

Thiourea Derivatives Restore Dysfunctional Mitochondria in Chronic Hepatitis B Infection

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ABSTRACT

Background: Chronic Hepatitis B (CHB) infection and the Hepatitis B virus X protein (HBx) are major risk factors associated with Hepato Cellular Carcinoma (HCC). In CHB infection, HBx induces mitochondrial dysfunction, exhaustion and impaired function in hepatocytes. Restoring hepatocyte health along with reduction in virus replication could be an ideal treatment for CHB. Thiourea derivatives are well known for their antiviral properties, though their effect on mitochondrial and/or hepatocyte health remains obscure. This study focuses on the repurposing of thiourea derivatives (DSA-00, DSA-02 and DSA-09) for hepatocyte replenishment.

Methods: HepG2.2.15 cells were treated with thiourea derivatives, alongside Entecavir (ETV). HBV DNA, RNA_s and antigens, measured by qPCR, Quantitative Reverse Transcriptase Polymerase Chain Reaction (RT-qPCR) and Enzyme-Linked Immunosorbent Assay (ELISA), respectively. Followed by proteomic analysis by Weighted Protein Co-expression Network Analysis (WPCNA) and Fluorescence Activated Cell Sorting (FACS) used for the validation of results.

Results: The proteomics analysis showed both DSA-00 and ETV were enriched with proteins associated with antiviral responses. In addition, DSA-00 additionally showed an increase in proteins linked to mitochondrial response. Whereas DSA-02 exhibited associations with the innate immune system and citric acid cycle and DSA-09 displayed pathways similar to DSA-00 and ETV. The treated groups exhibited an enhanced bio-energetic and antiviral response as compared to the untreated group. FACS analysis revealed the restoration of exhausted hepatocytes by thiourea derivatives through targeting mitochondria.

Conclusions: Our findings suggest that thiourea derivatives hold potential as a novel therapeutic agent that seems to restore mitochondrial health along with an antiviral response in CHB.

Keywords: Antiviral; Thiourea derivatives; Hepatitis B virus; Chronic hepatitis B infection; Mitochondria dysfunction; Exhausted hepatocytes

INTRODUCTION

Chronic Hepatitis B (CHB) infection is caused by Hepatitis B Virus (HBV) that lasts for more than six months and leading to long-

term liver disease. Currently, 257 million people around the world had a CHB infection [1,2]. CHB often leads to major problems with the liver, such as cirrhosis, liver failure and liver cancer. As the illness persists longer, there is more liver inflammation

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Received: 25-Aug-2023, Manuscript No. JPB-23-26284; Editor assigned: 28-Aug-2023, Pre-QC No. JPB-23-26284 (PQ); Reviewed: 11-Sep-2023, QC No. JPB-23-26284; Revised: 18-Sep-2023, Manuscript No. JPB-23-26284 (R); Published: 25-Sep-2023, DOI: 10.35248/0974-276X.23.16.652

Citation: Kumar J, Tyagi P, Singh RP, Saini PK, Sharma D, Maras JS, et al. (2023) Thiourea Derivatives Restore Dysfunctional Mitochondria in Chronic Hepatitis B Infection. J Proteomics Bioinform. 16:652.

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Surgical Materials To Thiourea And Thiourea Derivatives

Mohammad Jawaid, Faruq Mohammad



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Table of Contents Surgical Materials To Thiourea And Thiourea Derivatives

1. Understanding the eBook Surgical Materials To Thiourea And Thiourea Derivatives
 - The Rise of Digital Reading Surgical Materials To Thiourea And Thiourea Derivatives
 - Advantages of eBooks Over Traditional Books
2. Identifying Surgical Materials To Thiourea And Thiourea Derivatives
 - Exploring Different Genres
 - Considering Fiction vs. Non-Fiction
 - Determining Your Reading Goals
3. Choosing the Right eBook Platform
 - Popular eBook Platforms
 - Features to Look for in an Surgical Materials To Thiourea And Thiourea Derivatives
 - User-Friendly Interface
4. Exploring eBook Recommendations from Surgical Materials To Thiourea And Thiourea Derivatives
 - Personalized Recommendations
 - Surgical Materials To Thiourea And Thiourea Derivatives User Reviews and Ratings
 - Surgical Materials To Thiourea And Thiourea Derivatives and Bestseller Lists
5. Accessing Surgical Materials To Thiourea And Thiourea Derivatives Free and Paid eBooks
 - Surgical Materials To Thiourea And Thiourea Derivatives Public Domain eBooks
 - Surgical Materials To Thiourea And Thiourea Derivatives eBook Subscription Services
 - Surgical Materials To Thiourea And Thiourea Derivatives Budget-Friendly Options

6. Navigating Surgical Materials To Thiourea And Thiourea Derivatives eBook Formats
 - ePub, PDF, MOBI, and More
 - Surgical Materials To Thiourea And Thiourea Derivatives Compatibility with Devices
 - Surgical Materials To Thiourea And Thiourea Derivatives Enhanced eBook Features
7. Enhancing Your Reading Experience
 - Adjustable Fonts and Text Sizes of Surgical Materials To Thiourea And Thiourea Derivatives
 - Highlighting and Note-Taking Surgical Materials To Thiourea And Thiourea Derivatives
 - Interactive Elements Surgical Materials To Thiourea And Thiourea Derivatives
8. Staying Engaged with Surgical Materials To Thiourea And Thiourea Derivatives
 - Joining Online Reading Communities
 - Participating in Virtual Book Clubs
 - Following Authors and Publishers Surgical Materials To Thiourea And Thiourea Derivatives
9. Balancing eBooks and Physical Books Surgical Materials To Thiourea And Thiourea Derivatives
 - Benefits of a Digital Library
 - Creating a Diverse Reading Collection Surgical Materials To Thiourea And Thiourea Derivatives
10. Overcoming Reading Challenges
 - Dealing with Digital Eye Strain
 - Minimizing Distractions
 - Managing Screen Time
11. Cultivating a Reading Routine Surgical Materials To Thiourea And Thiourea Derivatives
 - Setting Reading Goals Surgical Materials To Thiourea And Thiourea Derivatives
 - Carving Out Dedicated Reading Time
12. Sourcing Reliable Information of Surgical Materials To Thiourea And Thiourea Derivatives
 - Fact-Checking eBook Content of Surgical Materials To Thiourea And Thiourea Derivatives
 - Distinguishing Credible Sources
13. Promoting Lifelong Learning
 - Utilizing eBooks for Skill Development
 - Exploring Educational eBooks
14. Embracing eBook Trends
 - Integration of Multimedia Elements

- Interactive and Gamified eBooks

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