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Bacterial Outer Membrane Proteins – Dependent Complement Activation

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Editorial

Complement (C) plays a pivotal role in the innate defence against microorganisms that invade animal and human bodies. Its activation through the classical (CP), lectin (LP) and alternative (AP) pathways lead to opsonisation and lysis of pathogens by incorporation of the membrane attack complex (MAC) into the membrane surrounding the microorganism's body. Bacteria getting into contact with human blood or plasma have developed a variety of strategies to evade C attack. Of special interest are outer membrane proteins (OMP) located in the outer membrane (OM) of gram-negative bacteria, which were shown to be involved in interactions with complement's factors [1]. Some OMP bind host's C regulatory proteins, while some of the others directly inactivate C components. Bacterial OMP may provide resistance against bactericidal action of the C system; however some of them may increase sensitivity of bacteria to serum [2]. Finding factors that control C components deposition on bacterial cells is the way to explain the sophisticated mechanism of bacteraemia leading to sepsis. Additionally, the mechanisms of OMP-mediated activation are currently intensively investigated, because of its high diversity and principal antigen vaccine potential. OMP are surface factors that are often utilized by gram-negative bacteria to avoid C-mediated recognition and destruction. Firstly, many OMP can bind specific fluid-phase regulators, such as factor H or C4bp protein. Respiratory pathogen *Moraxella catarrhalis* directly interacts with C_3, as it produces C_3-binding protein UspA [3]. The analysis of C_3 activation on Salmonella isolates belonging to the O48 serogroup showed that OMP in the range of molecular weights of 35-48 kDa determined their sensitivity to normal human serum (NHS) by C_3 activation [4]. It on the bacteria does not guarantee is worth mention that activation of the C system by surface structures the elimination of the microorganisms' cells from the host fluids. For example, no association between C_{3b} deposition on the *N. meningitidis* cells and their lysis was found [5]. What is more, there are numerous OMP, which cleave complement's components or interfere with a correct formation of MAC, the final step in C activation. Well documented is the research on human *enteropathogen Yersinia enterocolitica* strain lacking OmpR regulator protein. OmpR exhibited extremely high resistance to the bactericidal activity of NHS through Ail (factor involved in the serum-resistant (SR) phenotype) expression compared with the wild-type strain [6]. Within OMP isolated from *Salmonella* O_{48} serogroup, surface proteins characteristic of the bacterial strains sensitive or resistant to the bactericidal action of normal cord serum were appointed [7]. Interesting data were published for urinary tract pathogen Proteus mirabilis treated by the sequential passage in 90% normal bovine serum. Serum sensitive *P. mirabilis* O_{18} strain after prolonged treatment by animal serum produced certain classes of surface proteins in excess, which were related in their quantity to these isolated from the resistant strain *P. mirabilis* O_3 [8]. Component C_4bp regulates both CP and LP of C by preventing the assembly of C_4b_2a (the CP/LP C_3 convertase) and accelerating the decay of this complex. Many pathogens are equipped with protein surface factors that bind C_4bp. They are found for instance in bacterial species of Neisseria meningitidis, *Neisseria meningitidis, Neisseria gonorrhoeae, and Y. enterocolitica* [9-11]. The major OMP of *N. gonorrhoeae* is Poor, which comprises 60% of the protein content of OM. The binding of C_4bp to Por_1A represents the C evasion mechanism [10]. It was demonstrated that serogroup B *N. meningitidis* that produce Pores also bind C4bp. The results of serum bactericidal assay showed that the strains expressing PorA are more resistant to C lysis than PorA-negative strains [9]. *Y. enterocolitica* has two classes of OMP: YadA and Ail, which act as receptors for C_4bp. These proteins are the main SR determinants of these bacteria [11]. The fact is that the AP spontaneously initiates in serum. What is more, this pathway enhances C activation initiated by the CP and the LP. To protect own tissues organisms are equipped with membrane-bound C inhibitors and fluid-phase inhibitors. A significant, soluble-phase, the AP regulator is fH that act as cofactors for factor I in C_3b inactivation; it competes with factor B for C_3b binding and, for this reason, prevent C_3bBb (the C3 convertase of AP) formation. In addition, it accelerates the decay of C_3bBb [12]. Factor H binding is a frequent mechanism used by different pathogens such as *Borrelia burgdorferi, N. gonorrhoeae, and Haemophilus influenzae* [12-14]. In turn, the virulence factor PgtE (outer membrane protease) of *Salmonella enterica* not only cleaves fH, but also other C components: factor B, C3, and C_3b [15]. In the context of mobilization of C components of the distinct pathways, porins of *Klebsiella pneumoniae* were more effective activators of the CP. The molecule isolated from this pathogen named OmpK36 interacted directly with C_1q complement protein independently of antibodies [16,17]. Former report suggested that OMP of molecular weights of 34 kDa and 36 kDa of *Salmonella Typhimurium* were involved in C activation. It has been shown that these porins enabled AP and CP pathways initiation [18]. Less information is available about the initiation of the LP by the presence of OMP. Lectin pathway begins with the binding of mannose-binding lectin (MBL) to repeating sugar moieties on the bacteria. Mannose-binding lectin was shown to bind to *N. meningitidis* surface proteins Opa and PorB, independent of the calcium ions [19].

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