TOPIC: APOPTOSIS

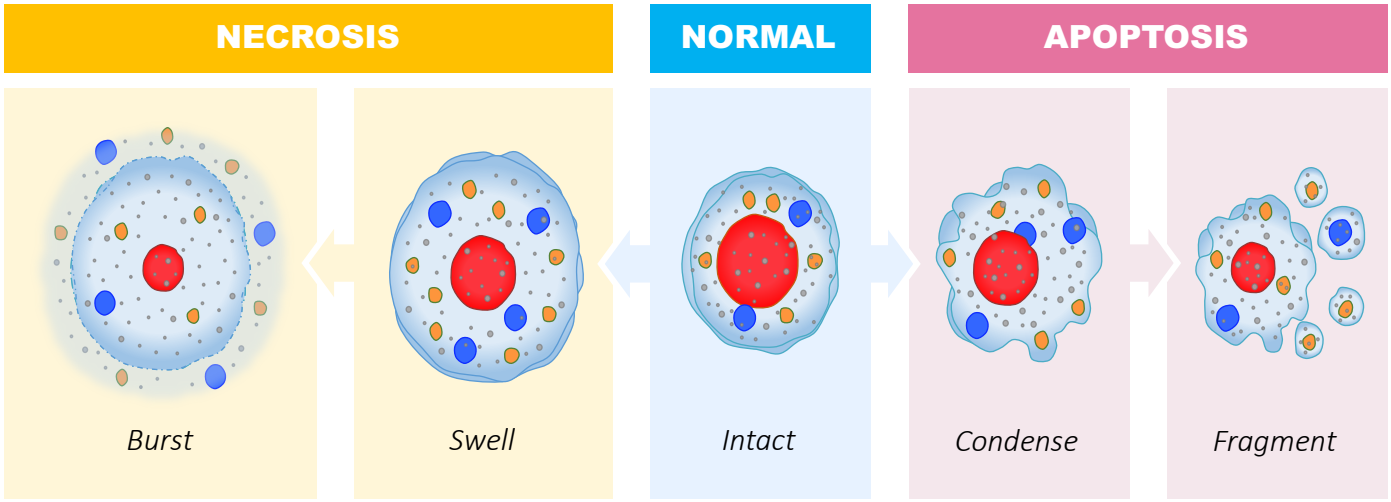
Key Knowledge:

- Apoptosis as a regulated process of programmed cell death
- Disruption to the regulation of the cell cycle and malfunctions in apoptosis that may result in deviant cell behaviour: cancer and the characteristics of cancer cells

CELL DEATH

Cell death can be either uncontrolled (necrosis = cell 'homicide') or occur via a sequence of controlled and coordinated steps (apoptosis = cell 'suicide'). While necrosis is detrimental to a multicellular organism and causes inflammation, apoptosis is a necessary process that is characterised by the following events:

- Apoptotic enzymes (caspases) are produced and cleave specific proteins in the cytoplasm and nucleus
- Cytoplasmic components, including the cytoskeleton, are digested, causing the cell to begin to shrink
- The cell membrane undergoes irregular bulging (blebbing) and the cell fragments into apoptotic bodies



APOPTOTIC PATHWAYS

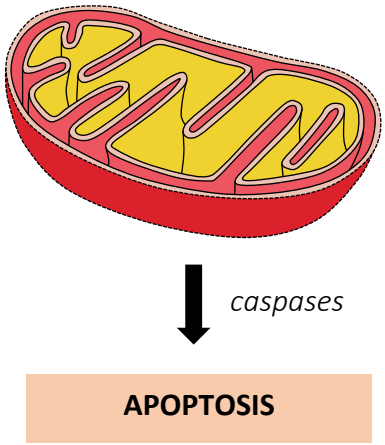
Apoptosis may be triggered by signals that originate either within the cell or externally. Internal signals will trigger an intrinsic process called the mitochondrial pathway, while external signals will trigger an extrinsic process called the death receptor pathway. Both pathways cause apoptosis via the production of caspases.

1. INTRINSIC PATHWAY

Apoptosis can be induced by a variety of intracellular signals, such as DNA damage, nutritional deprivation or oxidative stress responses.

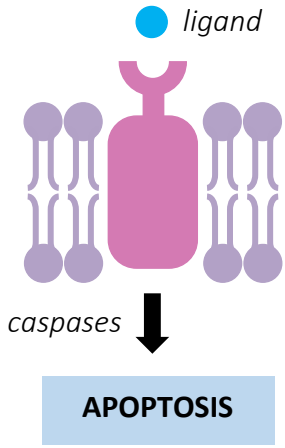
These intrinsic triggers result in the following cellular responses:

- The internal signals cause the mitochondrial membrane to become more permeable and release apoptotic proteins into the cytosol.
- The apoptotic proteins then activate caspases, which digest cellular proteins within the cytoplasm and nucleus, leading to apoptosis.
- The cell contents are packaged into apoptotic bodies and recycled via phagocytosis as the membrane blebs and the cell fragments.



2. EXTRINSIC PATHWAY

Apoptosis can also be induced by extracellular signals, such as chemicals that are released from surrounding cells to cause programmed cell death.



These extrinsic triggers result in the following cellular responses:

- The external signalling molecules (ligands) bind to a death receptor on the plasma membrane of the cell that is targeted for apoptosis.
- The death receptor initiates a signal transduction cascade that will activate apoptotic proteins, resulting in the production of caspases.
- Caspases will break down the cytoskeleton, which will lead to the fragmentation of the cell and the formation of apoptotic bodies.

FUNCTIONS OF APOPTOSIS

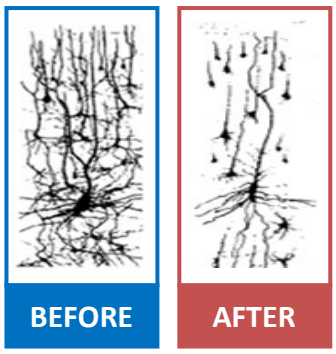
Apoptosis plays a vital role in organism development and survival, by removing cells that are not needed or by recycling excess cells to reduce energy costs. Examples of processes that involve apoptosis include:

- The foetal development of fingers and toes (as a result of the controlled loss of tissue between digits)
- The reinforcement and restructuring of synaptic connections within the brain via neural pruning
- The removal of excess plasma cells after a successful immune response or the targeting of cancer cells

Malfunctions to normal apoptotic processes can result in a wide variety of disease conditions, depending on whether levels of apoptosis are suppressed (below normal levels) or excessive (above normal levels).

NEURODEGENERATION

Excessive amounts of apoptosis can lead to neurodegeneration in brain tissue. This can lead to debilitating diseases such as Parkinson's disease or Alzheimer's disease. The progressive atrophy of nerve tissue is a very common consequence of ageing, which is associated with higher levels of DNA mutations and greater frequencies of oxidative stress responses. Blocking apoptotic processes in those with neurodegenerative conditions could decrease the development of symptoms associated with diseases.



CANCER

Insufficient amounts of apoptosis can lead to the development of cancers (uncontrolled cell proliferation). Cancers result in abnormal cellular growths (called tumours) that can be benign if they remain in their original tissue, or malignant if they spread to neighbouring tissues (metastasis). Cancers are caused by mutations to cancer-causing oncogenes (which promote unrestricted cell division) or tumour-supressing anti-oncogenes (which normally function to suppress tissue growth via apoptosis). Environmental factors that can cause mutations are called mutagens, and if they also cause cancer they are called carcinogens.