

LETTER

Inflammasome and caspase-1 inhibition caused by Bcl-2 and Bcl-X, may influence cytokine responses of lipopolysaccharide-stimulated peripheral blood mononuclear cells from septic patients

Zhao-Jun Liu, Jia-Lin Liu and Hong-Ping Qu*

See related research by Wu et al., http://ccforum.com/content/15/5/R224, and Giamarellos-Bourboulis et al., http://ccforum.com/content/15/1/R27

In recent issues of Critical Care, Wu and colleagues [1] and Giamarellos-Bourboulis and colleagues [2] observed that cytokine responses in different concentrations of lipopolysaccharide (LPS) (1 and 10 pg/μL, respectively) stimulated peripheral blood mononuclear cells (PBMCs) of septic patients and healthy controls. Wu and colleagues found that interleukin-1beta (IL-1β) production of PBMCs from patients with sepsis was significantly higher than that from controls, whereas Giamarellos-Bourboulis and colleagues found the opposite result. In light of previous research, we would like to offer some remarks.

LPS can lead to the activation of nuclear factor-kappa-B (NF-κB) and the subsequent generation of pro-IL-1β [3], which is readily processed into IL-1\beta by inflammasome-activated caspase-1 [4]. NF-κB also induces Bcell lymphoma 2 (Bcl-2) and B-cell lymphoma-extra large (Bcl-X₁), both of which could suppress the activation of caspase-1 by inhibiting NLRP1 (pyrin-containing nonobese diabetic-like receptor 1) and thus suppress the cleavage of pro-IL-1ß [5]. When PBMCs were stimulated with low concentrations of LPS, the expression of pro-IL-1β could be predominant and functions of inflammasomes and caspase-1 were still reserved and thus IL-1β production was increased. When PBMCs were stimulated with high concentrations of LPS, the expression of Bcl-X,/Bcl-2 could greatly increase and lead to significant inhibition of caspase-1 and thus the production of IL-1β was decreased, although the expression of pro-IL-1β may not have been influenced significantly [2]. That may be the reason why the results of the two sets of authors were conflicting.

Since Bcl-2/Bcl-X_t could be differently produced according to various concentrations of LPS, inhibiting Bcl-2/Bcl-X, with reagents like ABT-737 in order to make sure that inflammasome and caspase-1 are not suppressed in vitro would be necessary when trying to use LPS stimulation to assess the status of PBMCs from patients with sepsis.

Abbreviations

Bcl-2, B-cell lymphoma 2; Bcl- X_1 , B-cell lymphoma-extra large; IL-1 β , interleukin-1beta; LPS, lipopolysaccharide; NF-kB, nuclear factor-kappa-B; PBMC, peripheral blood mononuclear cell.

Competing interests

The authors declare that they have no competing interests.

Published: 8 February 2012

References

- Wu HP, Shih CC, Lin CY, Hua CC, Chuang DY: Serial increase of IL-12 response and human leukocyte antigen-DR expression in severe sepsis survivors. Crit Care 2011, 15:R224
- Giamarellos-Bourboulis EJ, van de Veerdonk FL, Mouktaroudi M, Raftogiannis M. Antonopoulou A. Joosten LA. Pickkers P. Savva A. Georgitsi M. van der Meer JW, Netea MG: Inhibition of caspase-1 activation in gram-negative sepsis and experimental endotoxemia. Crit Care 2011, 15:R27.
- Rittirsch D, Flierl MA, Ward PA: Harmful molecular mechanisms in sepsis. Nat Rev Immunol 2008, 8:776-787
- Schroder K, Tschopp J: The inflammasomes. Cell 2010, 140:821-832.
- Bruey JM, Bruey-Sedano N, Luciano F, Zhai D, Balpai R, Xu C, Kress CL, Bailly-Maitre B Li X Osterman A Matsuzawa S Terskikh AV Faustin B Reed IC: Bcl-2 and Bcl-XL regulate proinflammatory caspase-1 activation by interaction with NALP1. Cell 2007, 129:45-56.

*Correspondence: hongpingqu@yahoo.com.cn

Department of Critical Care Medicine and Respiratory Intensive Care Unit, RuiJin Hospital, Shanghai Jiao Tong University School of Medicine, No. 197 The second RuiJin Road, 200025 Shanghai, China



Cite this article as: Liu Z-J, et al.: Inflammasome and caspase-1 inhibition caused by Bcl-2 and Bcl-X, may influence cytokine responses of lipopolysaccharide-stimulated peripheral blood mononuclear cells from septic patients. Critical Care 2012, 16:410.