Poster Presentation

MS16.P14

Structural insights into SraP-mediated S. aureus adhesion to host cells

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Staphylococcus aureus, a Gram-positive bacterium causes a number of devastating human diseases, such as infective endocarditis, osteomyelitis, septic arthritis and sepsis. S. aureus SraP, a surface-exposed serine-rich repeat glycoprotein (SRRP), is required for the pathogenesis of human infective endocarditis via its ligand-binding region (BR) adhering to human platelet. It remains unclear how SraP interacts with human host. Here we report the 2.05 Å crystal structure of the BR of SraP, revealing an extended rod-like architecture of four discrete modules. The N-terminal legume lectin-like module specifically binds to N-acetylneuraminic acid. The second module adopts a β-grasp fold similar to Ig-binding proteins, whereas the last two tandem repetitive modules resemble eukaryotic cadherins but differing in calcium coordination pattern. Small-angle X-ray scattering and molecular dynamic simulation indicated the three C-terminal modules function as a rigid stem to extend the N-terminal lectin module outward. Further structure-guided mutagenesis analyses showed that SraP binding to sialylated receptors promotes S. aureus adhesion to and invasion into host epithelial cells. Our findings have thus provided novel structural and functional insights into the SraP-mediated interaction of S. aureus with host epithelial cells.

Keywords: Staphylococcus aureus, serine-rich repeat glycoprotein, lectin