Crystal Structures of Sortase B from *Staphylococcus aureus* and *Bacillus anthracis* Reveal Catalytic Amino Acid Triad in the Active site

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Surface proteins of Gram-positive bacteria perform critical biological functions during the pathogenesis of human infections. These functions are only carried out when they are attached to the cell wall envelope. The anchoring process of the surface protein is accomplished by sortases via a transpeptidation reaction involving a C-terminal sorting signal containing a conserved five-amino acid motif. Sortase B recognizes NPQ**T**N in *S. aureus*, and NPKTG in *B. anthracis*, cleaves the polypeptide after the Thr residue and attaches the mature protein to the cell wall peptidoglycan. The catalytic mechanism for similar reaction has been proposed. Questions whether a thiol ion pair intermediate plays a key role in the sortase-catalyzed reaction and which residues constitute the active site remain unsolved. In this paper, we report 1.6 and 2.0 Å resolution crystal structures of SrtB from *B. anthracis and S. aureus,* respectively, provide a first detailed view of the active site and enables the design of new experiments with a goal to target the protein for new class of drugs that would inhibit cell wall anchoring in gram-positive bacteria.

Keywords: sortase, bacillus anthracis, structural genomics