



Kemijski inštitut
Ljubljana
Slovenija

National
Institute of Chemistry
Slovenia

<http://www.ki.si>

VABILO NA INŠTITUTSKO PREDAVANJE / INVITATION TO THE INSTITUTE LECTURE

Prof. Dr. Muriel DELEPIERRE

Unité de RMN des Biomolécules CNRS URA 2185,
Institut Pasteur, Paris

Petek/ Friday, 20. 11. 2009, ob / at 13:00

Velika predavalnica Kemijskega inštituta / Lecture Hall at the
National Institute of Chemistry; Hajdrihova 19, Ljubljana

The HasA_{sm} bacterial hemophore

Povzetek / Abstract

Heme transport systems in bacteria are required and might be potential target for antibacterial drugs. The heme acquisition system, Has, exists in pathogenic as well as in opportunistic bacteria but only for the latter one extensive studies have been conducted, constituting as such a model system. The outer membrane receptor HasR, the central component of this system, functions in synergy with a secreted high affinity heme binding protein, the hemophore HasA. HasA extracts heme from host hemoproteins and returns it to HasR. Then, the energy given by a protein complex of the inner membrane is used to allow heme entrance across the bacterial membrane and to eject the empty hemophore from the receptor. The hemophore plays a dual function both in heme scavenging and transfer to the receptor and as an initiator of a regulatory cascade controlling gene expression *via* its fixation to the receptor in the presence of heme. Reconstitution of this heme acquisition system in *E. coli*, overexpression and purification of its various components have allowed us to obtain sufficient amount of protein to perform NMR and biophysical studies to analyse at the molecular level the different steps of heme acquisition by HasR.

Presentation will describe this transport system and the work achieved over the years to understand all molecular mechanisms involved in this process from the hemophore secretion, to heme delivery to the cell via the heme uptake and release to the outer membrane receptor using various biophysical approaches. Attention will be drawn on the complex formed between the membrane receptor HasR (98 kDa) and its two ligands, heme and HasA hemophore (19kDa). CRINEPT-TROSY NMR experiments in DPC micelles used to obtain information on the intermediate HasA-HasR complex indicate that a stable protein-protein adduct is formed in the presence of heme or not. The spectral fingerprint shows that: *i)* upon complex formation the heme group is readily transferred from holoHasA to HasR and *ii)* the surface contact area of HasA is independent of the presence of the heme and involves loop L1, loop L2, and the β 2- β 6 strands. This study represents the first structural characterization of the HasA-HasR complex.

Vljudno vabljeni! / Kindly invited!

Info: prof. dr. Janez Plavec; janez.plavec@ki.si