CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP130020

Project Title:
Investigating PI3K inhibition-mediated feedback regulation in renal cancer treatment

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
The University of Texas M.D. Anderson Cancer Center

Lay Summary:

How to choose the most effective targeted cancer therapy strategy for individual cancer patient is an important and challenging issue. Single-agent therapy usually targets one particular molecule or pathway; however, such therapy often activates other cancer signaling pathways, resulting in drug resistance over time. A more effective therapy may therefore require a combination of agents to inhibit the other cancer signaling pathways that are activated by a particular drug. However, combination therapies generally involve problems with toxicity. Also, only a fraction of cancer patients typically benefit from combination therapies, which means many other patients who receive these therapies do not improve and may even experience unnecessary complications. Thus, there is an increasingly urgent need for more in-depth understanding of the underlying mechanisms driving the response to targeted therapy. This proposal focuses on targeting the PI3K signaling pathway in renal cell carcinoma (RCC), one of the 10 most frequently occurring cancers in the United States and the sixth most commonly diagnosed cancer in Texas. The PI3K pathway is a very important target in cancer treatment, and several drugs to inhibit this pathway are currently in preclinical or clinical trials. However, complications resulting from inhibiting this pathway, such as the activation of other cancer-causing signaling pathways, will likely limit the use of PI3K-inhibiting drugs for treating RCC. Currently, the appropriate use of combination therapy to target the PI3K enzyme and other cancer-causing targets in RCC is unclear. We propose to study the underlying mechanisms associated with inhibiting the PI3K pathway in RCC treatment. Our proposed studies may identify new agents that will enhance the effectiveness of PI3K inhibitors; they may also lead to novel biomarkers that can distinguish patients who would benefit more from single-agent therapies from those who respond better to combination therapies.