

Apoptosis :- suicide, program death, regulated deth.

- degrade DNA & nuclear & cytoplasmic ptn. (by enzyme caspases)
- Greek word falling off
- Doesn't elicit inflammation
- plasma membrane intact.
- Apoptotic body become target for phagocyte before their content leak out.

Apoptosis

pathologic

- ① DNA damage
 - intrinsic
 - Activation by BH3
- ② misfolded ptn
 - intrinsic
 - Activation by BH3 or direct activation of Caspases
- ③ Infection (viral)
 - intrinsic + Extrinsic
 - Activation by viral ptn. or cytotoxic T lymphocyte

physiologic

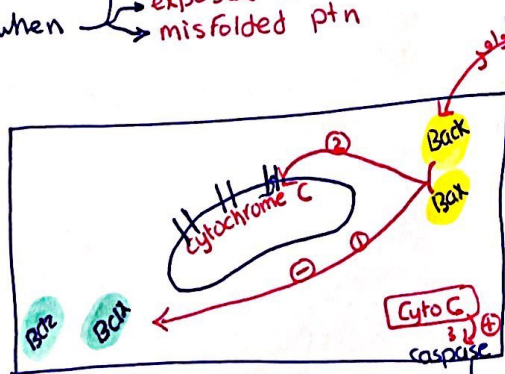
- ① During embryogenesis
- ② Turnover of proliferative tissue
- ③ Involution of hormone-dependent tissue
testosterone & progesteron
- ④ Decline of leukocyte number
at the end of immune response
- ⑤ Elimination of potentially harmful self reactive lymphocytes

Apoptosis is regulated by 2 pathway.
 ↳ intrinsic pathway (Mitochondrial)
 ↳ extrinsic pathway (Death receptor)

1 Intrinsic pathway.

- Mitochondria contain ptn that can inducing Apoptosis → Cytochrome C
 ↑ mitochondria permeability, ↑ permeable membrane. ↑ Cyto C leaks → caspases 9

BH3
 ↳ sensors ptn.
 ↳ Activated when
 ↳ deprivation of growth factor
 ↳ exposed to DNA damage.
 ↳ misfolded ptn



- ① inhibition of Bcl2, BclXL.
- ② forming channel to leak cyto C
- ③ Cyto C with activate caspase 9
 ↳ Apoptosis

- BH3 sensor (proapoptotic)
- Bcl2, BclXL (Antiapoptotic)
- mitochondria

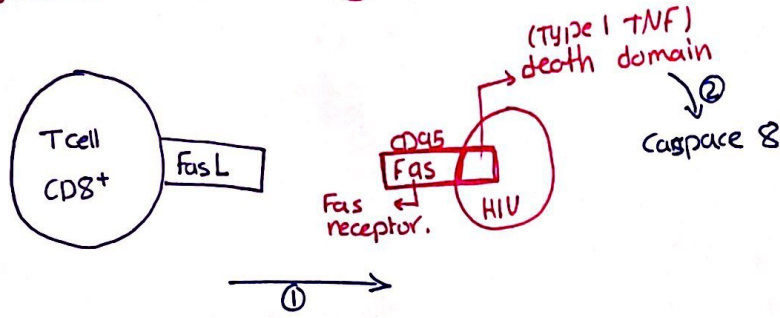
9 intrinsic
 8 extrinsic

2. Extrinsic pathway. (ligand + receptor)

① Attachment between FAS + FASL (cross linked)

② Activated cas 8
↓
Apoptosis.

A.



*After cas 8 + 9 is activated → Activation more caspases → Active enzyme = Apoptosis.

clearance of apoptosis

- ① entice phagocyte → by eat-me signal
- ② flips phospholipid (outer leaflet) + expose phosphatidylserine
- ③ Happen before the cell membrane damage.

Morphology

- ↳ small cluster.
- ↳ cell shrink rapidly
- ↳ formation cytoplasmic buds
- ↳ fragmentation → apoptotic bodies
- ↳ phagocyte will eliminate from apoptotic bodies before inflammatory response.

OTHER PATHWAY OF CELL DEATH

① Necroptosis

- ↳ necrosis + Apoptosis
- ↳ initiation by TNF receptors
- ↳ receptor interacting ptn RIP (Kinases)

③ Autophagy

- ↳ self eating.
- ↳ Nutrient deprivation
- ↳ survival pathway

② pyroptosis

- ↳ activation of inflammasome.
- ↳ pyro → fire
- ↳ used by infectious microbe
- ↳ inflammation + fever +