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0521529565 - Apoptosis in Health and Disease: Clinical and Therapeutic Aspects
Edited by Martin Holcik, Eric C. LaCasse, Alex E. MacKenzie and Robert G. Korneluk
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Apoptosis in Health and Disease

Clinical and Therapeutic Aspects

The process of programmed cell death or apoptosis has, in the past decade, been shown to be centrally involved in the pathogenesis of the significant majority of human illnesses and injury states. The cellular attrition observed in most degenerative conditions is apoptotic in nature; conversely, a failure of apoptosis has been proposed to underlie many forms of cancer. The central role of apoptosis in human disease clearly brings with it clinical promise: for example, the strong possibility exists that attenuation of apoptotic death will significantly modulate the severity of degenerative disorders. Similarly, conditions such as cancer, autoimmune disease, psoriasis, and endometriosis, in which aberrant cellular proliferation is observed, may benefit from enhanced rates of apoptosis. This book surveys the underlying molecular mechanisms of apoptosis, investigates its role in degenerative and other diseases, and evaluates potential therapies that will permit appropriate activation or inhibition of apoptosis in disease and injury states.

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Preface

Multicellular organisms are remarkable in their complexity, comprised of an almost unimaginably diverse array of molecular mechanisms enabling the propagation, differentiation, and maintenance of their component cells. But just as there exist precisely programmed mechanisms to generate and maintain the cellular constituents of metazoans, so too there exist elaborate means of ending the lives of cells. Homeostasis is achieved at the cost of a certain intolerance; cells have defined life spans, limited ability to deal with physical, chemical, electrical, thermal, or biologic stress, and a narrow scope of acceptable behavior, deviation from which rapidly results in death. Thus, cells which have served their purpose in development, have reached the end of their natural life span post-development, have sustained an injury, or in some way have become dysregulated conduct a rapid self-disassembly and then die efficiently, committing suicide. This programmed cell death or apoptosis is a natural ongoing process, necessary for life. As logical as this state of affairs may appear in hindsight, a full appreciation has only come over the last two decades.

Although, as might be expected, the number of molecular pathways enacting this cellular attrition pales in comparison with that required to generate a cell, they are nonetheless remarkably complex. The past decade has witnessed the delineation of many, and likely most, of the central molecular mechanisms and the constituent parts by which apoptosis occurs. This gratifying molecular progress leads directly to the question of therapeutic relevance. Just as “normal” programmed cell death is essential for life, dysregulated programmed cell death is observed in the significant majority of diseases and injury states. The ubiquity of such dysregulation invokes the obvious question: does the pharmacologic or biologic modulation of this process impact disease severity? In the following pages, internationally recognized experts attempt to address this central and still largely unanswered question showing where we are in the pursuit of apoptosis modulation-based therapies.

This book attempts to summarize some of the key apoptosis findings and how they apply to medicine. This general subject is vast and cannot be justly covered in a single chapter or book. In addition, we apologize to our many colleagues whose work could not be cited for lack of space.