



Book Review

Cell death; a survival strategy? Perspectives and mechanisms

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When Cells Die. A comprehensive evaluation of apoptosis and programmed cell death. Edited by Richard A Lockshin, Zahra Zakeri and Jonathan L Tilly. Wiley-Liss, New York: 1998. Pp. 504. ISBN: 0-471-16569-7

The initial intention of the Editors of this overview of cell death was to provide an introduction for newcomers to the field, and to help them appreciate the meaning and impact of apoptosis in their own spheres of interest. However, the distinguished group of contributors that the Editors have selected have provided a much broader and conceptual evaluation which remains accessible to neophytes while being a stimulating and rewarding read for more established thanatologists.

The book is divided into five main sections, each of several chapters. The first looks at the whole phenomenon of cell death in organisms ranging from prokaryotes to multicellular plants and mammals, not forgetting that well known worm *Caenorhabditis*. Also covered here, both by Benjamin Trump and Irene Berezsky and by Zahra Zakeri are the different types of cell death, and the role of these in development of insect, bird and mammalian tissues. The second, on 'Themes and Approaches to Cell Death' is a detailed look at two families of apoptotic executioners—the caspases and the endonucleases. Sections three and four consider cell death in dividing cells (such as lymphocytes) and in long lived terminally differentiated cells (such as neurons) respectively, while section five focuses on the clinical relevance of apoptosis, although other clinical implications are also mentioned elsewhere.

Three themes permeate the volume. One is that apoptosis is essentially a constructive event, a survival strategy. In this context, Jean-Claude Ameisen reviews the evidence for a form of apoptosis in bacteria and single celled eukaryotes, and suggests we think of apoptosis in a much longer and broader evolutionary and indeed Darwinian context than as an essential coevolutionary accompaniment of multicellularity. In multicellular organisms, damage to or malfunction of an individual cell disturbs the dynamic balance between pro- and anti-apoptotic gene products and results in its 'altruistic' suicide for the benefit of host survival. This, of course, enhances the likelihood of reproduction of the host genome. Ameisen sees a parallel here in the acquisition of the toxin/antitoxin genetic package in bacteria. While this may be 'selfish' in the sense of killing competing heterologous bacteria that do not possess the package, it may at the same time be or become 'altruistic' since it carries the potential for the suicide of individual bacterial cells in the longer term interests of the whole bacterial colony. The big question here is whether 'selfishness' and 'altruism' appear

simultaneously in bacterial evolution or whether acquisition of the first phenotype precedes the second. Is (or perhaps was, since the ability to commit suicide for the greater good seems so evolutionarily beneficial) a bug out there that can kill other bugs but not itself? Equally importantly, do pro- and anti-apoptotic 'altruistic' proteins in multicellular organisms have other, 'selfish' functions?

A second theme is the essentially unitary nature of apoptosis, whatever subtle difference in morphology and molecular mechanisms may be found in different cell types under different conditions. One aspect of this is seen by the emphasis on a general role for caspases, reviewed by Vincent Cryns and Junying Yuan, and their specific involvement in apoptosis of lymphocytes, neurons and the ovary. Even oncosis, as a variant of apoptosis discussed by Trump and Berezsky, appears to require these enzymes. In their review of endonuclease activities, however, Marianna Sikorska and Roy Walker emphasise that classic internucleosomal DNA fragmentation is not an invariant feature of apoptosis although the larger molecular weight fragmentation is a necessary and sufficient process to cause chromatin collapse with the characteristic nuclear morphology. Indeed, different cell types differ markedly in the degree to which their DNA becomes fragmented during apoptosis, and the still commonly used internucleosomal ladder may give a falsely negative indication of a genuinely apoptotic process.

The third theme is more of a plea. It is that rather than focus on measuring the late stages of apoptosis (counting the dead cells), we should concentrate more on studying earlier events (counting the challenged cells). By this, I understand the Editors to be referring to the possible definition of an irreversible point(s) of commitment and the sequence of molecular events that lead up to it, for these have the greater potential for therapeutic manipulation. Indeed, several authors display a healthy scepticism of the adequacy of many classical markers such as shrinkage, blebbing and internucleosomal DNA fragmentation since these are consequences of earlier events such as Ca entry and proteolytic damage to the cytoskeleton. The importance of the mitochondrial-cytosolic interface, the role of cytochrome C release and the mitochondrial membrane as the site of action of Bcl family members is also recognised by several authors, though perhaps not given quite the emphasis we should do now. However, perhaps we should

remember this scepticism, since further experiments—such as those involving anaerobic organisms which lack mitochondria—may cause us to revise our dogmas again.

Inevitably, the unavoidable delay between preparation of the reviews and publication means that recent data in a rapidly expanding field (in this case after 1997) is not included. Indeed, in an age where we are used to the virtually instantaneous dissemination of information via the internet, some may therefore question the value of books

such as this. However, this very immediacy of information delivery may threaten those powers of critical detachment and conceptual thinking that are essential in any scientist. If the book can evolve by losing (?by apoptosis) its sole role as an information carrier, it may gain a survival advantage in information technology as provider of the longer term perspective. This book is a prime example of its fully evolved form and I strongly recommend it to all whether touched by or submerged in cell death.