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丙酮酸脱氢酶与肿瘤

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Pyruvate Dehydrogenase and Tumor

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摘要

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摘要

丙酮酸脱氢酶是丙酮酸生成乙酰辅酶A的关键酶, 而乙酰辅酶A是葡萄糖进入三羧酸循环有氧化化的首要原料。丙酮酸脱氢酶活性可以抑制丙酮酸脱氢酶的活性。肿瘤细胞的总体丙酮酸脱氢酶表达增加, 造成丙酮酸脱氢酶活性降低, 导致肿瘤细胞主要通过糖酵解的方式获取能量。恶性肿瘤糖酵解活跃能促进细胞增殖和抑制细胞凋亡, 而形成肿瘤细胞糖酵解的微环境可保护肿瘤细胞逃避宿主免疫杀伤并减轻化疗药物损伤, 还有利于肿瘤细胞的侵袭和转移。因此, 丙酮酸脱氢酶在肿瘤的发生发展过程中起作用。事实上胚胎干细胞以及成体干细胞也主要是以糖酵解的方式获取能量。由此推断, 丙酮酸脱氢酶的活性可能与肿瘤细胞的干性相关。

关键词: 丙酮酸脱氢酶, 糖酵解, 肿瘤, 丙酮酸, 三羧酸循环

Abstract:

Pyruvate dehydrogenase is a key enzyme which transforms pyruvate into acetyl-coenzyme A (acetyl-CoA) by pyruvate decarboxylation. Acetyl coenzyme A is the primary raw material for aerobic oxidation of glucose into the Krebs cycle. The activity of pyruvate dehydrogenase can be negatively regulated by pyruvate dehydrogenase kinase. The overall expression of pyruvate dehydrogenase kinase is increased in tumor cells, which results in the decreasing activity of pyruvate dehydrogenase with an increased glycolysis for energy even in the presence of oxygen. The increased glycolytic activity of malignant tumor cells can promote cell proliferation and inhibit apoptosis. The glycolytic microenvironment protects tumor cells from host immune system and chemotherapy resistance, and promotes tumor cells invasion and metastasis. Embryonic and adult stem cells rely on glycolysis for energy. Thus, the activity of pyruvate dehydrogenase plays an important role in regulation of cancer cell stemness.

Key words: Pyruvate dehydrogenase Glycolysis Tumor Pyruvate Krebs cycle

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