Structural insight into dual function of Neisserial lactoferrin binding protein B

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Lactoferrin binding protein B (LbpB) is a surface exposed lipoprotein that plays dual roles in iron import from host lactoferrin protein, and protection against antimicrobial cationic peptide lactoferricin. LbpB is an attractive target for antimicrobial drugs and vaccine design. However, molecular mechanisms of LbpB's functions are unclear. In the current study, we determined the structures of Neisseria meningitidis and N. gonorrhoeae LbpBs in complex with human lactoferrin using X-ray crystallography and cryo-electron microscopy. The structures depict the bi-lobe architecture of LbpB and revel the binding interface with the lactoferrin. Structural and functional analysis of the LbpB proteins indicate that iron-loaded lactoferrin selectively binds to N-lobe of LbpB. In contrast, we show that lactoferricin binding site is in the C-lobe of LbpB. Furthermore, our data suggests that lactoferrin and lactoferricin binding to LbpB are independent. Together, these results provide insights into lactoferrin and lactoferricin recognition, and create a framework for understanding the dual function of LbpB in mediating Neisserial pathogenesis.