PREFACE

This book is concerned with a group of proteins, denoted small Heat shock (or stress) proteins (sHsps), that play major roles in human diseases. sHsps, which are denoted so because of their small molecular masses (15 to 30 kDa), belong to the family of Heat shock proteins (Hsps) originally characterized in cells exposed to heat shock. Nowdays, Hsps are also denoted stress proteins consequently of the large spectrum of conditions or agents that induce or stimulate their expression in virtually all living organisms, including procaryots. It is now well established that Hsps expression in response to stress results of cellular alterations in protein folding and membrane integrity. In addition, Hsps, which encompass a large number of related proteins, are also constitutively expressed in several types of cells, particularly those in pathological conditions. The family of human small stress proteins contains ten (or eleven, see table below) members sharing a C-terminal structural domain, refered as the α-crystallin domain, first detected in the mammalian lens protein α-crystallin. Up until recently, these proteins were designated as HspXX, where XX corresponded to the first digits of the apparent molecular weights with the exception of αA- and αB-crystallin which were called by their own name. A new nomenclature, presented below, has been proposed to better characterize human sHsps: the HspB1 to HspB10 terminology. HspB1 refers to Hsp27, one of the first sHsps to be characterized. Only HspB1, HspB4, HspB5, HspB8 plus the less conserved Hsp16.2 polypeptide share an ATP-independent chaperone « holdase » activity that favors their interaction, through dynamic and complex modulations of their hetero- and homo-oligomerization/phosphorylation profiles, with misfolded polypeptides. By doing so, sHsps attenuate the irreversible and deleterious aggregation of stress-altered polypeptides. The chaperone activity of sHsps is therefore different from that of the ATP-dependent « foldase » chaperones (Hsp70, Hsp90 and Hsp60) aimed at refolding stress-induced misfolded polypeptides. However, the holdase and foldase chaperones are part of a coordinated protein refolding network that provide cells with a better resistance to numerous different types of aggressions, such as those that can be encountered in several human diseases.

The aim of this book is therefore to bring together chapters written by top scientific leaders to give a comprehensive view of the fast emerging contrasting roles played by sHsps in human diseases as diverses as neurodegenerations, myopathies, cardiomyopathies, cataracts and cancers. For example, sHsps attenuate stress- or pathologically-induced protein aggregation and can therefore be beneficial to counteract pathologies induced by aggregation-prone proteins (i.e Alzheimer, Parkinson, Huntington). On the other hand, the protective

activity of sHsps, particularly against apoptosis, can be deleterious for cancer patients as it can protect cells that should normally be eliminated.

After an introductory chapter providing an overview of these proteins, the book is divided in four main sections each of which deals with one important aspect of sHsps. The first section contains chapters that deals with the beneficial protecting effects mediated by sHsps in diseases related to protein conformation, cytoskeleton, redox state and autophagy as well as their role in protecting neuronal and cardiac cells. The second section of this book deals with the pathological state and amyloid structures induced by mutations in sHsps genes. Pathologies such as cataract, myopathies, cardiopathies and neuropathies are described. In contrast to the preceding sections, the third one contains chapters describing the deleterious effect of the protective activity of sHsps against apoptosis; a phenomenon which leads to tumorigenesis and tumor expansion. The newly described but distantly related Hsp16.2 polypeptide expressed in tumor cells fits well in this section. Finally, the use of sHsp as prognosis cancer markers is discussed. The last section of the book describes different therapeutic approaches aimed at either inhibiting sHsps expression or modulating their chaperone activity by specific peptides. The last chapter summarizes these approaches and points to the complex protective role of sHsps: beneficial when it protects cells that should not die (i.e neurons, cardiomyocytes) and deleterious by protecting cells that should die, such as cancer cells. Hence, future therapeutic drugs will have to be carefully designed to overcome these problems.

Overall, it is hoped that this book will provide a comprehensive review of the many features the small stress proteins and their dual and contrasting role play in human pathologies. We are most grateful to all authors who contributed so efficiently to this book and to the Editorial board of Nova Sciences for its support and strong interest.

Stéphanie Simon and André-Patrick Arrigo
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