Poster Presentation

MS110.P07

Visualizing ATP hydrolysis in a viral DNA-packaging molecular motor

L. Tang[1], H. Zhao[1], T. Christensen[1], Z. Lin[1], A. Lynn[1]

[1]*University of Kansas, Department of Molecular Biosciences, Lawrence, Kansas, USA*

Many DNA viruses encode powerful molecular machines to package viral genome into preformed protein shells. These DNA-packaging motors contain an ATPase module that converts the chemical reaction of ATP hydrolysis to physical motion of DNA. We previously determined the structures of the DNA-packaging motor gp2 of Shigella phage Sf6 in the apo form and in complex with ADP and ATP-gamma-S (Zhao et al, 2013, PNAS, 110, 8075). Here we report the structure of gp2 in complex with its substrate ATP at 2.0 Angstrom resolution. To our knowledge, this is the first time to capture, at high resolution, a precatalytic state for ASCE-superfamily ATPases, which include a large group of nucleic acid helicases and translocases involved in a broad range of cellular and viral processes. The structure reveals the precise architecture of the ATP-bound state of the motor immediately prior to catalysis. Comparison with structures of the apo and ADP-complexed forms unveils motions of the Walker A motif coupled with ATP and Mg2+ binding and ATP hydrolysis. In the Walker B motif, residue E118 undergoes a side chain conformational switching coupled with the ATP hydrolysis, whereas residue E119 locks residue R51 side chain to a conformation that is readily reachable to residue E118 side chain. Residue E121 in the Walker B motif deprotonates a water molecule, which acts as a nucleophile to attack the gamma-phosphorous, leading to ATP hydrolysis. The alpha-helix (residue G182-R194) in the linker domain undergoes a translational motion against the ATPase domain triggered by ATP hydrolysis, serving as a mechanism for translating the energy from the chemical reaction into physical movement of DNA. We further observed the time course of ATP hydrolysis by gp2 by determining structures of gp2:ATP complexes captured at various incubation time. These structures have made it possible to delineate, at atomic detail, the complete cycle of ATP hydrolysis of this viral DNA-packaging molecular motor.

Keywords: ATP hydrolysis, chemomechanical coupling, DNA packaging