


Small heat shock proteins operate as molecular chaperones in the mitochondrial intermembrane space

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Mitochondria are complex organelles with different compartments, each harbouring their own protein quality control factors. While chaperones of the mitochondrial matrix are well characterized, it is poorly understood which chaperones protect the mitochondrial intermembrane space. Here we show that cytosolic small heat shock proteins are imported under basal conditions into the mitochondrial intermembrane space, where they operate as molecular chaperones. Protein misfolding in the mitochondrial intermembrane space leads to increased recruitment of small heat shock proteins. Depletion of small heat shock proteins leads to mitochondrial swelling and reduced respiration, while aggregation of aggregation-prone substrates is countered in their presence. Charcot–Marie–Tooth disease-causing mutations disturb the mitochondrial function of HSPB1, potentially linking previously observed mitochondrial dysfunction in Charcot–Marie–Tooth type 2F to its role in the mitochondrial intermembrane space. Our results reveal that small heat shock proteins form a chaperone system that operates in the mitochondrial intermembrane space.

Mitochondria are composed of more than 1,100 proteins, of which the nuclear genome encodes more than 99% (refs. 1–3). Most mitochondrial proteins are therefore imported from the cytosol, and this poses a considerable burden on mitochondrial surveillance systems^{4,5}. The mitochondrial matrix is equipped with multiple chaperone systems, including mtHSP60 and mtHSP70 (refs. 1–6). However, classical

chaperones, like the Hsp70 and Hsp90 families, were not found in the mitochondrial intermembrane space (IMS)⁷.

The only IMS chaperones known so far are the small translocases of the inner mitochondrial membrane (TIMMs), CHCHD4 (Mia40 in yeast) and ClpB (Skl3 in yeast). The small TIMMs and Mia40/CHCHD4 protect, respectively, transmembrane and disulphide-rich proteins during

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The Biology Of Heat Shock Proteins And Molecular Chaperones

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The Biology Of Heat Shock Proteins And Molecular Chaperones:

The Biology of Heat Shock Proteins and Molecular Chaperones Richard I. Morimoto, Alfred Tissières, Costa Georgopoulos, 1994 Biology of Heat Shock Proteins and Molecular Chaperones ,1994 **Biology of Heat Shock Proteins and Molecular Chaperones** Cold Spring Harbor Laboratory, 1994 *Regulation of Heat Shock Protein Responses* Alexzander A A Asea, Punit Kaur, 2018-05-01 This books provides the most up to date reviews on current advances in our understanding of the regulation of heat shock protein responses Key basic scientists and clinical research laboratories from major universities academic medical centers and pharmaceutical companies around the world have contributed chapters that review present research activity and importantly project this field into the future For easy readability the book is sub divided into four sections including Section I HSP and Stress Responses Section II Chaperone Functions of HSP Section III HSP in Human Diseases Section IV Prognosis Diagnosis of HSP The book is a must read for researchers involved in biomedical research drug discovery and design to improve human health The Biology of Extracellular Molecular Chaperones Derek J. Chadwick, Jamie A. Goode, 2008-04-30 The heat shock or cell stress response was first identified in the polytene chromosomes of Drosophila This was later related to the appearance of novel proteins within stressed cells and the key signal stimulating this appearance was identified as the presence of unfolded proteins within the cell It is now known that this is a key mechanism enabling cells to survive a multitude of physical chemical and biological stresses Since the promulgation of the molecular chaperone concept as a general cellular function to control the process of correct protein folding a large number of molecular chaperones and protein folding catalysts have been identified and it has been recognized that not all molecular chaperones are stress proteins and vice versa The discovery of molecular chaperones as folding proteins went hand in hand with their recognition as potent immunogens in microbial infection It was subsequently shown that administration of molecular chaperones such as Hsp60 Hsp70 or Hsp90 could inhibit experimental autoimmune diseases and cancer More recently evidence has accumulated to show that certain molecular chaperones are also present on the surface of cells or in extracellular fluids A new paradigm is emerging at least some molecular chaperones are secreted proteins with pro or anti inflammatory actions regulating the immune response in human diseases such as coronary heart disease diabetes and rheumatoid arthritis In addition to having direct effects on cells molecular chaperones can bind peptides and present them to T cells to modulate immune responses This may be significant in the treatment of cancer This is the first book bringing leading researchers in this field together to review and discuss our current knowledge of cell stress response and molecular chaperones the changing paradigms of protein trafficking and function cell stress proteins as immunomodulators and pro and anti inflammatory signalling molecules the role of these proteins in various chronic diseases and their potential as preventative or therapeutic agents The Biology of Extracellular Molecular Chaperones is of particular interest to immunologists cell and molecular biologists microbiologists and virologists as well as clinical researchers working

in cardiology diabetes rheumatoid arthritis and other inflammatory diseases **Guidebook to Molecular Chaperones and Protein-Folding Catalysts** Mary-Jane Gething,1997-11-27 The precise shape of a protein is a crucial factor in its function How do proteins become folded into the right conformation Molecular chaperones and protein folding catalysts bind to developing polypeptides in the cytoplasm and ensure correct folding and transport This Guidebook catalogues the latest information on nearly 200 of these molecules including the important class of heat shock proteins each entry is written by leading researchers in the field The Biology of Heat Shock Proteins and Molecular Chaperones Richard I.

Morimoto,Alfred Tissières,Costa Georgopoulos,1994 Chaperones Stuart K. Calderwood,Thomas L. Prince,2023-08-04 This second edition volume expands on the previous edition with new discussions on the latest techniques used to study molecular chaperones and the stress response The chapters in this book cover such as analysis of the initiation and regulation of the stress response the role of heat shock protein 90 Hsp90 in gene expression through chromosome immunoprecipitation features of chaperone function and biology the emerging role of the extracellular HSPs and the use of chaperones as biomarkers Written in the highly successful Methods in Molecular Biology series format chapters include introductions to their respective topics lists of the necessary materials and reagents step by step readily reproducible laboratory protocols and tips on troubleshooting and avoiding known pitfalls Cutting edge and thorough Chaperones Methods and Protocols Second Edition is a valuable resource for all researchers who want to learn more about this interesting and developing field

The biology of heat shock proteins and molecular chaperones ,2002 **Heat Shock Proteins and Whole Body Adaptation to Extreme Environments** Michael B. Evgen'ev,David G. Garbuz,Olga G. Zatsepina,2014-10-24 For many years the authors have investigated the adaptive role of heat shock proteins HSPs in different animals including the representatives of homothermic and poikilothermic organisms that inhabit regions with contrasting thermal conditions This book will summarize the data accumulated in the course of these studies and describe the general molecular mechanisms underlying the adaptation of various organisms to aggressive environments We also concentrate on different evolutionary trends characteristic for HSP systems in the course of adaptation to fluctuating environmental conditions In addition we describe the peculiarities in the regulatory regions of heat shock genes necessary for fine tuning of these systems providing the adaptation to adverse conditions Special emphasis is given to the role of mobile elements in the evolution and functioning of various groups of HSP genes The book combines the results of field studies and laboratory analysis of stress genes systems

Molecular Chaperones in Health and Disease Matthias Gaestel,2005-09-27 Molecular chaperones are involved in a wide variety of essential cellular processes in living cells A subset of molecular chaperones have been initially described as heat shock proteins protecting cells from stress damage by keeping cellular proteins in a folding competent state and preventing them from irreversible aggregation Later it became obvious that molecular chaperones are also expressed constitutively in the cell and are involved in complex processes such as protein synthesis intracellular protein transport post translational

modification and secretion of proteins as well as receptor signalling Hence it is not surprising that molecular chaperones are implicated in the pathogenesis of many relevant diseases and could be regarded as potential pharmacological targets Starting with the analysis of the mode of action of chaperones at the molecular cellular and organismic level this book will then describe specific aspects where modulation of chaperone action could be of pharmacological and therapeutic interest

Molecular Chaperones in the Cell Peter A. Lund, 2001 Interest in molecular chaperones has grown exponentially over the last decade Molecular Chaperones recognise nascent and unfolded polypeptide chains and are often essential for their folding proteolytic processing intracellular targeting and secretion They are vital for cell growth with key roles in processes as diverse as signal transduction and stress survival Much work has already been done in understanding the structure and function of the major molecular chaperones and more recently the emphasis in research has shifted toward exploring their precise roles in many different processes with which they are involved inside the cell This aspect of molecular chaperone biology is the focus of this book Here the field's leading experts synthesise our body of knowledge into succinct chapters and the reader gains not only a fuller understanding of the roles of chaperones in the context of cellular processes but also an insight into the nature of these proteins and their breadth of definition This book represents an invaluable summary of the state of research in this fast moving highly important branch of molecular biology which has ramifications for understanding not only many diverse cellular processes but also give important insights into diseases such as BSE CJD and Alzheimer's disease which involve protein misfolding

Molecular Chaperones and Folding Catalysts Bernd Bakau, 2003-09-02 One of the most intriguing discoveries in molecular biology in the last decade is the existence of an evolutionary conserved and essential system consisting of molecular chaperones and folding catalysts which promotes the folding of the proteins in the cell This text summarizes our current knowledge of the cellular roles the regulation and the mechanism of action of this system It has a broad scope covering cell biological genetic and biochemical aspects of protein folding in cells from bacteria to man Particularly appropriate to researchers working in basic and applied aspects of molecular medicine this volume should also prove useful as an up to date reference book and as a textbook for specialized university courses

Heat Shock Proteins and Cytoprotection Alexander E. Kabakov, Vladimir L. Gabai, 2012-12-06

Heat Shock Proteins and Stress Alexander A. Asea, Punit Kaur, 2018-10-24 The book *Heat Shock Proteins and Stress* provides the most comprehensive review on contemporary knowledge on the role of HSP in Stress Using an integrative approach to understanding the regulation of HSP responses the contributors provide a synopsis of novel mechanisms by which HSP responses are regulated under normal physiological and pathophysiological conditions Key basic and clinical research laboratories from major universities and academic medical hospitals around the world contribute chapters that review present research activity and importantly project the field into the future The book is a must read for researchers postdoctoral fellows and graduate students in the fields of Translational Medicine Clinical Psychologists Human Physiology Zoologists Botanists Biotechnology Molecular

Medicine Infectious Diseases Experts and Pathologists *Molecular Chaperones* R.J. Ellis,R.A. Laskey,G.H.

Lorimer,2012-12-06 Currently one of the hottest topics in biochemistry the concept of molecular chaperones has challenged the paradigm of protein self assembly Key figures in many disciplines review all aspects of molecular chaperones in this volume which arises from a Royal Society discussion meeting Overview chapters discuss the significance of chaperones in biochemistry molecular genetics and cell biology Each chapter is well referenced providing access to the literature

Molecular Aspects of the Stress Response: Chaperones, Membranes and Networks Peter Csermely,László

Vígh,2007-08-09 We are extremely happy to present the reader this book containing a summary of a well known research field the phenomenon of cellular stress defense from two new angles networks and membranes The volume starts with an introduction to the concept of molecular chaperones in their original sense R John Ellis the founder of the chaperone concept describes chaperones as mediators of correct assembly and or misassembly of other macromolecular complexes This sets the tone of the book where later chapters give detailed examples of the richness of chaperone action by hundreds of other proteins and membrane structures The reader will learn the role of chaperone classes such as Hsp27 or Hsp90 the action of highly organized chaperone networks in various cellular compartments such as the ER or mitochondrial ER networks as well as the molecular details of the signaling mechanisms leading to chaperone induction during stress Various special stress defense mechanisms against oxidative stress or dryness will also be covered Membranes comprise a surprising mixture of stability and dynamics in the cell Their role in the regulation of the stress response has been accepted only slowly in the field Two chapters summarize this important aspect of the stress response showing the importance of membrane hyperstructures lipid species composition protein membrane interactions and cold adaptation **Heat Shock Proteins in Veterinary**

Medicine and Sciences Alexzander A. A. Asea,Punit Kaur,2018-03-21 This books provides up to date reviews on current advances of the role of HSP in veterinary medicine and research Key basic and clinical research laboratories from major universities veterinary hospitals and pharmaceutical companies around the world have contributed chapters that review present research activity and importantly project this field into the future For easy readability the book is sub divided into sections on HSP in the following aspects of Veterinary Medicine including I Domestic Animals II Poultry III Aquatic and IV Parasites The book is a must read for heat shock protein researchers in general and specifically those involved in clinical and research in veterinary medicine **Molecular Chaperones** Stuart K. Calderwood,Thomas L. Prince,2016-08-23 The

proteome consists of a complex mixture of proteins each of which need to be folded correctly in order to function for the health of the organism and many of these proteins require molecular chaperones to reach the correct conformation and in some cases to remain in a folded form In *Molecular Chaperones Methods and Protocols* expert researchers address a wide variety of approaches to the study these mechanisms featuring the workings of heat shock proteins and heat shock transcription factors in vitro and in vivo Written in the highly successful *Methods in Molecular Biology*™ series format

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Table of Contents The Biology Of Heat Shock Proteins And Molecular Chaperones

1. Understanding the eBook The Biology Of Heat Shock Proteins And Molecular Chaperones
 - The Rise of Digital Reading The Biology Of Heat Shock Proteins And Molecular Chaperones
 - Advantages of eBooks Over Traditional Books
2. Identifying The Biology Of Heat Shock Proteins And Molecular Chaperones
 - Exploring Different Genres
 - Considering Fiction vs. Non-Fiction
 - Determining Your Reading Goals
3. Choosing the Right eBook Platform
 - Popular eBook Platforms
 - Features to Look for in an The Biology Of Heat Shock Proteins And Molecular Chaperones
 - User-Friendly Interface
4. Exploring eBook Recommendations from The Biology Of Heat Shock Proteins And Molecular Chaperones
 - Personalized Recommendations
 - The Biology Of Heat Shock Proteins And Molecular Chaperones User Reviews and Ratings
 - The Biology Of Heat Shock Proteins And Molecular Chaperones and Bestseller Lists
5. Accessing The Biology Of Heat Shock Proteins And Molecular Chaperones Free and Paid eBooks
 - The Biology Of Heat Shock Proteins And Molecular Chaperones Public Domain eBooks
 - The Biology Of Heat Shock Proteins And Molecular Chaperones eBook Subscription Services
 - The Biology Of Heat Shock Proteins And Molecular Chaperones Budget-Friendly Options
6. Navigating The Biology Of Heat Shock Proteins And Molecular Chaperones eBook Formats
 - ePub, PDF, MOBI, and More
 - The Biology Of Heat Shock Proteins And Molecular Chaperones Compatibility with Devices
 - The Biology Of Heat Shock Proteins And Molecular Chaperones Enhanced eBook Features
7. Enhancing Your Reading Experience
 - Adjustable Fonts and Text Sizes of The Biology Of Heat Shock Proteins And Molecular Chaperones
 - Highlighting and Note-Taking The Biology Of Heat Shock Proteins And Molecular Chaperones
 - Interactive Elements The Biology Of Heat Shock Proteins And Molecular Chaperones

8. Staying Engaged with The Biology Of Heat Shock Proteins And Molecular Chaperones
 - Joining Online Reading Communities
 - Participating in Virtual Book Clubs
 - Following Authors and Publishers The Biology Of Heat Shock Proteins And Molecular Chaperones
9. Balancing eBooks and Physical Books The Biology Of Heat Shock Proteins And Molecular Chaperones
 - Benefits of a Digital Library
 - Creating a Diverse Reading Collection The Biology Of Heat Shock Proteins And Molecular Chaperones
10. Overcoming Reading Challenges
 - Dealing with Digital Eye Strain
 - Minimizing Distractions
 - Managing Screen Time
11. Cultivating a Reading Routine The Biology Of Heat Shock Proteins And Molecular Chaperones
 - Setting Reading Goals The Biology Of Heat Shock Proteins And Molecular Chaperones
 - Carving Out Dedicated Reading Time
12. Sourcing Reliable Information of The Biology Of Heat Shock Proteins And Molecular Chaperones
 - Fact-Checking eBook Content of The Biology Of Heat Shock Proteins And Molecular Chaperones
 - Distinguishing Credible Sources
13. Promoting Lifelong Learning
 - Utilizing eBooks for Skill Development
 - Exploring Educational eBooks
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 - Integration of Multimedia Elements
 - Interactive and Gamified eBooks

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