Format: Abstract

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Loss of ALDH1L1 folate enzyme confers a selective metabolic advantage for tumor progression.

Krupenko SA[1], Krupenko NI[2].

Author information

1 Department of Nutrition, UNC-Chapel Hill, UNC Nutrition Research Institute, Kannapolis, NC, 28081, United States. Electronic address: sergey_krupenko@unc.edu.

2 Department of Nutrition, UNC-Chapel Hill, UNC Nutrition Research Institute, Kannapolis, NC, 28081, United States.

Abstract

ALDH1L1 (cytosolic 10-formyltetrahydrofolate dehydrogenase) is the enzyme in folate metabolism commonly downregulated in human cancers. One of the mechanisms of the enzyme downregulation is methylation of the promoter of the ALDH1L1 gene. Recent studies underscored ALDH1L1 as a candidate tumor suppressor and potential marker of aggressive cancers. In agreement with the ALDH1L1 loss in cancer, its re-expression leads to inhibition of proliferation and to apoptosis, but also affects migration and invasion of cancer cells through a specific folate-dependent mechanism involved in invasive phenotype. A growing body of literature evaluated the prognostic value of ALDH1L1 expression for cancer disease, the regulatory role of the enzyme in cellular proliferation, and associated metabolic and signaling cellular responses. Overall, there is a strong indication that the ALDH1L1 silencing provides metabolic advantage for tumor progression at a later stage when unlimited proliferation and enhanced motility become critical processes for the tumor expansion. Whether the ALDH1L1 loss is involved in tumor initiation is still an open question.

KEYWORDS: ALDH1L1 promoter methylation; Cofilin; Folate metabolism; JNK; Tumor suppression; p53

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