Chapter 43

**Lipopolysaccharides of Yersinia**

*An overview*

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1. **INTRODUCTION**

Lipopolysaccharides (LPSs) are the endotoxins of Gram-negative bacteria and well known for their immunological, pharmacological and pathophysiological effects displayed in eucaryotic cells and organisms. To date, much emphasis has been put on the elucidation of the chemical structures of LPSs and on their relation, or that of substructures, to the various biological effects. Lipopolysaccharides (Alexander and Rietschel, 2001) can be classified into two types which are characterized by the size of the saccharide portion, i.e. smooth- and rough-form (S- and R-form). Both types consist of lipid A and, covalently linked to it, a saccharide portion composed of up to fifteen sugars, the core region (Holst, 1999; Holst, 2002). In S-form LPS, this core region is substituted by the O-specific polysaccharide (Knirel and Kochetkov, 1994; Jansson, 1999). Both LPS types are present in wild-type Gram-negative bacteria, S-form for example in *Escherichia coli* or *Vibrio cholerae*, and R-form in *Neisseria meningitidis* or *Bordetella pertussis*. Since mutants that are not able to synthesize a minimal core structure are not viable, the core region and lipid A represent a common structural unit occurring in all LPSs and important for viability and membrane function of Gram-negative bacteria. The lipid part of LPS, the lipid A, was proven to represent the toxic principle of endotoxin. However, lipid A toxicity depends strongly on its structure, and is influenced by the core region.
2. LPS OF YERSINIA

This short overview deals mainly with structures and biological functions of LPSs from the three major human pathogenic species, i.e. *Yersinia enterocolitica*, *Y. pestis* and *Y. pseudotuberculosis*. Structures of lipid A and the core regions of LPSs from the first two species have been elucidated, as were some biological properties of the lipid A moieties. Of *Y. pseudotuberculosis*, only a partial core structure was reported, and no structure of lipid A. With regard to O-specific polysaccharide structures, quite a number of LPSs from *Y. enterocolitica* and *Y. pseudotuberculosis* are known. *Y. pestis* LPSs are of the rough type and, thus, do not possess any O-specific polysaccharides.

2.1 Lipid A structures

In *Y. enterocolitica*, the structures of the lipid A from LPSs of the serotypes O:3, O:8, O:9, O:11,23 and O:11,24 (Figs. 1 and 2) have been elucidated (Aussel *et al.*, 2000; Oertelt *et al.*, unpublished.). The structures of the major lipid A molecules are all very similar, i.e. they consist of a β-(1→6)-linked 2-amino-2-deoxy-D-glucopyranose (GlcN) disaccharide that is bisphosphorylated at positions C-1 and C-4' and that is hexa-acylated. Two amide- and two ester-linked 3-hydroxymyristic acid [14:0(3-OH)] residues are present. Whereas in serotypes O:3, O:8 and O:9 the acyloxyacyl pattern at the non-reducing GlcN is identical, that of serotypes O:11,23 and O:11,24 differs by the presence of an 14:0[3-O(12:0)] that is amide-linked to the non-reducing GlcN. In serotype O:8, the structure of the lipid A was found to be temperature-dependent (Figure 2) (Oertelt *et al.*, unpublished). The above described hexa-acylated lipid A was the major component in LPSs of bacteria grown at 21°C. In LPSs of bacteria grown at 37°C, the major components were a tri- and a tetra-acylated lipid A. This preparation contained also small amounts of hexa-acylated lipid A, as contained the preparation from the bacteria grown at 37°C small amounts of the tri- and a tetra-acylated lipid A. Unfortunately, it was not possible to isolate pure tri- and a tetra-acylated lipid A fractions, thus, their biological properties could not be established.

The lipid A structures of LPSs from serotypes O:11,23, O:11,24, O:3, O:8 and O:9 are very similar to the structure of lipid A in LPSs of *Escherichia coli* (Zähringer *et al.*, 1994).

Similar to the lipid A of *Y. enterocolitica*, the structures of lipid A of LPSs from *Y. pestis* vary with the growth temperature (Figure 3). Again, the hexa-acylated carbohydrate backbone is produced as major component at lower temperature (27°C), whereas at 37°C two less acylated lipid A