

Bacterial Lipopolysaccharide-Dependent Complement Evasion

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Editorial

Finding factors that control complement (C) components deposition on bacterial cells is the way to explain the sophisticated mechanism of bacteraemia. Lipopolysaccharide (LPS, endotoxin) is a surface antigen found in the cell walls of Gram-negative bacteria, such as Salmonella [1]. LPS action on the human body is often considered in the context of sepsis, which is characterized by an excessive inflammatory response in the presence of endotoxin. At low concentrations, LPS stimulates innate immune system, which helps the host to eliminate the invader, but at high levels, it causes shock and even death [2]. Moreover, recent LPS characterization supports the development of a new vaccine against non-typhoidal Salmonellae for Africa [3]. From the point of view of pathogens, LPS-dependent resistance to C-mediated killing is an essential virulence property. In this paper, I want to highlight the main findings on the role of LPS in bacterial C-dependent serum susceptibility. To introduce, it is worth bringing forward a general structure of endotoxin. LPS of smooth strains (S) consists of three structural domains: lipid A, which anchors the whole molecule in the bacterial cell wall, core oligosaccharide, and O-specific polysaccharide chains (O antigen, O-Ag). Lipooligosaccharide (LOS) is analogous to the LPS, but it lacks O-Ag. When the LPS is connected to the bacterium, the outermost fragment - O antigen determines the response of the inflammatory system. In case of killing or disruption of bacterial cells with drugs (i.e. antibiotics) results in a lipid A release, the most toxic domain of endotoxin [1]. The role of LPS and its chemotypes in the resistance of bacteria to C has not been investigated thoroughly. Since the 80's, it has been known that long-chain LPS with complete O-specific chains confers bacterial resistance to serum by promoting the deposition of C components at a distance from the cell wall, thus preventing its disruption with the C5b-9 complexes. It was demonstrated that the amount of LPS O-Ag and its chain length distribution are important factors that protect for example *Salmonella* strains from C-mediated lysis [4,5]. The protective role of LPS and O antigen in serum resistance was also highlighted by an interesting study investigating the serum resistance of *Escherichia coli* ST131 [6]. Partial or total loss from the LPS of the sugars responsible for O-antigenicity (rough strains, R) often results as increased sensitivity to the bactericidal effect of serum, however, such loss is not necessary for serum sensitivity [7]. For instance, smooth *Proteus mirabilis* strains were sensitive to C-mediated killing, despite C binding by their LPS [8]. Gram-negative bacteria lacking the polysaccharide side chains within O-Ag activate C via the classical pathway (CP) [9]. In turn, smooth strains with complete LPS activate C via the alternative pathway (AP) [10], but the binding of MBL to the complex carbohydrate structures of microorganisms is poorly understood. Some results support the hypothesis that LPS structure is a major determinant of MBL binding [11]. O-Ag plays a significant role in blocking the early deposition of C3 on bacterial surfaces. However, no direct correlation between the C3 deposition pattern and

bacterial resistance was observed [12]. It was also shown that C3 activation by LPS via the AP was sensitive to slight variations in the chemical structure, but not to large changes in the length of the O-Ag polysaccharide side chain of LPS [13]. Endotoxin isolated from a serum-sensitive *Shigella flexneri* strain deposited more C3 fragments than LPS from serum-resistant strains [14]. O-antigen chemical variation helps the invaders to evade host's immune response until specific antibodies appear. Of particular interest is the presence of sialic acid (Sia) moieties in LPS or LOS, molecules typical for mammal tissues. Pathogenic bacteria, especially those living in association with higher organisms may incorporate Sia into their surface structures. Sialylation of eukaryotic membrane surfaces enhances the interaction between C3b and factor H, resulting in cleavage of C3b to iC3b by factor I. Possessing of Sia by bacteria results in increased conversion of bound C3b to iC3b on the organism, which may be a mechanism for their serum resistance in vivo. Sialylation of *Neisseria gonorrhoeae* LOS converts serum-sensitive strains to serum resistant [15]. This corresponds to the observation that sialylation of gonococcal LOS is essential in the modulating of C action through inhibition of the AP [16]. In contrast, the presence of Sia in the structure of Salmonella O48 LPS was not sufficient to block the AP activation [17] and serum-sensitive Salmonella O48 with sialylated LPS poorly converted C3 to C3c [18]. In other study on *Campylobacter jejuni* blood isolates, susceptibility to human serum was not attributable to the ability to sialylate LOS [19]. Although microorganisms are well characterized with their virulence factors, they are still able to evade host defense mechanisms. Gram-negative bacteria with their potential to change the chemical structure of LPS may become distinct strains containing the unique surface antigens pattern. It may generate serious clinical problems of global interest to eliminate bacteria occurring systemic infections with current available drugs.

References

1. Raetz C (1990) Biochemistry of endotoxins. *Biochem* 59: 129-170.
2. O'Hagan DT, MacKichan ML, Singh M (2001) Recent developments in adjuvants for vaccines against infectious diseases. *Biomol Eng* 18: 69-85.
3. Onsare RS, Micoli F, Lanzilao L, Alfani R, Okoro CK, et al. (2015) Relationship between antibody susceptibility and lipopolysaccharide O-antigen characteristics of invasive and gastrointestinal nontyphoidal Salmonellae isolates from Kenya.
4. Grossman N, Schmetz MA, Foulds J, Klima EN, Jimenez-Lucho VE, et al. (1987) Lipopolysaccharide size and distribution determine serum resistance in Salmonella montevideo. *J Bacteriol* 169: 856-863.
5. Bravo D, Silva C, Carter JA, Hoare A, Alvarez SA, et al. (2008) Growth-phase regulation of lipopolysaccharide O-antigen chain length influences serum resistance in serovars of Salmonella. *J Med Microbiol* 57: 938-946.
6. Phan MD, Peters KM, Sarkar S, Lukowski SW, Allsopp LP, et al. (2013) The serum resistance of a globally disseminated multidrug resistant uropathogenic *Escherichia coli* clone.

7. Nelson BW, Roantree RJ (1967) Analyses of lipopolysaccharides extracted from penicillin-resistant, serum-sensitive salmonella mutants. *J Gen Microbiol* 48: 179-188.
8. Kaca W, Literacka E, Sjöholm AG, Weintraub A (2000) Complement activation by *Proteus mirabilis* negatively charged lipopolysaccharides. *J Endotoxin Res* 6: 223-234.
9. Cooper NR (1983) Activation and regulation of the first complement component. *Fed proc* 42: 134-138.
10. Bjornson AB, Bjornson HS (1977) Activation of complement by opportunist pathogens and chemotypes of *Salmonella minnesota*. *Infect Immun* 16: 748-753.
11. Devyatyarova-Johnson M, Rees IH, Robertson BD, Turner MW, Klein NJ, et al. (2000) Lipopolysaccharide structures of *Salmonella enterica* serovar Typhimurium and *Neisseria gonorrhoeae* determine the attachment of human mannose-binding lectin to intact organisms. *Infect Immun* 68: 3894-3899.
12. Biedzka-Sarek M, Venho R, Skurnik M (2005) Role of YadA, Ail, and lipopolysaccharide in serum resistance of *Yersinia enterocolitica* serotype O:3. *Infect Immun* 73: 2232-2244.
13. Grossman N, Leive L (1984) Complement activation via the alternative pathway by purified *Salmonella* lipopolysaccharide is affected by its structure but not its O-antigen length. *J Immunol* 132: 376-385.
14. Fudala R, Doroszkiewicz W, Niedbach J, Gamian A, Weintraub A, et al. (2003) The factor C3 conversion in human complement by smooth *Shigella flexneri* lipopolysaccharides. *Acta Microbiol Pol* 52: 45-52.
15. Lewis LA, Gulati S, Burrowes E, Zheng B, Ram S, et al. (2015) α -2,3-Sialyltransferase expression level impacts the kinetics of lipooligosaccharide sialylation, complement resistance, and the ability of *Neisseria gonorrhoeae* to colonize the murine genital tract. *mBio* 6: e02465-14.
16. Ram S, Sharma AK, Simpson SD, Gulati S, McQuillen DP, et al. (1998) A novel sialic acid binding site on factor H mediates serum resistance of sialylated *Neisseria gonorrhoeae*. *J Exp Med* 187: 743-752.
17. Bugla-Płoskońska G, Rybka J, Futoma-Koloch B, Cisowska A, Gamian A, et al. (2010) Sialic acid-containing lipopolysaccharides of *Salmonella* O48 strains-potential role in camouflage and susceptibility to the bactericidal effect of normal human serum. *Microb Ecol* 59: 601-613.
18. Futoma-Koloch B, Godlewska U, Guz-Regner K, Dorotkiewicz-Jach A, Klaus E, et al. (2015) Presumable role of outer membrane proteins of *Salmonella* containing sialylated lipopolysaccharides serovar Ngozi, sv. Isaszeg and subspecies arizonae in determining susceptibility to human serum. *Gut Pathog* 7: 18.
19. Ellström P, Feodoroff B, Hänninen M-L, Rautelin H (2014) Lipooligosaccharide locus class of *Campylobacter jejuni*: sialylation is not needed for invasive infection. *Clin Microbiol Infect* 20: 524-529.