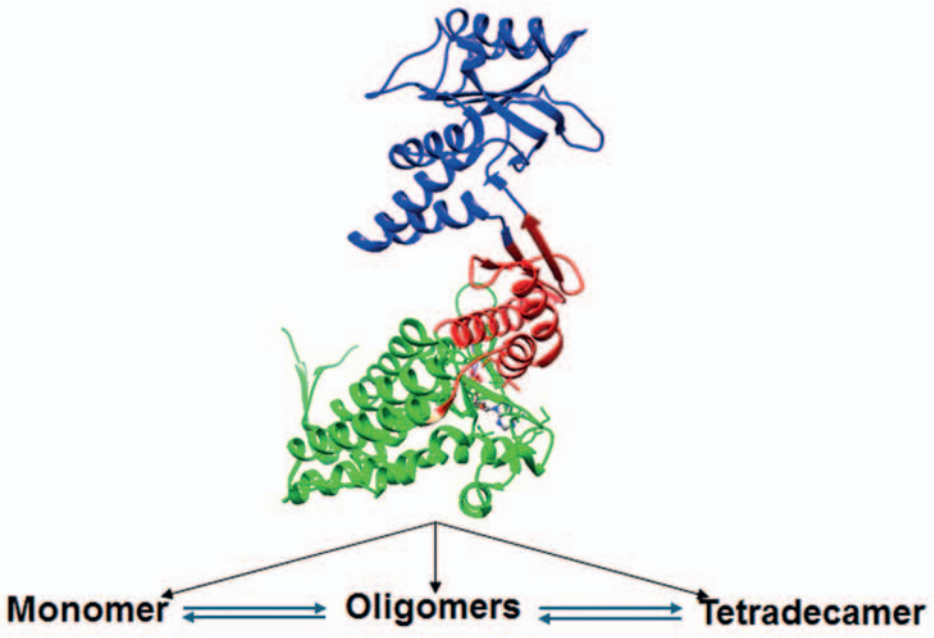
The multitasking molecular chaperone Hsp60

Structure, function, and impact on health and disease



Edited by
Francesco Cappello
Everly Conway de Macario
Alberto J. L. Macario

Preface

The Chaperone System (CS) is key to development, growth, and survival in the face of stress caused by all stressors in all life forms. It is a physiological system, most likely very ancient in evolution from its simplest primitive versions in the primeval unicellular organisms to the complexity found today in the most advanced multicellular eukaryotes, such as humans. In these, the CS is composed of molecular chaperones, chaperone cofactors, cochaperones, and chaperone interactors and receptors. The canonical functions of the CS pertain to the maintenance of protein homeostasis, and, in this, it interacts and collaborates with the ubiquitin proteasome system and the chaperone-mediated autophagy machinery. The CS also has noncanonical functions, for instance, those pertaining to inflammation, autoimmunity, carcinogenesis, and other pathophysiological processes, and, in these, its main interactor is the immune system. Although the CS is typically cytoprotective, key to molecular integrity of proteins and, thereby, to cell and organismal health, it may also play etiopathogenic roles in many diseases, the chaperonopathies. The chief components of the CS are the molecular chaperones, some of which are named heat shock protein (Hsp), and one of them is Hsp60, the central character of this book. Its canonical function in humans consists of maintaining protein homeostasis within mitochondria. Because of this, Hsp60 is essential for life, but if defective can cause serious diseases, the Hsp60 chaperonopathies. In addition, Hsp60 resides and functions outside mitochondria and outside cells and, therefore, its abnormalities may affect functions elsewhere. Thus, Hsp60 appears in a variety of locations and molecular forms, monomer, oligomer, and homotetradecamer. This book's main goal is to present research on Hsp60 functions and their abnormalities in Hsp60 chaperonopathies. These can be genetic or acquired, and both are amenable, at least in theory, to chaperonotherapy. This can be positive in cases of chaperonopathies by defect, in which a defective chaperone must be boosted, for example, using docking compounds, or replaced with the normal protein, or by providing the normal gene via genetic engineering. Instead, negative chaperonotherapy is indicated in chaperonopathies by excess or by mistake. In both instances, the pathogenic chaperone must be inhibited/blocked, or its gene silenced. In this book, the various aspects of Hsp60 chaperonopathies affecting human physiological systems, for example, digestive, cardiovascular, nervous, genitourinary, respiratory

systems, and so on, are described and discussed, including descriptions of molecular mechanisms, and clinical and pathological manifestations. In each case, the possible uses of Hsp60 as biomarker in diagnosis, prognostication, and patient monitoring are examined, as well as the potential of chaperonotherapy. An important objective is to present to healthcare professionals the field of chaperonology, focusing on the CS and its diseases caused by Hsp60 abnormalities, their clinical and pathological manifestations, diagnosis, and treatment. The field is emerging, and many questions are still unanswered, and, because of this, it is very attractive for the curious mind, for both the basic researcher who wants to discover new pathogenic pathways and their molecular players, and the practitioner, pathologist, or clinician, interested in understanding as yet unexplained cyto- and histopathological lesions and symptoms.

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Everly Conway de Macario, Alberto J. L. Macario,
Francesco Cappello
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Contents

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Edited by
Francesco Cappello [a,b]

Everly Conway de Macario [b,c]

Alberto J. L. Macario [b,c]

[a]Department of Biomedicine, Neuroscience and Advanced Diagnostics (BIND), University of Palermo, Palermo, Italy.
[b]Euro-Mediterranean Institute of Science and Technology (IEMEST), Palermo, Italy.
[c]Department of Microbiology and Immunology, School of Medicine, University of Maryland at Baltimore-Institute of Marine and Environmental Technology (IMET), Baltimore, MD, USA.

The multitasking molecular chaperone Hsp60: Structure, function, and impact on health and disease provides an overview of this key component of the Chaperone System (CS). Over the last several years, the importance of the CS as a physiological system has been brought to prominence and its roles in health and disease made clear. The molecular chaperones, including Hsp60, are the key components of the CS that are typically cytoprotective, but they can also be etiopathogenic factors, causing diseases named chaperonopathies. This book covers various areas of medicine in which Hsp60 chaperonopathies have been identified. Various chapters discuss the Hsp60 structure, localization, functions, and participation in disease mechanisms both genetic and acquired, focusing on humans but also presenting data obtained from pro- and eukaryotic experimental models. The main goal is to provide information accessible to all healthcare professionals in a way that can be understood by nonspecialists and that would stimulate clinical and pathological detection of Hsp60 chaperonopathies. Molecular mechanisms are briefly described with the purpose of illuminating roads toward accurate diagnosis, treatment, and patient monitoring. Consequently, the possibility of developing/applying chaperonotherapy centered on Hsp60, as a therapeutic tool or target, is analyzed in many sections of this book, across a variety of medical specialties.

This book is an invaluable reference for practitioners, researchers, and students in medicine, biology, molecular biology, biochemistry, biophysics, pharmacology, and related life sciences.

Key Features

- Discusses strategies for diagnosis, patient monitoring, and treatment of disorders in which Hsp60 plays a role and can be used as biomarker and therapeutic target or agent.
- Explains the fundamental biophysics, genetics, physiology, and pathogenicity of Hsp60.
- Explores the mechanisms involving Hsp60 abnormalities causing disease, including carcinogenesis, inflammation, autoimmunity, and neurodegenerative disorders.

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