Journal of Leukemia
ISSN: 2329-6917
OPEN ACCESS Freely available online
Perspective

The Role of Bone Marrow Nutrient Gradients in Leukemia Cell Adaptation and Survival

Sabine Hoffmann*

Department of Medical Oncology and Hematology, University Hospital Frankfurt, Frankfurt, Germany

DESCRIPTION

Leukemia represents one of the most biologically complex malignancies, not only because of its genetic diversity but also due to the profound metabolic reprogramming that accompanies its development, progression and therapeutic resistance. Leukemic cells do not merely proliferate because of oncogenic mutations; they survive, expand and evade therapy by fundamentally reshaping their metabolic circuits and exploiting host-derived nutrients, stromal interactions, and energy pathways. This metabolic plasticity offers leukemia cells a profound survival advantage in an often hostile environment, enabling them to adapt to nutrient scarcity, oxidative stress and cytotoxic drugs.

One of the defining features of leukemic metabolism is the preferential reliance on glycolysis, even in the presence of oxygen a phenomenon known as the Warburg effect. While initially understood as a consequence of mitochondrial impairment, it is now clear that glycolytic reprogramming is a deliberate survival strategy that provides rapid ATP generation, biosynthetic precursors and redox balance. Leukemic blasts often upregulate glucose transporters and glycolytic enzymes, enabling them to sustain high proliferative rates. This metabolic shift also allows the cells to acidify their microenvironment through increased lactate production, which further promotes leukemic growth while suppressing immune cell function. Interestingly, glycolytic dependency varies among leukemia subtypes, and some forms, particularly subsets of Acute Myeloid Leukemia (AML), maintain functional mitochondria and utilize oxidative phosphorylation, challenging the assumption that glycolysis is universally dominant. The interplay between glycolysis and mitochondrial metabolism in leukemia is more interconnected than once believed, with cells often toggling between pathways depending on environmental limitations.

Mitochondrial metabolism remains a central component of leukemic survival, especially within the stem and progenitor cell population. Leukemia Stem Cells (LSCs), which are responsible for disease initiation, relapse, and therapeutic resistance, demonstrate a unique metabolic signature characterized by heightened oxidative phosphorylation. Rather than relying solely on glycolytic flux, LSCs use mitochondrial respiration to generate ATP, maintain stemness, and resist chemotherapeutic stress. This reliance makes them particularly vulnerable to inhibitors of electron transport chain components. However, LSCs also exhibit exceptional metabolic flexibility, allowing them to compensate for mitochondrial inhibition by shifting toward fatty acid oxidation or amino acid metabolism, thereby sustaining survival under therapeutic pressure. This ability to alternate between metabolic pathways underscores why targeting metabolism must be approached with precision and combination modalities.

Glutaminolysis provides leukemic cells with carbon and nitrogen for nucleotide synthesis, lipid metabolism, and maintenance of redox homeostasis. Glutamine also fuels the Tricarboxylic Acid (TCA) cycle, supporting mitochondrial respiration. Fatty acid oxidation, in particular, supports energy production, redox balance and resistance to apoptosis. LSCs frequently engage lipid catabolism, especially when residing within adipose-rich bone marrow niches. Adipocytes can directly transfer fatty acids to leukemia cells, creating a metabolic symbiosis that enhances leukemia fitness and contributes to therapeutic resistance. Hypoxia also plays a profound role in shaping leukemic metabolism. Bone marrow niches often present low-oxygen environments, forcing leukemic cells to adopt metabolic strategies that prioritize survival over proliferation. Hypoxia-Inducible Factors (HIFs) orchestrate this metabolic shift by promoting glycolysis, reducing mitochondrial oxygen consumption and enhancing angiogenesis. Leukemia cells positioned within hypoxic zones exhibit increased chemoresistance and stem-like properties, complicating efforts to eradicate minimal residual disease.

Correspondence to: Sabine Hoffmann, Department of Medical Oncology and Hematology, University Hospital Frankfurt, Frankfurt, Germany, E-mail: hoffmanns@gmail.com

Received: 04-Sep-2025, Manuscript No. JLU-25-39209; **Editor assigned:** 08-Sep-2025, PreQC No. JLU-25- 39209 (PQ); **Reviewed:** 22-Sep-2025, QC No. JLU-25-39209; **Revised:** 29-Sep-2025, Manuscript No. JLU-25-39209 (R); **Published:** 06-Oct-2025, DOI: 10.35248/2329-6917-25.13.458

Citation: Hoffmann S (2025). The Role of Bone Marrow Nutrient Gradients in Leukemia Cell Adaptation and Survival. J Leuk. 13:458.