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Kinetic characterization of malate dehydrogenase in normal and malignant human breast tissues

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Background: Aerobic glycolysis rate is higher in breast cancer tissues than adjacent normal tissues in order to supply ATP, lactate and anabolic precursors needed for tumourgenesis and metastasis. High aerobic glycolysis requires NAD as a vital cofactor in order to guarantee its flow. Malate dehydrogenase (MDH) as an important enzyme in cancer metabolism could be a source of NAD beside to famous LDH to allow the continued functioning of glycolysis even in the absence of oxygen. Enzyme kinetic characteristics are related to environment-involved the enzyme and tumor microenvironment has distinct features relative to adjacent normal tissues. 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 effect of diverse tumor microenvironment on kinetic enzyme.

Methods: MDH activity was measured from crude human breast tumors and normal tissues, which were obtained directly from operating room. The Michaelis-Menten constant (Km) and maximum velocity (Vmax) was then determined in the crude extracts.

Results: Tumor MDH affinity in forward reaction was same as normal MDH but Vmax of cancerous MDH was higher relative to normal MDH. In reverse reaction, affinity of tumor MDH for malate and NAD+ was lower than normal MDH.

Conclusions: The lower MDH affinity for malate and NAD+ is a valuable tool for preserving NAD and malate by cancer cells in order to use them in other pathways such as glycolysis and malate decarboxylation to pyruvate. The increasing MDH affinity for malate and decreasing the MDH activity and expression in forward reaction may be a valid molecular target to abolish its probable effect on tumourgenesis also kinetic characteristics of MDH could be a novel diagnosis parameter for human breast cancer.

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