Journal of Cancer Research and Immuno-Oncology

OPEN ACCESS Freely available online

Commentary

Metabolic Pathways in Cancer: A Primer on Cellular Energy and Growth

Ruixiang Shamsabadipour*

Department of Radiotherapy, Payame Noor University, Tehran, Iran

DESCRIPTION

Cancer is a multifaceted disease characterized by uncontrolled cell growth and division. Historically, the focus of cancer research has primarily centered on genetic mutations and signaling pathways that drive tumorigenesis. However, an emerging field of study has shed light on the critical role of metabolism in cancer development and progression. Cancer cells exhibit distinct metabolic alterations that support their rapid proliferation, survival, and invasion. This essay explores the fascinating world of cancer metabolism, delving into its fundamental principles, key metabolic pathways, and the implications of targeting metabolism for cancer treatment.

The basics of cancer metabolism

Warburg effect: One of the hallmark features of cancer metabolism is the Warburg effect, named after the Nobel laureate Otto Warburg, who observed that cancer cells preferentially rely on glycolysis, a less efficient form of glucose metabolism, even in the presence of oxygen (aerobic glycolysis). This metabolic switch allows cancer cells to generate energy quickly and produce essential building blocks for rapid cell division.

Altered nutrient uptake: Cancer cells exhibit increased uptake of glucose and other nutrients, such as amino acids and fatty acids, to sustain their high metabolic demands. These nutrients serve as the raw materials for energy production and the synthesis of macromolecules needed for cell growth and division.

Redox homeostasis: Cancer cells often experience oxidative stress due to their elevated metabolic activity. To counteract this, they upregulate antioxidant defenses, such as the glutathione system, to maintain redox homeostasis and prevent damage from Reactive Oxygen Species (ROS).

Key metabolic pathways in cancer

Glycolysis: Glycolysis is a central metabolic pathway that converts glucose into pyruvate, producing a small amount of Adenosine Triphosphate (ATP) and Nicotinamide Adenine Dinucleotide (NADH). In cancer cells, glycolysis is upregulated to meet the energy and biosynthetic demands of rapid proliferation. The resulting lactate production contributes to the acidic microenvironment of tumors.

Glutaminolysis: Glutaminolysis is the process by which cancer cells catabolize the amino acid glutamine to generate ATP and produce key intermediates for nucleotide and amino acid synthesis. Glutamine addiction is a common feature of many cancer types.

Pentose phosphate pathway: The PPP is a metabolic pathway parallel to glycolysis that generates ribose-5-phosphate and NADPH. Ribose-5-phosphate is essential for nucleotide synthesis, while NADPH is crucial for maintaining redox balance and supporting fatty acid synthesis. Cancer cells often activate the PPP to fuel their growth.

Fatty acid synthesis: Cancer cells exhibit increased de *novo* fatty acid synthesis to generate lipids for cell membranes and energy storage. This process involves the conversion of glucose-derived carbon into fatty acids through a series of enzymatic reactions.

Mitochondrial metabolism: While the Warburg effect suggests that cancer cells rely solely on glycolysis for energy, many cancer cells maintain functional mitochondria and utilize oxidative phosphorylation (OXPHOS) to varying degrees. Mitochondrial metabolism provides additional ATP and supports redox homeostasis.

Metabolic adaptations to tumor microenvironment

Hypoxia: Tumor microenvironments are often hypoxic due to inadequate blood supply. In response, cancer cells activate Hypoxia-Inducible Factors (HIFs) to promote glycolysis and angiogenesis, enabling them to thrive in low-oxygen conditions.

Acidosis: The accumulation of lactate from increased glycolysis contributes to the acidic pH of the tumor microenvironment. Acidosis can promote cancer cell invasion, immune evasion, and resistance to therapy.

Nutrient competition: Within tumors, cancer cells compete with surrounding normal cells for limited nutrients, leading to a nutrient-deprived environment that can further drive metabolic adaptations.

Correspondence to: Ruixiang Shamsabadipour, Department of Radiotherapy, Payame Noor University, Tehran, Iran, E-mail: sruixiang@pu.com.ir

Received: 01-Sep-2023, Manuscript No. JCRIO-23-26896; **Editor assigned:** 04-Sep-2023, PreQC No. JCRIO-23-26896 (PQ); **Reviewed:** 18-Sep-2023, QC No. JCRIO-23-26896; **Revised:** 25-Sep-2023, Manuscript No. JCRIO-23-26896 (R); **Published:** 02-Oct-2023; DOI: 10.35248/2684-1266.23.9.183

Citation: Shamsabadipour R (2023) Metabolic Pathways in Cancer: A Primer on Cellular Energy and Growth. J Cancer Res Immunooncol. 9:183.

Implications for cancer treatment

Targeting glycolysis: Therapeutic strategies that target glycolysis aim to disrupt the Warburg effect and starve cancer cells of their energy source. Small molecules targeting glycolytic enzymes, such as hexokinase and pyruvate kinase, are under investigation as potential anticancer agents.

Glutaminolysis inhibition: Inhibiting glutaminolysis has emerged as a promising therapeutic approach, particularly in cancers with high glutamine dependence. Agents targeting glutaminase, an enzyme critical for glutamine catabolism, are being explored in clinical trials.

Metabolic vulnerabilities: Identifying specific metabolic vulnerabilities in cancer cells, such as reliance on particular nutrient transporters or enzymes, offers opportunities for targeted therapy. Precision medicine approaches aim to match patients with therapies that exploit these vulnerabilities.

Immunotherapy and metabolism: Immune checkpoint inhibitors, such as anti-PD-1 and anti-CTLA-4 antibodies, have shown success in treating certain cancers. Recent research has uncovered links between metabolism and immune response, opening avenues for combination therapies that enhance the effectiveness of immunotherapy.