Clinics in Oncology

Mini Review
Published: 07 Oct, 2022

Glucose Metabolism Regulation of the Antiviral Innate Immunity against SARS-CoV-2

*Hua Li[1], Chaofeng Han[2] and Tengfei Zhang[3]**

[1]Shanghai No.2 Homeless Aid Station, Shanghai, China

[2]Department of Histology and Embryology, Shanghai Key Laboratory of Cell Engineering, Naval Medical University, China

[3]Department of Gynecology and Obstetrics, The People's Hospital of Zhuji, The Affiliated Zhuji Hospital of Wenzhou Medical University, China

Abstract

Host induces antiviral innate immunity responses by inducing type I interferon's through Pattern-Recognition Receptors (PRRs), which requires energy supply quickly. On the same time, virus also hijacks glucose, lipid metabolism of host cell to escape anti-viral immune and replicate itself. Severe Acute Respiratory Syndrome-related Coronavirus 2 (SARS-CoV-2) has been found inhibits antiviral innate immunity through its Non-Structure (NS) and Open Reading Frame (ORF) proteins. Recent research found that the high glucose or enhanced glycolysis in host cell aggravated SARS-CoV-2 infection, which needs to be discussed. Here we summarized the recent progress of glucose metabolism during SARS-CoV-2 infection.

Introduction

The innate immune system of host recognizes Pathogen-Associated Molecular Patterns (PAMPs) such as RNA or DNA of viruses through Pattern-Recognition Receptors (PRRs) including Toll-Like Receptors (TLRs) in the endosome, retinoic acid-inducible (RIG)-1-like receptors (RLRs) and cyclic GMP-AMP (cGAMP) synthase (cGAS) in the cytoplasm. The activation of the PRRs induce anti-viral innate responses through producing type I interferon's and inflammatory cytokines majorly depending on the transcription factor Interferon Regulatory Factors (IRF) and Nuclear Factor κB (NF-κB) [1,2].

Upon infection host cells adapt to reprogram from Tricarboxylic Acid Cycle (TCA) to aerobic glycolysis to quick and huge energy supply, in which HIF-1α has a central role by inducing various genes involved in metabolism such as the glucose transporter GLUT1, Lactate Dehydrogenase (LDH) and Pyruvate Dehydrogenase Kinase (PDK1). The expression of HIF-1α under normoxic condition is very low regulated by Prolyl Hydroxylase (PHD). However, upon infection will lead to the mitochondria ROS increment and inactivation of PDH, which stabilizes and accumulation HIF-1α expression. After then, the energy supply for producing inflammatory cytokine adaptively reprogram to anabolic glycolysis [3].

On the other side, viruses also adaptively hijack glucose, lipid metabolism of host cells to acquire enough nucleoside acid and membrane substrates for replication. SARS-CoV-2, the single RNA virus, does not encode metabolic enzymes required for viral genomic replication, protein synthesis, and lipogenesis and alters host cell metabolism to replicate itself. For example, SARS-CoV-2 boosted lipid biosynthesis to support the generation of lipid bilayer-enveloped virions in a fashion similar to other coronaviruses [3,4]. Palma first found that evaluated glucose level enhanced SARS-CoV-2 replication and inflammatory cytokines in monocyte [5]. Furthermore, monocytes and macrophages in lung adapted their metabolism to upon SARS-CoV-2 infection and became highly glycolytic regulated by mitochondria ROS and HIF-1α accumulation, which facilitates virus replication. Inhibition of HIF-1α limited viral replication significantly. The research did not explain how HIF-1α promoted viral replication. Interestingly, ORF3a of SARS-CoV-2 was found to induce mitochondrial damage and Mito-ROS production and promote HIF-1α expression, which subsequently facilitates SARS-CoV-2 infection and cytokines production [6]. However, the mechanism of negative function of HIF-1α in antiviral innate immunity was not addressed. Recently, HMGB1 was found to induce inflammation and glycolysis via HIF-1α, then HIF-1α suppresses IRF5 and IRF3 transcription and sequential type I IFN expression [7].

OPEN ACCESS

Correspondence:
Tengfei Zhang, Department of Gynecology and Obstetrics, The People's Hospital of Zhuji, The Affiliated Zhuji Hospital of Wenzhou Medical University, Wenzhou, China, E-mail: sxyjb2008@126.com

Received Date: *22 Sep 2022*
Accepted Date: *03 Oct 2022*
Published Date: *07 Oct 2022*

Citation:
Li H, Han C, Zhang T. Glucose Metabolism Regulation of the Antiviral Innate Immunity against SARS-CoV-2. Clin Oncol. 2022; 7: 1952.

ISSN: 2474-1663

Thus, above research collectively demonstrates that high blood glucose and highly glycolysis level will be susceptible to SARS-CoV-2 infection, which also raises a question whether ketogenic diet will protect SARS-CoV-2 infection by inhibiting glycolysis.

References

1. Liu J, Qian C Cao X. Post-translational modification control of innate immunity. Immunity. 2016;45(1):15-30.
2. Cao X. Self-regulation and cross-regulation of pattern-recognition receptor signaling in health and disease. Nat Rev Immunol. 2016;16(1):35-50.
3. Wu F, Zhao S, Yu B, Chen YM, Wang W, Song ZG, et al. A new coronavirus associated with human respiratory disease in China. Nature. 2020;579:265-9.
4. Zhu L, She ZG, Cheng X, Qin JJ, Zhang XJ, Cai J, et al. Association of blood glucose control and outcomes in patients with COVID-19 and pre-existing type 2 diabetes. Cell Metab. 2020;31(6):1068-77.e3.
5. Tian M, Liu W, Li X, Zhao P, Shereen MA, Zhu C, et al. HIF-1α promotes SARS-CoV-2 infection and aggravates inflammatory responses to COVID-19. Signal Transduct Target Ther. 2021;6(1):308.
6. Codo AC, Davanzo GG, Monteiro LB, de Souza GF, Muraro SP, Virgilio-da-Silva JV, et al. Elevated glucose levels favor SARS-CoV-2 infection and monocyte response through a HIF-1α/glycolysis-dependent axis. Cell Metab. 2020;32(3):437-46.e5.
7. Peng T, Du SY, Son M, Diamond B. HIF-1α is a negative regulator of interferon regulatory factors: Implications for interferon production by hypoxic monocytes. Proc Natl Acad Sci U S A. 2021;118(26):e2106017118.