

Advances in Experimental Medicine and Biology 770

Germana Meroni *Editor*

TRIM/RBCC Proteins

LANDES
BIOSCIENCE

 Springer

TRIM/RBCC Proteins

ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY

Editorial Board:

NATHAN BACK, *State University of New York at Buffalo*

IRUN R. COHEN, *The Weizmann Institute of Science*

ABEL LAJTHA, *N.S. Kline Institute for Psychiatric Research*

JOHN D. LAMBRIS, *University of Pennsylvania*

RODOLFO PAOLETTI, *University of Milan*

Recent Volumes in this Series

Volume 761

OOCYTE BIOLOGY AND FERTILITY PRESERVATION

Sam Kim

Volume 762

HIV INTERACTIONS WITH DENDRITIC CELLS: INFECTION AND IMMUNITY

Li Wu and Olivier Schwartz

Volume 763

BIOLOGY AND REGULATION OF BLOOD-TISSUE BARRIERS

C. Yan Cheng

Volume 764

HOT TOPICS IN INFECTION AND IMMUNITY IX

Andrew J. Pollard

Volume 765

OXYGEN TRANSPORT TO TISSUE XXXIV

Palm Welch and Harrison Bruley

Volume 766

DIGENETIC TREMATODES

Rafael Toledo and Bernard Fried

Volume 767

DNA HELICASES AND DNA MOTOR PROTEINS

Maria Spies

Volume 768

TEN YEARS OF PROGRESS IN GW/P BODY RESEARCH

Edward K.L. Chan and Marvin J. Fritzler

Volume 769

TANDEM REPEAT POLYMORPHISMS: GENETIC PLASTICITY, NEURAL DIVERSITY AND DISEASE

Anthony J. Hannan

Volume 770

TRIM/RBCC PROTEINS

Germana Meroni

A Continuation Order Plan is available for this series. A continuation order will bring delivery of each new volume immediately upon publication. Volumes are billed only upon actual shipment. For further information please contact the publisher.

TRIM/RBCC Proteins

Edited by

Germana Meroni, PhD

Cluster in Biomedicine, CBM S.c.r.l., AREA Science Park, Trieste, Italy

Springer Science+Business Media, LLC

Landes Bioscience

Springer Science+Business Media, LLC
Landes Bioscience

Copyright ©2012 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.

Springer Science+Business Media, LLC, 233 Spring Street, New York, New York 10013, USA
<http://www.springer.com>

Please address all inquiries to the publishers:
Landes Bioscience, 1806 Rio Grande, Austin, Texas 78701, USA
Phone: 512/ 637 6050; FAX: 512/ 637 6079
<http://www.landesbioscience.com>

The chapters in this book are available in the Madame Curie Bioscience Database.
<http://www.landesbioscience.com/curie>

TRIM/RBCC Proteins, edited by Germana Meroni. Landes Bioscience / Springer Science+Business Media, LLC dual imprint / Springer series: Advances in Experimental Medicine and Biology.

ISBN 978-1-4614-5397-0

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

TRIM/RBCC proteins / edited by Germana Meroni.

p. ; cm. -- (Advances in experimental medicine and biology ; v. 770)

Includes bibliographical references and index.

ISBN 978-1-4614-5397-0 (alk. paper)

I. Meroni, Germana, 1964- II. Series: Advances in experimental medicine and biology ; v. 770. 0065-2598

[DNLM: 1. Carrier Proteins. WI AD559 v.770 2012 / QU 55.2]

572'.696--dc23

2012031700

DEDICATION

To Eugenia and Franco,
For the privilege and delight of sharing your genes

PREFACE

The genomic ‘golden age’ has delivered the sequence of numerous novel genes while leaving us with many unanswered questions about their function. This is particularly true for gene families as, often, members are annotated based on homology rather than function. The tripartite motif family belonged to this category, although, during the last few years, the field boosted an important wealth of biochemical, cellular and physiological breakthrough data. In the first part of this book, we attempt to offer an overview of state-of-the-art basic findings on the tripartite motif (TRIM, also known as RBCC) family members and to deal in the second part with their relevant and growing physiological and pathological roles.

TRIM/RBCC Proteins begins with a general introduction on the genomic organization of the TRIM family and of its evolution, which produced one of the largest RING-containing protein families. TRIM proteins’ conserved multi-domain structure is reviewed in Chapter 2 and translation into the ability to function as E3 ubiquitin ligases, the enzymes needed for the ubiquitin-modification of specific substrates, is dealt with in Chapter 3. The shared domain structure not only underscores the E3 ligase activity but also other common features, in particular TRIM proteins ability to often demarcate defined subcellular structures. Some are well-characterized compartments, such as the PML nuclear bodies, whereas others are still undefined cytoplasmic and nuclear structures (Chapter 4). Within the nucleus, some of the TRIM family members are involved in epigenetic control of transcription (Chapter 5). Moreover, a sub-class of TRIM members can also decorate cytoskeletal structures through their capacity to associate with the microtubular apparatus (Chapter 6).

TRIM family members implication in such an important process as ubiquitination makes them vulnerable to alteration in crucial physiological processes leading to a plethora of pathological conditions that are recapitulated in the second part of the book. Known for a long time, the acute promyelocytic leukemia t(15;17) translocation results in an oncogenic PML (a TRIM member)-retinoic acid receptor- α fusion protein. Since then, several other TRIM proteins have been implicated in tumorigenesis and are addressed in Chapter 7. However, one of the most recent arenas in which TRIM proteins were discovered to have a predominant and growing role is innate immunity, in which a good share of family

members are key players via direct interactions with pathogens, above all TRIM5 as one of the main HIV-1 restriction factors, and participating as sensors of 'danger' signaling pathways (Chapter 8). However, TRIM proteins can also be enriched in preferential tissues. This is the case of the skeletal muscle members, heavily implicated in trophic and metabolic muscle physiology as well as in genetic muscular dystrophies (Chapter 9). Other genetic disorders implicate the TRIM genes in developmental processes, and in this field the study of TRIM homologs in invertebrate and rodent models contributed to the understanding of their role in embryonic patterning and determination (Chapter 10).

Much of the TRIM family function has been discovered, but there is still a long way to go. I hope this volume provides the foundation to contribute to foster novel discoveries in the rapidly evolving field of TRIM proteins biology.

*Germana Meroni, PhD
Cluster in Biomedicine, CBM S.c.r.l., AREA Science Park
Trieste, Italy*

ABOUT THE EDITOR...



GERMANA MERONI is a graduate of the University of Milan, Italy. She was a post-graduate fellow at the Department of Biotechnology of the San Raffaele Hospital in Milan, Italy, and then post-doctoral fellow at the Department of Human and Molecular Genetics of Baylor College of Medicine, Houston, TX (USA). She established her research group at the Telethon Institute of Genetics and Medicine (TIGEM) in Naples and then moved as leader of the Functional Genomics Laboratory at the Cluster in Biomedicine within AREA Science Park in Trieste, Italy. Her main research interest is the genetics and biochemistry of the Tripartite Motif family in health and disease.

PARTICIPANTS

Elizabeth C. Batty
Macromolecular Structure
and Function Group
Division of Molecular Biosciences
Imperial College London
South Kensington
London
UK

Valeria Cambiaghi
Department of Experimental Oncology
European Institute of Oncology, IEO
Milan
Italy

Florence Cammas
Department of Functional Genomics
Institut de Génétique et de Biologie
Moléculaire et Cellulaire
CNRS/INSERM/ULP/Collège de France
Illkirch
France

Evelyne Chaignat
Center for Integrative Genomics
University of Lausanne
Lausanne
Switzerland

Pierre Chambon
Department of Functional Genomics
Institut de Génétique et de Biologie
Moléculaire et Cellulaire
CNRS/INSERM/ULP/Collège de France
Illkirch
France

Timothy C. Cox
Division of Craniofacial Medicine
Department of Pediatrics
University of Washington
and
Center for Tissue and Cell Sciences
Seattle Children's Research Institute
Seattle, Washington
USA
and
Department of Anatomy
and Developmental Biology
Monash University
Clayton, Victoria
Australia

Paul S. Freemont
Macromolecular Structure
and Function Group
Division of Molecular Biosciences
Imperial College London
South Kensington
London
UK

Carmela Fusco
Laboratory of Medical Genetics
IRCCS Casa Sollievo della Sofferenza
San Giovanni Rotondo
Italy

Virginia Giuliani
Department of Experimental Oncology
European Institute of Oncology, IEO
Milan
Italy

Kazuhiro Ikeda
Division of Gene Regulation
and Signal Transduction
Research Center for Genomic Medicine
Saitama Medical University
Saitama
Japan

Satoshi Inoue
Division of Gene Regulation
and Signal Transduction
Research Center for Genomic Medicine
Saitama Medical University
Saitama
and
Departments of Geriatric Medicine
and Anti-Aging Medicine
Graduate School of Medicine
The University of Tokyo
Tokyo
Japan

Kirsten Jensen
Macromolecular Structure
and Function Group
Division of Molecular Biosciences
Imperial College London
South Kensington
London
UK

Konstantin Khetchoumian
Department of Functional Genomics
Institut de Génétique et de Biologie
Moléculaire et Cellulaire
CNRS/INSERM/ULP/Collège de France
Illkirch
France

Siegfried Labeit
Universitätsmedizin Mannheim
University of Heidelberg
Mannheim
Germany

Sara Lombardi
Department of Experimental Oncology
European Institute of Oncology, IEO
Milan
Italy

Régine Losson
Department of Functional Genomics
Institut de Génétique et de Biologie
Moléculaire et Cellulaire
CNRS/INSERM/ULP/Collège de France
Illkirch
France

Cristiano Marinelli
Department of Experimental Oncology
European Institute of Oncology, IEO
Milan
Italy

Olga Mayans
School of Biological Sciences
University of Liverpool
Liverpool
UK

Giuseppe Merla
Laboratory of Medical Genetics
IRCCS Casa Sollievo della Sofferenza
San Giovanni Rotondo
Italy

Germana Meroni
Cluster in Biomedicine
CBM S.c.r.l.
AREA Science Park
Trieste
Italy

Lucia Micale
Laboratory of Medical Genetics
IRCCS Casa Sollievo della Sofferenza
San Giovanni Rotondo
Italy

PARTICIPANTS

xiii

Pier Giuseppe Pelicci
Department of Experimental Oncology
European Institute of Oncology, IEO
and
Dipartimento di Medicina
Chirurgia e Odontoiatria
University of Milano
Milan
Italy

Francesca Petrera
Cluster in Biomedicine
CBM S.c.r.l.
AREA Science Park
Trieste
Italy

Alexandre Reymond
Center for Integrative Genomics
University of Lausanne
Lausanne
Switzerland

Jonathan P. Stoye
Division of Virology
National Institute for Medical Research
London
UK

Francesca Toffalorio
Department of Experimental Oncology
European Institute of Oncology, IEO
Milan
Italy

Melvyn W. Yap
Division of Virology
National Institute for Medical Research
London
UK

CONTENTS

1. GENOMICS AND EVOLUTION OF THE TRIM GENE FAMILY	1
Germana Meroni	
Abstract.....	1
Introduction	1
The Human TRIM Family	2
TRIM Family Evolution	6
Conclusion	8
2. THE TRIPARTITE MOTIF: STRUCTURE AND FUNCTION	11
Lucia Micale, Evelyne Chaignat, Carmela Fusco, Alexandre Reymond and Giuseppe Merla	
Abstract.....	11
Introduction	11
The Tripartite Motif.....	12
C-Terminal Region.....	18
Conclusion	21
3. TRIM PROTEINS AS RING FINGER E3 UBIQUITIN LIGASES.....	27
Kazuhiro Ikeda and Satoshi Inoue	
Abstract.....	27
Introduction	27
TRIM Proteins Are Involved in Protein Modification Pathway by Ubiquitin	28
Efp/TRIM25 Functions as E3 Ligase for Both Ubiquitination and ISGylation.....	29
E3 Ubiquitin Ligases in TRIM/RBCC Proteins	31
Conclusion	34

4. PML NUCLEAR BODIES AND OTHER TRIM-DEFINED SUBCELLULAR COMPARTMENTS39

Elizabeth C. Batty, Kirsten Jensen and Paul S. Freemont

Abstract.....	39
Introduction.....	39
PML Nuclear Bodies and Associated Proteins	42
The Tripartite Motif in PML.....	43
The Formation and Dissolution of PML Nuclear Bodies	44
PML Nuclear Body Dynamics—Number, Movement and Morphology.....	44
Isoforms of PML Protein.....	46
PML Nuclear Bodies and Disease.....	47
Nuclear Compartments Sharing Associations with PML Nuclear Bodies.....	48
TRIM Proteins That Localise to PML Nuclear Bodies.....	50
Other TRIM-Defined Subcellular Compartments.....	52
Conclusion	53

5. TRIM INVOLVEMENT IN TRANSCRIPTIONAL REGULATION59

Florence Cammas, Konstantin Khetchoumian, Pierre Chambon
and Régine Losson

Abstract.....	59
Introduction.....	59
The TIF1 Family Proteins in Gene-Specific Regulation.....	60
PML/TRIM19 in the Control of Transcription	65
RFP/TRIM27 in the Control of Transcription	67
Other TRIM Family Members in Transcriptional Regulation.....	71
Conclusion	72

6. TRIM PROTEINS IN CANCER.....77

Valeria Cambiaghi, Virginia Giuliani, Sara Lombardi, Cristiano Marinelli,
Francesca Toffalorio and Pier Giuseppe Pelicci

Abstract.....	77
Introduction.....	77
TRIM Proteins in Chromosomal Translocations.....	78
TRIM Proteins as E3-Ub Ligases	84
TRIM Proteins with Tumour Suppressor Functions or Involvement in p53 Pathways.....	86
Conclusion	87

7. TRIM PROTEINS AND THE INNATE IMMUNE RESPONSE TO VIRUSES.....93

Melvyn W. Yap and Jonathan P. Stoye

Abstract.....	93
Introduction.....	93

TRIM25 and Interferon β Induction.....	94
TRIM22 and Inhibition of HIV-1 Production.....	95
TRIM 28 and Retroviral Silencing.....	96
TRIM5 and Retroviral Restriction.....	97
Other TRIMs Associated with Viral Resistance.....	98
TRIM Proteins That Negatively Regulate the Innate Immune Response.....	98
Discussion and Conclusion.....	99

8. THE MICROTUBULE-ASSOCIATED C-I SUBFAMILY OF TRIM PROTEINS AND THE REGULATION OF POLARIZED CELL RESPONSES 105

Timothy C. Cox

Abstract.....	105
Introduction.....	105
MID1/TRIM18.....	106
MID2/TRIM1.....	107
TRIM9.....	112
TRIM36/Haprin.....	114
TRIFIC/TRIM46 and TNF/TRIM67.....	115
Conclusion.....	115

9. MuRFs: SPECIALIZED MEMBERS OF THE TRIM/RBCC FAMILY WITH ROLES IN THE REGULATION OF THE TROPHIC STATE OF MUSCLE AND ITS METABOLISM..... 119

Olga Mayans and Siegfried Labeit

Abstract.....	119
Introduction: Skeletal Muscle Plasticity and MuRFs.....	119
Discovery and Conserved Features of the MuRF Gene Family.....	120
The Molecular Structure of MuRFs.....	122
Physiological Roles and Cellular Targets of MuRF1.....	124
Outlook: Emerging Concepts on the Regulation of the Tropic State of Myocytes and Their Metabolism by Ubiquitin Ligases.....	126
Conclusion.....	128

10. TRIM PROTEINS IN DEVELOPMENT..... 131

Francesca Petrer and Germana Meroni

Abstract.....	131
Introduction.....	131
The TRIM-NHL Protein Group.....	132
The TRIM-FN3 Protein Group.....	135
Other TRIM Proteins Involved in Developmental Processes.....	138
Conclusion.....	138

INDEX..... 143

ACKNOWLEDGMENTS

As the editor of this book, I wish to acknowledge with gratitude the contributors' investment of time and knowledge and thank all the colleagues around the world involved in the different aspects of TRIM research.

My involvement in the study of the TRIM family is fruit of the support I have received from many people but in particular from Andrea Ballabio who introduced me to this field a long time ago. My deep gratitude goes to Graciana Diez-Roux for her incessant warm encouragement.

I also wish to thank Cynthia Conomos and Celeste Carlton at Landes Bioscience for the professional efforts in pulling this project together and for their patience.