Distinguished Visitor Programme

Prof Douglas Green
Head, Division of Cellular Immunology, La Jolla Institute for Allergy and Immunology

Biography

Prof. Green is the head of the Division of Cellular Immunology at the La Jolla Institute for Allergy and Immunology and Adjunct Professor of Biology, La Jolla Institute for Allergy and Immunology and also Adjunct Professor of Biology at the University of California, San Diego. Doug Green received his Ph.D. from Yale University. Before coming to San Diego, he was a faculty member in the Department of Immunology at the University of Alberta at Edmonton. He is head of the Division of Cellular Immunology at the La Jolla Institute for Allergy and Immunology.

Prof. Green's work can be found in several fields in ISI Essential Science Indicators Web product, including Clinical Medicine, Molecular Biology & Genetics, Biology & Biochemistry, and Immunology.

Their laboratory studies the process of apoptosis, or active cell death, and how it functions in the regulation of the immune system. At the center of this process is a set of proteases, the caspases, several of which make up the apoptotic "Executioner." During apoptosis these become active and orchestrate the death of the cell. Using cell-free and whole cell systems they are investigating how the Executioner becomes active, and exactly how it kills the cell. They and others have identified a number of proteins that are cleaved upon activation of the Executioner proteases, but, at this point, few of them unambiguously play a role in the apoptotic process. One endpoint, however, is the externalization of phosphatidylserine in the plasma membrane, and this is responsible for triggering the active removal of the apoptotic cell by phagocytic cells in vivo.

One mechanism of caspase activation involves the release of cytochrome c from mitochondria. Cytochrome c in the cytosol becomes part of a complex called the "apoptosome" which includes a caspase. Cytochrome c release from mitochondria is regulated to control apoptosis, and the nature of both the release and the regulation are under active study. One cell surface molecule that can trigger apoptosis when it is ligated is Fas, or CD95, found on activated lymphocytes and other cells. CD95 is bound and activated by its ligand, and therefore the regulation of expression of the CD95-ligand is important in the induction of apoptosis in the immune system. We are actively investigating the expression of the ligand, in lymphoid and nonlymphoid cells, and how this functions to regulate immune responses. They have found that the expression of CD95-ligand in nonlymphoid tissues controls the extent of immune responses in those tissues, leading to the phenomenon of immune "privilege."

Their research therefore extends from the role of apoptosis in the regulation of immune responses in the whole organism, to the fundamental molecular events directing the death of the cell.
Lecture Abstract

8 October 2003, 6.15 pm, Clinical Research Centre (CRC) Auditorium, Faculty of Medicine, MD 11, National University of Singapore, 10 Medical Drive, Singapore 117597

"The Mirror of Life: Cell Death in Health and Disease"

"We generally think that to "die a little every day" is a bad thing, and of course it can be. But it is also an essential part of the way our bodies work- the death of some of our cells is critically important in the prevention of diseases like cancer and autoimmunity. Whenever a cell divides, and this happens very often in our bodies, there is a chance that it can become a tumor; what helps to prevent this in the vast majority of cell divisions is the activation of programs that hold that cell on the "edge of death" so that it will die if it isn't in the right place at the right time. Similarly, in our immune systems, each time an immune lymphocyte is "born" it has the potential to cause devastating destruction of our own tissues; these cells are on the "edge of death" until what they can respond to is rigorously tested.

The cell death that our cells can undergo as part of these critical processes is called "apoptosis". Apoptosis is controlled in most cases by the mitochondria, the "energy factories" of the cell, but here the effect has nothing to do with energy - it is another completely different function of the mitochondria that controls apoptosis. We need mitochondria to keep our cells alive - it turns out that we also need them for our cells to die. And as a consequence, we can "die a little day" in the best possible ways"