Poster Presentation

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Structural basis of antibacterial peptide self-immunity by ABC transporters

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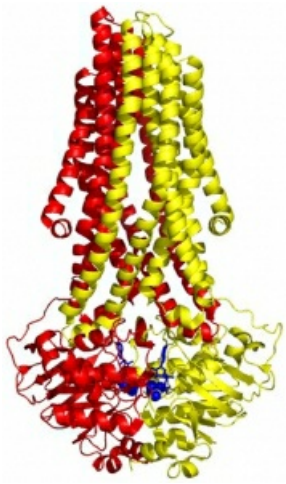
Bacteria under nutrient starvation secrete a class of toxic peptides called microcins. One such example is the microcin MccJ25 which can be exported using the ABC transporter McjD. Release of MccJ25 confers self-immunity to the producer strain, whilst uptake by neighbouring bacterial cells leads to inhibition of RNA polymerase activity. Previously, the high resolution structure of nucleotide-bound McjD was elucidated in a novel conformation termed 'outward-occluded', providing insights into the export cycle. However, in order to better understand the mechanism for MccJ25 secretion, it is important to trap the transporter in different conformational states.

In this work, two new X-ray crystal structures of McjD have been determined in distinct conformational states. These structures comprise (a) apo McjD and (b) ADP-VO4 bound McjD, the latter which represents a high energy transition state intermediate in the export cycle. Predictive cysteine cross-linking verifies the new conformations can be sampled in the native cell membrane, whilst ligand accessibility studies of the McjD cavity reveal substrate interactions spanning the length of the binding pocket. Furthermore, transport assays in liposomes indicate that MccJ25 can outcompete the fluorescent drug Hoechst for McjD export in an ATP-dependent manner. Taken together, these results provide a mechanistic rationale for antibacterial peptide self-immunity in ABC exporters.
[1] Choudhury, H. G. et al. (2014). PNAS, 111, 9145-9150.



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