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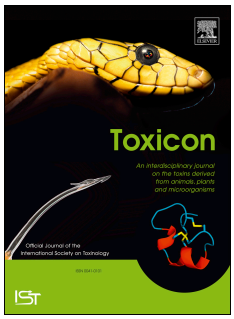

Exotoxins and endotoxins: Inducers of inflammatory cytokines

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Exotoxins and endotoxins: inducers of inflammatory cytokines

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ABSTRACT

Endotoxins and exotoxins are among the most potent bacterial inducers of cytokines. During infectious processes, the production of inflammatory cytokines including tumor necrosis factor (TNF), interleukin-1β (IL-1β), gamma interferon (IFNγ) and chemokines orchestrates the anti-infectious innate immune response. However, an overzealous production, leading up to a cytokine storm, can be deleterious and contributes to mortality consecutive to sepsis or toxic shock syndrome. Endotoxins of Gram-negative bacteria (lipopolysaccharide, LPS) are particularly inflammatory because they generate auto-amplificatory loops after activation of monocytes / macrophages. LPS and numerous pore-forming exotoxins also activate the inflammasome, the molecular platform that allows the release of mature IL-1β and IL-18. Among exotoxins, some behave as superantigens, and as such activate the release of cytokines by T-lymphocytes. In most cases, pre-exposure to exotoxins enhances the cytokine production induced by LPS and its lethality, whereas pre-exposure to endotoxin usually results in tolerance. In this review we recall the various steps, which, from the very early discovery of pyrogenicity induced by bacterial products, ended to the discovery of the endogenous pyrogen. Furthermore, we compare the specific characteristics of endotoxins and exotoxins in their capacity to induce inflammatory cytokines.

Highlights

- Endotoxins and exotoxins share the capacity to induce the production inflammatory cytokine.
- Macrophages are the main producers of endotoxin-induced cytokines.
- Macrophages and T-cells are the main producers of exotoxins/superantigens-induced cytokines.
- Endotoxins induce tolerance when exotoxins induce priming

Keywords: inflammation, inflammasome, superantigen, cytokine, priming, synergy

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