15.2: Apoptosis

Both cell proliferation and apoptosis (controlled/progammed cell death) are decisive processes within a cell. Keep in mind, apoptosis is distinct from cell necrosis, in which cell death is usually attributable to physical or chemical damage and rapidly spontaneous; think explosion.

Apoptosis is genetically programmed cell death, which leads to “tidy” breakdown and disposal of cells. Morphologically, apoptosis is characterized by shrinking of the cell, changes in the cell membrane (with the formation of small blebs known as “apoptotic bodies”), shrinking of the nucleus, chromatin condensation, and fragmentation of DNA. Macrophages and other phagocytic cells recognize this signal and remove apoptotic cells by phagocytosis without inflammatory phenomena developing. Apoptosis regulates the growth of normal tissues and removes unwanted cells in a controlled manner.

Caspases are a family of enzymes that control this process. These are cysteine proteases that cleave proteins next to aspartate residues when they become activated. When a cell receives an apoptotic signal, the procaspases become active and begin the process of protein degradation starting with the cleavage of laminins in the nuclear envelope, protein kinases, transcription factors, snRP proteins, and inhibitors of special DNAses, which are able to fragment the nuclear DNA (figure 15.6).
Figure 15.6: Comparison of intrinsic and extrinsic apoptosis pathways.

The extrinsic pathway for apoptosis is triggered on the cell surface by ligands that bind to receptors of the tumor necrosis factor family (TNFR, "death receptors"). These include Fas receptors, which are present on the plasma membrane of most cells in the body. When Fas ligands bind to a cell’s Fas receptors, trimerization of the receptors takes place via the adapter protein FADD ("Fas-associated death domain"), which activates the initiator caspases 8 and 10 inside the cell, setting in motion the apoptotic process.

The intrinsic, mitochondrial pathway is triggered by genotoxic (DNA damage) or oxidative stress. Aided by Bcl proteins, chemical stress makes the outer mitochondrial membrane leaky. As a result, mitochondrial proteins reach the cytoplasm. Cytochrome c in particular then triggers the caspase cascade by binding to the adapter protein Apaf1 and promoting formation of an apoptosome, a wheel-shaped heptamer that recruits initiator procaspase 9 and activates it to caspase 9.

The Bcl protein family not only includes proapoptotic proteins (Bax, Bak, and Bim) but also proteins that inhibit apoptosis (including Bcl2). Extracellular growth factors ensure inactivation of Bad or replication of Bcl 2, thus preventing apoptosis.

References and resources

Text

Clark, M. A. *Biology*, 2nd ed. Houston, TX: OpenStax College, Rice University, 2018, Chapter 9: Cell Communication, Chapter 10: Cell Reproduction.


Figures

Grey, Kindred, Figure 15.6 Comparison of intrinsic and extrinsic apoptosis pathways. 2021. https://archive.org/details/
Added Model № 2 of apoptosome formation and activation of caspase-9 and caspase-3 (hy) by Brat Ural. From Wikimedia Commons. Added ion channel by Léa Lortal from the Noun Project.