

## Series Preface

Cell death, or conversely cell survival, is a major biological phenomenon. Just as with cell proliferation and cell differentiation, cell death is a choice that a cell has to make, sometimes voluntarily, other times accidentally. As such, cell death serves a purpose in the biology of a multicellular organism. The machinery of cell death and that of cell protection are evolutionarily conserved and their elements can even be found in single-celled organism. The disruption of cell death mechanisms can often cause developmental abnormalities. Factors that can trigger cell death are diverse and the cell death process is intricately connected with other biological processes. Cell death directly contributes to the pathogenesis of many diseases, including cancer, neurodegenerative diseases, and tissue injury in organ failure.

The study of cell death and cell survival has become a multidisciplinary subject, which requires expertise from all fields of the modern biology. Exploring the role of cell death in disease development and the modulation of cell death for the prevention and treatment of devastating disease demands constant updating of our knowledge through the broadest interactions among all investigators, basic and clinical. The rapid expansion of our knowledge in this field has gone beyond what could be summarized in a single book. Thus, this timely series *Cell Death in Biology and Diseases* summarizes new developments in different areas of cell death research in an elaborate and systemic way. Each volume of this series addresses a particular topic of cell death that either has a broad impact on the field or that has an in-depth development in a unique direction. As a whole, this series provides a current and encyclopedic view of cell death.

We would like to sincerely thank the editors of each volume in the series and the authors of each chapter in these volumes for their strong commitment and great effort towards making this mission possible. We are also grateful to our team of professional Springer editors. They have worked with us diligently and

creatively from the initiation and continue this on the development and production of each volume of the series. Finally, we hope the readers will enjoy the reading, find the content helpful to their work, and consider this series an invaluable resource.

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# Book Preface

Over the past few decades, it has become widely appreciated that genetically programmed, active cell death processes are critically important for immune-mediated removal of infected or transformed cells, as well as self-elimination of damaged cells. This includes removal via cellular suicide of cells that have been damaged by conventional anti-cancer therapies such as chemotherapy and radiation. Concurrently, it has been determined that defects in cell death pathways can promote tumor development and progression, including the development of resistance to chemotherapy, radiation, immunotherapies, and biologic agents. These resistance mechanisms have devastating consequences for the successful treatment of cancer patients. A key goal in the development of new therapeutic strategies and agents for the treatment of cancer is to achieve selective and efficient killing of tumor cells. Assisting this goal are numerous ongoing studies and discoveries that have elucidated the molecular mechanisms of cell death pathways, including the extrinsic and intrinsic apoptosis pathways, and the proteins that act to regulate these pathways. Understanding of these cell death pathways is now making it possible to identify the specific cell death defects that occur in cancer cells, and is leading to the development of novel strategies and agents to overcome or correct these defects in cancer patients.

This volume summarizes current understanding of the molecular mechanisms that govern cell death in normal and malignant cells, and introduces cutting-edge opportunities for achieving selective killing of cancer cells by targeting these mechanisms in patient's tumors. A particular emphasis is placed on data emerging from the translation of basic research findings to clinical trials. The book begins by describing many of the common cell death defects that have been identified in primary patient specimens, including aberrant overexpression of anti-apoptotic proteins and oncoproteins, and mutation or loss of expression of pro-apoptotic proteins and tumor suppressors. The unique bioenergetics of cancer cells and unique characteristics of the tumor microenvironment are then discussed, along with opportunities for novel therapeutic interventions that are afforded by these distinctive features. The role of autophagy in regulating cancer cell death and current progress in targeting autophagy to improve responsiveness to conventional anti-cancer therapies is also presented. Additionally, a rapidly expanding field implicates microRNAs in the regulation of cell death proteins and pathways.

Recent descriptions of aberrant microRNA expression in cancer cells and the potential for targeting microRNAs are summarized. Further chapters describe preclinical and clinical approaches currently being used to target DNA repair pathways and protein chaperones as a means to provoke tumor cell death. New discoveries regarding the complex interplay between dying cancer cells and the immune system are also discussed, with an eye towards optimizing these interactions for therapeutic advantage. Finally, recent progress in targeting specific components of cell death signaling pathways is reviewed. These chapters highlight exciting advancements in the targeting of sphingolipid signaling, Bcl-2 family members, IAPs, death receptor signaling, the proteasome, and survival signaling mediated by the PI3K/AKT and RAS/RAF/MEK/ERK pathways.

*Cell Death Signaling in Cancer Biology and Treatment* will be particularly beneficial to biochemists, molecular biologists, and systems biologists interested in basic mechanisms of cell death signaling, the nature of cell death defects in cancer, and the impact of basic biological processes on cell death regulation. Scientists interested in the translation of findings from basic cell death research to clinical trials will appreciate the emphasis each chapter places on these important advances. Moreover, industry and academic scientists interested in anti-cancer drug development will learn of unique opportunities and approaches being taken to develop and evaluate highly selective agents with potent killing activities against tumors cells resistant to radiation or conventional chemotherapy drugs.

The work presented in this book is built on the foundation of many excellent studies and discoveries from a vast number of scientists. I wish to acknowledge those whose work is not presented, or whose area is not a specific focus of this book. In addition, I would like to thank the inspirational guidance of the late Stanley Korsmeyer, who introduced me to the fascinating field of cell death. I am particularly thankful for the authors who are respected leaders in their areas of research. Special thanks also go to my close colleagues in this field, with whom I have had many helpful discussions, including Pam Hersherberger, John Lazo, Changyou Li, Hannah Rabinowich, Shivendra Singh, Xiao-Ming Yin, Jian Yu, Yan Zang, and Lin Zhang. This book represents the first in a new book series entitled *Cell Death in Biology and Diseases* (Springer) with Series co-editors Xiao-Ming Yin and Zheng Dong. I am indebted to the co-editors for helping to develop the content of this book, as well as to Aleta Kalkstein and Renata Hutter, editors from Springer. Lastly, I wish to thank my children, Rachel, Josiah, and Matthew, for their patience, inspiration, and laughter.

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