CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP150676

Project Title:
Identification of Novel Melanoma Metastasis Driver Genes through Transposon-Mediated Mutagenesis

Award Mechanism:
High Impact/High Risk

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

Lay Summary:

Cancer is caused by mutations or alterations in DNA that promote uncontrolled cell growth or inappropriate cell survival. Melanoma is one type of cancer which affects the skin. In most cases, if the melanoma is detected early, surgery will cure the patient. However, once the melanoma spreads to distant organs of the body, in a process called metastasis, the survival of these patients drops dramatically. Our collaborators have obtained melanoma tumors directly from human patients after surgery. After transplantation of these human cells into mice, they observed that the behavior of the melanoma cells in mice predicted the clinical outcome in patients. Melanomas that efficiently metastasized in mice also formed metastases in patients from which they they were removed. In contrast, melanomas that metastasized inefficiently in mice were usually cured in the patient by surgery. This shows that there are differences among melanomas in their ability to metastasize. The primary goal of this proposal is to identify new genes that are critical for a melanoma to spread to distant organs of the body. To accomplish this, we have developed a powerful method that creates specific mutations to DNA of human melanoma cells, and we can implant these cells back into mice. By imaging the animals, we are able to observe the melanoma cells as they spread throughout the body. After collecting the metastases and isolating DNA, we can quickly identify the genes that have been altered. Using inefficiently metastasizing cells, we will employ this method to identify genes that drive metastasis in mice. Genes identified in this screen will then be tested to see if they can promote metastasis on their own. If successful, these studies will identify new targets for distinguishing melanomas that metastasize from those that do not metastasize and may accelerate the development of diagnostic strategies or targeted therapies for this disease.