

LETM1 as a novel target for warburg effects in human cancers

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Leucine zipper/EF hand-containing transmembrane-1 (LETM1) is a mitochondrial inner membrane protein that was first identified in Wolf-Hirschhorn syndrome, and was deleted in nearly all patients with the syndrome. LETM1 encodes for the human homologue of yeast Mdm38p, which is a mitochondria-shaping protein of unclear function. Here, we describe LETM1-mediated regulation of mitochondrial ATP production and biogenesis. We show that LETM1 overexpression can induce necrotic cell death in HeLa cells, in which LETM1 reduces mitochondrial biogenesis and ATP production. LETM1 acts as an anchor protein and associates with mitochondrial ribosome protein L36. Adenovirus-mediated overexpression of LETM1 reduced mitochondrial mass and expression of many mitochondrial proteins. LETM1-mediated inhibition of mitochondrial biogenesis enhanced glycolytic ATP supply and activated protein kinase B activity and cell survival signaling. The expression levels of LETM1 were significantly increased in multiple human cancer tissues compared with normals. These data suggest that LETM1 serves as an anchor protein for complex formation with the mitochondrial ribosome and regulates mitochondrial biogenesis. The increased expression of LETM1 in human cancer suggests that dysregulation of LETM1 is a key feature of tumorigenesis.

Biography

Jongsun Park has completed his Ph.D on 2001 at Basel University, Switzerland, focusing on the roles of PDK1 function in insulin signaling pathway. Dr. Park spends 3 years for postdoctoral studies from Friedrich Miescher Institute, which is supported by Novartis pharmaceutical company. Now, he is the head of department of Pharmacology, College of Medicine, Chungnam National University, South Korea. He has published more than 30 papers in reputed journals, such as Cancer Research, JBC and Cellular Signaling. Dr. Park is serving as an editorial board member of WJBC and JBM. He is also a managing editor in Frontiers in Bioscience.

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