CRITICAL CARE

LETTER

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

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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-1β by inflammasome-activated caspase-1 [4]. NF-κB also induces B-cell lymphoma 2 (Bcl-2) and B-cell lymphoma-extra large (Bcl-X_L), both of which could suppress the activation of caspase-1 by inhibiting NLRP1 (pyrin-containing non-obese diabetic-like receptor 1) and thus suppress the cleavage of pro-IL-1β [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_L/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_L could be differently produced according to various concentrations of LPS, inhibiting Bcl-2/Bcl-X_L 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_L, B-cell lymphoma-extra large; IL-1β, interleukin-1beta; LPS, lipopolysaccharide; NF-κB, nuclear factor-kappa-B; PBMC, peripheral blood mononuclear cell.

Competing interests

The authors declare that they have no competing interests.

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