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A Synthetic Peptide AWRK6 Alleviates Lipopolysaccharide-Induced Liver Injury

Lili Jin [1], Qiuyu Wang [1], Hanyu Zhang [1], Sijia Tai [1], Hongsheng Liu [2] and Dianbao Zhang [3,*]

[1] School of Life Science, Liaoning University, Shenyang 110036, China; lilijin@lnu.edu.cn (L.J.); qiuyuwang@lnu.edu.cn (Q.W.); zhanghanyu.lnu@gmail.com (H.Z.); taisijia.lnu@gmail.com (S.T.)

[2] Research Center for Computer Simulating and Information Processing of Bio-macromolecules of Liaoning Province, Liaoning University, Shenyang 110036, China; liuhongsheng@lnu.edu.cn

[3] Department of Stem Cells and Regenerative Medicine, Key Laboratory of Cell Biology, National Health Commission of China and Key Laboratory of Medical Cell Biology, Ministry of Education of China, China Medical University, Shenyang 110122, China

* Correspondence: zhangdianbao@gmail.com; Tel.: +86-24-3193-9318

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Abstract: During lipopolysaccharide (LPS)-induced sepsis, the liver plays central roles in toxins phagocytosis and clearance to protect the whole body. The liver cells were constantly irritated by LPS which leads to liver injury. While most anti-LPS agents showed little clinical activity against LPS-induced liver injury. Here, the protective effects of the synthetic peptide AWRK6 against LPS-induced liver injury have been investigated in vivo and in vitro. In mice liver homogenate, LPS administration elevated ALT (alanine aminotransferase), iNOS (inducible nitric oxide synthase) and repressed SOD (superoxide dismutase) activities and these changes were remarkably reversed by AWRK6. Histologically, AWRK6 effectively alleviated the histological changes and repressed LPS-induced neutrophils infiltration. By TUNEL assay on liver sections, AWRK6 was proven to inhibit apoptosis induced by LPS in mice livers, which was also verified by the protein levels of cleaved-caspase 9, Bax and Bcl-2. In addition, by in vitro study using HepG2 cells, AWRK6 was found to recover the LPS-reduced cell viability and reduce LPS-induced apoptosis. For mechanisms, AWRK6 was demonstrated to alleviate the LPS-induced phosphorylation of ERK, JNK and p38 MAPK, indicating the involvement of MAPKs in the protection of AWRK6 against liver injury. In summary, we have found the synthetic peptide AWRK6 as a promising novel agent for LPS-induced liver injury, by inhibiting cell apoptosis through MAPK signaling pathways, which might bring new strategies for the treatment of acute and chronic liver injuries.

Keywords: AWRK6; synthetic peptide; lipopolysaccharides (LPS); liver injury; apoptosis

1. Introduction

Lipopolysaccharides (LPS), a major component of gram-negative bacteria outer membrane, can induce sepsis and the mortality exceeds 20% [1]. During sepsis, the liver plays central roles in toxins phagocytosis and clearance to protect the whole body and the liver itself [2]. The liver cells were constantly irritated by LPS, leading to liver injury [3,4]. Most anti-LPS agents, such as antibiotics and antibodies, showed little clinical activity against liver injury, such as the polymyxin antibiotics colistin and polymyxin B (PMB), which became clinically available for LPS neutralization in the 1950s before being shortly restricted due to its toxicity [5,6]. Nowadays, the drug-resistant bacteria and LPS release caused by the use of large amounts of antibiotics make the problems more serious [7]. Therefore, it is urgent to develop novel agents and strategies against LPS, especially for liver injury.

Antimicrobial peptides are important group of innate immunity effectors with broad-spectrum antibiosis, found among almost all classes of animals [8]. Recent studies revealed that antimicrobial