Ефремова Валерия Викторовна – студент медико-диагностического факультета, Гомельский государственный медицинский университет, Республика Беларусь, г. Гомель.
Денисенко Маргарита Витальевна – студентка медико-диагностического факультета, Гомельский государственный медицинский университет, Республика Беларусь, г. Гомель.

Information about authors:
Belous Ekaterina Mikhailovna – Lecturer at the Department of Biological Chemistry, Master of Biological Sciences, Gomel State Medical University, Republic of Belarus, Gomel.
Efremova Valeria Viktorovna – student of the Medical Diagnostic Faculty, Gomel State Medical University, Republic of Belarus, Gomel.
Denisenko Margarita Vitalievna – student of the Medical Diagnostic Faculty, Gomel State Medical University, Republic of Belarus, Gomel.

МЕТАБОЛИЧЕСКИЙ ПЕРЕПРОГРАММИНГ ПРИ ОСТРОМ МИЕЛОИДНОМ ЛЕЙКОЗЕ

Белоус Е. М., Айман Ашраф

Гомельский государственный медицинский университет,

Республика Беларусь, г. Гомель

METABOLIC REPROGRAMMING IN ACUTE MYELOID LEUKEMIA

Belous E. M., Aiman Ashraf

Gomel State Medical University, Republic of Belarus, Gomel

Аннотация: Данная статья представляет обзор современных представлений о метаболическом репрограммировании при остром миелоидном лейкозе. Рассматривается роль эффекта Варбурга и мевалонатного пути в патогенезе заболевания. Особое внимание уделяется потенциальным терапевтическим мишеням, включая ингибирование изопреноидного синтеза с помощью бисфосфонатов. Статья обобщает экспериментальные данные и обсуждает клинические перспективы.

Ключевые слова: Острый миелоидный лейкоз, метаболическое репрограммирование, эффект Варбурга, иммунометаболизм.

Abstract: This article provides an overview of current concepts of metabolic

reprogramming in acute myeloid leukemia. The role of the Warburg effect and the mevalonate pathway in disease pathogenesis is discussed. Particular attention is paid to potential therapeutic targets, including inhibition of isoprenoid synthesis by bisphosphonates. The article summarizes experimental data and discusses clinical perspectives.

Keywords: Acute myeloid leukemia, metabolic reprogramming, Warburg effect, immunometabolism.

Introduction

Acute myeloid leukemia (AML) is a heterogeneous and aggressive hematological malignancy originating from myeloid progenitor cells in the bone marrow. Globally, cancer remains a leading cause of mortality, and AML accounts for a significant proportion of leukemia-related deaths. In the United States alone, acute leukemia causes more than ten thousand deaths annually [1].

Recent studies have demonstrated that, in addition to genetic abnormalities, alterations in cellular metabolism play a critical role in leukemogenesis. Metabolic reprogramming is now recognized as a hallmark of cancer, enabling tumor cells to modify energy production and biosynthetic pathways to support rapid proliferation. One of the most characteristic features of this process is the Warburg effect, which is defined by increased glycolysis even under normoxic conditions [3].

This review aims to summarize the general characteristics of AML, discuss the mechanisms of metabolic reprogramming, and explore therapeutic opportunities targeting the mevalonate pathway.

Study objects and methods

This article used literary sources from databases such as PubMed, eLibrary, and others. Special attention is paid to studies that examined the role of metabolic reprogramming in acute myeloid leukemia.

Research results and their discussion

AML is characterized by abnormal proliferation of myeloid blasts in the bone marrow and peripheral blood, leading to disrupted hematopoiesis. The disease exhibits unique clinical features, including a higher incidence in males, a median age at presentation, and variable blast counts. Leukemia stem cells (LSCs), a subpopulation of hematopoietic stem cells, possess self-renewal capacity and give rise to both identical stem cells and differentiated progeny, thereby sustaining the malignant clone [1]. Current treatment strategies include intensive chemotherapy, venetoclax combined with azacitidine or low-dose cytarabine, and allogeneic stem cell transplantation.

Metabolic reprogramming is not limited to cancer cells but also occurs in immune cells. Immunometabolism describes the biochemical synergy between metabolic pathways and immune cell activation. Depending on their phenotype, immune cells adopt specific metabolic patterns involving glycolysis, oxidative phosphorylation, fatty acid oxidation, and amino acid signaling [5]. These shifts can promote either pro-inflammatory or anti-inflammatory responses, influencing disease initiation and progression. In AML, metabolic alterations within the bone marrow microenvironment contribute to immune evasion and therapy resistance.

The Warburg effect, characterized by enhanced aerobic glycolysis, provides cancer cells with rapid ATP production and metabolic intermediates for biosynthesis. In AML, this metabolic switch supports blast proliferation and survival. Key enzymes involved in glycolysis are often overexpressed, making them attractive therapeutic targets. However, targeting glycolysis alone may be insufficient due to metabolic plasticity of leukemic cells [3].

Beyond glucose metabolism, lipid biosynthesis pathways are frequently upregulated in AML. The mevalonate pathway, responsible for cholesterol synthesis, plays a critical role in cellular transformation. It produces isoprenoid intermediates such as farnesyl pyrophosphate (FPP) and geranylgeranyl pyrophosphate (GGPP), which are essential for the prenylation of small GTP-binding proteins including Ras,

Rho, Rac, and Rab. These proteins regulate cell survival, membrane dynamics, and intracellular trafficking [4].

Bisphosphonates, particularly aminobisphosphonates like zoledronate, inhibit farnesyl pyrophosphate synthase, a key enzyme in the mevalonate pathway. This inhibition reduces FPP and GGPP levels, disrupting prenylation and subsequent signaling pathways involved in clonal expansion and differentiation block in AML. Preclinical studies have demonstrated antitumor activity of bisphosphonates in AML models, and their combination with conventional chemotherapy represents a promising strategy [4].

Conclusion

Metabolic reprogramming, including the Warburg effect and activation of the mevalonate pathway, is a fundamental feature of acute myeloid leukemia. These metabolic alterations not only support rapid proliferation but also contribute to therapy resistance and immune evasion. Targeting the mevalonate pathway with bisphosphonates, such as zoledronate, disrupts isoprenoid synthesis and prenylation of critical signaling proteins, leading to antileukemic effects. Future clinical studies are needed to evaluate the efficacy of bisphosphonate-based regimens in AML patients. Integrating metabolic inhibitors into existing chemotherapy protocols represents a promising direction for improving treatment outcomes.

Acknowledgments

The work was carried out within the framework of the BRFFI project M26MP-040 "My First Grant".

References:

1. Shimony S., Stahl M., Stone R. M. Acute Myeloid Leukemia: 2025 Update on Diagnosis, Risk-Stratification, and Management. American Journal of Hematology. 2025;100(5):860-891.

2. Hu T., Liu C. H., Lei M., Zeng Q., Li L., Tang H., Zhang N. Metabolic regulation of the immune system in health and diseases: mechanisms and interventions.

Signal Transduction and Targeted Therapy. 2024;9(1):268.

3. Chiarella E., Nisticò C., Di Vito A., Morrone H. L., Mesuraca M. Targeting of Mevalonate-Isoprenoid Pathway in Acute Myeloid Leukemia Cells by Bisphosphonate Drugs. Biomedicines. 2022;10(5):1146.

4. Hanahan D., Weinberg R.A. Hallmarks of Cancer: The Next Generation. Cell. 2011;144(5):646-674.

5. O'Donnell J.S., Teng M. W. L., Smyth M.J. Cancer immunoediting and resistance to T cell-based immunotherapy. Nature Reviews Clinical Oncology. 2019;16(3):151-167.

Сведения об авторах:
Белоус Екатерина Михайловна – преподаватель кафедры биологической химии, магистр биологических наук, Гомельский государственный медицинский университет, Республика Беларусь, г. Гомель.
Айман Ашраф – обучающийся факультета иностранных студентов, Гомельский государственный медицинский университет, Республика Беларусь, г. Гомель.

Information about authors:
Belous Ekaterina Mikhailovna – Lecturer at the Department of Biological Chemistry, Master of Biological Sciences, Gomel State Medical University, Republic of Belarus, Gomel.
Aiman Ashraf – student at the Faculty of Foreign Students, Gomel State Medical University, Republic of Belarus, Gomel.

СОВРЕМЕННЫЕ МЕТОДЫ ХИРУРГИЧЕСКОГО ЛЕЧЕНИЯ ЗАБОЛЕВАНИЙ ЖЕЛУДКА

Белоусова М. В., Блинова А. А.

Кемеровский медицинский государственный университет,

Россия, г. Кемерово

MODERN METHODS OF SURGICAL TREATMENT OF GASTRIC DISEASES

Belousova M. V., Blinova A. A.

Kemerovo State Medical University, Russia, Kemerovo