J Cell Biochem. 2018 Jun;119(6):4907-4917. doi: 10.1002/jcb.26718. Epub 2018 Mar 7.

ER stress mediated regulation of miR23a confer Hela cells better adaptability to utilize glycolytic pathway

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PMID: 29377281 DOI: 10.1002/jcb.26718

Abstract

Cancer cells exhibit increased dependency on aerobic glycolysis, a phenomenon referred as the "Warburg effect" and therefore, blocking glycolysis by using non-metabolizable analogues of glucose, like 2-Deoxy glucose (2-DG), has been proposed to be of huge therapeutic importance. One of the major drawbacks of using 2-DG as a chemotherapeutic agent is that it can induce ER stress. ER stress is a hall mark in many solid tumors and the unfolded protein response (UPR) associated with it initiates many survival mechanisms in cancer cells. In the present study, we report a novel survival mechanism associated with ER stress, by which the cancer cells become more adapted to aerobic glycolysis. When ER stress was induced in Hela cells by treating them with 2-DG or Thapsigargin (TG) the expression and activity of LDH was significantly up regulated, conferring the cells a greater glycolytic potential. A simultaneous decrease was observed in the expression of miR-23a, which was predicted in silico to have target site on the 3'UTR of LDH A and B mRNAs. miRNA over expression studies and mRNA degradation assays suggest that miR-23a could target LDH A and LDH B mRNAs. Further on the basis of our results and previous scientific reports, we propose that "c-Myc," which is over expressed during ER stress, repress the expression of miR-23a, which in turn regulates the expression of its target genes viz., LDH A and LDH B, thereby making the cells more competent to survive in tumor microenvironment, which requires efficient use of aerobic glycolysis.

Keywords: 2-DG; ER stress; LDH A; LDH B; aerobic glycolysis; c-Myc; miR-23a; thapsigargin.

Related information

GEO Profiles
Gene
Gene (GeneRIF)
MedGen
Nucleotide (RefSeq)