



CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP160842

Project Title:
Novel roles for NIK in high-grade glioma: regulation of mitochondrial dynamics to control cell migration and invasion

Award Mechanism:
High Impact/High Risk

Principal Investigator:
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Entity:
Texas A&M University System Health Science Center

Lay Summary:

A key feature of all aggressive tumors, such as high-grade gliomas, is their ability to invade healthy tissue. The property of tumor cells to invade healthy organs is associated with high energy expenditure and extensive changes in cell morphology of the invading cancer cells. In this application, we will investigate the role of the enzyme protein NF-kappaB-inducing kinase (NIK) in this process. NIK is known to play an important role in immunity, and misregulation of NIK has been associated with many hematological and solid cancers. Although NIK is expressed in the brain, its role in the CNS in general, and in brain tumors specifically, is poorly understood. My laboratory has established a critical role for NIK in promoting the migratory and invasive potential of glioma cells and we have shown that this tumorigenic activity of NIK is mainly controlled via the non-canonical NF-kappaB signaling pathway. Recently, we made the intriguing observation that NIK is localized to mitochondria, which are important organelles that are essential for cellular energy production and survival. Specifically, loss of NIK in glioma cells dramatically alters cell morphology, mitochondria abundance, and localization of mitochondria within cells. Here, we will investigate how NIK regulates mitochondrial mass, dynamics and subcellular distribution to supply the energy requirements for glioma cell migration and invasion.

Completion of this study is anticipated to have a significant impact on acquiring new knowledge about the molecular and cellular mechanisms of how NIK functions in mitochondria to drive glioma cell invasion and pathogenesis. This proposal will open new lines of research into the understanding mitochondrial dysfunction in cancer, and facilitate the design of drugs that specifically target NIK in the mitochondria to attenuate tumor invasion and improve treatment outcomes for glioma patients.