جامعة الملك سعود
King Saud University

college of sciences
Zoology Department

Cell Biology and Physiology

ZOO (242)

Apoptosis (programmed cell death)

Learning objectives

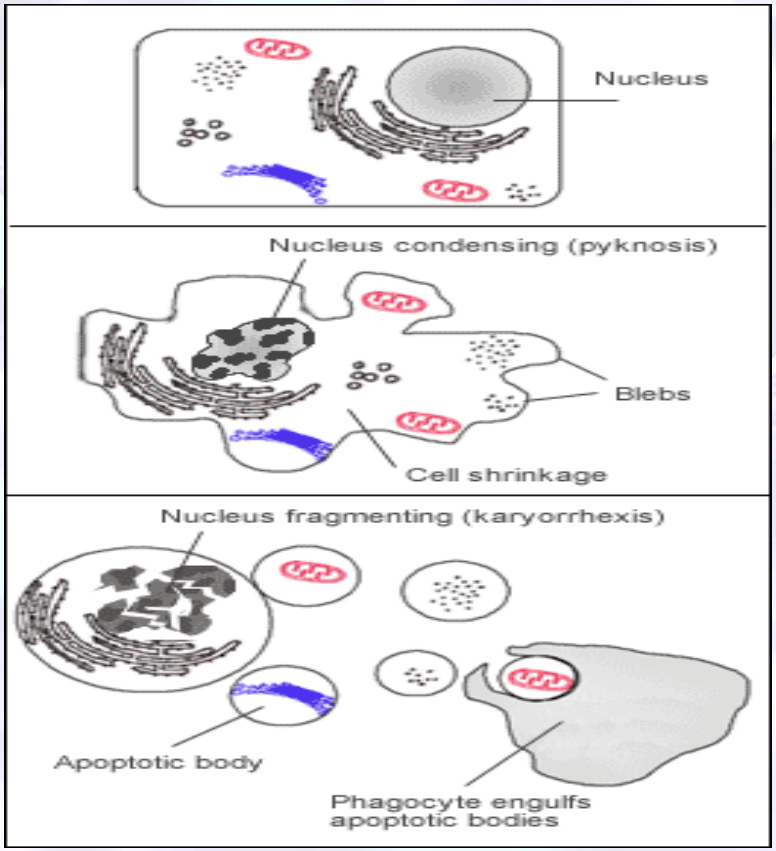
- Through this lecture the students will be able to
- Understand apoptosis, the difference between programmed cell death and necrosis.
- The morphological events of apoptosis.
- Describe the role of apoptosis in diseases Describe the events that may trigger signals from within or outside of a cell to trigger apoptosis.

Introduction

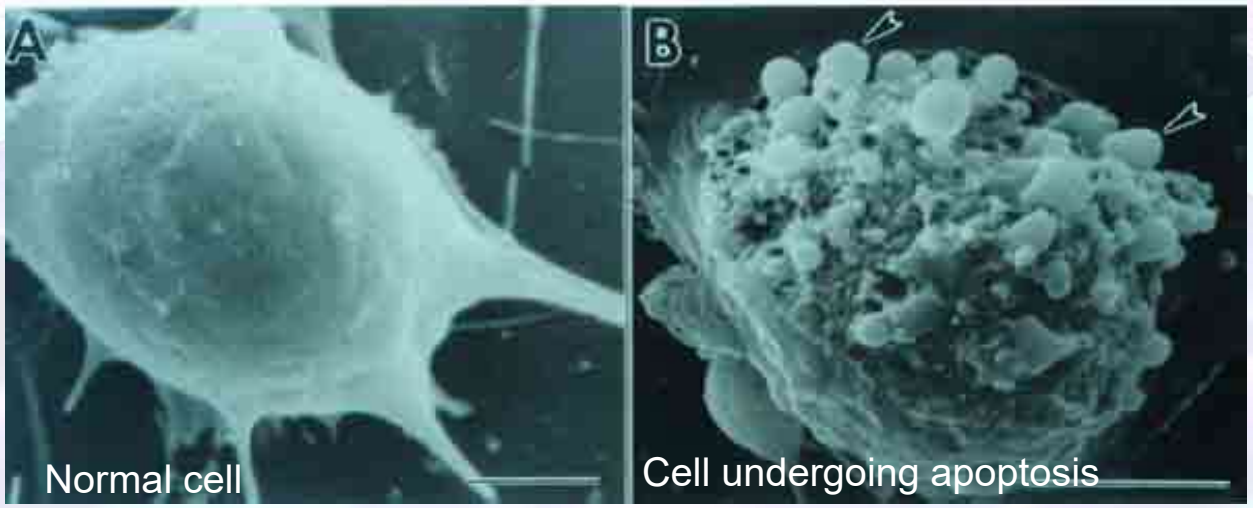
- Apoptosis is the process of programmed cell death that may occur in multicellular organisms.
- There are two ways that a cell can die: Either by necrosis or apoptosis.
- **Necrosis** occurs when a cell is damaged by an external force, such as poison, a bodily injury, an infection or getting cut off from the blood supply (which might occur during a heart attack or stroke). When cells die from necrosis, it's a rather messy affair. The death causes inflammation that can cause further distress or injury within the body.
- **Programmed cell death (Apoptosis)** is the process by which cells in plants and animals die through self –destruction through a built-in cell suicide mechanism rather than due to injury.

Events of apoptosis

- During this process, cellular agents chop up the DNA and fragment the organelles and other cytoplasmic components.
- The cell shrinks and becomes lobed (also called "blebbing"), and the cell's parts are packaged up in vesicles that are engulfed and digested by specialized scavenger cells, leaving no trace.
- Apoptosis protects neighboring cells from damage that they would otherwise suffer if a dying cell merely leaked out all its contents, including its many digestive enzymes



Scanning electron micrograph of cell undergoing apoptosis



Neuroscience Research Slides from UCI
http://www.neuroscience.uci.edu/research/resslides.htm

What cause a cell to go under apoptosis?

- Apoptosis is a general and convenient way to remove cells that should no longer be part of the organism.

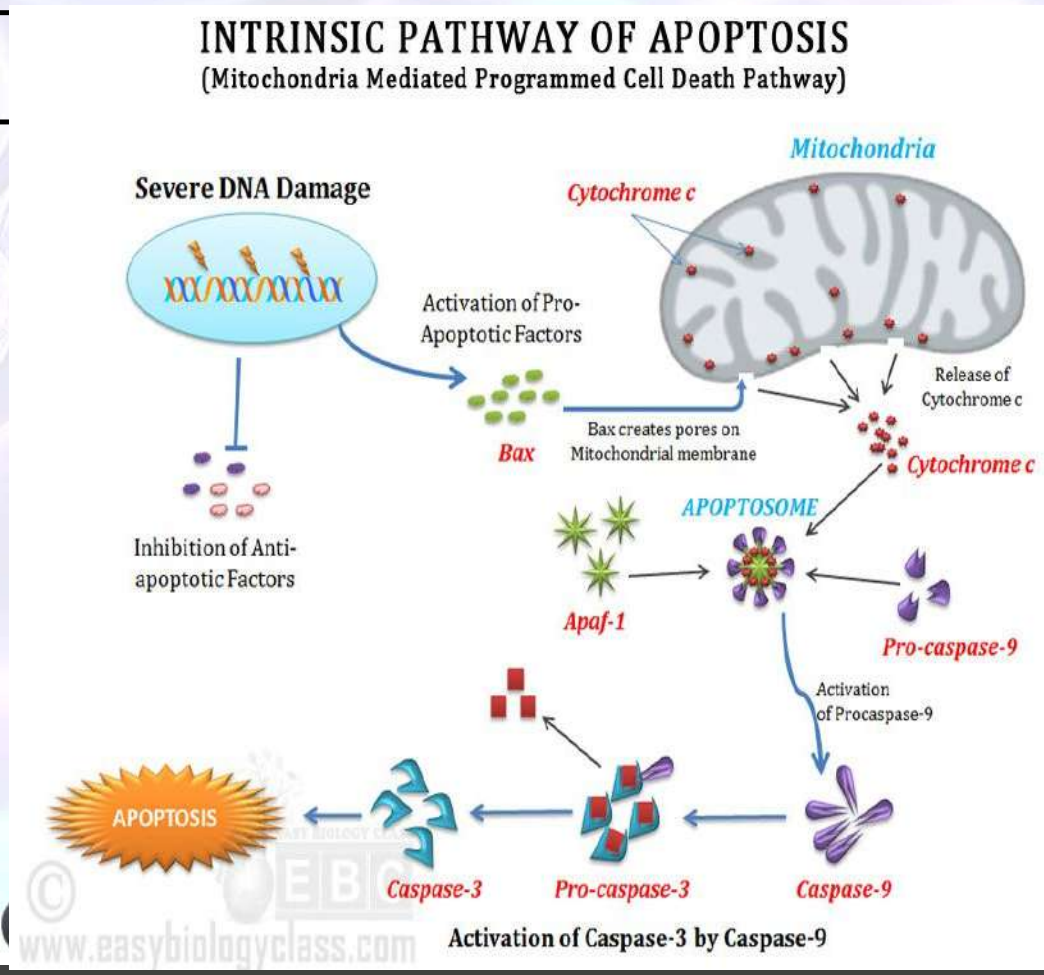
- cells may need to be “deleted” during development and some may be harm to the other cells (they are abnormal cells with DNA damaged or virally infected .

Regulation of apoptosis

- Before the actual process of cell death is triggered by enzymes, apoptotic signals must cause regulatory proteins to initiate the apoptosis pathway. This step allows those signals to cause cell death, or the process to be stopped (the cell no longer need to die). The apoptosis is controlled by various internal (intrinsic) or external (extrinsic) signals.
- **Intrinsic pathway** Several proteins are involved, but two main methods of regulation have been identified:
  - ❖ Targeting of mitochondria functionality.
  - ❖ Direct transducing the signal via adaptor proteins to the apoptotic mechanisms.
- **An extrinsic (external) pathway:** the initiation of apoptosis by external signal has been identified in several toxin studies.

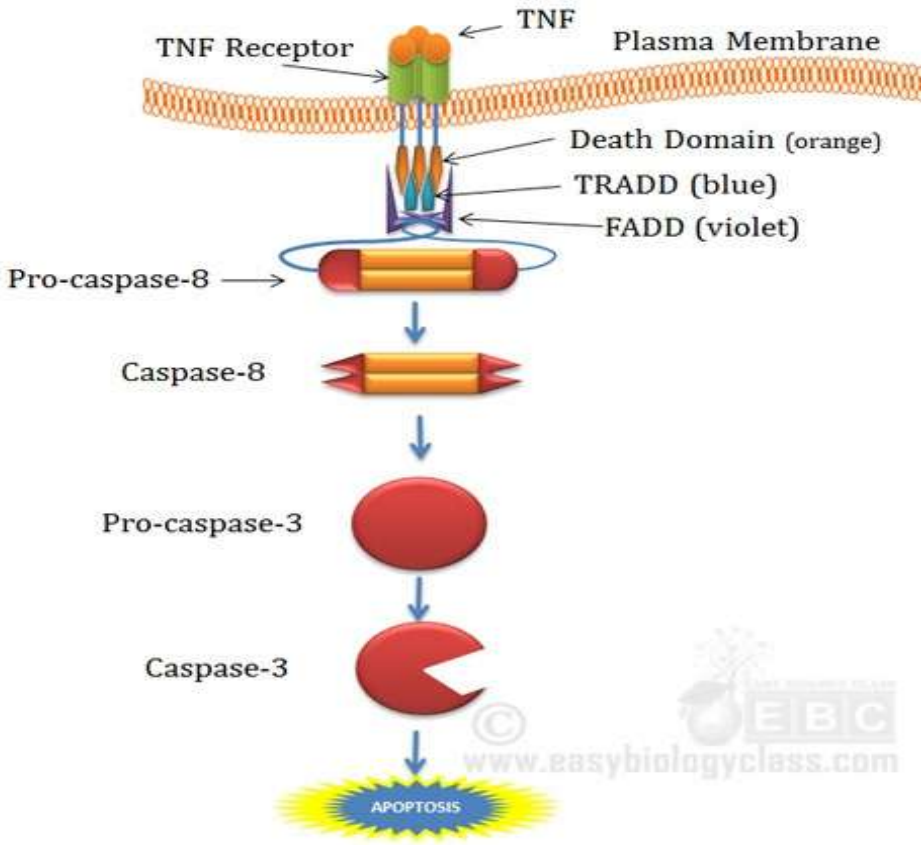
Intrinsic pathway

- The key gene is P53, which inhibit BCL2 and cause Cytochrome C release from mitochondria and initiate cell death through caspase 9.



An extrinsic (external) pathway

- Two theories of the direct initiation of apoptotic mechanisms in mammals have been suggested:
  - The TNF-induced (tumour necrosis factor) model and the
  - Fas-Fas ligand-mediated model recepotor on membrane,
  - And then activate key genes (Caspase genes) leading to cell death.
- Both involving receptors of the TNF receptor (TNFR) family coupled to extrinsic signals.



Extrinsic Pathway of Apoptosis

The morphological events of apoptosis

1. Cell shrinkage and rounding are shown.
2. The cytoplasm appears dense, and the organelles appear tightly packed.
3. Chromatin undergoes condensation into compact patches against the nuclear envelope.
4. The cell membrane shows irregular buds known as blebs.
5. The cell breaks apart into several vesicles called apoptotic bodies, which are then phagocytosed.

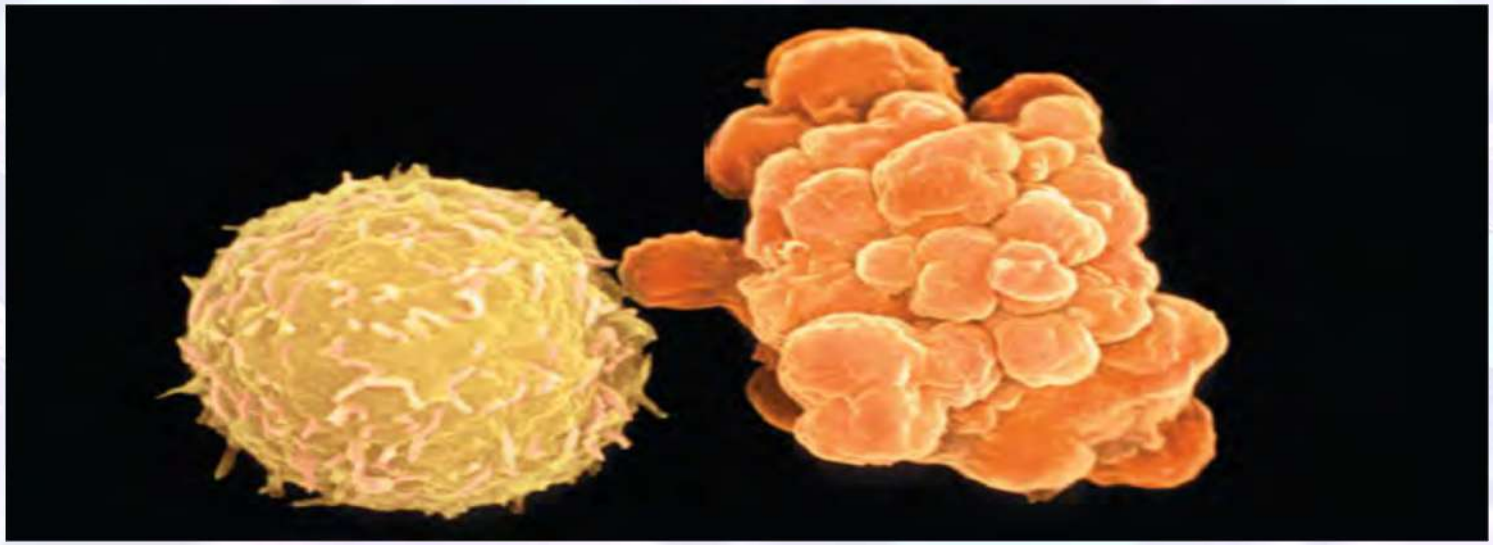


Figure: Apoptosis of a human white blood cell. We can compare a normal white blood cell (left) with a white blood cell undergoing apoptosis (right). The apoptotic cell is shrinking and forming lobes ("blebs"), which eventually are shed as membrane bounded cell fragments (colorized SEMs).

Implication in disease

- **Inhibition of apoptosis**
- The normal functioning of the apoptotic pathway has been disrupted in such a way as to impair the ability of the cell to undergo normal apoptosis.
- This results in a cell that lives past its "use-by-date" and is able to replicate and pass on any faulty machinery to its progeny, increasing the likelihood of the cell's becoming cancerous or diseased.
- Inhibition of apoptosis can result in a number of cancers, autoimmune diseases, inflammatory diseases, and viral infections.
- The cancer was originally believed to be associated with accumulation of cells due to an increase in cellular proliferation, but it is now known that it is also due to a decrease in cell death.

Dysregulation of p53

- p53 prevents the cell from replicating by stopping the cell cycle at G1, or interphase, to give the cell time to repair, however it will induce apoptosis if damage is extensive and repair efforts fail.
- The tumor-suppressor protein p53 accumulates when DNA is damaged due to a chain of biochemical factors. Any disruption to the regulation of the p53 gene will result in impaired apoptosis and the possible formation of tumors.

Summary

- **Apoptosis** is a type of programmed cell death in which cell components are disposed of in an orderly fashion, without damage to neighboring cells.
- Several apoptotic signaling pathways exist in the cells of humans and other mammals, and these pathways may be triggered in several ways.
- Signals eliciting the apoptotic response can originate from outside or inside the cell.
- A major pathway involves pore formation in the outer mitochondrial membrane, which leads to release of factors that activate caspases.

References

- Green, Douglas (2011). Means to an End: Apoptosis and other Cell Death Mechanisms. Cold Spring Harbor, NY: Cold Spring Harbor Laboratory Press.
- Molecular Biology of the Cell (textbook) (5th ed.) by Alberts Bruce,(2008). "Chapter 18 Apoptosis: Programmed Cell Death Eliminates Unwanted Cells".