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Preface

Molecular chaperones and intracellular protein transport

It is now recognized that chaperones accompany proteins in all periods of their biogenesis, including synthesis, membrane translocation, folding, assembly, and disposal. How the common features of chaperones and other protein biogenesis factors are employed to assist these fundamentally different processes is topic of this issue.

One of the central dogmas of biology is that the information contained in the amino acid sequence of any protein is sufficient to allow for its spontaneous and autonomous folding. However, in a living cell, the situation is more complicated. Here, protein biogenesis does not start with a full-length, denatured protein but as soon as the ribosome has catalyzed the formation of the first few peptide bonds between individual amino acids. Specific interactions of nascent polypeptides occur already within the ribosomal polypeptide exit tunnel and these interactions can result in the induction of secondary structure within segments of the nascent polypeptide. In many cases folding should only proceed when a protein has reached its final destination. To that end, the first decision upon exit from the ribosomal tunnel is whether or not a protein should remain in the cytosol or should be delivered to one of the cellular compartments. Ribosome-associated protein biogenesis factors, many of which are chaperones, assist this sorting process. All proteins that do not remain in the cytosol have to be sorted into or across membranes. Translocation across membranes requires sophisticated protein translocation machineries, which consist of a core channel that allows for the passage of the polypeptide plus accessory subunits, which can differ depending on where exactly the translocated polypeptide should end up. A detailed understanding of the structure and dynamic composition of the different translocation machineries is a prerequisite to understand their function on a mechanistic level. While the basic process of membrane translocation or integration to any compartment follows similar principals, the machineries are not evolutionary conserved and a variety of different translocation mechanisms have developed. In many cases chaperones are involved in activity, driving translocation as motors fuelled by ATP hydrolysis, or by assisting the delivery of translocated proteins. In eukaryotic cells protein sorting is a major challenge because specific targeting routes for each of the compartments, as for example the mitochondria, the ER, the peroxisome, and the chloroplast have to be defined. A special case is also the assembly of large membrane complexes. Often membrane translocation requires an intimate coupling between translation and translocation machineries. Finally, many proteins not only have to be translocated across a membrane once, but shuttle, for example, in and out of the nucleus in a regulated manner. Once a protein has reached its destination it has to fold into its native structure. As all compartments of a cell are crowded with proteins and other macromolecules, displaying sticky surfaces, this can interfere with spontaneous protein folding and result in aggregation. Also, it is recently becoming more clear that many protein complexes are highly dynamic entities, which assemble and disassemble in a regulated manner, a process which again requires the action of chaperones. Finally, even correctly folded and assembled proteins have a limited life time because oxidative damage and other spontaneously occurring modifications render proteins non-functional or destabilize their native structure. Such defective proteins have to be disposed by degradation and in many cases this final step of protein biogenesis is assisted by chaperones.

This special issue of BBA-Molecular Cell research highlights recent advances of our understanding on molecular chaperones and their roles in protein folding, protein translocation and assembly. Moreover, since protein folding is tightly coupled to transport of polypeptides as well as cellular quality control processes, it aims to provide insight into our current knowledge of how proteins are transported across biological membranes and by which means malfolded proteins are recognized and removed. We are indebted to the colleagues who contributed their review articles to this issue, the colleagues that acted as reviewers and performed careful evaluation of the articles, and the editorial staff of the journal for their interest into the topic and their support during the preparation of this special issue.

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Dr. Sabine Rospert is Professor of Biochemistry and Molecular Biology at the Medical Faculty of the University of Freiburg. She received her PhD in Microbiology from the Philipps-University, Marburg in 1991. From 1992, Dr. Rospert worked as a PostDoc in the laboratory of Dr. Jeff Schatz at the Biocenter in Basel. In 1999, she moved to Halle/Saale to become an independent junior group leader at the Max Planck Research Unit "Enzymology of Protein Folding." In 2003, she accepted a professorship in Freiburg. Since 2005 she is a full professor focusing on the function of ribosome-bound protein biogenesis factors in eukaryotic cells.

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