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.