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Transketolase regulates dynamic switch of glucose metabolism to control breast cancer cell metastasis via α-KG signaling pathway

Metabolic reprogramming including glucose metabolism is associated with progression of tumor growth. To identify the important players in such reprogramming, we employed 4T1/BALB/c syngeneic model to compare tumors of varying sizes. We identified the glycolytic enzyme transketolase (TKT) to be up-regulated in the bigger tumors. We found TKT expression levels were the highest in lymph node metastases compared with primary tumor and normal tissues of patients. Patients with higher TKT levels had poor overall survival. Reduced TKT attenuated cancer cell growth and metastatic behaviors by in vitro and in vivo assays. Depletion of TKT elevated the expression of alpha-ketoglutarate (α -KG), which was able to inhibit cancer cell growth and metastasis. Reduced TKT or addition of α -KG switched glucose metabolism from glycolysis to TCA cycle through the regulation of enzymes involved in those pathways. These results suggest that TKT-mediated α -KG signaling pathway may be exploited for anti-metastasis therapy in breast cancer.

Biography

Lu-Hai Wang has completed his PhD in Molecular Biology at University of California-Berkeley in 1976 and has been dedicated to the research in cancer biology. He holds the Professorship in The Rockefeller University and Mount Sinai School of Medicine since 1979 and 1988, respectively. He was recruited as the Distinguished Investigator and Director of the Institute of Molecular and Genomic Medicine at National Health Research Institute in 2008 and went back to Taiwan. In 2010, he was elected as the Academician, which is the highest honor in academia in Taiwan. In 2012, he was awarded Fellow of TWAS, The World Academy of Sciences. His research interests lie in the molecular mechanism for tumor progression and metastasis. His laboratory has identified several miRNAs involved in regulating, migration, invasion and metastasis of breast, ovarian, and oral cancer cells. He is currently the Vice President of the China Medical University (CMU) in Taiwan and a Chair Professor in the Graduate Institute of Chinese and Western Integrated Medicine, CMU.

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