CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP170114

Project Title:
Mechanisms of melanoma metastasis

Award Mechanism:
Individual Investigator

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

Lay Summary:

Most cancer deaths are caused by distant metastasis, in which cancer cells spread throughout the body. Cancers that do not metastasize are almost always curable because they can be surgically removed. Yet little is known about the molecular mechanisms that allow cancer cells to spread through the blood to other parts of the body. Distant metastasis is known to be a very inefficient process in which most cancer cells that enter the blood die before they are able to form distant metastases, but it has not been understood why. We recently discovered that the metastasis of human melanoma cells is limited by oxidative stress, caused by the generation of highly reactive molecules, called reactive oxygen species, inside cancer cells. Most melanoma cells that enter the blood die from oxidative stress. The rare melanoma cells that survive during metastasis undergo metabolic adaptations that allow them to withstand the oxidative stress. By better understanding these metabolic adaptations we may be able to develop pro-oxidant therapies that block metastasis.

We hypothesize that changes in specific metabolic pathways enable metastasizing melanoma cells to survive. We will test this by transplanting melanoma cells from patients into specialized mice that allow human melanoma cells to form tumors and to metastasize in a way that mirrors their behavior in patients. We will genetically manipulate the cells to alter their ability to activate specific metabolic pathways and test whether this affects their ability to form primary or metastatic tumors. By better understanding these mechanisms we hope to develop new therapies that prevent metastasis by exacerbating oxidative stress or by preventing the metabolic adaptations required to survive oxidative. This work represents a fundamental shift in strategy away from the use of anti-oxidants for cancer therapy, which appear to promote cancer cell survival and which have been shown in clinical trials to promote cancer progression.