Introduction

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When the subject of responses to injury or wound healing arises, the discussion usually pertains to reparative processes at the tissue or organ system level. Until recently, relatively little attention has been paid to the healing of wounded cells. Although much is known about the responses of individual cells to injury, and about their repair processes, there has not been a collective synthesis published that integrates the interdisciplinary aspects of the cellular healing responses. This *Annals* volume represents the first endeavor to bring this subject into focus.

Each of the many and various molecular processes involved in cell repair are the subject of active research efforts scattered over numerous biomedical science research fields. When viewed collectively, it becomes clear that cellular wound-healing activities are highly organized and complex. By comparison, the reparative processes involved in tissue wound-healing reflects the outcome of complex coordinated events involving many cells and cell types. Reparative processes at the cell level are also complex and coordinated, involving highly orchestrated series of molecular events designed to detect and repair injured components of the cell. As opposed to healing of tissue injury, which often occurs by replacement of damaged tissue with scar, cellular wound-healing processes are more regenerative and, when successful, the repair is more precise.

Cell Injury: Mechanisms and Repair is concerned chiefly with describing the processes of injury and healing at the molecular level. In the spring of 2004, a conference was organized at The University of Chicago to bring together experts on the various aspects of cell injury and repair, to share information and consider each aspect of the healing response in light of all the other processes that are simultaneously occurring in cells while they are healing and responding to injury. The symposium has since evolved into a graduate-level core course in molecular medicine and pathology at The University of Chicago. Like the original symposium, this book is organized in four sections, which progress from basic structure and physical integrity of the mammalian cell to modes of cell injury and cellular responses to ways in which we may be able to utilize our understanding of these types of injury and subsequent responses for therapeutic strategies that limit injury or enhance repair.

Part I of this *Annals* volume focuses on the structural factors which are deterministic of cell integrity and the physicochemical modes of cell injury. It is essentially a materials-science approach to cell injury. The chapters review basic aspects of mammalian cell structure, including not only the biophysical nature and responses

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of specific cell components such as the plasma membrane but also interactions with the extracellular and intracellular "matrix of life," water. This pertains to basic determinants of protein stability, protein assemblies and organelles. Thus, information about the energetics of passage through intermediate steps leading to aggregation of unfolded proteins and about the role of the biological solvent (water) as an active player in all these molecular events is discussed in the context of their role in the pathogenesis of cell injury. Physical and chemical aspects of interactions within and between proteins are reviewed and the effects of temperature and molecular crowding on these interactions are discussed.

In Part II, several different biophysical modes of cell injury are reviewed in a series of chapters that examine electrical injury to cells such as electroporation of the lipid bilayer and electrical denaturation of membrane proteins, as well as the effects of temperature extremes on cells. In these latter chapters, effects of excessive heat on individual cells and their components, as well as the effects of freezing and thawing on cells in both cryo-injury and biopreservation attempts are considered. Thus, the chapters in this section give the reader an overview of the types of direct cell injury which promote cellular responses and for which we are currently seeking and testing therapeutic strategies.

Part III of this volume is devoted to the healing responses of cells. In the opening chapter of this section, a tutorial overview of endogenous and therapeutic mechanisms of cell membrane repair is presented, giving the reader an introduction to key experiments in the elucidation of these concepts. Subsequent chapters in this section review the roles of endogenous substances, including calcium and heat shock proteins, in responses to cell injury. Molecular mechanisms involved in the induction of and the cellular response to DNA damage are also detailed in this section. Considerations of genetic syndromes and the clinical phenotypes resulting from aberrations in DNA repair are included. This part of the text concludes with a treatise on autophagy, a relative newcomer to the spectrum of endogenous protective responses to injury and stress, and discusses the pathological implications of deregulation of the autophagic response in mammalian cells.

The final components of the text deal with therapeutic strategies to rescue injured cells by augmenting the cell's natural healing responses. Many of the strategies discussed are those we considered when resuscitating damaged tissues and organs. These include inhibition of injurious factors such as reactive oxygen species, as well as direct repair of membranes through the use of specific polymers or through stimulated enhancement of endogenous repair mechanisms. By distinguishing cellular wound-healing process from tissue and organ wound-healing processes, it is hoped that the therapeutic goals will be better defined, and that this will result in more effective clinical resuscitation efforts.

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