I-4 13:00 - 13:40

The 3.0Å-resolution crystal structure of the HslVU peptidase-ATPase complex reveals an ATP-dependent proteolysis mechanism

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E. coli heat shock locus HslU ATPase and HslV peptidase form an ATP-dependent HslVU protease, a homologue of the eukaryotic 26S proteasome. ATP-dependent proteases are responsible for degradation of the majority of proteins in the cell. They degrade unstable regulatory protein factors, which provides the temporal control of many cellular processing, and also degrade abnormally folded proteins, which is essential for cellular maintenance.

We present the 3.0Å-resolution crystal structure of HslVU in the $U_6V_6V_6$ configuration. The bound dADP is in anti conformation. The nucleotide binding controls the HslU conformations in domain I as the putative binding sites for unfolding proteins and the central pore through which unfolded polypeptides would likely be translocated into HslV. The structure reveals a protein unfolding-coupled translocation mechanism for ATP-dependent proteases. The formation of HslVU involves extensive hydrophilic interactions. The binding of HslU to HslV opens its pores and induces its asymmetric changes in electrostatic potential, surface curvature, pore size, and peptidase active site.