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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.

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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.

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