Mortalin Biology: Life, Stress and Death

Sunil C. Kaul • Renu Wadhwa
Editors

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Springer

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Foreword

The heat shock response was originally discovered over 40 years ago in the fruit fly and heat shock proteins were subsequently identified in all organisms. It was found that these protect organisms against exposure to suboptimal temperatures and numerous other stresses many of which are also inducers of the response. Research on the mechanisms of action of these stress proteins was aided by development of molecular technologies, identification and cloning of new genes encoding stress proteins in a variety of assay systems both at the cellular and organism levels and it became clear that these proteins have essential constitutive functions in normal unstressed conditions. While *in vivo* animal systems are necessary to make certain firm conclusions, culture cell systems still offer an excellent platform to dissect the molecular mechanisms of action of a protein and to uncover the signal transduction pathways involved in the response. In my view, mortalin is an excellent example of this. Besides its cloning in the normal and cancer cell hybrid screening assay, many of its characteristics such as multiple subcellular residences, impact on p53 protein activity and carcinogenesis, and involvement in neuro-degenerative pathologies have been found since its discovery. The present book offers a single volume reading on the discovery of mortalin biology by experts from different fields and different parts of the globe. It is a unique volume compiling structural, evolutionary and functional aspects of a single stress protein in a variety of model systems ranging from invertebrates to human cells in culture and clinical samples. Besides making an easily understandable reading, it will be very helpful in asking further questions and designing experiments to advance mortalin-based diagnostics and therapeutics.

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Preface

Since the discovery of heat shock response by Ferruccio Ritossa in 1962, the phenomenon has been well characterized in a variety of cells and organisms as induction of a family of proteins called “heat shock proteins” (HSP). Based on their molecular weight, these proteins are classified into, at least, 6 major subfamilies named as HSP100, HSP90, HSP70, HSP60, HSP40 and small HSPs. The fact that the heat shock protein synthesis can be triggered by a variety of other stress conditions such as, infection, inflammation, exercise, starvation, oxygen-, nitrogen- or water-deprivation and exposure to chemical and physical toxins, they are also classified as “stress proteins”. Then came the surprise that the HSP also exist under non-stressful conditions and perform housekeeping functions, such as folding and assisting in the establishment of correct protein conformation, mediating protein-protein interactions, intra-cellular trafficking of other proteins, preventing unwanted protein aggregation and channelizing their degradation. A new term “chaperones” evolved to express such functionality of this highly conserved class of proteins.

A new member of HSP70 family of proteins was first cloned in 1993 in a cell hybrid protein-screening assay. Since it was identified to be associated with cellular mortal phenotype, it was named ‘mortalin’. Endorsing its multiple functionality, mortalin made its manifestation in many independent experimental regimes, such as those aimed to identify molecules involved in antigen processing, stress-survival and mitochondrial functions. With nearly two decades of experimentation, mortalin has been recognized as an essential protein that not only acts as a chaperone and stress-survival factor but also plays a key role in mitochondrial import motor function, energy generation, ROS management, immune response, control of centrosome duplication and activities of tumor suppressor protein p53. Stemming from these multiple functions is its role in human cancers on one-hand and neurodegenerative diseases on the other. With an aim to introduce mortalin at the graduate and advanced undergraduate levels, this book is organized as a chapter-wise description of structure, evolution and functional role of mortalin in normal and diseased physiology. We hope that this sketch of mortalin biology by the team of experts will help in asking new questions, advancing knowledge and developing mortalin-based diagnostic and therapeutic reagents and technologies.

We are very grateful to all the authors for their interest, enthusiasm and devotion to mortalin research that made this book necessary and possible. Without their hard work to contribute chapters, it was not possible to accomplish this volume suitable for general and specialized reading.

Sunil C. Kaul
Renu Wadhwa

Contents

Part I Structure and Function of Mortalin

- 1 Birth of Mortalin: Multiple Names, Niches and Functions Connecting Stress, Senescence and Cancer** 3
Renu Wadhwa and Sunil C. Kaul
- 2 Mortalin's Machinery** 21
Custer C. Deocaris, Sunil C. Kaul and Renu Wadhwa
- 3 The Role of Mortalin in Iron Homeostasis** 31
Wen-I Luo and James A. Cowan
- 4 Functional Characteristics of Mortalin** 55
Walter A. Baseler, Tara L. Croston and John M. Hollander

Part II Mortalin in Evolution

- 5 Mortalin and *Drosophila* DmHsp22: Two Mitochondrial Chaperones Regulating Aging and Carcinogenesis** 83
Marie Le Pécheur, Geneviève Morrow and Robert M. Tanguay
- 6 Mortalin in Invertebrates and The Induction of Apoptosis by Wild-Type p53 Following Defeat of Mortalin-Based Cytoplasmic Sequestration in Cancerous Clam Hemocytes** 97
Charles W. Walker, Ben Low and S. Anne Böttger
- 7 Mortalin and Stem Cells: A Study from Planarians** 115
Renata Batistoni

Part III Mortalin in Health and Disease

- 8 Mortalin in Cell Protection from Immune Attack** 129
Moran Saar, Oren Moskovich and Zvi Fishelson
- 9 Mortalin in Neurological Diseases** 139
Jinghua Jin, Travis J. Cook, Jake G. Hoekstra and Jing Zhang

10 Loss of Mortalin Function in Parkinson's Disease-Supporting the Mitochondrial Pathway of Neurodegeneration	159
Lena F. Burbulla and Rejko Krüger	
11 Hsp75/mortalin and Protection from Ischemic Brain Injury	179
Robin E. White, Yi-Bing Ouyang and Rona G. Giffard	
12 Catecholamine Regulated Protein (CRP40), A Splice Variant of Mortalin-2: Functional Role in CNS Disorders	191
Joseph P. Gabriele, Sarah E. Groleau, Ritesh P. Daya, Zdenek B. Pristupa and Ram K. Mishra	
13 Chaperonopathies: Diseases in Which Mortalin and Other Hsp-Chaperones Play a Role in Etiology and Pathogenesis	209
Alberto J. L. Macario, Francesco Cappello and Everly Conway de Macario	
Part IV Mortalin and Cancer	
14 Many Faces of Mortalin and Tid1	225
Ohad Iosefson and Abdussalam Azem	
15 Mortalin: A Positive Regulator of Centrosome Duplication and Amplification	245
Masayuki Kanai and Kenji Fukasawa	
16 Mortalin Expression in Normal and Neoplastic Tissues	257
Angheliki Nomikos, Sinclair R. Dundas and Graeme I. Murray	
17 Mortalin-p53 Interaction as a Target for Liver Cancer Therapy	267
Wen-Jing Lu, Nikki P. Lee, Renu Wadhwa and John M. Luk	
18 Mortalin Targeting Gadgets for Cancer Therapy	279
Chae-Ok Yun and Renu Wadhwa	
Part V Mortalin Based Technologies	
19 Cell Internalizing Anti-Mortalin Antibody for Generation of Illuminating MSCs for Long-Term <i>In vitro</i> and <i>In vivo</i> Tracking ..	295
Toshimasa Uemura, Masanori Nishi, Sunil C. Kaul and Renu Wadhwa	
20 Mortalin Staining Pattern as a Reporter for Cell Based Anti-Cancer Drug Screening	307
Ran Gao, Zeenia Kaul, Tomoko Yaguchi and Renu Wadhwa	
21 Cell Internalizing Anti-mortalin Antibody as a Nanocarrier	323
Zeenia Kaul, Tomoko Yaguchi, Renu Wadhwa and Sunil C. Kaul	
Index	337

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