CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP180880

Project Title:
Targeting BRAF- and RAS-Mutant Cancers by Small Molecule-Induced Proteolysis of ERK1/2

Award Mechanism:
High Impact/High Risk

Principal Investigator:
Dalby, Kevin

Entity:
The University of Texas at Austin

Lay Summary:

Melanoma is a deadly form of skin cancer killing approximately ten thousand Americans per year, with a disproportionate number residing in Texas. Diagnoses are expected to increase by 26% over the next 16 years, and will have a proportionally greater impact on young adults as well as on African-American and Hispanic populations in Texas. There is an urgent need for novel drugs for treating patients with drug-resistant melanomas. The focus of this proposal is to address this unmet medical need and to develop an entirely novel therapeutic modality with a triple mechanism of action against an enzyme called ERK which is critical for melanoma. These mechanisms are – 1) inhibiting ERK activation, 2) inhibiting ERK signaling, and 3) inhibiting ERK expression. Thus, compounds designed to inhibit and eradicate ERK from tumors will be developed into preclinical candidates for treating melanomas. The objectives of this proposal are to develop and synthesize a potent and selective ERK degrader and to validate it in an in-vivo model of BRAF mutant melanoma.