P06-197

ATP-DRIVEN MOTIONS OF 70-KDA HEAT SHOCK PROTEINS (HSP70S): INSIGHTS INTO STRUCTURAL DYNAMICS OF THE HSP70 POWER STROKE

Yi-Wei Chang,[a,b] Chung Wang,[a] and Chwan-Deng Hsiao[a]

[a]*Institute of Molecular Biology, Academia Sinica, Taipei, 11529, Taiwan;* [b]*Institute of Bioinformatics and Structural Biology, National Tsing Hua University, Hsinchu, 300, Taiwan*

The 70-kDa heat shock proteins (Hsp70s) are interspecific highly conserved molecular chaperones which participate in many crucial cellular functions, such as promoting the correct folding of nascent or stress-denatured polypeptides, assisting the protein translocation across membranes, and helping the assembly/disassembly of protein complexes.. Under particular control by the J-domain ATPase activating proteins and nucleotide exchange factors (NEFs), Hsp70s process their substrates in ATP-driven cycles. Previous studies clearly defined that Hsp70 protein can be distributed into two major functional domains, the NH2-terminal nucleotide-binding domain (NBD) and the COOH-terminal substrate-binding domain (SBD). To date, the ATP dependent allosterically regulating mechanism between these two domains has been long explored. However, precise structural understanding of the interdomain communication during ATPase cycle is still limited. In this report, we have determined the X-ray structures of ATP form intact Hsp70 chaperone proteins in various species, including the DnaK in eubacterium *Geobacillus kaustophilus HTA426* and the 70-kDa heat shock cognate protein (Hsc70) in mammalian *Rattus norvegicus*. Together with the result of detecting the solvent accessibility of a Trp reporter on the domain-domain interface, the structures reveal typical domain releasing behaviors of Hsp70s upon ATP binding and hydrolysis. This is in good agreement with previous studies that the hydrolysis of ATP may drives large domain movement of SBD related to NBD and provides power to allow Hsp70s serving as motors in processes such as protein translocation trough transport channels. Furthermore, the insertion of the hydrophobic linker region of gkDnaK into another crystallographic symmetry molecule's substrate binding pocket suggests a characteristic cooperative mechanism of Hsp70s. These important findings demonstrate exciting insights into structural dynamics of Hsp70 family proteins during chaperone cycles.