Pathology - Research and Practice 251 (2023) 154905

Contents lists available at ScienceDirect

Pathology - Research and Practice

journal homepage: www.elsevier.com/locate/prp

Review

The role of endoplasmic reticulum stress in promoting aerobic glycolysis in cancer cells: An overview

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ARTICLE INFO

Keywords:
Aerobic Glycolysis
Endoplasmic Reticulum Stress
Metabolic Adaptation

ABSTRACT

Aerobic glycolysis, also known as the Warburg effect, is a metabolic phenomenon frequently observed in cancer cells, characterized by the preferential utilization of glucose through glycolysis, even under normal oxygen conditions. This metabolic shift provides cancer cells with a proliferative advantage and supports their survival and growth. While the Warburg effect has been extensively studied, the underlying mechanisms driving this metabolic adaptation in cancer cells remain incompletely understood. In recent years, emerging evidence has suggested a potential link between endoplasmic reticulum (ER) stress and the promotion of aerobic glycolysis in cancer cells. The ER is a vital organelle involved in protein folding, calcium homeostasis, and lipid synthesis. Various cellular stresses, such as hypoxia, nutrient deprivation, and accumulation of misfolded proteins, can lead to ER stress. In response, cells activate the unfolded protein response (UPR) to restore ER homeostasis. However, prolonged or severe ER stress can activate alternative signaling pathways that modulate cellular metabolism, including the promotion of aerobic glycolysis. This review aims to provide an overview of the current understanding regarding the influence of ER stress on aerobic glycolysis in cancer cells to shed light on the complex interplay between ER stress and metabolic alterations in cancer cells. Understanding the intricate relationship between ER stress and the promotion of aerobic glycolysis in cancer cells may provide valuable insights for developing novel therapeutic strategies targeting metabolic vulnerabilities in cancer.

1. Introduction

Cancer, one of the most pressing challenges in modern healthcare, holds tremendous significance on multiple fronts. Its importance lies not only in its impact on individual lives but also in its broader societal and economic implications [1,2]. Cancer is a leading cause of morbidity and mortality globally. As per the World Health Organization (WHO) report, it was responsible for approximately 10 million deaths in 2020, which corresponds to nearly one in six deaths [3]. Conventional treatment methods for cancer, such as chemotherapy, and radiation therapy suffer from a lack of specificity towards cancer cells and often result in significant side effects [4,5]. The complex nature of cancer and its ability to develop resistance to conventional therapies necessitates a deeper understanding of cancer biology to devise novel and more effective treatment methods [6].

In this review, we have focused on the intriguing crosstalk between ER stress and aerobic glycolysis in cancer cells, highlighting the interplay between these two prominent features of cancer biology. The dysregulated energy metabolism characterized by enhanced aerobic glycolysis and the activation of ER stress pathways intertwine to shape the tumor microenvironment, influence cancer cell survival, and impact treatment responses. By elucidating the intricate connections between ER stress and aerobic glycolysis, this review aims to contribute to the understanding of the molecular mechanisms underlying cancer

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https://doi.org/10.1016/j.prp.2023.154905
Received 29 July 2023; Received in revised form 19 October 2023; Accepted 24 October 2023
Available online 24 October 2023