the potential to assist clinicians and pathologists in outcome prediction and patient stratification for therapy.