Quick guide

Chaperonins

R. John Ellis

What are they? The chaperonins are one family of 'molecular chaperone', a class of proteins that assist in correct protein assembly. As their name suggests, molecular chaperones are there to ensure the right molecules meet and that nothing untoward happens when they do. The chaperonins themselves fall into two subfamilies: the GroE subfamily (or Group I chaperonins) and the TCP-1 subfamily (or Group II chaperonins).

Where are they found? Everywhere. The GroE subfamily members occur in mitochondria, chloroplasts and other plastids, and in the Bacteria. TCP-1 subfamily members occur in the eukaryotic cytosol and in the Archaea. Chaperonins aren't easy to spot by their names alone, which include: bacterial common antigen, 65 kDa antigen, Hsp60, Hsp10, HuCha60, mitonin, Rubisco subunit binding protein, thermosome and thermophilic factor 55.

How do they work? After a period of intense debate, there is general agreement that the chaperonins function as molecular 'test tubes' (called Anfinsen, or folding, cages) that prevent the aggregation of certain newly synthesized or stress-denatured protein chains. They also increase the apparent rate of folding of some proteins.

Does protein aggregation matter? Yes. Aggregation is a severe biological problem caused by the high concentrations of proteins in the cell. Chaperonins provide one way of preventing aggregation during the protein folding process.

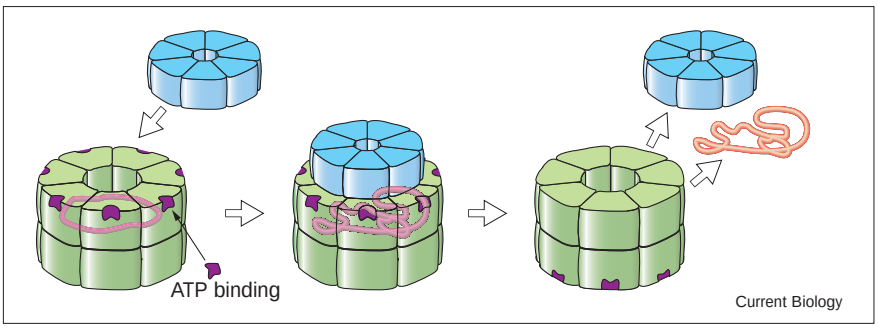
What is an Anfinsen cage made of? Both chaperonin subfamilies consist of a subunit of about 60 kDa, generically termed chaperonin 60. All types of chaperonin 60 make up a large oligomeric structure (called GroEL in *Escherichia coli*) consisting of two stacked rings of 60 kDa subunits. Each ring contains a central 'cage' in which a partially folded protein chain can bind. The GroE subfamily also contains a chaperonin 10 subunit, seven of which form a single oligomeric ring (called GroES in *E. coli*) that binds to one or both ends of the chaperonin 60 oligomer (see Figure). Binding of GroES to GroEL results in conformational changes that enlarge the central cage so that it can accommodate partially folded proteins of up to about 70 kDa in size.

They first came to prominence ... in 1988, when Sean Hemmingsen spotted the sequence similarity between the Rubisco subunit binding protein and GroEL, and proposed a new family of molecular chaperones. Chaperonins peaked around 1996, when the Anfinsen cage model, after surviving some initial ridicule, was agreed in outline. Chaperonins are now respectable and starting to appear in standard student texts.

What don't we know about them? Plenty. Besides the need for further details of their function in protein folding, there are indications of chaperonin involvement in other processes such as the immune response, cytokine production, recovery from stress and mRNA degradation.

Do say ... "Don't leave home without one." Abolition of chaperonin function in *E. coli* results in protein aggregation followed by cell death.

Don't say ... "Aren't they called 'molecular chaperonins'?" This is a nonsense term still seen in some respectable journals and is no more sensible than the term 'molecular immunoglobulin'.



The Anfinsen cage binds and releases newly synthesized polypeptides in an ATP-dependent cycle. A single partially folded protein chain (pink) binds inside one chaperonin 60 cage (green), which is then enlarged and closed by the binding of chaperonin 10 (blue), which acts as a 'bung' for the molecular 'test tube'. The binding of chaperonin 10 and ATP (purple) releases the chain into the cage, where it has about 15 seconds (at 23°C) to continue to fold, this time being determined by the rate of ATP hydrolysis. The unbinding of chaperonin 10 releases the more folded chain into the cytoplasm with a reduced risk of it aggregating with similar partially folded chains.

Where can I find out more?

Ditzel L, Lowe J, Stock D, Stetter K-O, Huber H, Huber R, Steinbacher S: Crystal structure of the thermosome, the archaeal chaperonin and homolog of CCT. *Cell* 1998, 93:125-138.

Ellis RJ (Ed.): *The Chaperonins*. San Diego: Academic Press Inc; 1996.

Ellis RJ, Hartl FU: Principles of protein folding in the cellular environment. *Curr Opin Struct Biol* 1999, 9:102-110.

Hemmingsen SM, Woolford C, van der Vies SM, Tilly K, Dennis DT, Georgopoulos GC, Hendrix RW, Ellis RJ: Homologous plant and bacterial proteins chaperone oligomeric protein assembly. *Nature* 1988, 333:330-334.

Xu Z, Horwich AL, Sigler P: The crystal structure of the asymmetric GroEL–GroES–(ADP)7 chaperonin complex. *Nature* 1997, 388:741-750.

Address: Department of Biological Sciences, University of Warwick, Coventry, CV4 7AL, UK.