CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP110202

Project Title:
Role of TMEM127 in the endomembrane system and mTOR signaling

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
The University of Texas Health Science Center at San Antonio

Lay Summary:

Discovery of novel cancer genes is important to shed light on the genetic underpinnings of cancer and can offer opportunities for diagnosis and development of new treatments. We recently found a novel tumor predisposing gene, TMEM127, by studying families affected by pheochromocytoma, a tumor of brain-derived cells known as neural crest cells. Mutations of TMEM127, a gene of unknown function, were detected in various affected individuals and families with this tumor. The mutations were all inherited, and the genetic pattern of the tumors in patients with mutations suggested that TMEM127 may be a tumor suppressor gene, i.e, mutations are likely to lead to loss of TMEM127 function, which prompts tumor growth. Our studies also showed that the TMEM127 protein is located in many structures within the cell that have a membrane, namely endosomes, Golgi complex and lysosomes. This finding suggests that TMEM127 shuttles between these locations within the cell and thus might function in trafficking and/or sorting of proteins. In addition, we found that when TMEM127 is reduced, cells turn on the mTOR pathway, which suggests that under normal circumstances TMEM127 works by restraining mTOR. mTOR is an enzyme that controls many important functions of the cell, including growth, survival, protein production, response to nutrients and various stresses. Many cancers have abnormally increased mTOR function. Thus, understanding the function of genes and proteins that control mTOR can have an impact on a variety of cancer types. Current treatments that target excessive mTOR activation of cancers have limited efficacy. Hence, development of novel drugs that exploit less known aspects of mTOR function may offer opportunities for new therapies in the future. In this proposal, our goal is to define the mechanisms by which TMEM127 hinders the mTOR pathway. These studies will shed light on mTOR regulation and will begin to reveal the importance of the intracellular movement in cancer.