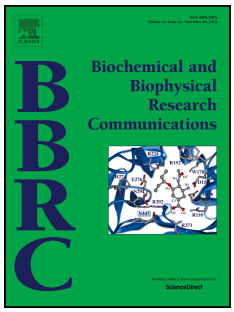
Accepted Manuscript



Hydrogen protects against hyperoxia-induced apoptosis in type II alveolar epithelial cells via activation of PI3K/Akt/Foxo3a signaling pathway

Dan Wu, Mulin Liang, Hongxing Dang, Fang Fang Feng Xu, Chengjun Liu

PII: S0006-291X(17)32370-7

DOI: 10.1016/j.bbrc.2017.11.193

Reference: YBBRC 38986

To appear in: *Biochemical and Biophysical Research Communications*

Received Date: 24 November 2017

Accepted Date: 28 November 2017

Please cite this article as: D. Wu, M. Liang, H. Dang, F.F. Feng Xu, C. Liu, Hydrogen protects against hyperoxia-induced apoptosis in type II alveolar epithelial cells via activation of PI3K/Akt/Foxo3a signaling pathway, *Biochemical and Biophysical Research Communications* (2017), doi: 10.1016/j.bbrc.2017.11.193.

Hydrogen protects against hyperoxia-induced apoptosis in type II alveolar epithelial cells via activation of PI3K/Akt/Foxo3a signaling pathway

Dan Wu, Mulin Liang,Hongxing Dang, Fang Fang Feng Xu, Chengjun Liu

Department of Pediatric Intensive Care Unit, Children's Hospital of Chongqing Medical University, Ministry of Education Key Laboratory of Child Development and Disorders; China International Science and Technology Cooperation Base of Child Development and Critical Disorders; Chongqing Key Laboratory of Pediatrics, Chongqing, China

Corresponding author:
Chengjun Liu
No. 136, 2nd Zhongshan Rd, Yuzhong District, Chongqing, China; 86-13983296275;
E-mail: liucwd@163.com

Abstract Oxidative stress is regarded as a key regulator in the pathogenesis of prolonged hyperoxia-induced lung injury, which causes injury to alveolar epithelial cells and eventually leads to development of bronchopulmonary dysplasia (BPD). Many studies have shown that hydrogen has a protective effect in a variety of cells. However, the mechanisms by which hydrogen rescues cells from damage due to oxidative stress in BPD remains to be fully elucidated. This study sought to evaluate the effects of hydrogen on hyperoxia-induced lung injury and to investigate the underlying mechanism. Primary type II alveolar epithelial cells (AECIIs) were divided into four groups: control (21% oxygen), hyperoxia (95% oxygen), hyperoxia+hydrogen, and hyperoxia+hydrogen+LY294002 (a PI3K/Akt inhibitor). Proliferation and apoptosis of AECIIs were assessed using MTS assay and flow cytometry (FCM), respectively. Gene and protein expression were detected by quantitative polymerase chain reaction (q-PCR) and western blot analysis. Stimulation with hyperoxia decreased the expression of P-Akt, P- FoxO3a, cyclinD1 and Bcl-2. Hyperoxic conditions increased levels of Bim, Bax, and Foxo3a, which induced proliferation restriction and apoptosis of AECIIs. These effects of hyperoxia were reversed with hydrogen pretreatment. Furthermore, the protective effects of hydrogen were abrogated by PI3K/Akt inhibitor LY294002.The results indicate that hydrogen protects AECIIs from hyperoxia-induced apoptosis by inhibiting apoptosis factors and promoting the expression of anti-apoptosis factors. These effects were associated with activation of the PI3K/Akt/FoxO3a pathway.

Keywords: Hyperoxia; Hydrogen; AECIIs;LY294002;PI3K/Akt/FoxO3a pathway

1.Introduction

Oxygen therapy is commonly used in the treatment of respiratory diseases. However, prolonged exposure to high concentrations of oxygen can result in chronic