Apoptosis && autophagy

Cell death

Necrosis

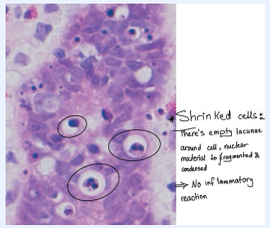
Uncontrolled,damaging death

- ➢ Cell size —> Enlarged (swelling)
- ➢ Nucleus —> Pyknosis, Karyorrhexis,Karyolysis.
- ➢ Plasma membrane —> Disrupted
- ➢ Cellular content —> Enzymatic digestion, may leak out of cell
- ➢ Adjacent inflammation —> Frequent
- ➢ Physiologic or pathologic role —> always pathologic

Apoptosis

Programmed, controlled death

- ➢ Cell size —> Reduced (shrinkage)
- ➢ Nucleus —> Fragmentation into nucleosome- size fragments < we can say pyknosis and karyorrhexis>
- ➢ Plasma membrane—> Intact, altered structure, especially orientation of lipids
- ➢ Cellular content —> Intact, may be released in apoptotic bodies.
- ➢ Adjacent inflammation—> No
- ➢ Physiologic or pathologic role —> often physiologic and may be pathologic



Causes of apoptosis

Physiologic

- ➢ embryogenesis
- ➢ Involution of tissues upon hormone deprivation (Cyclic endometrium, lactating breast)
- ➢ Steady state population (Gut, Skin) “rapid turnover“
- ➢ End of function/life (neutrophils at end of inflammation)
- ➢ Self reacting lymphocytes

Pathologic

- ➢ DNA damage (Rx, chemoTx, temperature, UV, hypoxia)
- ➢ Accumulation of misfolded proteins
- ➢ Some infections (adenovirus, HIV, hepatitis viruses)

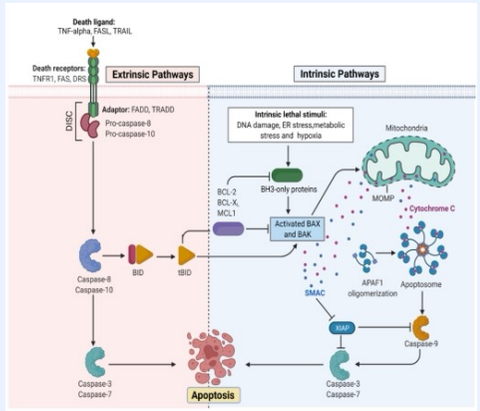
Mechanisms of apoptosis

Intrinsic pathway (Mitochondrial pathway)

- ➢ in most physiological and pathological situations
- ➢ The lack of survival signals, activate sensors as **BH3** that is located in cytoplasm those sensors **inhibit BCL2(antiapoptic proteins)** and **activation of BAX and BAK**, the BAX and BAK will dimerise forming a channel where **cytochrome c** leak outside the mitochondria and activate **caspases *9***. And a series of the actions until the cellular proteins and organelles go through apoptosis.

Extrinsic pathway

- ➢ **TNF** receptor family, cytoplasmic death domain
- ➢ Prototypes: Type 1 TNF receptor and **Fas**
- ➢ Fas ligand on activated T lymphocytes
- ➢ Fas –FasL interaction activates death domain which in turn activates **caspase *8***



Autophagy

- Self-eating
  May lead to the adaptive mechanism atrophy —> failure of adaptation leads to apoptosis
- membrane bound vacuoles form in the cells, these vacuoles are **derived from ER** membrane, and they are called **autophagic vacuoles.**
  These vacuoles fuse with **lysosomes** making **autophagolysosome**, then the **lysosomal enzymes** will start the process of **digestion**.
- Survival mechanism in times of nutrient deprivation.
  Recycling cells contents to provide nutrients and energy in times of starvation