Structural basis of Neisserial lactoferrin binding protein B function

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Neisseria are exclusive human pathogens causing meningitis, septicemia, and gonorrhea. Neisserial pathogens acquire iron from host proteins such as transferrin, lactoferrin, and hemoglobin using outer membrane protein systems. The lactoferrin binding protein (Lbp) system, composed of integral membrane protein LbpA and lipoprotein LbpB, has been proposed to selectively hijack iron from lactoferrin protein. LbpB also provides protection against host antimicrobial peptide lactoferricin. The molecular mechanisms for Lbp system functions remain unknown. In the current study, we determined the structure of LbpB in complex with lactoferrin. We show that the N-lobe of LbpB interacts with the C-lobe of lactoferrin. Structural alignment analysis indicates virtually no conformational changes upon complex formation. Our structure also provides insight into LbpB's specificity towards holo-lactoferrin over apo-lactoferrin. We show that lactoferrin and lactoferricin binding to LbpB are independent. We propose that LbpB binding locks lactoferrin in an iron-bound state for efficient iron scavenging during Neisserial infections.

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