

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

Edited by

Peter Csermely

Department of Medical Chemistry, Semmelweis University, Budapest, Hungary

László Vigh

*Institute of Biochemistry, Biological Research Center of the Hungarian Academy
of Sciences, Szeged, Hungary*

Springer Science+Business Media, LLC

Landes Bioscience / Eurekah.com

G101 101 594



Copyright ©2007 Landes Bioscience and Springer Science+Business Media, LLC

All rights reserved.

No part of this book may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopy, recording, or any information storage and retrieval system, without permission in writing from the publisher, with the exception of any material supplied specifically for the purpose of being entered and executed on a computer system; for exclusive use by the Purchaser of the work.

Printed in the U.S.A.

Springer Science+Business Media, LLC, 233 Spring Street, New York, New York 10013, U.S.A.

Please address all inquiries to the publishers:

Landes Bioscience / Eurekah.com, 1002 West Avenue, Second Floor, Austin, TX 78701, U.S.A.

Phone: 512/ 637 6050; FAX: 512/ 637 6079

<http://www.eurekah.com>

<http://www.landesbioscience.com>

Molecular Aspects of the Stress Response: Chaperones, Membranes and Networks, edited by Peter Csermely and László Vigh, Landes Bioscience / Eurekah.com / Springer Science+Business Media, LLC dual imprint / Springer series: Advances in Experimental Medicine and Biology

ISBN-10: 0-387-39974-7

ISBN-13: 978-0-387-39974-4

While the authors, editors and publisher believe that drug selection and dosage and the specifications and usage of equipment and devices, as set forth in this book, are in accord with current recommendations and practice at the time of publication, they make no warranty, expressed or implied, with respect to material described in this book. In view of the ongoing research, equipment development, changes in governmental regulations and the rapid accumulation of information relating to the biomedical sciences, the reader is urged to carefully review and evaluate the information provided herein.

Library of Congress Cataloging-in-Publication Data

A C.I.P. Catalogue record for this book is available from the Library of Congress.

CONTENTS

1. PROTEIN MISASSEMBLY: MACROMOLECULAR CROWDING AND MOLECULAR CHAPERONES 1

R. John Ellis

Introduction	1
Inside the Cell	1
The Principle of Protein Self-Assembly: Yesterday and Today	3
The Molecular Chaperone Concept	4
The Problem of Protein Misassembly	6
Macromolecular Crowding	7
Stimulation of Misassembly by Crowding Agents	10
How do Chaperones Combat Misassembly?	11
The Molecular Chaperone Function	11

2. THE CELLULAR “NETWORKING” OF MAMMALIAN HSP27 AND ITS FUNCTIONS IN THE CONTROL OF PROTEIN FOLDING, REDOX STATE AND APOPTOSIS 14

André-Patrick Arrigo

Introduction	14
Hsp27 in Cells Exposed to Heat Shock	15
Hsp27 in Cells Exposed to Oxidative Stress	17
Hsp27 in Cells Committed to Apoptosis	19
Conclusions and in Vivo Perspectives	21

3. MOLECULAR INTERACTION NETWORK OF THE HSP90 CHAPERONE SYSTEM 27

Rongmin Zhao and Walid A. Houry

Introduction	27
Mapping the Hsp90 Physical Interaction Network	29
Mapping the Hsp90 Genetic Interaction Network	30
The Hsp90 Interactome	31
Perspectives and Future Directions	34

4. ORGANIZATION OF THE FUNCTIONS AND COMPONENTS OF THE ENDOPLASMIC RETICULUM	37
Yuichiro Shimizu and Linda M. Hendershot	
Introduction	37
Overview of Protein Biosynthesis in the ER	37
The ER Possesses a Unique Environment for Protein Folding	39
The ER Quality Control System	39
Chaperone Selection during Protein Maturation in the ER	41
Organization of a Subset of Chaperones into Large Prefomed Complexes	42
Components of the Calnexin/Calreticulin System and Their Organization	43
Possible Advantages and Constraints That an Organization of ER Chaperones Might Impose	44
5. MOLECULAR CRIME AND CELLULAR PUNISHMENT: ACTIVE DETOXIFICATION OF MISFOLDED AND AGGREGATED PROTEINS IN THE CELL BY THE CHAPERONE AND PROTEASE NETWORKS	47
Marie-Pierre Hinault and Pierre Goloubinoff	
The Criminal Nature of Protein Aggregation in the Cell	47
Defence Mechanisms against Protein Aggregation in the Cell	48
Aging and Conformational Diseases: Failures of Law Enforcement Leading to Lawlessness	52
6. CHAPERONES AS PARTS OF CELLULAR NETWORKS	55
Peter Csermely, Csaba Söti and Gregory L. Blatch	
Introduction: Cellular Networks and Chaperones	55
Chaperones in Cellular Networks	58
Chaperone-Mediated Emergent Properties of Cellular Networks	59
Chaperone Therapies	60
Conclusion	60
7. CHAPERONES AS PARTS OF ORGANELLE NETWORKS	64
György Szabadkai and Rosario Rizzuto	
Introduction	64
Biogenesis of the ER and Mitochondrial Networks: A Role for Chaperones in Interorganellar Communication?	65
ER-Mitochondrial Ca²⁺ Transfer: A Major Example of Organelle Interactions	67

**Chaperone Control of ER-Mitochondrial Interaction along the Ca²⁺ Signal
Transmission Pathway 68**
**Perspectives: The Role of Chaperone Mediated ER-Mitochondria
Coupling in Cell Death 71**
Conclusions 73

**8. HEAT SHOCK FACTOR 1 AS A COORDINATOR
OF STRESS AND DEVELOPMENTAL PATHWAYS 78**

Julius Anckar and Lea Sistonen

Introduction 78
Functional Domains of HSF1 79
Activation Mechanisms of HSF1 80
Regulation of *hsp* Gene Transcription by HSF1 81
Stress-Specific Activation of HSF1 82
HSF1 as a Developmental Regulator 83
HSF1-Mediated Expression of Cytokines 83
Heat Shock Factors Working Together 84
Future Perspectives 85

**9. CHAPERONE REGULATION OF THE HEAT SHOCK
PROTEIN RESPONSE 89**

Richard Voellmy and Frank Boellmann

Introduction 89
**Feedback Regulation of the Heat Shock Protein Response
by Stress-Inducible Chaperones 90**
Hsps and Co-Chaperones Repress Activation of HSF1 90
**HSP90-Containing Multichaperone Complexes Regulate HSF1 Oligomeric
Status and Transcriptional Competence 91**
**Regulation of HSF1 by CHIP as Part of the Protein Quality
Control System 93**
Synopsis 94

**10. MECHANISMS OF ACTIVATION AND REGULATION
OF THE HEAT SHOCK-SENSITIVE
SIGNALING PATHWAYS 100**

Sébastien Ian Nadeau and Jacques Landry

Introduction 100
Major Signaling Pathways Activate Heat Shock 101
Molecular Origin of the Heat Shock Signal 106
Conclusion 107

11. MEMBRANE-REGULATED STRESS RESPONSE: A THEORETICAL AND PRACTICAL APPROACH	114
László Vigh, Zsolt Török, Gábor Balogh, Attila Glatz, Stefano Pioletto and Ibolya Horváth	
Introduction	114
The Evolution of the “Membrane Sensor” Hypothesis with the Aid of Unicellular Stress Models: The Beauty of Simplicity	115
Evidence Concerning the Operation of Membrane-Associated Stress Sensing and Signaling Mechanisms in Mammalian Cells. Membrane Lipids May Provide the Molecular Switch for Stress Sensing and Signaling	119
Stress Response Profiling: Can We “Zoom In” on Membrane Hyperstructures Engaged in the Generation of Stress Signal?	122
Can We Point to Lipid Molecular Species Engaged in Stress Sensing and Signaling?	123
Computational Methods for the Design of Subtle Interactions between Lipids and Proteins of Membranes	124
Conclusions	127
12. BEYOND THE LIPID HYPOTHESIS: MECHANISMS UNDERLYING PHENOTYPIC PLASTICITY IN INDUCIBLE COLD TOLERANCE	132
Scott A.L. Hayward, Patricia A. Murray, Andrew Y. Gracey and Andrew R. Cossins	
Introduction	132
Cold Adaptation and the Lipid Hypothesis	133
Evidence in Prokaryotes	133
Evidence in Plants	134
Evidence in Animals	134
<i>Caenorhabditis elegans</i> Cold Tolerance and the Contribution of Desaturases	135
Nonlipid Mechanisms of Cold Tolerance	137
Interaction and Compensatory Mechanisms	137
Conclusions	138
13. TREHALOSE AS A “CHEMICAL CHAPERONE”: FACT AND FANTASY	143
John H. Crowe	
Sugars and Stabilization of Biological Materials	143
Origins of the Trehalose Myth	144
The Mechanism of Depression of T_m	145
Trehalose Stabilizes Microdomains in Membranes	145
There Is More Than One Way to the Same End	147

Trehalose Has Useful Properties, Nevertheless	147
Glass Transitions and Stability	148
Nonenzymatic Browning and Stability of the Glycosidic Bond	149
Sugar Glasses in Plant Anhydrobiotes	150
Lessons from Nature Can Be Used to Preserve Intact Cells in the Dry State	151
Successful Freeze-Drying of Trehalose-Loaded Cells	152
Can Nucleated Cells Be Stabilized in the Dry State?	153
What Is the Role of p26 in Stabilizing Dry Nucleated Cells?	153
Summary and Conclusions	154

14. CHAPERONES AS PART OF IMMUNE NETWORKS 159

Zoltán Prohászka

Introduction	159
Activation of Innate Immunity by Heat Shock Proteins	159
Immunological Protection of Heat Shock Proteins	160
Role of Natural Autoantibody Networks in Regulation of Autoimmunity	161
Heat Shock Proteins as Negotiators between Promotion of Inflammation or Control of Autoimmunity	162
Heat Shock Proteins as Elements of Multiple Networks	163

15. THE STRESS OF MISFOLDED PROTEINS:

C. ELEGANS MODELS FOR NEURODEGENERATIVE DISEASE AND AGING 167

Heather R. Brignull, James F. Morley and Richard I. Morimoto

Introduction	167
Models of Neurodegenerative Disease	168
<i>C. elegans</i> Model of polyQ Disease	168
The <i>C. elegans</i> polyQ Series in Neurons	169
Biophysical Properties of polyQ Proteins in Neurons of Live Animals	170
PolyQ Length-Dependent Aggregation Correlates with Neuronal Dysfunction	172
Dynamic Biophysical Properties of Intermediate polyQ Tracts in the Ventral Nerve Cord	173
Neuron-Specific Responses to polyQ Proteins	175
The <i>C. elegans</i> polyQ Series in Muscle Cells	175
Aging Influences the Threshold for polyQ Aggregation and Toxicity	176
Longevity Genes Influence Aging-Dependent Aggregation and Toxicity of polyQ Proteins	178
Genome-Wide RNAi Screening Identifies Novel Regulators of polyQ Aggregation and Toxicity	179
Global Disruption of Folding Homeostasis by polyQ Proteins	181
Conclusion	185

16. HSP90 AND DEVELOPMENTAL NETWORKS 190
Suzannah Rutherford, Jennifer R. Knapp and Peter Csermely

Introduction 190
Hidden Genetic Variation 191
Hsp90 and Signal Transduction Thresholds 193
Nonlinearity in Developmental Responses to Signal Transduction 195
A Pivotal Role for Hsp90 in Network Evolvability? 195

INDEX 199