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Recent advances in biosensor based endotoxin detection

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ABSTRACT

Endotoxins also referred to as pyrogens are chemically lipopolysaccharides habitually found in food, environment and clinical products of bacterial origin and are unavoidable ubiquitous microbiological contaminants. Pernicious issues of its contamination result in high mortality and severe morbidities. Standard traditional techniques are slow and cumbersome, highlighting the pressing need for evoking agile endotoxin detection system. The early and prompt detection of endotoxin assumes prime importance in health care, pharmacological and biomedical sectors. The unparalleled recognition abilities of LAL biosensors perched with remarkable sensitivity, high stability and reproducibility have bestowed it with persistent reliability and their possible fabrication for commercial applicability. This review paper entails an overview of various trends in current techniques available and other possible alternatives in biosensor based endotoxin detection together with its classification, epidemiological aspects, thrust areas demanding endotoxin control, commercially available detection sensors and a revolutionary unprecedented approach narrating the influence of omics for endotoxin detection.

Contents

1. Introduction

Endotoxins are complex lipopolysaccharides (LPS) which form an inherent fraction of the outer cell wall of all gram negative bacteria and are responsible for the organization

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and stability of the cell wall (Kim et al., 2012). These are composed of three distinct regions: O-specific antigen forming the surface antigen, core polysaccharide and a non-polar lipid A. Endotoxins are responsible for toxic effects causing fever (Su et al., 2013), multi organ failure (Lawrence, 2011), septic shock (Ding et al., 2007), sepsis (Gutsmann et al., 2010) meningococcemia and severe morbidities like neurologic disability, hearing loss and loss of a limb (Kofyman and Takayesu, 2011). Fig. 1 corresponds to flow diagram representing the lethal effects of endotoxin.

Severe endotoxin infections coupled with septic shock transmit an elevated mortality rate in spite of proper antibiotic treatment and intensive care (Goscinski et al., 2004). Detection of endotoxin is essential for quality control in biological products, medical devices, serological products, parenteral drugs, recombinant therapeutic products and food & water security (Yeo et al., 2011; Lazcka et al., 2007). These necessities are the need for a rapid and sensitive biosensor for detection and monitoring of endotoxin levels even in extremely small concentrations (Su et al., 2012). Biosensors are compact analytical detection devices that use living organisms or biologically derived molecules such as antibodies, nucleic acids, or enzymes, to recognize specific target analyte or a group of closely related analytes in the sample matrix through discrete or continuous electrical signal, colorimetric or fluorescent indicators (Turner 2013a, 2013b). Despite of the large arena of biosensor applications, the field of biosensor has been virtually classified into two broad categories (i) high throughput expensive instruments delivering high sensitivity and selectivity with capable of measuring complex limitless biological interactions and components and (ii) inexpensive, portable and easy to use by layman and even capable of home analysis (Turner 2013a, 2013b). Recently focus has also been geared up for development of diverse strategies for endotoxin detection, for example, biosensors based on bioluminescence using luciferase enzyme (Noda et al., 2010), fluorescent dyes (Voss et al., 2007), mass change (Ooe et al., 2007), frequency–amplitude responses (Ong et al., 2006) and endotoxin recognition systems that use endotoxin-specific substances such as endotoxin neutralizing proteins (Kaconis et al., 2011), endotoxin binding proteins (Davis et al., 2011), cationic antibacterial proteins (Ding et al., 2007), peptides (Voss et al., 2007), artificial molecules like synthetic receptor (i.e. amino acid-functionalized polydiacetylene liposome) (Rangin and Basu, 2004) and pyrene derivatives (Zeng et al., 2010). A comprehensive literature survey has been reviewed over the past ten years with an emphasis on biosensor based endotoxin detection (Fig. 2).

List of potential gram negative bacterias (Table 1) corresponding with their toxin produced, causal diseases, and its sources are mentioned. With an annual worldwide incidence of approximately 18 million, it is the largest cause of mortality in intensive care units. It represents a growing concern and significant problem in high-risk patients with an associated 30–40%

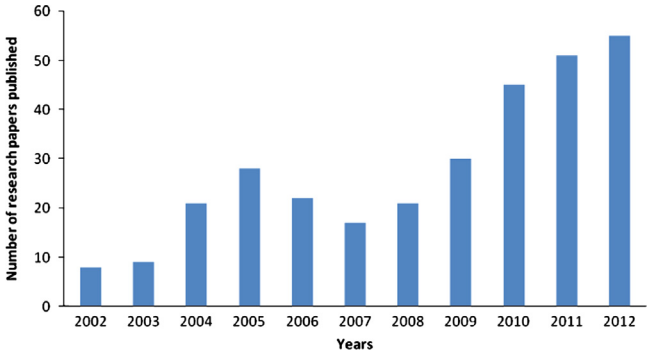

Fig. 2. Graph of a search on the term "biosensor based endotoxin detection" during the period 2002–2013, using the SCI database. This graph clearly depicts a linear increase in manuscripts published on biosensor based endotoxin detection with the highest number of papers published in the year 2012.

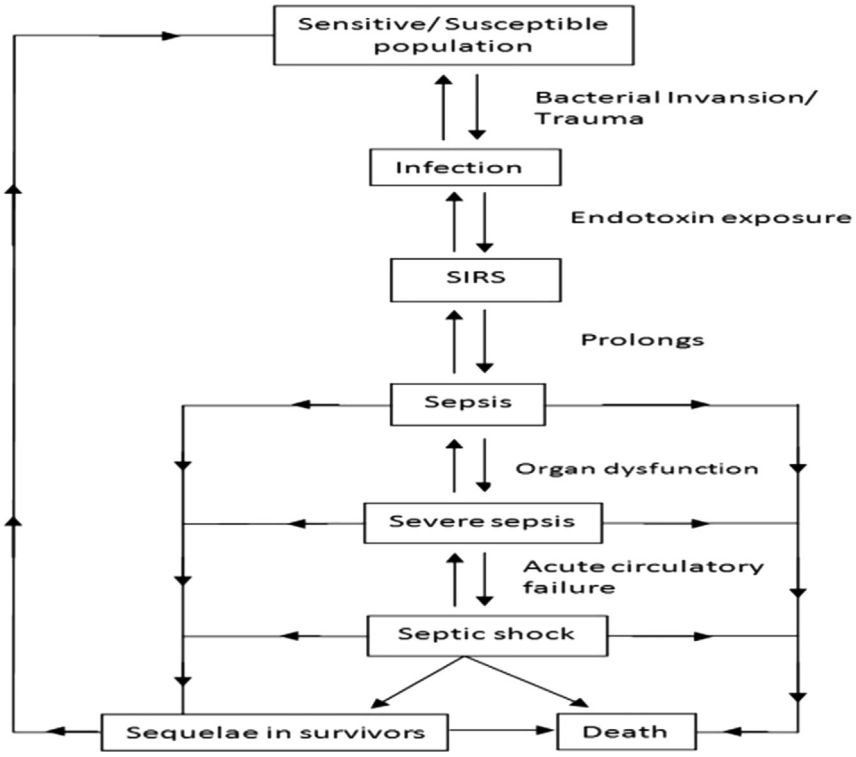

Fig. 1. Flow diagram representing the lethal effects of endotoxin. Whenever a sensitive or susceptible population due to bacterial infection or trauma get infected and finally get exposed to endotoxin, they develop SIRS. If left untreated or unchecked it prolongs to sepsis. Sepsis coupled with organ dysfunction leads to severe sepsis, which coalesces with acute circulatory failure to finally give rise to septic shock followed by irreversible sequelae in survivors and death.