

Preface

Death proclaims creation, although sounds utterly oxymoronic, is the most befitting description of programmed cell death *aka* apoptosis. With almost 50–60 billion ageing and physiologically impaired cells being replaced daily in a normal adult human, apoptosis makes way for healthy tissues to rebuild and regenerate, thus preserving the positive force of life. It's been a long journey since 1950s when the concept of programmed cell death began to take shape which later burgeoned exponentially so as to become an integral part of biomedical research. Groundbreaking discoveries in the early 1990s brought into forefront the role of proteases mainly caspases in the complex network of apoptosis activation process. This family along with other lesser known proteases, such as granzymes, calpains, cathepsins and HtrAs, initiate, activate, execute and modulate the entire apoptotic cascade through coordinated and precise mechanisms thus maintaining a delicate balance between cell survival and death. Perturbation in this equilibrium leads to several diseases of major medical significance such as cancer and neurodegenerative disorders which underscores the potential of these enzymes as current and future therapeutic targets.

In this book, we have described the role of proteases in programmed cell death. Apart from providing a broad overview on these proteases, this book also annotates the recent developments in various methodologies for studying their role under normal and diseased conditions. It also discusses significant contributions of these proteins in translational research and their future prospects in therapeutic intervention.

The book is organized in six chapters. The first chapter provides an introductory note on apoptosis in general, different pathways, molecules involved in these critical pathways and diseases associated with its deregulation. The second chapter introduces the reader to the caspase family of cysteinyl proteases. It focuses on structural and functional classification of caspases, their mechanisms of activation, substrates, inhibitors and role in different apoptotic pathways.

Molecules associated with alternate cell death mechanisms are emerging as potential therapeutic targets especially in cases where traditional pathway fails to activate and are covered in detail in the third and fourth chapters. The fifth chapter elaborates structural and functional assays on mechanism of these proteases

and their involvement in apoptosis. This chapter brings together a wide array of complementary techniques that have been developed for the specific detection and analysis of these proteases and their activities. Finally, the sixth chapter concludes with a vivid description and review of animal models and non-invasive imaging modalities in developmental therapeutics targeting proteases in apoptotic pathways. Taken together, the different chapters of the book deal with important aspects of the proteases associated with programmed cell death along with challenges and recent advancements in the field of research.

This book aims at providing up-to-date information on proteases associated with different cell death pathways with thorough discussions on current and potential preclinical and clinical applications. It also intends to inform and inspire undergraduate and graduate students alike and stimulate them towards pursuing biomedical research.

I am grateful to all the contributing authors for providing their expertise and thoughtful insights on proapoptotic proteases. I also thank all my students, lab members and friends who spent considerable amount of time proofreading and giving invaluable comments.

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