The choline-binding protein PspC of *Streptococcus pneumoniae* interacts with the C-terminal heparin-binding domain of vitronectin.


Abstract

Adherence of *Streptococcus pneumoniae* is directly mediated by interactions of adhesins with eukaryotic cellular receptors or indirectly by exploiting matrix and serum proteins as molecular bridges. Pneumococci engage vitronectin, the human adhesive glycoprotein and complement inhibitor, to facilitate attachment to epithelial cells of the mucosal cavity, thereby modulating host cell signaling. In this study, we identified PspC as a vitronectin-binding protein interacting with the C-terminal heparin-binding domain of vitronectin. PspC is a multifunctional surface-exposed choline-binding protein displaying various adhesive properties. Vitronectin binding required the R domains in the mature PspC protein, which are also essential for the interaction with the ectodomain of the polymeric immunoglobulin receptor and secretory IgA. Consequently, secretory IgA competitively inhibited binding of vitronectin to purified PspC and to PspC-expressing pneumococci. In contrast, Factor H, which binds to the N-terminal part of mature PspC molecules, did not interfere with the PspC-vitronectin interaction. Using a series of vitronectin peptides, the C-terminal heparin-binding domain was shown to be essential for the interaction of soluble vitronectin with PspC. Binding experiments with immobilized vitronectin suggested a region N-terminal to the identified heparin-binding domain as an additional binding region for PspC, suggesting that soluble, immobilized, as well as cellularly bound vitronectin possesses different conformations. Finally, vitronectin bound to PspC was functionally active and inhibited the deposition of the terminal complement complex. In conclusion, this study identifies and characterizes (on the molecular level) the interaction between the pneumococcal adhesin PspC and the human glycoprotein vitronectin.

Beteiligte Abteilungen und Gruppen

Infektionsbiologie

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