



CANCER PREVENTION & RESEARCH
INSTITUTE OF TEXAS

Award ID:
RP100535

Project Title:
A single nucleotide polymorphism in Mdm2 regulates p53 activity

Award Mechanism:
Individual Investigator

Principal Investigator:
Lozano, Guillermina

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

Lay Summary:

Normal variations exist in the human genome. One such variation occurs in the Mdm2 gene. Mdm2 is an important inhibitor of the p53 tumor suppressor. In normal cells p53 levels are very low, but in response to signals that damage DNA, p53 levels rise and prevent cell proliferation or kill the cell. Tumor cells often delete or mutate the p53 tumor suppressor. Tumor cells that retain a normal p53 gene often have high levels of the p53 inhibitor Mdm2 effectively inactivating p53. The variation that exists in the human Mdm2 gene is one that allows higher levels of Mdm2 to be made. The variation is associated with an increased cancer risk in humans in some cases. To directly address the importance of the Mdm2 variation to cancer risk, we generated a mouse model containing the human variation in Mdm2. In this model, higher levels of Mdm2 result in lower levels of p53 and an increased cancer risk. The proposed work involves treating mice with a low dose of ionizing radiation or the carcinogen found in tobacco smoke to ask whether the Mdm2 variation cooperates with these environmental factors to alter tumor risk. Lastly, the variation will be introduced into a different strain of mice that is at risk of developing breast cancer to see if the Mdm2 variant contributes to the risk of breast cancer specifically.