nature insight

Apoptosis

Cover illustration
Coloured scanning electron micrograph showing a killer T lymphocyte (orange) inducing a cancer cell (mauve) to undergo programmed cell death or apoptosis. Mauve vesicles are apoptotic bodies emerging from the cancer cell. (Image courtesy of A. Liepins/SPL.)

Programmed cell death, or apoptosis, is currently one of the hottest areas of modern biology. It describes the orchestrated collapse of a cell, staging membrane blebbing, cell shrinkage, protein fragmentation, chromatin condensation and DNA degradation followed by rapid engulfment of corpses by neighbouring cells.

The excitement ensued when it became clear that apoptosis is an essential part of life for any multicellular organism and that the way in which most cells die is conserved from worm to mammal. Optimum body maintenance means that about 10 billion of our cells will die on a normal day just to counter the numbers of new cells that arise through mitosis. During development apoptosis helps to sculpture the body, shape the organs, and carve out fingers and toes. Both the nervous system and the immune system arise through overproduction of cells followed by the death of those that fail to establish functional synaptic connections or productive antigen specificities, respectively. Apoptosis is necessary to purge the body of pathogen-invaded cells, but is also needed to eliminate activated or auto-aggressive immune cells.

Such massacre has to be tightly regulated as too little or too much cell death may lead to pathology, including developmental defects, autoimmune diseases, neurodegeneration or cancer. Not surprisingly then that the hunt is on to understand which cells die when, why and how precisely, and to find drugs that interfere with specific steps along the pathway. Naturally, with over 50,000 publications on the subject to date (source: ISI–Web of Science), it is impossible to be comprehensive, but we hope that this *Nature* Insight provides our readers with a taster of the latest developments in this rapidly moving field.

Michael Hengartner sets the stage on page 770 and introduces the assassins and victims in this molecular 'murder mystery'. On page 777 Andrew Wyllie and co-workers discuss why and how DNA damage results in apoptosis in some cells but not in others and what the consequences are if cells with damaged genomes fail to die. Once a cell is committed to die, its corpse must be removed and destroyed by phagocytic cells, as discussed by John Savill and Valerie Fadok on page 784. Peter Krammer outlines the importance of apoptosis for the immune system on page 789, focusing on the role of the infamous CD95 death receptor. On page 796 Gerard Evan and colleagues outline the molecular mechanisms that bring about apoptosis during development of various organisms, and highlight the conservation of cell death mechanisms during evolution. The role of programmed cell death in the construction and pathological deconstruction of the brain is discussed on page 802 by Junying Yuan and Bruce Yankner. It is evident from reading these reviews that death or serious illness may result if cells that should die survive, or cells that should live die. There is clearly huge therapeutic potential, but will apoptosis deliver its promise to medicine? On page 810 Donald Nicholson discusses the opportunities and limitations of taking apoptosis from the bench to the clinic.

We are indebted to all of the contributors to this Insight for their considerable efforts, despite space and time constraints, in producing an enlightening and thought-provoking collection of reviews.

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