MS10-P7 **Structural details for the disassembly of the AAA-ATPase VCP/p97 by ASPL**
Yvette Roske,[a] Anup Arumughan,[a] Erich Wanker,[a] Udo Heinemann,[a,b] [a]*Max-Delbrück-Centrum for Molecular Medicine, Robert-Rössle-Straße 10, 13125 Berlin, Germany,* [b]*Institute for Chemistry and Biochemistry, Freie Universität Berlin, 14195 Berlin, Germany*
E-mail: yroske@mdc-berlin.de

VCP/p97 is an essential multifunctional AAA+ ATPase interacting with a variety of adaptor proteins to perform diverse cellular functions. Previous studies indicate that direct binding of ubiquitin regulatory-X (UBX) domain-containing proteins control VCP activity in a spatio-temporal manner. However, the molecular details of how UBX proteins specifically regulate VCP function are poorly understood. Here, we show that the human UBX protein ASPL (alveolar soft-part sarcoma locus) associates with VCP and disassembles VCP hexamers into highly stable VCP:ASPL heterotetramers. The crystal structure of VCP bound to a C-terminal fragment of ASPL revealed that peptide regions around the canonical UBX domain adopt a unique helical lariat structure which wraps around the N-terminal domain of VCP and results in the disruption of inter-protomer interactions of the VCP hexamer. The VCP-D2 domain undergoes a dramatic domain movement, facilitating the formation of the VCP:ASPL heterotetramer and masking residues critical for VCP hexamer reassembly. Site-directed mutagenesis of residues either mediating VCP:ASPL contacts or stabilizing the VCP:ASPL heterotetramer abrogated the disassociation of VCP hexamers in vitro and in vivo.

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MS10-P8 **Structural and Functional Insights into *Mycobacterium tuberculosis* and *Mycobacterium smegmatis* Enhanced intracellular survival protein.**
Hye-Jin Yoon, Kyoung Hoon Kim, Doo Ri An, Ji Young Yoon, Hyoun Sook Kim, Ha Na Im, Jieun Kim, Se Won Suh, *Seoul National University, Korea*
E-mail: yoonhj@snu.ac.kr

Enhanced intracellular survival protein (Eis), a secreted protein encoded by the Rv2416c gene of *M. tuberculosis*, enhances intracellular survival of *M. smegmatis* in macrophages. It modulates the host immune responses by suppressing macrophage autophagy, inflammation, and cell death through the inhibition of reactive oxygen species (ROS) generation. Its GCN5-related N-acetyltransferase (GNAT) domain at the N-terminus is essential for the regulation of ROS generation and proinflammatory responses. It is also capable of acetylating kanamycin to confer resistance. To provide insights into its role in pathogenesis, we have determined the crystal structure of *M. tuberculosis* Eis. It is a homo-hexamer of 32 symmetry and each subunit comprises three domains. Domain 1 possesses the GNAT fold. Unexpectedly, domain 2 is also folded into the GNAT structure, while domain 3 structurally resembles the sterol carrier protein-2 domains with a hydrophobic cavity. Either acetyl CoA or CoA is observed to be bound to domain 1 only in the crystal, implying a functional difference between *M. tuberculosis* Eis domain 1 and domain 2. We have also confirmed that *M. tuberculosis* Eis is active as an N-acetyltransferase. Mutagenesis of Tyr132 indicates that the catalytic activity resides in domain 1. In addition, we have also determined the crystal structure of the Eis protein from *M. smegmatis*, as a complex with CoA, which is bound to domain 1 only.

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