

Key Event in Cell Death Occurs as Single, Quick Event

August 3 2006

Scientists at St. Jude Children's Research Hospital have demonstrated that a key event during apoptosis (cell suicide) occurs as a single, quick event, rather than as a step-by-step process. Apoptosis eliminates extraneous cells from the developing body; and disposes of cells that sustain irreparable harm to their DNA or are infected with microorganisms.

The researchers photographed individual cells undergoing that process, allowing investigators to observe the release of certain proteins from pores in the membranes of mitochondria. These cellular structures contain enzymes that extract energy from food molecules, and the space within the membrane surrounding them holds a variety of proteins that are released during apoptosis.

Results of the study indicate the formation of pores in the mitochondrial membranes is a rapid process that allows a nearly simultaneous rather than a sequential release of many apoptosis proteins, according to Douglas Green, Ph.D., chair of the St. Jude Department of Immunology. Green is senior author of a report on this work that appears in the August 1 issue of *Proceedings of the National Academy of Sciences*. The process of pore formation, called mitochondrial outer membrane permeabilization (MOMP), allows apoptosis proteins stored underneath the membrane to escape and orchestrate the cell's destruction.

MOMP is controlled by a family of proteins called Bcl-2; some of these support apoptosis and others interrupt the process. The pro- and anti-



apoptotic Bcl-2 proteins cooperate to weigh and balance cell signals that promote survival or death, in this way determining the final outcome. During apoptosis, these proteins are either already on the mitochondrial membranes or migrate to the membranes, where they trigger MOMP.

"The slow, continuous release of one of the proteins, apoptosis-inducing factor (AIF), suggests that the pore formed during MOMP remains open for many hours," Green said. "Our finding of nearly simultaneous rather than sequential release of the mitochondrial membrane proteins helps to explain the timing of the movement of these apoptosis proteins following MOMP. The findings also suggest that release of these proteins is not controlled by multiple levels of regulators, but rather occurs as a single event."

The study also highlights the importance of the Bcl-2 family in regulating the formation of pores in the mitochondrial membrane and emphasizes how critical the formation of these pores is to the regulation of apoptosis, Green said.

The team found that after cells were treated with a chemical that triggers apoptosis, it took three to 10 minutes for several proteins, cytochrome c, Smac, Omi and adenylate kinase-2 to escape together immediately following MOMP.

However, the AIF protein escaped from the mitochondrial membrane much more slowly and incompletely, starting with the release of cytochrome c but continuing during the next few hours. The St. Jude researchers concluded that while AIF is known to regulate other cellular processes, the protein itself is not involved in triggering apoptosis.

The researchers made the movement of the proteins visible by attaching fluorescent tags to make them glow when observed under a special microscope equipped with a laser that scanned the cells.



Source: St. Jude Children's Research Hospital

Citation: Key Event in Cell Death Occurs as Single, Quick Event (2006, August 3) retrieved 2 May 2024 from <u>https://medicalxpress.com/news/2006-08-key-event-cell-death-quick.html</u>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.