Haem-binding Properties and Crystallisation of the Bacterial Protein HemS

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Iron is one of the most important nutrients for the majority of living organisms due to its essential role in many biological processes like respiration and oxygen transport. Despite being one the most abundant chemical elements, iron is scarcely available under physiological conditions, because of its insolubility and toxicity.

Pathogenic bacteria rely on their host as source of iron and have evolved several strategies to circumvent their iron dependency. One mechanism relies on "stealing" iron in the form of haem from host's haem proteins through a set of inter-linked haem transporters [1]. These unique systems have intriguing molecular biology mechanisms.

The haem uptake system of the gastrointestinal pathogen *Yersinia enterocolitica* consists of 5 proteins. Located on the outer membrane, the receptor HemR sequesters haem from host haem proteins or directly binds free haem. When internalised, the ligand is taken up by the periplasmatic carrier HemT and passed onto the hetero-dimer HemUV, an integral inner membrane permease. In the cytosol, haem is held by the soluble protein HemS [1,2,3].

HemS purifies red from *E. coli*, has a soret peak at 412 nm and binds haemin in vitro in a pH- and buffer-dependent manner. Homologues of HemS can only be found in the phylum of the Proteobacteria, with a sequence identity greater than 30%. Sequence alignments show three conserved histidine and one conserved methionine residues which might be involved in haem-iron coordination. Since tertiary structure predictions showed no significant similarity to any known structure, HemS could adopt a novel fold.

Feraldo-Gomez J., Sansom M., *Nat. Rev. Mol. Cell. Biol.*, 2003, 4, 105-116.
Stojilikovic I., Hantke K., *Mol. Microbiol.*, 1994, 13, 719-732.
Wilks A., *Arch. Biochem. Biophys.*, 2001, 387, 137-142.

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