عنوان مقاله:

Malate dehydrogenase can help lactate dehydrogenase to support glycolysis pathway in breast cancer

محل انتشار:

یازدهمین کنگره بین المللی سرطان پستان (سال: 1394)

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خلاصه مقاله:

Background: High aerobic glycolysis as one of the hallmarks of cancer cells requires NAD+ as a vital cofactor in order to guarantee its flow. Malate dehydrogenase (MDH) as an important enzyme in cancer metabolism can be a source of NAD+ beside to famous Lactate Dehydrogenase (LDH). The aim of current study was to elucidate the kinetic parameters of MDH in human breast cancer by considering two points of views; the probable role of MDH in supporting of NAD+ pool and the influence of tumormicroenvironment on MDH kinetic. Methods: The Michaelis-Menten constant (Km) and maximum velocity (Vmax) of MDH was determined in the crude extracts of human breast tumors and normal tissues, also from MDA-MB 231 and MCF-7 cell lines. To check the potential role of MDH in glycolysis, MDH activity was measured when LDH activity was inhibited by different concentration of Oxamate as the inhibitor of LDH. Results: Km of Tumor MDH in forward reaction was same as normal MDH but Vmax of cancerous MDH (C-MDH) was higher relative to normal MDH. The MDH kinetic in MDA-MB 231 is different fundamentally from those of other samples. MDH activity was increased in the absence of LDH in MDA-MB 231 cell lines. Conclusions: The higher tendency of C-MDH for NAD+ and malate generation in cancer cells is a valuable tool for supporting glycolysis. Increasing MDH activity in the absence of LDH confirms the supporting role of MDH in glycolysis in more malignant cell lines. Therefore, decreasing MDH activity and expression in forward reaction may be a valid molecular target to abolish its probable effect on tumor metabolism, also kinetic characteristics of MDH can be a novel diagnosis parameter for human breast cancer.

کلمات کلیدی:

Malate dehydrogenase, enzyme kinetic, aerobic glycolysis, breast cancer