Preface

The establishment that cells responded to stress by the induction of specific gene expression led to the identification, in the 1980s, of heat shock or cell stress proteins and the realisation that these proteins are involved in the folding, re-folding, and prevention of aggregation, of client proteins. Such protein-folding proteins are now known as molecular chaperones, with the term protein-folding catalysts (PFCs) being applied to proteins such as thioredoxin and peptidyl prolyl isomerases that involve an enzymic step in the protein folding mechanism. Initially, these proteins were thought to be exclusively intracellular. However, in 1988 evidence was presented for the secretion and uptake of Hsp70 proteins by cultured cells suggesting that at least one molecular chaperone underwent aberrant cellular trafficking. Some years later the aberrant cytoplasmic and cell surface location of the mitochondrial Hsp60 protein began to be defined. These finding suggested a potentially wider remit for the function of molecular chaperones within the cell than had previously been considered.

A growing number of reports in the 1990s established that a number of molecular chaperones and PFCs had cell signalling actions when applied externally to cultured cells, and this realisation has prompted a rapid expansion of work in this field. Despite being dogged by suggestions that the biological and immunological properties of extracellular stress proteins results from contaminants in the preparations used, it is now becoming accepted that cell stress proteins can indeed be released from cells and that, in the extracellular environment, they elicit a number of regulatory functions. This line of work has culminated in the finding that a number of molecular chaperones and PFCs are present in the circulation and that levels of these proteins may reflect tissue and organismal pathology.

Since the beginning of the twenty-first century there has been a rapid increase in our understanding of the cellular trafficking mechanisms of molecular chaperones both in eukaryotes and in prokaryotes. In the former, molecular chaperone trafficking can occur between the various cellular compartments, with concomitant movement of other proteins and in some instances at least, the release of molecular chaperones from cells. In bacteria, molecular chaperones are involved in the trafficking of other proteins and are themselves released into the external milieu. There is an increasing appreciation of the role of molecular chaperones and PFCs in the interplay between bacteria and the cells of their hosts and this is now an important area of research for understanding the mechanisms of infectious diseases.

This volume brings together experts in the biochemistry, cellular biology, immunology and molecular biology of molecular chaperones and PFCs with a focus on the mechanisms of cellular trafficking of these proteins and the role of these variegated trafficking mechanisms in both human and animal health and disease. To guide readers who may be unfamiliar with this, now voluminous, field of research, this book starts with a number of introductory chapters which provide a historical background to the key aspects of molecular chaperone biology. The second section focuses on intracellular trafficking of molecular chaperones and their interactions with different cellular compartments and cellular components and the roles that such trafficking plays in the maintenance of cell health and in controlling the death of the cell. The third section deals with the roles played by molecular chaperones in the control of selected receptors that can play roles in immunological homeostasis. Section 4 deals with the unexpected finding that molecular chaperones can actually exist in the extracellular milieu and the consequences of such release for health and disease.

This book should be of interest to a wide range of biomedical scientists.

Brian Henderson
A. Graham Pockley

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Henderson, B.; Pockley, A.G. (Eds.)

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