

# Book Preface

Cell death is a fundamental aspect of cell biology closely associated with health and disease. So far, various forms of cell death have been recognized and extensively studied. In contrast to apoptosis, well defined as a form of programmed cell death, necrosis used to be considered as accidental (i.e., non-programmed) cell death, usually in response to a severe injury. In the past decade, there is accumulating evidence suggesting that necrosis is also programmed and is controlled by distinctive “death machinery” in response to various stimuli such as cell death ligands, pathogen-associated molecular patterns (such as viral RNA), oxidative stress, and DNA damage. Necroptosis, a particular form of necrotic cell death, has gained particular attention. This form of necrosis is highly regulated by RIP kinases (RIPK); scientists have now developed inhibitors that block these kinases. These inhibitors allow us to explore the role of these kinases in many experimental disease models in inflammation, ischemia-reperfusion damage, degenerative diseases, and infection and hopefully will soon reach the clinic to save lives.

To keep pace with the fast developments in this important research theme, we are pleased to present this book focusing on necrotic cell death as the second volume in the newly launched series *Cell Death in Biology and Diseases*. In this book we attempt to give a comprehensive coverage of programmed necrosis with contributions from the leading experts in this field around the world. The book starts with the history of necrosis research and also immediately jumps to how molecular insights and availability of inhibitors have rapidly led to potentially important therapeutic applications (Chap. 1). The book is divided, like many processes and good things in life, into seven parts. The first part involves a detailed description of the major regulators of necroptosis including the role and regulation of RIPK1 (Chap. 2) and RIPK3 (Chap. 3). The important role of Inhibitors of Apoptosis Proteins (IAPs) and ubiquitylation processes are elaborated as important regulators in the life–death bifurcation of RIPK1 (Chaps. 4 and 5). Caspase 8 is a crucial negative regulator of necroptosis and is paradoxically a pro-apoptotic molecule (Chaps. 6 and 7).

The second part deals with important cellular processes that modulate necrosis such as DNA damage, PARP activation, oxidative stress, and reactive oxygen species (Chaps. 7–9). They may represent different subroutines that result in particular forms of programmed necrosis. The third part of the book examines the intercellular aspects of necrosis and its role in immunity, inflammation, and viral infection (Chap. 10). In the fourth part, the complex relationship between p53, autophagy, autophagic cell death, and necrosis and how this determines cellular fate following stress are described (Chaps. 11–13). The fifth part elaborates on necrosis in model organisms including microbes, yeast, and *C. elegans* (Chaps. 14 and 15). The sixth part deals with the important quest for small molecule inhibitors of necroptosis and their potential implication for a plead of inflammatory, degenerative, and infectious diseases (Chaps. 16 and 17). Finally, in the seventh part, we discuss some methods and techniques for measuring necrosis and discuss the possible pitfalls (Chap. 18).

With the extensive studies on necrosis in the past several years, it is clear that regulated necrosis started as an ugly duckling besides the overwhelming beauty of apoptosis, and it has now become an admired and proud swan in the vast lake of cell death research. It is conceivable that in pathophysiological situations, targeting necrosis may become a dominant paradigm. We hope that this book, as the first one devoted to regulated or programmed necrosis, will become a useful source of reference for the growing number of researchers in this emerging field. We especially thank all the authors and editors for their patience and understanding during the making of this book.

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