CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP140649

Project Title:
Realizing Personalized and Precision Medicine for Melanoma: A Rapid Assay for Measuring ERK Activity

Award Mechanism:
High Impact/High Risk

Principal Investigator:
Dalby, Kevin N

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. Patients with melanoma have a poor prognosis, because while current targeted therapies are initially effective against the most common forms of melanoma containing a specific type of mutant BRAF kinase, their efficacy is limited by the near universal acquisition of resistance and resulting progressive disease. Our multi-disciplinary team at UT Austin, and MD Anderson has created a way to rapidly quantify the efficacy of current BRAF and MEK inhibitor therapies in melanoma cell lines. We have created a first-generation ERK sensor whose specificity against other MAPKs we will optimize to enable its use in quantifying the pharmacodynamics end point of BRAF and MEK inhibitors in primary human melanoma biopsies. Our long-term goal is to develop point-of-care multiplex assays with the capacity to simultaneously quantify tumorigenic kinase signaling pathways in human biopsies. In this proposal our central hypothesis is that “fluorescent peptide sensor-based assays can be developed with sufficient specificity to allow the quantification of key signaling nodes in human tumor samples.“ We have already shown that dose-dependent ERK pathway inhibition of BRAF-mutant melanoma cell lines following treatment with BRAF inhibitors can be measured by a fluorescent sensor we created and correlated to western blot analysis and inhibition of cell proliferation. Furthermore, we have the appropriate in-vivo tools and access to human melanoma samples on and off treatment to validate our assay. In this project, we will optimize our sensor and analytical procedures to develop the most robust, selective and sensitive assay for ERK activity in melanoma. We expect this study to lead to appropriate technology and biospecimen processing to enable reliable melanoma profiling for personalized precision cancer care.