Chaperon in Protein synthesize

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Protein is one of the most important molecules in biology and it is composed of 20 kinds of amino acid residues which are coded in the sequence of DNA. [1] A codon which is composed of three-nucleotide sequence can be translated into one kind of amino acid. However, we know that protein is folded in the 3-D space and it cannot has the biological function unless the sequence of amino acid residue is folded properly. Many artifical protein in the same amino acid residues sequence does not has the biological activity because it has different folding form from the native state.[1] How to make it folded in a right way?

Firstly, let us review how the protein is made in the cell. It can be divided into five step:[2]

1. Genes(DNA) are transcribed into RNA by the enzyme RNA polymerase
2. RNA transcripts are subjected to post-transcriptional modification and control
3. mRNA molecules are translated by ribosomes (rRNA + ribosomal proteins) which match the 3-base codons of the mRNA to the 3-base anticodons of the appropriate tRNA molecules
4. Newly synthesized proteins are often modified after translation (post-translation)
   (a) proteins undergo a final conformation adaptation in conjunction with **chaperon** proteins
   (b) soluble proteins may have sugars added
   (c) ...
5. the protein carries out its function

Chaperon plays a great role in step 4. It has been studied with several kinds of techniques.

Chaperonins are found in all organisms and symbiotic organelles.[3] The structures of some chaperon has been studied with the electron microscopy reconstructions [4] and small-angle neutron scattering[5]. They are large double ring structures consisting of 14, 16 or 18 subunits and mediate protein folding

in an ATP-dependent reaction.[3] Sometimes, the newly polypeptides fold spontaneously. And sometimes they fold with the help of chaperonins. It has been suggested that the two chaperone systems form a lateral network of cooperating proteins. Then, the network interact with newly synthesized polypeprides and help it fold correctly.

The group of Frydman has studied the function of chaperon *in vitro* with photoactivatable crosslinkers and fluorescent probes[6]. Double-ring chaperonin complexes are key mediators of cellular protein folding. Their essential function results from the cytosolic conditions of high protein concentration and volume occupancy, which present an unfavorable environment for spontaneous protein folding. Based on their ability to bind unfolded polypeptides within their ring cavities, chaperonins prevent off-pathway reactions and promote productive protein folding to the native state in an ATP-dependent manner. [6]

In addition to their role in folding, there is evidence that chaperones participate in the degradation of damaged or misfolded proteins. [6]

A approach involves pulse-chase protocols followed by the stabilization and analysis of the complexes between folding substrates and endogenous chaperones can be used in experiments *in vivo*. With this technique, the group of Frydman [6] has found that most newly synthesized polypeptides reach the native state spotanaeously without the assistance of the chaperone they used *in vitro*. But they weren't sure about whether there were some new uncharacterized chaperone responsible for it or not. More studies *in vivo* with biochemical approaches are necessary.

We should notice that these results are got mostly *in vitro* and with only a few substates. The generality of conclusions based on these experiments remains to be established. And furthermore, I am quite curious why the polypeprides can fold spontaneously. The native state of protein chain is not the thermal state with the lowest energy. Then how most of polypeprides fold to that state and stay in that state? It also need more study.

References

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