



CANCER PREVENTION & RESEARCH  
INSTITUTE OF TEXAS

Award ID:  
RP180192

Project Title:  
Dissecting the interplay between BAP1 and PBRM1 in renal cancer

Award Mechanism:  
Individual Investigator

Principal Investigator:  
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Entity:  
The University of Texas Southwestern Medical Center

Lay Summary:

Our lab discovered that the gene BAP1 is inactivated in 15% of kidney tumors. Another gene, PBRM1, is inactivated in roughly 50% of kidney tumors. We found that tumors with BAP1 mutations tend not to have mutations in PBRM1. Interestingly, we discovered that tumors with PBRM1 mutations exhibit low grade features and are associated with better prognosis, whereas BAP1-mutant tumors are associated with aggressive features (high tumor grade) and a worse prognosis. Prognosis, however, is the worst in tumors that have mutations in both genes. These findings establish the foundation for a precise classification of kidney cancer that is based on cancer genes (rather than on how the cancer appears under the microscope). In this application, we seek to understand why mutations in BAP1 and PBRM1 tend not to occur together in the same tumor, but when they occur, the tumors are most aggressive. We conjecture that there are mutation contexts permissive to the combined mutations and propose to evaluate their impact in mice. The proposed studies should shed light into how these mutations drive tumors, and may pave the way for better treatments for patients with this aggressive subtype of kidney cancer.