



CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP140329

Project Title:
Opening the Central Nervous System to Immunotherapy by Blocking
TREK1

Award Mechanism:
High Impact/High Risk

Principal Investigator:
Curran, Michael

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

Lay Summary:

To maintain the integrity of the brain and central nervous system, the body maintains a blood-brain barrier which blocks many drugs and compounds as well as potentially destructive elements of the host's own immune system from crossing. Although beneficial in most instances, in the setting of primary or metastatic cancer of the brain this barrier acts to block the immune system from attacking these tumors by denying access. For corporeal cancers such as melanoma, restoring the capacity of the immune system to attack and destroy cancers, a treatment known as immunotherapy, has shown the capacity to eliminate previously untreatable, metastatic tumors. Immunotherapy has given new hope of long-term survival to patients with many types of advanced cancers; however, those with cancers which have originated in or spread to the brain have been largely denied the benefits of this new class of therapies. A receptor known as TREK1 has been shown to act as gatekeeper of the blood brain barrier – denying the immune system access to the brain when engaged and permitting it when shut down. The goal of our study is to discover how to shut down TREK1 to allow the host immune system, boosted and targeted to the cancer by immunotherapy, to cure tumors of the brain. We propose to test existing drugs which block some functions of TREK1, as well as to make customized antibodies to disengage TREK1 in other ways, in order to find the best way to open the gates the brain and allow the immune system to enter and kill tumors. For patients with tumors of the central nervous system, the prognosis is poor and the type of long-term survival which immunotherapy can provide is virtually non-existent. If successful, this work has the potential to immediately impact both prognosis and quality of life for patients suffering from brain tumors, as the immune system has a unique potential to eradicate malignant lesions while sparing normal tissue and thus preserving cognitive function.