
Preface

The year 2003 marked the 25th anniversary of the discovery that the small molecule ubiquitin plays a critical role in the regulated degradation of proteins. Since that time, many other major advances have been made—including the discovery of the enzymes that regulate covalent attachment of ubiquitin to substrates; the purification and characterization of the proteasome; the association of targeted protein degradation with such specific cellular events as cell cycle regulation; and the discovery that defects in protein degradation are linked to specific human pathologies. Although many had once thought of protein degradation as a relatively nonspecific phenomenon, we now know that the ubiquitin–proteasome system is tightly regulated and exhibits precise temporal and substrate specificity.

The central relevance of the ubiquitin–proteasome system was highlighted in 2004 when the Nobel Prize in Chemistry was bestowed on three figures who played crucial roles in the early discoveries in this field: Aaron Ciechanover (a contributor to this book), Avram Hershko, and Irwin Rose. Many others have made great contributions as well, and a debt of gratitude is owed to all the early pioneers by those of us who now work in this growing area of biomedical science.

Because the ubiquitin–proteasome system plays a critical role in so much that goes on within a cell, more and more scientists from different backgrounds—cellular and molecular biology, genetics, pharmacology, pathology, and others—find that they must know how to manipulate this system to address questions in their own areas of research. *Ubiquitin–Proteasome Protocols* is designed for those investigators. We have sought contributions from the scientists who originally developed the protocols that other investigators will find necessary for their work. Because the field of ubiquitin-dependent proteolysis is so broad, the topics in this book cover much ground, from basic biochemistry to cellular assays to discovery techniques using mass spectroscopic analysis. Whether one is new to the field or a long-standing contributor, we hope that *Ubiquitin–Proteasome Protocols* will serve as a useful tool to accelerate discovery and enhance productivity.

We extend our deepest thanks and appreciation to all the contributors to our work. We solicited the leading contributors to this field, and we were thrilled by their willingness to participate, their enthusiasm for this project, and the hard work they invested to make this book as good as it possibly could be. We thank all of our colleagues, coworkers, and trainees for their continued inspiration and devotion to work in this field. We especially thank Edward Dornsmith, Liz Garman, and Chris Horaist for their hard work in helping us prepare the manuscript of this book for submission. We are grateful to Humana Press for the invitation to assemble *Ubiquitin–Proteasome Protocols*, and we thank John Walker for his assistance in making this work a reality.

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