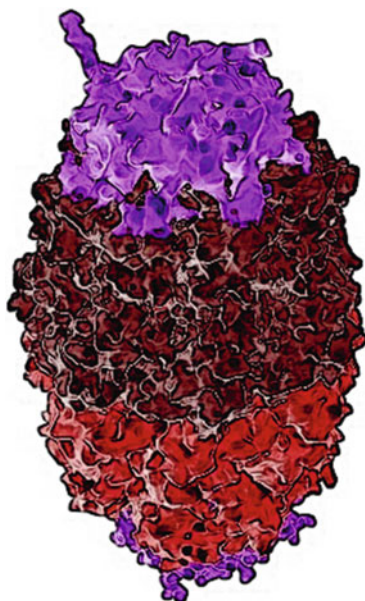


Preface

A still highly fascinating and perplexing scientific riddle is termed the protein folding problem: how do proteins fold into their three-dimensional structure? The molecular basis for life on earth has been greatly illuminated by breakthroughs in science in the last 70 years. We now understand to a large degree the basics of how living organisms replicate themselves, how the different types of organisms have evolved and still evolve, and also what limits and endangers the lives of organisms. We even have some clues to the human-centered enigma of aging and the limited lifespan of organisms. It is strange recapitulating that less than 100 years ago it was discovered that chromosomes are the carriers of heredity and that DNA was identified to carry the genetic information during my lifetime. While the basics of genetics are now well understood and are part of school education there are still enigmatic hurdles to capture the basis of the very pivotal last step of realization of genetic information: folding of polypeptide chains to the wide variety of three-dimensional structures that form the nanomachines and nano-devices that in biological systems perform most of the work and confer the dynamics to adapt to the environment. We know the basic 20 amino acid building blocks of polypeptides and can determine the structure of folded proteins—the nanomachines—by X-ray diffraction and a couple of other methods but we still lack a deeper understanding of how these polypeptide chains, in the short time period they get in a cellular environment, acquire the structure which confers function and renders them able to escape the degradation “police”. This statement may sound overexaggerated given the large body of research and knowledge on protein folding and unfolding, on the forces determining the interactions that guide and stabilize protein structures, and the many in vitro folding and computer simulation studies of protein folding that have been accumulated in the last 50 years. However, we have now known for more than 50 years that the sequence of amino acids, at least in principle, carries all the information necessary for a protein to fold into its structure. A bunch of proteins fold correctly in the test tube. We are still puzzled that this also happens in a living cell where the conditions are very much less favorable than in the settings found to be necessary for folding in the test tube. Great enlightenment has come by the

discovery of molecular chaperones—proteins themselves that ‘assist’ folding in the crowded cellular environment where all kinds of physicochemical disturbances for protein folding prevail. A special class of molecular chaperones, the chaperonins, is the subject of this booklet. These proteins fulfill, by virtue of their special structural organization that leads to encapsulation of proteins undergoing folding in a secluded chamber, in principle the requirements for a protein structure casting machine that shapes proteins into their structure. However, it was soon clear that chaperonins and molecular chaperones in general are ‘just’ facilitators of protein folding that moderate the effects of cellular disturbances for folding and help to reverse misfolding but do not confer structural information. The angle of knowledge, research activity, and speculation arising from the studies of the chaperonins—with special emphasis on the human mitochondrial chaperonin—will be discussed in this volume, trying to communicate the fascination of this subject and describing the steps on the way to a deeper understanding of protein folding this can contribute.



The human Hsp60/Hsp10 complex. Snapshot based on pdb coordinates 4pj1

The Hsp60 Chaperonin

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