Structural and Thermodynamic Insights into Adhesin-Mediated Pathogenesis in Enterococci

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Gram-positive Enterococci account for a significant fraction of hospital-acquired infections but are often difficult to treat due to their proficiency in colonizing damaged host tissues, forming biofilms, and acquiring and spreading antimicrobial resistance (AMR). These AMR genes and other virulence factors often spread by conjugation through a Type 4 Secretion System (T4SS). Adhesion proteins stabilize cell-cell contacts during the DNA transfer, and importantly, these same adhesion proteins promote biofilm formation and binding to host cells during infection. One such adhesin is PrgB, encoded on the conjugative pCF10 plasmid from *Enterococci faecalis*. A subset of PrgB binding partners involved in biofilm formation has been previously characterized, but the features of PrgB-host interactions required for infection remain unknown. This project aims to identify host-derived extracellular factors that interact with PrgB, quantify the thermodynamic parameters of binding, and structurally resolve important binding interfaces. Two important classes of extracellular molecules currently under investigation are divalent cations and sulfated glycosaminoglycans (GAGs). Results show that PrgB preferentially binds calcium with micromolar affinity and PrgB-mediated biofilm maturation requires divalent cations. Also, PrgB can bind GAGs through non-specific electrostatic interactions, but any alternate binding modes remain to be discovered. Ongoing structural studies will reveal molecular details that explain how these adhesins confer virulence by promoting pathogenic colonization of host tissues, stabilizing mating pairs during conjugation, and initiating biofilm formation.