**NEUROSCIENCE
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UNIT**

Heat Shock Proteins in Neural Cells

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*To my mother Elisabeth, and my brother,
Thomas Landsberg, whose thoughts cannot fly any more*

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PREFACE

Heat shock proteins (HSPs), also called stress proteins, are not only induced in response to elevated temperatures, but also as a result of various stress situations, including environmental strains, viral infection, ischemia, anoxia and oxidative stress. These stress situations trigger cellular defence mechanisms that act as an emergency system capable of combatting the toxic consequences due to the accumulation of misfolded proteins.

Heat shock proteins are involved in many physiological processes, including development and differentiation, organisation of the cytoarchitecture by binding to cytoskeletal elements and regulation of the balance between cell death and survival. Many heat shock proteins work as molecular chaperones. In this role, they contribute to *in vivo* protein folding and prevent nonproductive interactions with other proteins and cellular components. In recent years it has been found that the chaperone system and the proteolytic machinery work closely together, and that proteasomal inhibition causes the upregulation of stress proteins. Impairment of the proteasomal machinery and chaperone functions lead to protein damage, which contributes to neurodegenerative disorders and to the aging process.

The brain is the most sensitive target for traumatic events. Many disorders of the nervous system are caused by intracellular or extracellular deposits of protein aggregates. Stress responses in the brain, as monitored by the induction of heat shock proteins, occur in distinct regions and affect nerve cells and glia in a cell-type-specific manner. Hence, stress proteins may serve as biomarkers and provide diagnostic tools that allow us to identify stress specificity and localize pathological processes. Their critical involvement during neurodegeneration in brain disorders, such as Alzheimer's, Parkinson's and Huntington's diseases, and multiple sclerosis, makes them promising candidates for therapeutic intervention and drug development.

The authors of this book address the role of heat shock proteins and cellular stress responses in the brain, with a major focus on nerve cells and glia, namely oligodendrocytes and astrocytes. Chapter 1 summarizes the classification and functional roles of heat shock proteins which are particularly abundant in brain cells. The next chapters deal with the physiological functions of heat shock proteins in the regulation and maintenance of the cytoskeleton (Chapter 2), their role in the regulation of neuronal differentiation and development (Chapter 3), and cell death (Chapters 4 and 5). Chapter 4 discusses the specific antioxidant capacity of the small stress protein HSP32 (the heme oxygenase-1), a heat shock protein with enzymatic functions. This chapter also highlights acetylcarnitine, a compound with neuroprotective benefits. Chapter 5 concentrates on the role of heat shock proteins in the regulation of programmed cell death in association with neurodegenerative

disorders. In particular, the authors review their interference with apoptotic pathways and damage of the mitochondria, which play a key role during apoptosis. The following three chapters concentrate on heat shock proteins in neuropathological processes: Chapter 6 deals with the basic cellular role of the ubiquitin/proteasome pathway and its cooperation with the chaperone system, which is required to prevent the development of potentially toxic protein aggregates. Chapter 7 summarizes how stress proteins counteract common pathologies of “folding diseases” by reversing early synaptic and axonal abnormalities. Chapter 8 demonstrates the potential impact of certain families of heat shock proteins in multiple sclerosis, emphasizing their role in the generation of the immune response in more chronic phases of the disease process.

Research in the field of heat shock proteins is very active, and the authors of this book hope that their contributions will help neuroscientists bring together disparate data sets and develop new experimental strategies that will further elucidate the roles of HSPs in the nervous system during health and disease.

Christiane Richter-Landsberg

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