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***Streptococcus pneumoniae* surface protein PfbA is a versatile adhesin binding to extracellular matrix molecules and glycans of host**

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Streptococcus pneumoniae, one of the major human respiratory pathogens, uses its repertoire of surface proteins to adhere to the epithelium of the nasopharynx and lungs leading to colonization. PfbA is a conserved surface protein of *S. pneumoniae* and helps the bacterium to colonize the host by recognizing the extracellular matrix (ECM) molecule fibronectin as well as blood proteins like plasminogen and human serum albumin. The crystal structure of rPfbA₁₅₀₋₆₀₇ revealed it to possess a beta helical region similar to those of carbohydrate-active enzymes. The structural analysis of revealed that C-terminal segment of rPfbA₁₅₀₋₆₀₇ resembles the fibronectin (Fn)-binding regions of Fn-binding proteins. To get more insight into PfbA's putative carbohydrate binding property and its binding to various host molecules we generated three different constructs of PfbA and characterized by ELISA, isothermal calorimetry and bio-layer interferometry experiments. The isothermal calorimetry experiments revealed that PfbA binds to different saccharides. Further, ELISA and bio-layer interferometry experiments identified that 1) apart from Fn and plasminogen, the beta helix of PfbA also binds to other ECM molecules 2) lysines are not responsible for PfbA's binding to plasminogen, 3) in comparison with native fibrinogen, deglycosylated-fibrinogen exhibits reduced binding affinity towards PfbA implying the importance of carbohydrate - PfbA interaction and 4) the C-terminal region of PfbA is exclusively binding to the N-terminal F1 modules of fibronectin. Thus, the results of this study show PfbA to be a versatile multidomain and multiligand binding protein employing different binding mechanisms. These results could be useful for structure-based designing of inhibitors against PfbA.

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