



Characteristics of Lactate and Tumor Glycolysis

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DESCRIPTION

Lactate, the primary byproduct of tumour glycolysis, is thought to be one of the most important metabolites in the tumour microenvironment. The reprogrammed cancer cell metabolism is closely related to the increased rate of tumour glycolysis, which results in excess lactate production and increased extracellular acidification. This decrease in pH near cancer cells is largely due to reprogrammed tumour glycolysis, substantial literature data suggest that lactate is not simply a byproduct of tumour glycolysis, despite serving as the primary fuel to meet the anabolic requirements of cancer cells. Lactate is essential for tumour growth, migration, and invasion, as well as tumour metastasis, tumour microenvironment, and immune modulation.

This study summarizes current knowledge on lactate's role in tumour glycolysis, its fate and transporters, the lactate shuttle, and metabolic symbiosis. It also summarizes the role of lactate in the tumour microenvironment, immune invasion, and therapeutic strategy development. The high mortality rate in patients with solid tumours is primarily due to the complex microenvironment and tumour recurrence after primary tumour treatment with surgery, chemo and radiotherapy. Cancer develops as a result of uncontrolled growth and proliferation of cancer cells, invasion, and metastasis, resistance to autophagy, immune avoidance, and evasion of growth suppressors. Cancer cells are distinguished from normal cells by their extraordinary ability to adapt, reprogrammed cellular energetics, and signalling pathways.

In many cancers, metabolic reprogramming fosters the malignant phenotype imposed by the tumour microenvironment, facilitating cancer progression, invasion, angiogenesis, metastasis, and resistance to conventional therapies. As a result, metabolic reprogramming in cancer cells is regarded as a hallmark of the disease. Cancer cells are known for

their increased rate of tumour glycolysis, which is thought to be an ideal cancer hallmark that can control their metabolism to ensure tumour promotion, survival, angiogenesis, and metastasis. Otto Warburg discovered in 1927 that cancer cells use glucose as a primary energy source even in normoxic physiological conditions (enough energy) to meet their energy requirements, generating an excess of lactate through a process known as aerobic glycolysis.

Lactate, according to the lactogenesis hypothesis, is not a waste product but also serves as a fuel for cancer cells and has carcinogenic signalling functions. Lactate plays a role in a variety of biological processes, including carcinogenesis, angiogenesis, cell migration, metastasis, and immune escape. Lactate, for example, is a potential on metabolite in a variety of cancers, including breast cancer, and can regulate transcriptional activities involved in metabolic reprogramming, cell cycle, and cancer proliferation. Furthermore, lactate can be transported *via* Mobile Cardiac Telemetry (MCT) and used as a respiratory fuel in some cancers. The brain uses glucose as its primary source of energy *via* indirect glucose oxidation, in which astrocytes play a critical role by consuming glucose from the blood, which is then converted into lactate *via* glycolysis.

This lactate is then transported to neurons and oxidized. This resulted in the hypothesis that lactate is converted into pyruvate by neuronal Lactate Dehydrogenase (LDH) before entering the Tricyclic Antidepressant (TCA) cycle for complete oxidation. These findings support the concept of the "lactate shuttle," which states that under normoxic conditions, lactate can be freely switched between cells, tissues, and organs. Several studies have found that intratumoral lactate levels can reach 40 mm, compared to 1.8-2.0 mm in normal tissues, and that this is strongly linked to cancer resistance and poor outcomes. Lactate not only acts as a signalling molecule in cancer, but also in other diseases. As a result, a better understanding of lactate, its fate, and its role in cancer is critical.

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