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Apoptosis

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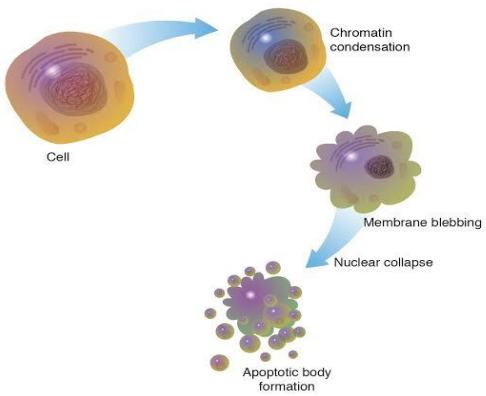
Abstract *— The term "apoptosis" originates from the Greek language, where it signifies the process of "dropping off" or "falling off." In the context of nature, it specifically refers to the shedding of petals from flowers or leaves from trees, reflecting a natural and orderly process of cellular elimination. In biological terms, apoptosis involves a meticulously orchestrated sequence of molecular events within a cell, leading to its systematic self-destruction. This process is tightly regulated and serves various crucial functions in maintaining tissue homeostasis, development, and eliminating damaged or unnecessary cells from the body. During apoptosis, the cell undergoes distinct morphological changes, including condensation of the nucleus, fragmentation of DNA, and formation of apoptotic bodies. These changes facilitate the efficient removal of the dying cell without causing inflammation or damage to neighboring cells. Once the cell has undergone apoptosis, it is typically engulfed and digested by neighboring cells, a process known as phagocytosis. This ensures the prompt and efficient clearance of cellular debris, preventing any potential harmful effects on the surrounding tissue. Overall, apoptosis plays a vital role in shaping the development and maintenance of multicellular organisms by eliminating unwanted or compromised cells, thereby contributing to tissue remodeling, immune response regulation, and overall organismal health.*

Keywords *— **Apoptosis, Programmed cell death, Cellular self-destruction, Molecular events, Tissue homeostasis***

INTRODUCTION

The term apoptosis can be defined as a natural biological process of programmed cell death in which the cells destroy themselves for maintaining the smooth functioning of the body.



Apoptosis occurs normally during development and aging and as a homeostatic mechanism to maintain cell populations in tissues. Apoptosis also occurs as a defense mechanism such as in immune reactions or

when cells are damaged by disease or noxious agents. Although there are a wide variety of stimuli and conditions, both physiological and pathological, that can trigger apoptosis, not all cells will necessarily die in response to the same stimulus. Irradiation or drugs used for cancer chemotherapy results in DNA damage in some cells, which can lead to apoptotic death through a p53-dependent pathway. Some hormones, such as corticosteroids, may lead to apoptotic death in some cells (e.g., thymocytes) although other cells are unaffected or even stimulated.

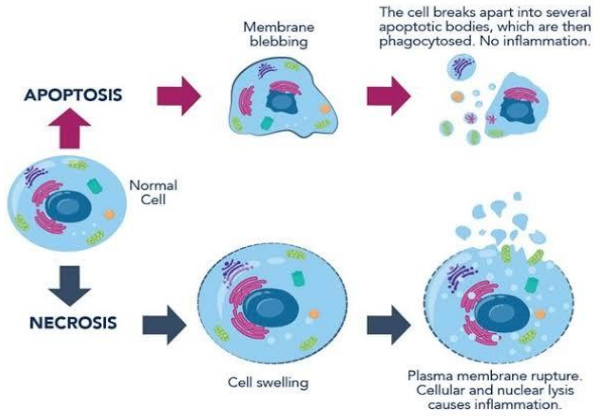
Cell death:

Cell die by one of two mechanisms-

- Necrosis - Death By Injury

-Apoptosis - Death By Suicide

Apoptosis and necrosis have different characteristics.



What is the difference between necrosis and apoptosis?

The main difference between apoptosis and necrosis is that apoptosis is a natural and controlled process of cell death while necrosis is an uncontrolled process of cell death. Apoptosis is important for the development and maintenance of healthy tissues while necrosis leads to tissue damage.

Apoptosis is a type of programmed cell death that occurs in response to various stimuli, such as DNA damage or viral infection. Apoptosis is characterized by several morphological changes, including cell shrinkage, plasma membrane bulging (known as blebbing), chromatin condensation, and formation of apoptotic bodies.

Necrosis, on the other hand, is a type of cell death that occurs in response to extreme stress, such as exposure to toxins or infection. Necrosis is characterized by cell swelling, membrane rupture, and release of inflammatory mediators.

Classic changes during apoptosis:

Cell shrinkage

Nuclear fragmentation

- Chromatin condensation
- Chromosomal DNA fragmentation
- Formation of cytoplasmic blebs& apoptotic bodies
- Phagocytosis

Significance of apoptosis:

• Helps sculpt hands and feet during embryonic development.

• Cells die by apoptosis when the structure is no longer needed e.g-when tadpole changes into a frog at

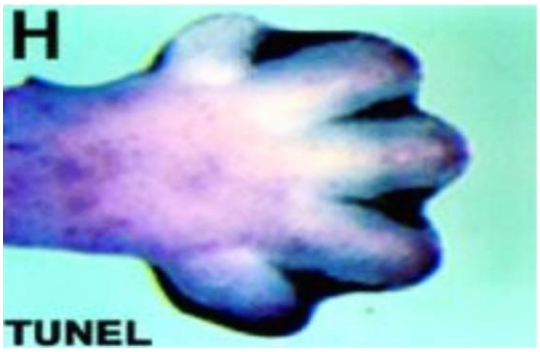
metamorphosis, the cells in the tail die b'coz tail is not needed by adult frog.

• Helps to eliminate cells that are abnormal, non-functional or potentially dangerous to the animal. In human body about one lakh cells are produced every second by mitosis and a similar number die by apoptosis.

• Animal cells recognize damage in cell organelles and can kill themselves-DNA damage can produce cancer promoting mutations, if not repaired. Cells undergo apoptosis if they cannot repair it.

Examples of apoptosis:

Apoptosis in bud formation during which many interdigital cells die. They are stained black by a TUNEL method



- Incomplete differentiation in two toes due to lack of

apoptosis

Pathways of apoptosis:

The process of apoptosis undergoes two pathways:

1. Extrinsic Pathway

2. Intrinsic Pathway

Extrinsic Pathway

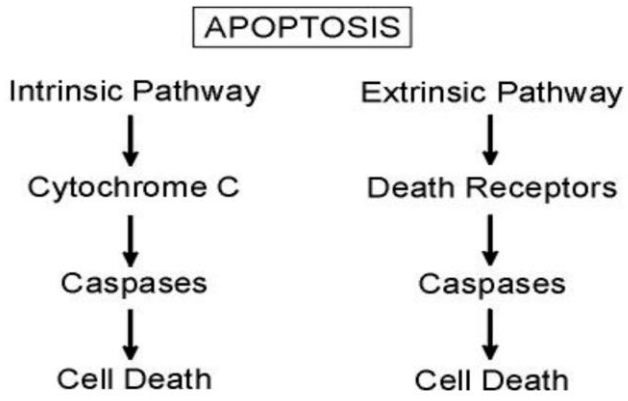
This pathway triggers apoptosis in response to external stimuli, like, ligand binding at death receptors on the cell surface. These receptors are members of the Tumor Necrosis Factor gene family. The receptor binding initiates caspase activation.

Intrinsic Pathway

This pathway triggers apoptosis in response to internal stimuli such as biochemical stress, DNA damage and lack of growth factors. This pathway is modulated by two groups of molecules- Bax, and Bcl-2. These groups of molecules determine whether a cell will survive or undergo apoptosis in response to the stimuli.

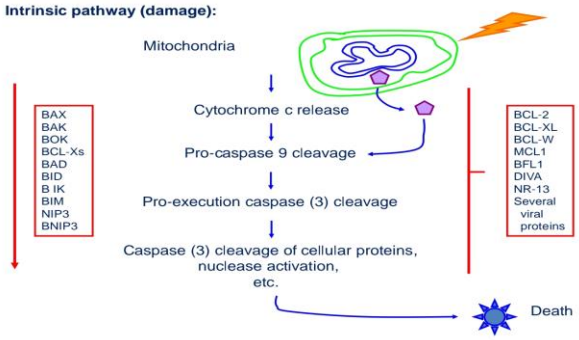
Apoptosis occurs by two activation pathways.

- Extrinsic (death receptor) pathway
- Intrinsic (mitochondrial) pathway



Inhibition of apoptosis

- Many cells produce inhibitory proteins that act to restrain the extrinsic pathway. Some cells produce protein FLIP (Flice-like Inhibitory Protein), which resembles an initiator caspase but has no protease activity b'coz it lacks the key cysteine in its active site. FLIP dimerizes with caspase-8 in the DISC, caspase-8 is not cleaved at the site required for its stable activation and the apoptotic signal is blocked. This prevents inappropriate activation of extrinsic pathway of apoptosis.



Role of apoptosis

1. Large number of apoptotic cells that have been detected in the brains of patients with neurodegenerative disorders. involving oxidative stress, perturbed calcium homeostasis, mitochondrial dysfunction and activation of cysteine proteases called caspases.

2. Apoptosis plays an important role in the body of an organism. Following are a few such roles performed by the process:

3. The separation of the fingers during the development of the foetus is due to apoptosis.It results in the closure of the neural tube in the dorsal part.

4. Programmed cell death results in the removal of vestigial remnants such as pronephros.

5. During the determination of sex of the foetus, the Wolffian ducts are removed by cell death.

6. In the urachus, apoptosis allows the removal of redundant tissues between the bladder and umbilicus.

Apoptosis: Role in Disease Cancer:

Virus associated cancer

•Several human papilloma viruses (HPV) have been implicated in causing cervical cancer. One of them produces a protein (E6) that binds and inactivates the apoptosis promoter p53.

•Epstein-Barr Virus (EBV), the cause of mononucleosis and associated with some lymphomas

– produces a protein similar to Bcl-2

– produces another protein that causes the cell to increase its own production of Bcl-2. Both these actions make the cell more resistant to apoptosis.

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