

## ***The Mechanism of Direct Heme Transfer from the Streptococcal Surface Protein Shp to HtsA of the HtsABC Transporter***

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**Background and Objective:** Heme is a source of essential iron for bacterial pathogens. How heme is acquired is poorly understood. The heme uptake system of *Streptococcus pyogenes* consists of the surface proteins Shr and Shp and transporter HtsABC. This study aims at elucidating the mechanism of heme transfer from Shp to HtsA as a model to understand how heme is transferred from one protein to another.

**Methods:** The kinetic mechanism of the transfer was determined. The molecular events were further explored by mutagenesis of Shp.

**Results:** HoloShp forms a complex with apoHtsA and then transfers heme exponentially to apoHtsA (J Biol Chem 281:20761). Ala replacements of the axial residues of the Shr heme iron altered the single-exponential transfer into a double-exponential reaction (J Biol Chem 282:31380).

**Discussion and Conclusion:** The reaction involves a mechanism of activated heme transfer, and the two axial bonds in holoHtsA are formed at the same time. Elimination of one axial bond in Shp results in a Shp-heme-HtsA intermediate. These results suggest a reaction model in which the axial ligands of the empty apoHtsA heme pocket slides into the axial positions of the heme in Shp to displace the axial bonds in Shp and pull out heme.

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