Adaptation

Apoptosis

Apoptosis or programmed cell death can be induced by intrinsic or extrinsic pathway.

Normally, growth factors bind to their receptors in the cells and prevent the release of cytochrome C and SMAC.

withdrawal or absence of growth factors can result in release of these mediators and initiate the intrinsic pathway.

Intrinsic pathway:

It is initiated by the release of cytochrome C and SMAC (second mitochondrial activator of caspases) from the mitochondrial inter-membrane space.

Release of cytochrome C with dATP, procaspase-9 and APAF- 1 (apoptosis activating factor -1) into the cytoplasm, leading to sequential activation of caspase-9 and effector caspases {Caspases- 3 and -7}.

Intrinsic pathway:

Release, SMAC binds and blocks the function of IAPs (Inhibitor of Apoptosis Proteins).

Normally, IAPs are responsible for causing the blocking the activation of caspases and keep cells alive and so, neutralization of IAPs permits the initiation of a caspase cascade.

Extrinsic pathway of apoptosis:

It is activated by:

Binding of Fas ligand to CD95 (Fas; member of TNF receptor family) or

Binding of TRAIL (TNF related apoptosis inducing ligand) to death receptors DR4 and DR5.

This induces the association of FADD (Fas- associated death domain) and procaspase-10 to death domain motifs of the receptors resulting in activation of caspase 10 which finally activates caspases- 3 and 7 that are final effector caspases.

Cellular proteins particularly a caspase antagonist called FLIP, binds to procaspase-10 but can not activate it.

This is important because some viruses produce homologues of FLIP and protect themselves from apoptosis.

Mitochondrion play a central regulatory structure of apoptosis.

Caspase 3 is the most important executioner caspase.

Condensation of nuclear chromatin is the most characteristic feature of apoptosis .

Glucocorticoids induce apoptosis while sex steroids inhibit apoptosis