Title: Molecular Pathways in Penile Cancer

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ABSTRACT

Penile cancer (PeCa) is a highly morbid disease, and it exhibits higher mortality among Puerto Ricans than among the rest of the US population. The etiology of penile cancer is incompletely understood. Transgenic penile cancer models allow the potential to probe the genetic and molecular basis of penile cancer. At MD Anderson, we recently developed the first genetically engineered mouse models of penile squamous cell carcinoma, the predominant histologic type of PeCa, through simultaneous deletion of tumor suppressor genes (SMAD4, APC, PTEN) in the penile epithelium. Our preliminary results using these models revealed fascinating molecular subtypes of penile cancer and potential mechanisms for cisplatin resistance. Signaling pathways driving the penile cancer formation in the mice may be similar to those mediating human papillomavirus (HPV) mediated and non-HPV mediated penile cancer in men. Thus, these novel models have opened an unprecedented opportunity to study the molecular genetics of penile cancer, and to accelerate the identification of biomarkers, therapeutic targets and resistance mechanisms. On the clinical side, at UPR we recently accrued a unique collection of penile cancer samples, which provides the material for the first study on transcriptomic profiling of PeCa in Puerto Ricans. The synergistic partnership of the two institutions will promote the integrated analysis of the mouse models and human data, with the aim to develop high-impact research data into a mature U54 project, competitive for external funding in 2 years.

The specific aims of this proposal are:
Aim 1. Investigate the molecular alterations and efficacy of combination therapy in mouse models.
Aim 2. Identify HPV-specific gene expression pattern and integrate human data with mouse models.