APOPTOSIS

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INTRODUCTION

- DEFINATION –
- ✓ apoptosis is a tightly regulated form of cell death. Also called the programmed cell death.
- ✓ Apoptosis is a type of cell death in which cell uses specialized cellular machinery to kill itself.
- ✓ Apoptosis is the deliberate suicide of unwanted cell, in multicelluler organism.
- ✓ Apoptosis is a normal physiological form of cell death that play a key role in the maintanace of adult tissues.
- ✓ Apoptosis is responsible for balancing cell proliferation and cell number in tissues.

WHY SHOULD A CELL COMMIT SUICIDE?

- (A) –PROGRAMMED CELL DEATH IS A NEEDED FOR PROPER DEVELOPMENT –

- EXAMPLE –

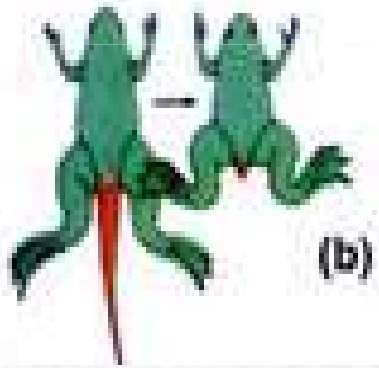
✓ The resorption of tadpole tail at the time of its metamorphosis into a frog occur by apoptosis.

✓ The formation of the fingers and toes of the fetus require the removal by apoptosis, of the tissues between them.

In the human body about 100,000 cells are produced every second by mitosis and a similar number die by apoptosis (Vaux and Korsmeyer, 1999, Cell) !

Development and Morphogenesis:

- 131 of the 1,090 somatic cells die during C.elegans development
- during limb formation separate digits evolve by death of interdigital mesenchymal tissue (a)
- ablation of cells no longer needed such as the amphibian tadpole tail during metamorphosis (b)
- demise of cells allows sculpturing of hollow structures (c)
- formation of reproductive organs (d)
  (Müllerian duct → uterus, deleted in males;Wolffian duct → male organs, deleted in females)
- massive cell death occurs during early development of the nervous system (> 50 percent of all neurons die)



- (B) PROGRAMMED CELL DEATH IS A NEEDED TO DESTROY CELL THAT REPRESENT A THEAT TO THE ORGANISM –
- EXAMPLE –
- ✓ Cells that are infected by viruses – one of the method by which cytotoxic T- lynphocytes (CTLs) kill viruses infected cell in by inducing apoptosis.
- ✓ Cell with DNA damage – to disrupt proper embrionic development leading to birth defect.
- ✓ Cancerous cell – radiation and chemical used in cancer theraphy induce apoptosis in some type of cancer cells.

WHAT MAKES A CELL TO COMMIT APOPTOSIS?

- There are two reason –
- ➢ THE WITHDRAWAL OF POSITIVE SIGNAL THAT IS NEEDED FOR SURVIVAL –
- ✓ Growth factor for nurons,

- RECEIPT TO NEGETIVE SIGNALS-
- Increased level of oxidant within the cell.
- Damage to DNA by – Uv rays, X- rays.

APOPTOSIS TRIGGER BY THE EXTERNAL SIGNAL

- In these type of cell death a death ligand act in the surface of cell, the signal of these ligand where accepted by a receptor which is present in the cell.
- Acceptor than activate the caspase.
- The process can be summarised as follows-
- Death receptor- death receptor mainly present in the membrane of cell. Example are- Fas/CD95, DR4/DR5, DR3 and TNFR(tumer necrosis factor receptor).
- Adaptor- they recceve the signal from receptor and transfer the signal to caspas.

- The examples are- FADD (fas associated death domain protein) and TRADD (TNFR associated death domain protein).
- Binding of death ligand induced trimerization of their receptor.
- Receptor then transfer the signal to adaptor, the procaspas are attached with the adaptor after geting signal adaptor activate the caspas.
- Activated caspas activate the other caspas and finally phagocytosis process occure.

CASPASE

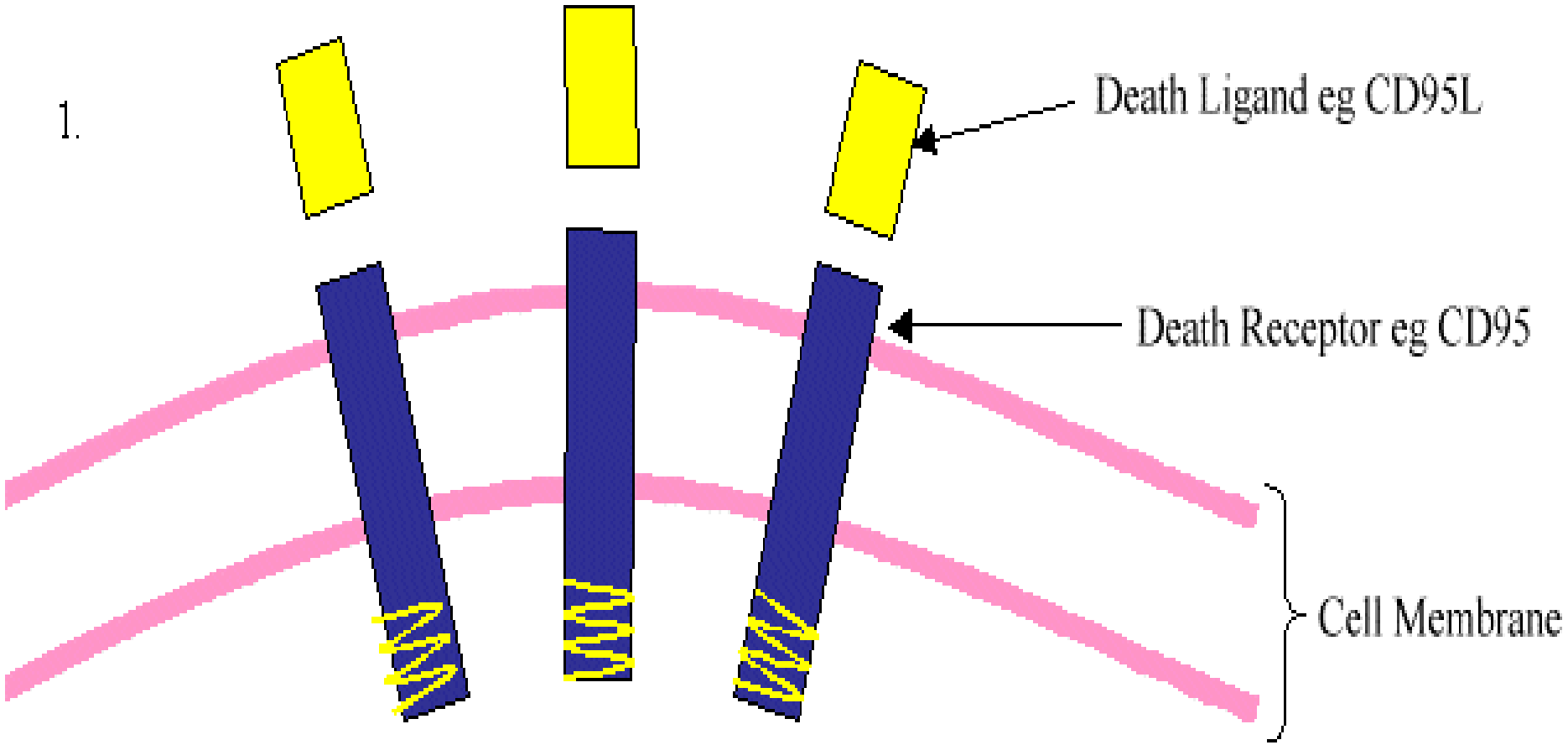
- Caspase (cysteine aspartate specific proteases).
- General characteristics-
- Highly spesific proteases,
- Cleave protein exclusively after asparted residues,
- Act in protein by hydrolysis of peptide bond.
- Type-

✓ 1 activator- caspase 2, 8,9,10

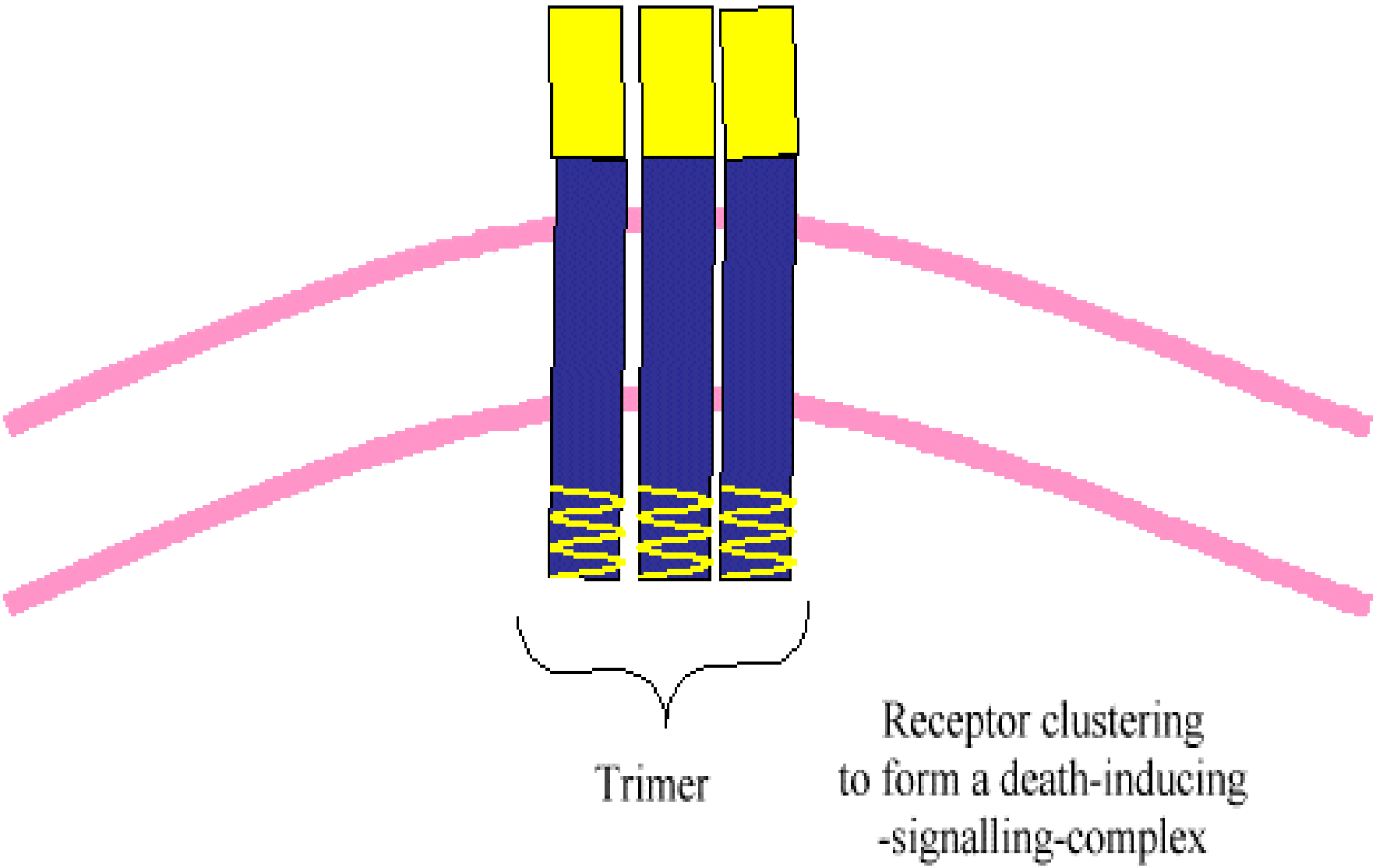
✓ 2 executionare- caspase 3,6,7

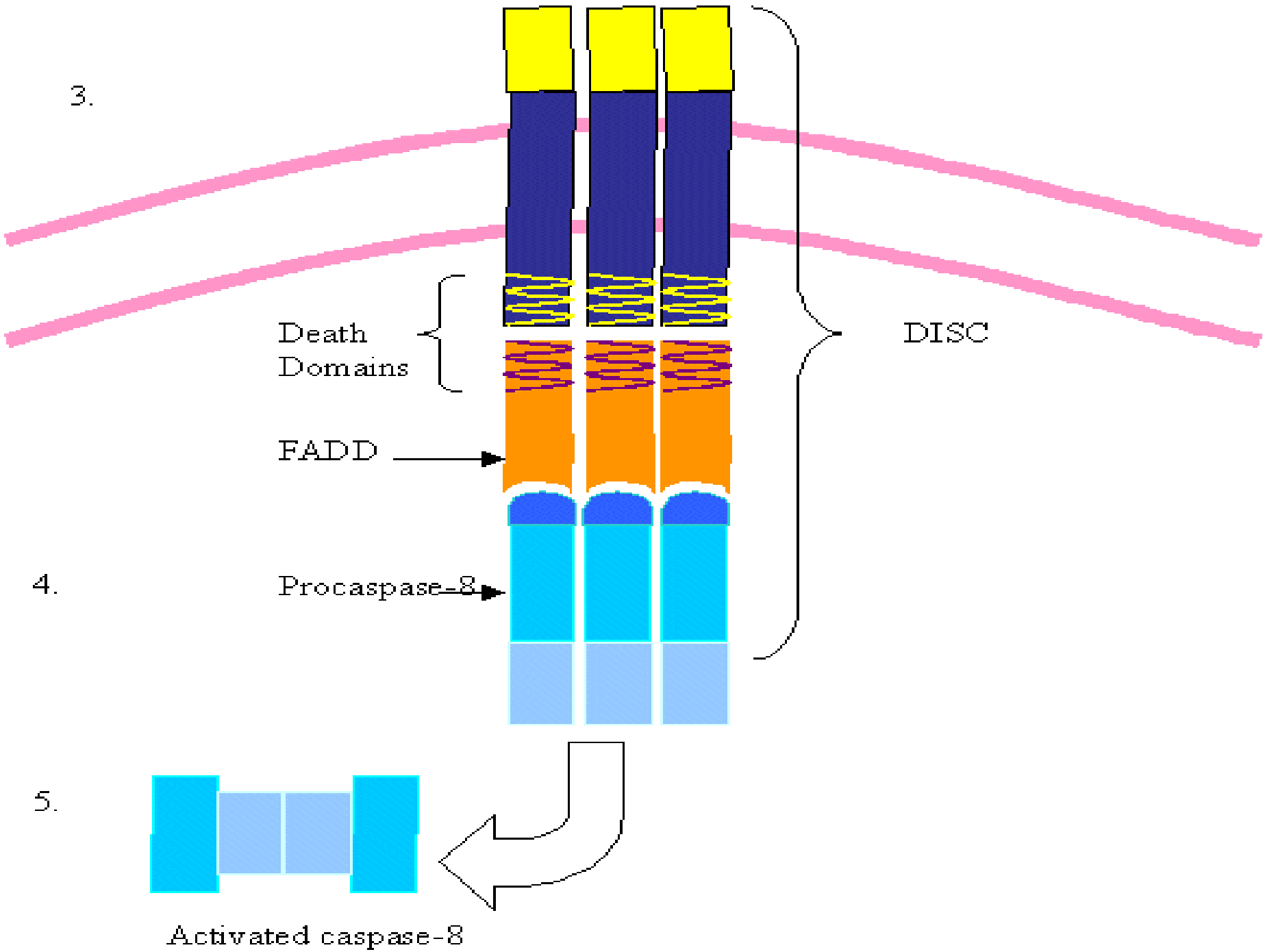
✓ 3 cytokin prossesor- caspase 1,4,5,11,12,13,14

- Inactive caspase called procaspase.


1.
Death Ligand eg CD95L
Death Receptor eg CD95
Cell Membrane

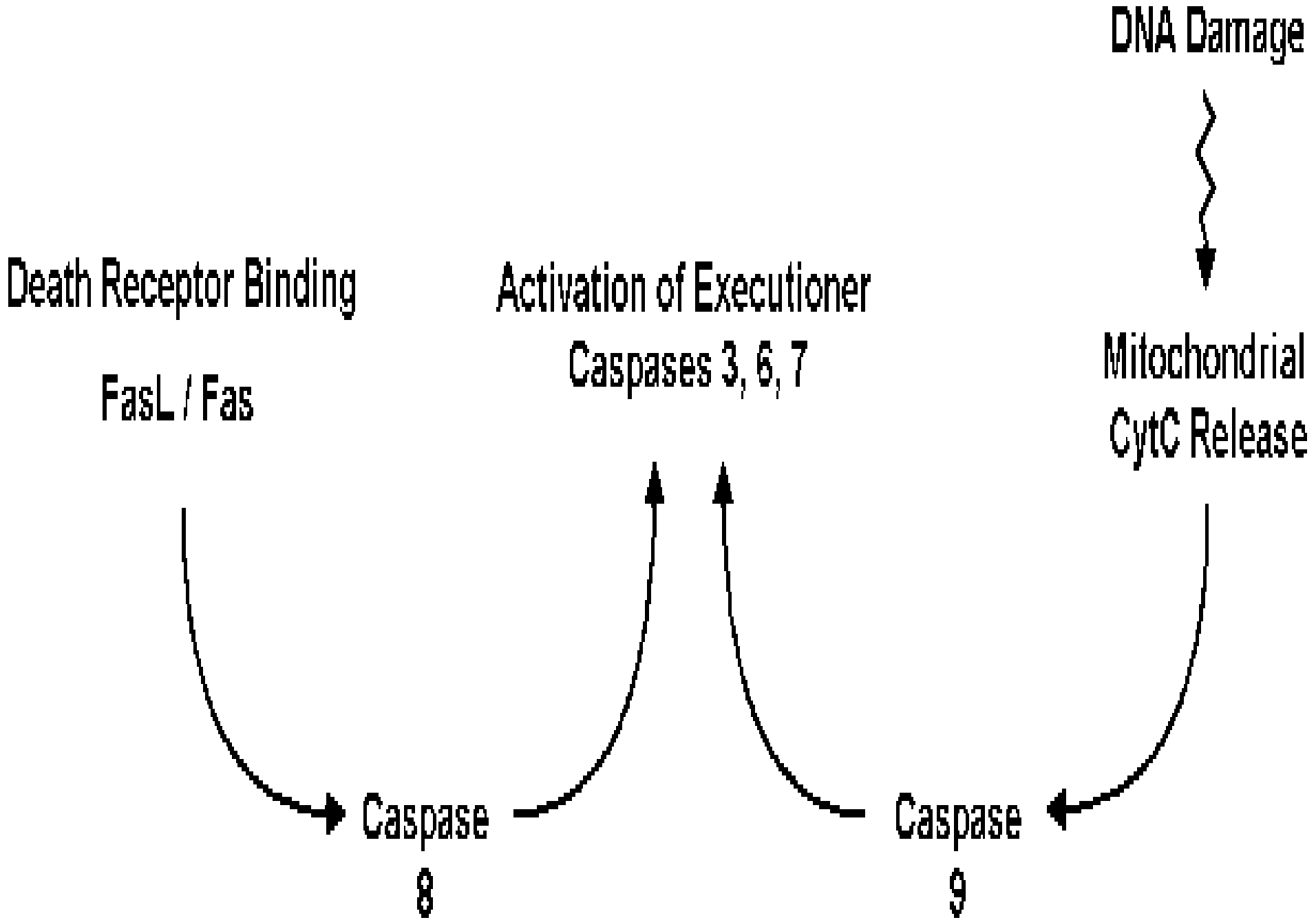
2.


Trimer
Receptor clustering
to form a death-inducing
-signalling-complex


3.
Death
Domains
DISC
FADD
4.
Procaspase-8
5.
Activated caspase-8

THE EXECUTION PHASE

- The two phase meet here. Downstream the initiator caspase 8,9,10 activate executionar caspase 3,6,7 which then cleave the cellular protein.


DNA Damage
Death Receptor Binding
FasL / Fas
Activation of Executioner
Caspases 3, 6, 7
Mitochondrial
CytC Release
Caspase
8
Caspase
9

Thankyou