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BOOK REVIEW

Not Only Death Molecules

(Review on "Caspases: Their Role in Cell Death and Cell Survival", Los, M., and Waczak, H., eds., Landes Bioscience, Georgetown, TX; Kluwer Academic/Plenum Publishers, New York, 2002, 273 p.)

For many centuries, the problems of the two extreme ends of life, birth and death, have been the most exciting and intriguing for humankind. After the discovery of the phenomenon of physiological cell death (most commonly known as apoptosis) it became clear that individual cells can die not only because they are accidentally injured, but also as a result of activation of specific mechanisms for cellular autodestruction. It has also become clear that enzymes targeting numerous structural and regulatory proteins in cells committed to death are the key effectors of apoptosis. These endopeptidases known as caspases are cysteine proteases with cleavage preference after aspartic acid residues. To date, about fifty members of the caspase family have been identified in eukaryotes.

As part of a series entitled "Molecular Biology Intelligence Unit", this volume summarizes recent seminal discoveries elucidating the role of caspases in apoptosis, inflammation, and other physiological functions, namely the mechanisms whereby various caspases become activated, the organization of the proteolytic cascades initiating and executing cell removal with molecules activating or inhibiting caspases, etc. The book being reviewed here was conceived by the authors as a compact compendium on caspases. The famous German scientists Marek Los and Henning Walczak, the editors of the book, have compiled 15 chapters written by more that forty contributors from Europe, Northern America, and Australia who are the leading experts in the field. It is noteworthy that the monograph was published in 2002, the same year Sydney Brenner, John Sulston, and Robert Horvitz were awarded the Nobel Prize in Physiology or Medicine for their combined work in elucidating the genetic pathway for apoptosis.

The first six chapters are introductory ones intended to familiarize the reader, especially those not specialized in this field of molecular biology, with the up-to-date basic concepts and principles of the subject. Chapter 1, the longest chapter, describes the primary structure of caspases, the stages of proteolytic processing of catalytically inactive caspase precursors (procaspases), specific cellular caspase substrates and their peptide analogs, as well as natural and synthetic caspase inhibitors. The following five chapters of the book are devoted to the analysis of caspase-dependent apoptosis, providing a very brief but useful outlook on the formation of death-inducing multiprotein complexes (DISC and apoptosome) and the general principles of the functioning of caspase cascades, including their control by cellular as well as virus-encoded caspase inhibitors. These chapters provide a thorough, concise, and up-to-date overview of the biochemistry and molecular biology of caspases.

Chapter 7 serves to present current knowledge on participation of caspases in crucial cellular processes besides apoptosis, including regulation of the cell cycle, cell proliferation, cell survival, and cell migration as well as triggering of surface receptor internalization.

The next two chapters are characterized by a deep endeavor into the problems related to the participation of caspases in production, activation, or degradation of cytokines and the importance of caspases for regulation of proinflammatory networks or the immune response.

Chapter 10 summarizes recent advances in understanding of the physiology of individual caspases. These data became available due to experiments with various caspase knockout mice. It is of interest to learn that the deficiency in caspase-7, -8, or -9 is associated with early embryonic death.

These are followed by four chapters on the applied aspects of caspase study. In particular, chapter 11 deals in details with the activation of caspase-dependent apoptosis in cancer cells upon chemotherapy. A modern methodology used to characterize an activity-based profile of caspases in live cells and crude cell lysates is also profoundly analyzed (chapters 12 and 13). In the following chapter, the authors discuss newly-developed therapeutic approaches that should prevent or stimulate the activation of caspases. This information will be extremely useful to basic researchers and clinicians interested in the pharmacotherapy of heart failure, stroke, rheumatoid arthritis, liver injury, sepsis, and cancer. Finally, by the end of the book, the alternative, caspase-independent cell death pathways are described with the emphasis on the role of non-caspase proteases (calpains, cathepsins, and granzymes), protein kinases (RIP, ASK1, and JNK) as

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well as endonucleases (endonuclease G). The various components of caspase-independent cell death pathways are to be taken into account as potential targets for future drug development.

Overall, the value of such a textbook is not limited to spreading the basic knowledge on caspases among specialists in the broad field of apoptosis. The book provides researchers with the contemporary developments in the strategies for further study. For anyone who would like to learn about apoptosis *Caspases: Their Role in Cell Death and Cell Survival* is the place to start. Of course, a Russian edition of this compendium would be welcomed.

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