Progress in Lipid Research 49 (2010) 97–107

Contents lists available at ScienceDirect

Progress in Lipid Research

journal homepage: www.elsevier.com/locate/plipres

Review

Lipopolysaccharide: Biosynthetic pathway and structure modification

Xiaoyuan Wang [a,*], Peter J. Quinn [b,1]

[a] State Key Laboratory of Food Science and Technology, Jiangnan University, 1800 Lihu Avenue, Wuxi 214122, China
[b] Department of Biochemistry, King's College London, 150 Stamford Street, London SE1 9NH, United Kingdom

ARTICLE INFO

Article history:
Received 6 May 2009
Received in revised form 16 June 2009
Accepted 17 June 2009

Keywords:
Gram-negative bacteria
Outer membrane
Lipopolysaccharide
Endotoxin
Lipid A
LPS biosynthesis

ABSTRACT

Lipopolysaccharide that constitutes the outer leaflet of the outer membrane of most Gram-negative bacteria is referred to as an endotoxin. It is comprised of a hydrophilic polysaccharide and a hydrophobic component referred to as lipid A. Lipid A is responsible for the major bioactivity of endotoxin, and is recognized by immune cells as a pathogen-associated molecule. Most enzymes and genes coding for proteins responsible for the biosynthesis and export of lipopolysaccharide in *Escherichia coli* have been identified, and they are shared by most Gram-negative bacteria based on genetic information. The detailed structure of lipopolysaccharide differs from one bacterium to another, consistent with the recent discovery of additional enzymes and gene products that can modify the basic structure of lipopolysaccharide in some bacteria, especially pathogens. These modifications are not required for survival, but are tightly regulated in the cell and closely related to the virulence of bacteria. In this review we discuss recent studies of the biosynthesis and export of lipopolysaccharide, and the relationship between the structure of lipopolysaccharide and the virulence of bacteria.

Contents

1. Introduction

Gram-negative bacteria have two distinct membranes: an inner membrane and an outer membrane. A prominent constituent of the outer leaflet of the outer membrane is lipopolysaccharide (LPS). The LPS components of many bacteria are toxic. The

Abbreviations: LPS, lipopolysaccharide; TLR4, toll-like receptor 4; Kdo, 3-deoxy-D-manno-octulosonic acid; Hep, L-glycero-D-manno-heptose; CAMPs, cationic antimicrobial peptides; α-L-Ara4N, 4-amino-4-deoxy-α-L-arabinose; Und-P-α-L-Ara4N, undecaprenyl phosphate-L-Ara4N.

* Corresponding author. Tel./fax: +86 (0)510 85329329.
E-mail addresses: xwang65@gmail.com (X. Wang), p.quinn@kcl.ac.uk (P.J. Quinn).
[1] Tel.: +44 (0)20 78484408; fax: +44 (0)20 78484500.

0163-7827/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.plipres.2009.06.002

discovery of endotoxin in the late 19th century was based on the demonstration that heat-killed cholera bacteria were themselves toxic rather than causing toxicity by secretion of a product from the living organism. Secreted toxins became broadly known as "exotoxins", and the toxic materials of bacteria as "endotoxin". The historical aspects of the role of endotoxins in bacterial pathogenesis and their chemical characterization as LPS have been the subject of a comprehensive review [1].

The LPS molecule can be divided into three parts: lipid A, core polysaccharides and O-antigen repeats (Fig. 1). Lipid A represents the hydrophobic component of LPS which locates in the outer leaflet of the outer membrane, while core polysaccharides and

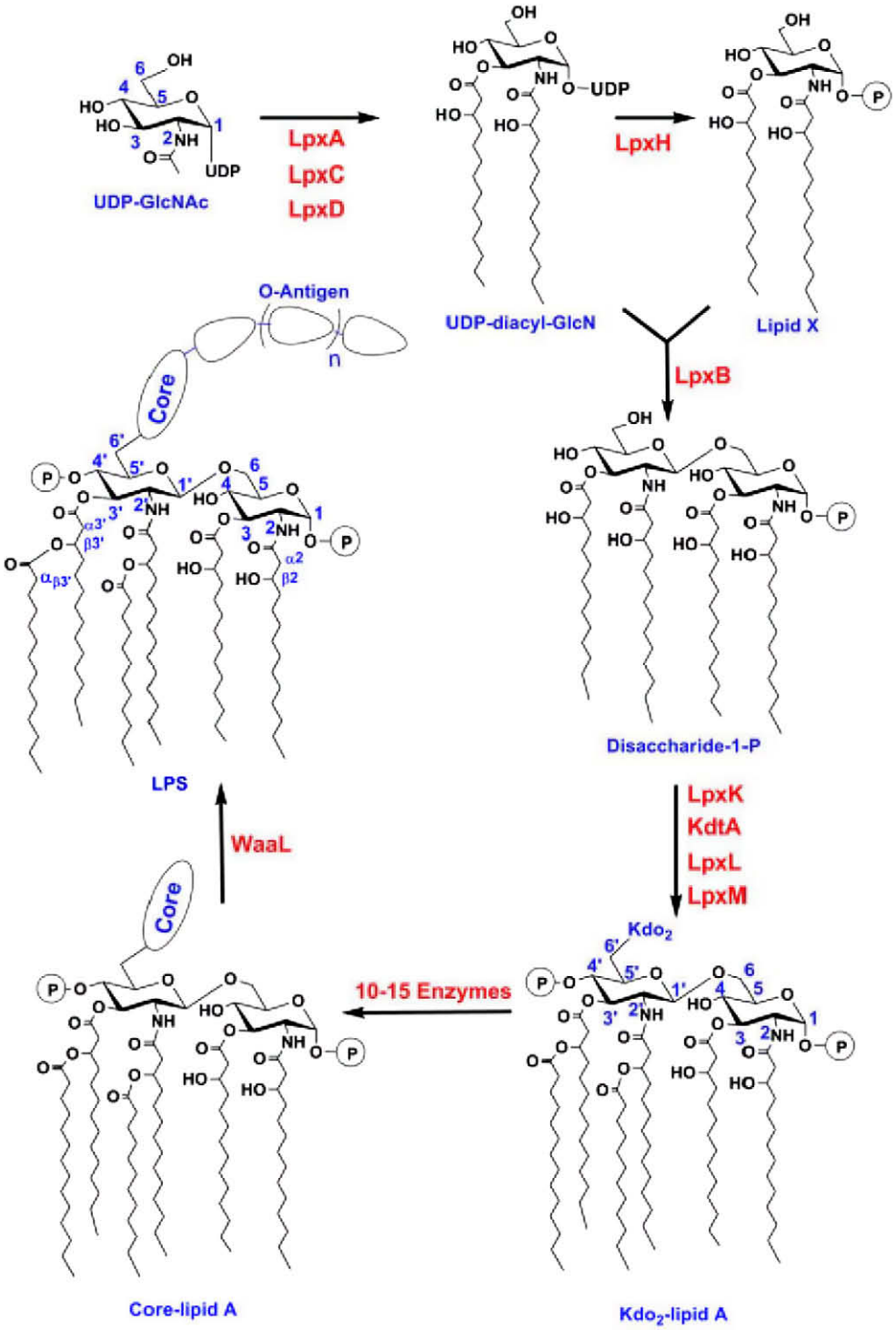

Fig. 1. Structure and biosynthetic pathway of LPS in *E. coli*. Each reaction is catalyzed by a single enzyme. The name of the enzyme is highlighted in red, and the name of the substrate in blue. The structure of lipid A is shown in detail, but structures of core oligsaccharides and O-antigen are simplified as symbols since there are many variations in these two regions. The genes encoding the enzymes of lipid A biosynthesis are present in single copy and highly conserved among bacteria [2,3]. The core region usually contains 10–15 monosaccharides. The O-antigen usually contains only a few monosaccharides, but can be repeated many times in LPS. Noncarbohydrate components are also found in these regions.