Structural basis for the teleost HSP60 chaperonin revealed the ring-association mechanism

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Abstract

Sixty-kDa heat shock proteins (HSP60) is one member of HSPs families, have been known that plays a chaperone role in mitochondria. Several studies have revealed that HSP60 are assembled from monomers to single-ringed heptamers, and two of which can associate to form a football-shaped tetradecamer for chaperone activity. In addition, HSP60 have been identified at the cell surface and extracellular medium and acts as a chemoattractant of the immune responses. It also reported the extracellular HSP60 promote cell proliferation and regeneration in marine teleost fish. To study the mechanism behind the multiple functions of HSP60 at different locations, we aimed to study its biochemical activity and multiple conformational structures. Here, we successfully produced the recombinant protein of *Epinephelus coioides* HSP60 (*Ec*HSP60) and determined the crystal structure of the monomeric *Ec*HSP60 at 3.4 Å resolution. The monomeric structure showed that the apical domain of *Ec*HSP60 are highly flexible before oligomeric assembling. In addition, we also found a mutant-type *Ec*Hsp60 that can form a stable heptameric single-ring conformation in the absence of co-chaperonin and nucleotide. The single-ring structure of the heptameric *Ec*HSP60 was also solved at 3.5 Å resolution and showed a unique ring-ring association without nucleotide binding. It has confirmed both of two forms to be states of their normal chaperon activity in mitochondria. Otherwise, we also investigate their ATPase and chaperone activity to compare the detailed difference between two types. Taken together, these data may provide insight into the detailed mechanism of extramitochondrial HSP60.

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