



CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP160340

Project Title:
The role of the Lats kinases in sarcomatoid renal cell carcinoma

Award Mechanism:
Individual Investigator

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

Lay Summary:

Renal cell carcinoma (RCC) is the most common type of kidney cancer. Scientific advances over the last several years have given us with a better understanding of this disease and provided us with a number of therapeutic options. However, one type of RCC, known as sarcomatoid RCC or sRCC, has evaded our understanding. sRCC is extremely fast growing and frequently spreads to other tissues. It is usually resistant to all types of treatment and patients diagnosed with sRCC usually do not survive a year. Based on DNA sequence data from human patients, we mutated two genes (Lats1 and 2) in the kidneys of mice. Amazingly, this resulted in sRCC formation with metastasis to the lungs. We found that the sRCC formation in Lats1/2 mutants was dependent on the inappropriate activation of two proteins known as Yap and Taz. Yap and Taz are transcription factors meaning they activate the expression of other genes. We will identify the genes activated by Yap and Taz in sRCCs, determine which ones are misregulated in human sRCCs as well as which appear to be responsible for sRCC formation as the identification of these genes may provide us with novel therapies for treating this disease. Finally, we will determine if two FDA approved drugs that regulate the activity of Yap and Taz are able to block sRCC formation in mouse models. Completion of this project will not only provide us with insight into the causes of sRCC but may also directly result in new therapeutic options for this devastating disease.