

Abstract No. yuan3

The Crystal Structure of the MJ0796 ATP-Binding Cassette: Implications for the Structural Consequences of ATP Hydrolysis in the Active Site of an ABC-Transporter

Y.R. Yuan, S. Blecker, O. Martsinkevich, L. Millen, P.J. Thomas, and J.F. Hunt (Columbia U.)

Beamline(s): X12C

The crystal structure of the MJ0796 ATP-binding cassette, a member of the o228 / LoID transporter family, has been determined with Mg-ADP bound at its active site. Comparing this structure to that of the ATP-bound form of the HisP ATP-binding cassette (Hong et al., 1998, Nature 396:703) shows a withdrawal of a phylogenetically-invariant glutamine residue from contact with the gamma-phosphate of ATP in the active site. This glutamine is located in a protein segment that links the rigid F1-type ATP-binding core of the enzyme to an ABC-transporter-specific alpha-helical subdomain that moves substantially away from the active site in the Mg-ADP-bound structure of MJ0796 compared to the ATP-bound structure of HisP. A similar conformational effect is observed in the Mg-ADP-bound structure of MJ1267 (Karpowich et al., Structure, in press), establishing the withdrawal of the glutamine and the coupled outward rotation of the alpha-helical subdomain as consistent consequences of gamma-phosphate release from the active site of the transporter. Considering this subdomain movement in the context of a leading model for the physiological dimer of cassettes present in ABC transporters indicates that it produces a modest mechanical change that is likely to play a role in facilitating nucleotide-exchange out of the ATPase active site. Finally, it is noteworthy that one of the intersubunit packing interactions in the MJ0796 crystal involves antiparallel beta-type hydrogen bonding interactions between the outermost beta-strands in the two core beta-sheets leading to their fusion into a single extended beta-sheet, a type of structural interaction that has been proposed to play a role in mediating the aggregation of beta-sheet-containing proteins.