CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP130310

Project Title:
Regulation of HECT E3 ubiquitin ligases by Rak kinase: a novel mechanism that links tyrosine phosphorylation to protein stability in breast tumor suppression

Award Mechanism:
Individual Investigator

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

Lay Summary:

Tumor suppressor proteins are proteins that suppress the development of tumors. Tumor suppressor proteins that are present in normal breast cells are often absent or present in only very low amounts in breast cancer cells. It is believed that the absence or reduction in the amount of tumor suppressor proteins in breast cancer cells is due to increased protein breakdown. In other words, in breast cancer cells, tumor suppressor proteins are produced, but then they are broken down rapidly. It is not known how normal breast cells prevent rapid breakdown of tumor suppressor proteins. In this application, we propose to establish a model to explain how normal cells prevent breakdown of such proteins. Our group previously reported that a protein called Rak interacts with an important tumor suppressor protein, PTEN. Recently, we found that Rak also interacted with and stabilized another tumor suppressor protein, BRCA1, in breast cells. BRCA1 helps cells repair DNA damage. Further, we found that Rak interacted with the enzymes that can cause degradation of these tumor suppressor proteins. These findings led us to hypothesize that Rak helps cells repair damaged DNA and that Rak prevents breakdown of tumor suppressor proteins by interacting with those proteins and the enzymes that can cause their breakdown. In this proposal, we will test our hypothesis by using breast cancer cells with normal and reduced levels of Rak and mice with normal level or no expression of Rak. If this study is successful, the results will provide important information about how breast cancer cells that lack Rak respond to DNA damage caused by radiotherapy or chemotherapy. That information could be used to guide treatment for patients with breast tumors that lack Rak. Also, the results of this study will identify new molecules that play an important role in breast cancer development. That information could be used to develop new treatments designed to target those molecules.