Preface

Individual cells face three choices: to divide (mitosis), to specialize (differentiate) or to commit suicide (cell death). The balance between these processes ensures that the number of cells in an organism remains essentially in functional equilibrium. While mitosis and differentiation have received detailed attention from cell and molecular biologists for well over a century, physiological cell death has become a major interest only in the last twenty years. Until recent times, most reports of cell death focussed on "accidental" cell death, or "cell killing", where a cell dies because a vital metabolic process necessary for its continued survival is blocked. We now know that in multicellular organisms cell death by suicide is far, far, more common than death of cells because they have been killed.

In retrospect, it is surprising that for a long time biologists never questioned the fate of so many duplicating cells in our body. If we imagine an 80-year-old person in which mitosis proceeded unopposed by any balancing homeostatic death process, he would have around two square km of skin, two tons of bone marrow and lymph nodes, and a gut 16 km long. Indeed, mitosis unchecked by cell death results in neoplastic pathology. Ironically, it was study of just such a neoplasia - follicular lymphoma - that led to identification of the first component of the mechanism for cell suicide. While determining more about the mechanisms for cell death have continued to reveal much about the origins of malignant disease, they have also provided new insights into diseases caused by too much or unregulated cell suicide, such as neurodegenerative diseases.

Searching journal articles in the last twelve months using the terms "cell death" or "apoptosis" yields about 20,000 publications, yet the same search in the year 1987 identifies only 439 publications. The reason for this tremendous growth in interest in cell death research is that many of the molecular mechanisms by which cells kill themselves have been discovered, and abnormalities in the regulation of cell death have been linked to human disease.

Unfortunately, because of the rapid growth of the field, many of the publications on cell death are not totally reliable, have been contradicted, or remain controversial, which can be misleading for students or clinicians new to the area. Nonetheless, several new drugs have been developed based on our current understanding of the molecular mechanisms of death, and many advanced clinical trials look highly promising.

Since cell death has now become translational, and therefore of interest to clinicians, pharmacologists and medical chemists, as well as to basic biologists, it seems an appropriate time to produce this book. In it, we have attempted to clarify the inconsistencies in the literature, in particular by referring to more definitive studies now available using transgenic or gene deleted mice. We have also tried to highlight those as yet unexploited molecular pathways susceptible to therapeutic intervention.

Our thanks go first to our publisher, who stimulated us in this endeavour, and to the scientists who dedicated some of their precious time writing the individual chapters. Our apologies go to our many colleagues who could not be mentioned and properly credited because of time and space limitations. We hope our readers find our efforts insightful and rewarding.

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