Poster Sessions

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Recognition of an unusual peroxisomal targeting signal 1 by the import receptor Pex5p

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The structure of the peroxisomal receptor Pex5p in the presence of a small model cargo revealed a large conformational change of the receptor upon cargo binding (Stanley et al., 2006). It, however, remained unknown whether the binding was cargo-specific and only indirect methods were applicable to test cargo activity during the translocation process. In order to investigate whether the previously observed type of cargo binding is generally applicable, we have determined the structure of Pex5p in complex with alanine-glyoxylate aminotransferase (AGT). The complex reveals how the unusual C-terminal KKL receptor recognition motif can be accommodated within the previously characterized central binding cavity. The present structure, similarly to the Pex5p-mSCP2 complex, reveals a secondary interaction site. From the receptor side the motif that participates in the interaction is the very same than the one in the Pex5p-mSCP2 structure. A common feature of all the available Pex5p crystal structures is that one of the seven TPR repeats of the receptor (TPR4) is not visible and thus can be considered as a highly flexible part of the molecule. Since most TPR proteins participate in various interactions it would not be surprising if the TPR4 segment was serving as an interaction site and stabilized by a binding partner in a later step of peroxisomal translocation. Important to note that TPR4 and the secondary binding motif are located on the opposite sides of the receptor. It is intriguing to hypothesize that secondary interactions are playing a role in the correct orientation of the cargo to ensure the accessibility of the TPR4 region during translocation process. Our structural and biochemical data also consistently show that AGT remains fully active when bound to the receptor.

Keywords: peroxisome, transport, Pex5p

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Crystal structure of L-CKS from *Haemophilus influenzae* in complex with KDO

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The enzyme 3-deoxy-manno-octulosonate cytidylyltransferase (CMP-KDO synthetase; CKS) catalyzes the activation of 3-deoxy-D-manno-octulosonate (or 2-keto-3-deoxy-manno-octonic acid, KDO) by forming L-CKS. In order to determine the structure of L-CKS from *H. influenzae*, we have crystallized it by hanging drop vapour-diffusion method at 296 K. The crystal of L-CKS is orthorhombic, belonging to the space group *P2_12_2_1*, with unit cell parameters of \( a = 48.42, b = 82.61, c = 115.71 \) Å. The presence of two monomers in the asymmetric unit gives a reasonable *V*_m of 2.05 Å³ Da⁻¹, with a solvent content of 40.0%. We determined the crystal structure of L-CKS from *H. influenzae* in complex with KDO at 2.30 Å resolution by the multiwavelength anomalous diffraction method. The overall protein structure is similar to that of K-CKS from *E. coli*. The C-terminal alpha-helix (Ala230-Asn254) of monomer A has a unique conformation. The structure of L-CKS from *H. influenzae* in complex with KDO will be useful in structure-based inhibitor design.


Keywords: antibacterial target, CKS, KDO

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Structure and function of the human histone chaperone C1A complexed with the bromodomain from TFIIID

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Histone modifications frequently function as a mark to induce nucleosome structure changes in a site-specific manner. Although many domains that specifically recognize histone modification have been identified, the molecular mechanism of the change in the nucleosome structure induced by histone modification remains elusive. We have therefore studied the functional interaction between the histone chaperone C1A, which has histone-(H3-H4)-tetramer disrupting activity, and an acetylated histone-recognizing domain of the TFIIID bromodomain. We have performed an X-ray crystallographic analysis and biochemical studies of the C1A-bromodomain complex to determine the structure and to understand how the complex is formed. The C1A-bromodomain complex is a protein-protein interaction governed by a high-affinity interaction between the bromodomain and a coiled-coil domain of C1A. In the complex, the bromodomain and Coa11 domains of C1A are associated with each other, and the coiled-coil domain of C1A is not associated with the Coa11 domains. Our results provide insights into the molecular mechanism of nucleosome structure changes induced by histone modifications.

Keywords: antibacterial target, CKS, KDO