CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP130389

Project Title:
Targeting the Warburg effect for human cancer treatment

Award Mechanism:
High Impact/High Risk

Principal Investigator:
Lu, Zhimin

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

Lay Summary:

Epidermal growth factor receptor (EGFR) overexpression or mutations, which have been detected in many human tumors, including glioma, promote tumor development. However, the EGFR inhibitors used in clinical cancer treatments have not been as effective as expected because of intrinsic and acquired resistance. Thus, identifying novel key regulators of EGFR-regulated tumorigenesis may provide an alternative approach for cancer treatment. Tumor cells have elevated rates of glucose uptake and lactate production in the presence of oxygen, a process known as aerobic glycolysis or the Warburg effect. Pyruvate kinase (PK) regulates the rate-limiting final step of glycolysis to generate ATP. PK M2 isoform (PKM2) is often overexpressed in human cancers and therefore defined as a tumor-specific isoform. PKM2 depletion in human cancer cells reverses the Warburg effect and profoundly inhibits tumor formation, indicating an essential role for PKM2 in cancer metabolism and tumor growth. Given the heterogeneous nature of human cancer, abrogating aberrant glycolysis, which is essential for tumorigenesis, by inhibiting PKM2 rather than regulating each individually oncogene or tumor-suppressor gene will likely be a highly effective strategy for treating cancer. Glioblastoma multiforme (GBM) is one of the most difficult cancers to treat. This proposal is aim to identify lead compounds that inhibit PKM2 activity and tumor growth. This novel approach for treating cancer by targeting a key regulator of cancer metabolism may provide a better, more efficient treatment for GBM.