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ORIGINAL RESEARCH

CD73 Attenuates Alcohol-Induced Liver Injury and Inflammation via Blocking TLR4/MyD88/NF-κB Signaling Pathway

Zhen-Ni Liu[1–3]
Xue Wu[1–3]
Qian Fang[1–3]
Zi-Xuan Li[1–3]
Guo-Qing Xia[1–3]
Jun-Nan Cai[1–3]
Xiong-Wen Lv[1–3]

[1]Inflammation and Immune Mediated Diseases Laboratory of Anhui Province, Anhui Institute of Innovative Drugs, School of Pharmacy, Anhui Medical University, Hefei, People's Republic of China; [2]The Key Laboratory of Anti-Inflammatory and Immune Medicines, Ministry of Education, Hefei, People's Republic of China; [3]Institute for Liver Diseases of Anhui Medical University, Hefei, People's Republic of China

Background: Alcoholic liver disease (ALD) is liver damage caused by long-term drinking. Inflammation plays a central role in the progression of ALD. CD73 is a ubiquitously expressed glycosylphosphatidylinositol-anchored glycoprotein that is a key enzyme that converts ATP into adenosine. Evidence has shown that CD73 plays an important role in many diseases, but the role and mechanism of CD73 in alcohol-induced liver injury and inflammation is still unclear.

Methods: The alcohol-induced liver injury and inflammation mouse model was established. The rAAV9-CD73 was used to overexpress CD73. Isolation of primary macrophages (MΦ) from the liver was conducted. The effects of CD73 on alcohol-induced liver injury and inflammation were evaluated by quantitative real-time PCR, Western blotting, ELISA, and immunohistochemical assay. Flow cytometry was used to detect the cell cycle and apoptosis.

Results: Our results showed that overexpression of CD73 can reduce alcohol-induced liver damage, lipid accumulation, and the secretion of inflammatory cytokines. pEX3-CD73 can promote RAW264.7 cells proliferation and inhibit apoptosis via suppressing the activation of TLR4/MyD88/NF-κB signaling pathway. Inhibition of TLR4 further enhanced the anti-inflammatory effect of overexpression of CD73.

Conclusion: Overexpression of CD73 can reduce alcohol-induced liver injury and inflammation. CD73 may serve as a potential therapeutic target for ALD.

Keywords: CD73, alcohol-induced liver injury and inflammation, TLR4/MyD88/NF-κB signaling pathway, apoptosis, RAW264.7 cells

Introduction

ALD is liver damage caused by long-term drinking, and is the leading cause of liver-related morbidity and mortality worldwide, characterized by liver inflammation.[1] Every year, 3.3 million deaths occur because of alcohol.[2] Studies have shown that alcoholic liver disease has become increasingly common in many parts of Asia, but it is declining in Western Europe. The situation of ALD in my country is not optimistic, and it should attract our attention.[3,4] Despite the great harm of ALD, there are still no FDA-a pproved drugs or nutritional therapies to treat patients and only behavioral intervention and drug intervention are used for alcohol withdrawal treatment.[5] The current academic view believes that liver damage, inflammation and liver fibrosis are important nodes in the progression of ALD. Inflammation plays a central role in the progression of ALD.[6]

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Correspondence: Xiong-Wen Lv
School of Pharmacy, Anhui Medical University, 81 Mei Shan Road, Hefei, Anhui Province, 230032, People's Republic of China
Email lyuxw@ahmu.edu.cn

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