# APOPTOSIS VS NECROSIS OVERVIEW

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# Apoptosis - Programmed Cell Death

**Why needed?** In adult tissues cell death exactly balances cell division

- In apoptosis the cell destroys itself from within and avoids leakage of the cell contents into the extracellular space

**Apoptosis causes** (Destroy cells that are a threat)

- Infected with virus
- Turn off immune response
- DNA damaged cells
- Cancer

# Apoptosis - Programmed Cell Death

**Apoptosis process – include a increase in the activity of Caspases and is an energy dependent (ATP) process**

- Cells do not release their cellular constituents into the surrounding interstitial tissue

- Cellular contents are quickly phagocytosed by macrophages or adjacent normal cells

- No inflammatory reaction

# Apoptosis - Enzymes

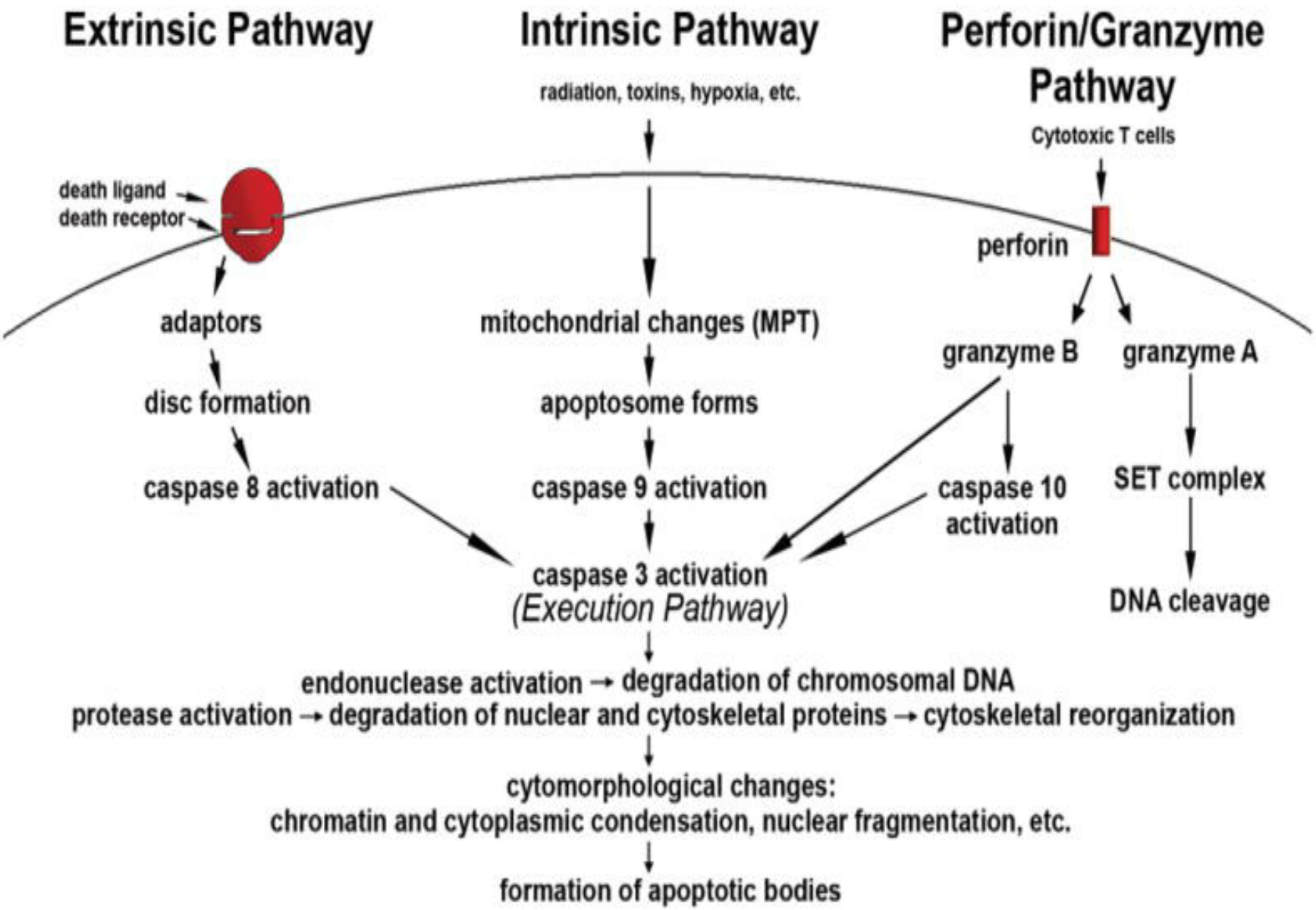
- 1. Caspase -Caspases (cysteine-aspartic proteases, cysteine aspartases or cysteine-dependent aspartate-directed proteases) are a family of protease enzymes

- Play an essential roles in programmed cell death

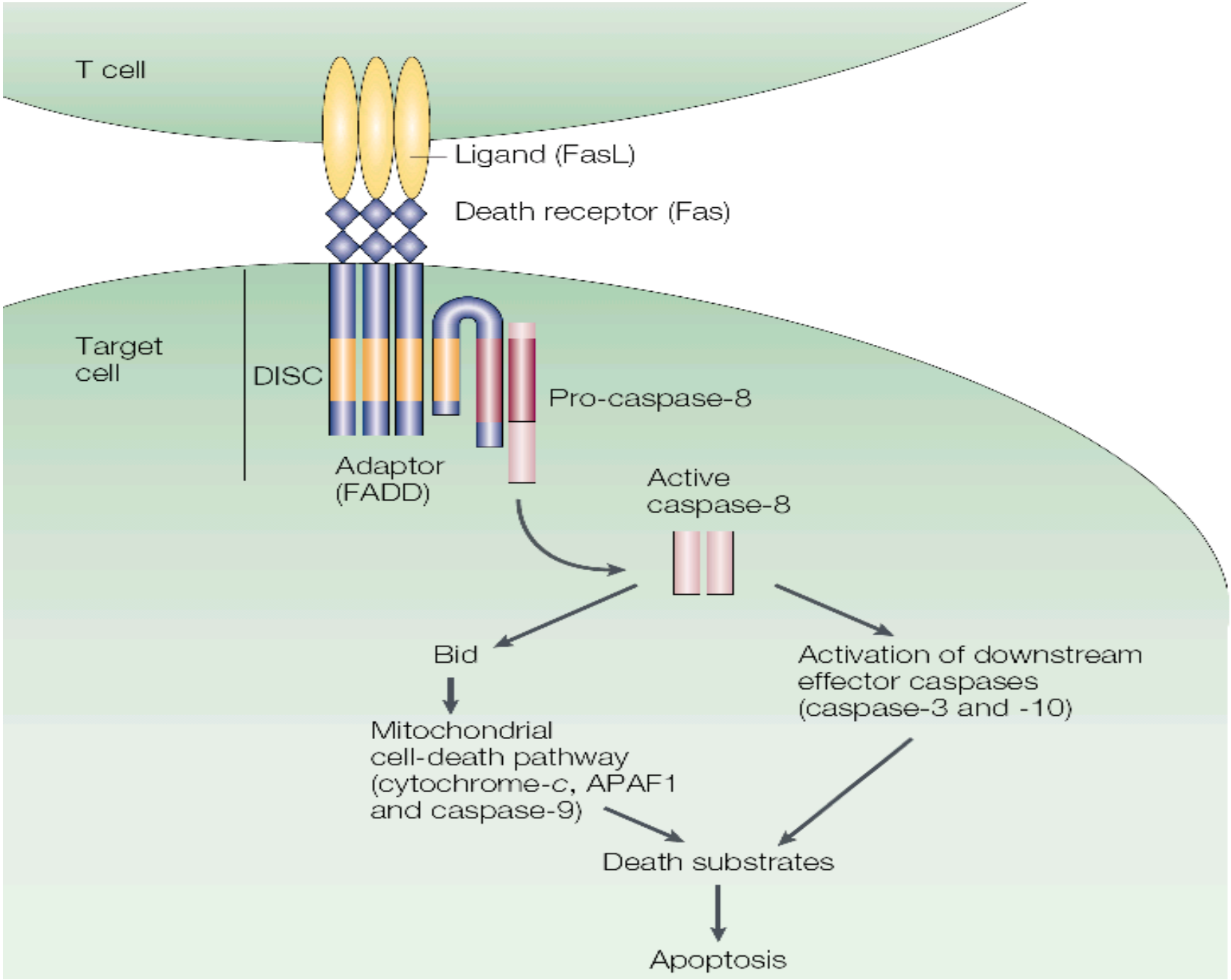
- Activation of Caspases ensures that the cellular components are degraded in a controlled manner, carrying out cell death with minimal effect on surrounding tissues

- These forms of cell death are important for protecting an organism from stress signals and pathogenic attack.

# Apoptosis – Activation pathways



# Apoptosis - FAS/FASL mediated pathway




*Source: Nature Reviews/Immunology 2002; 2: 273-281.*

# Importance of Apoptosis

- **Important in normal physiology / development**
- **Development:** Immune systems maturation, Morphogenesis, Neural development
- Adult: Immune privilege
- DNA Damage and wound repair
- **Excess apoptosis** -Neurodegenerative diseases
- **Deficient apoptosis-** Cancer, Autoimmunity

# Necrosis

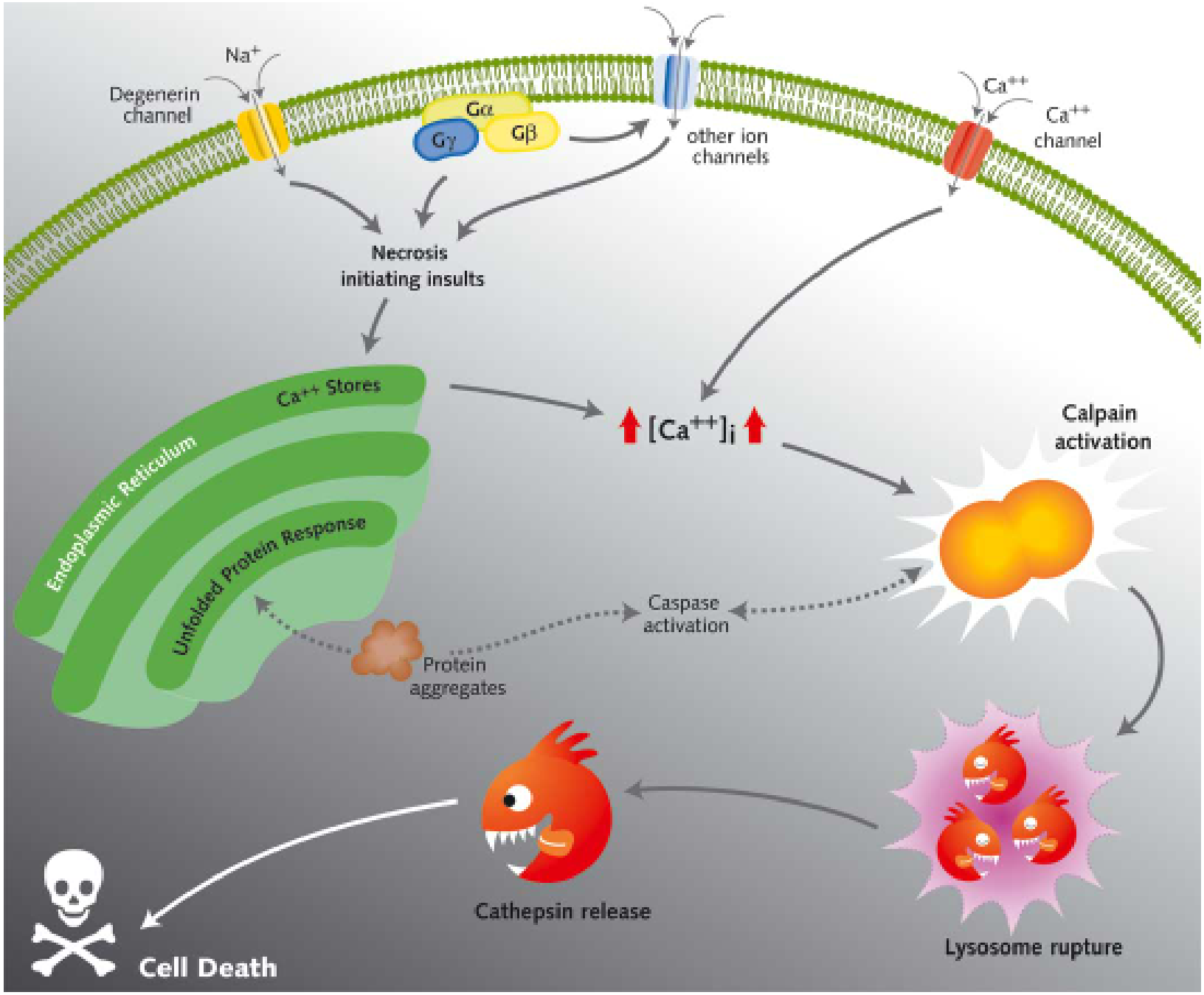
**Causes: Trauma (toxic chemicals, mechanical injury, heat, hypoxia)**

- Loss of ability to regulate internal environment
- Ca2+ influx accompanied by swelling
- Alteration of protein activity (Calpain, Cathepsin, Caspase)
- Production of toxic compounds (activation of cyclooxygenases) prostaglandins
- Inflammation

# Necrosis -Enzymes

- 1. Calpain are calcium dependent non-lysosomal cysteine proteases (proteolytic enzymes)
- Have been implicated in apoptotic cell death and essential component in necrosis
- 2. Cathepsin are proteases (enzymes that degrade proteins)

# Necrosis


Na+
Degenerin channel
Gα
Gγ
Gβ
other ion channels
Ca++
Ca++ channel
Necrosis initiating insults
Ca++ Stores
Endoplasmic Reticulum
Unfolded Protein Response
[Ca++]i
Calpain activation
Caspase activation
Protein aggregates
Cathepsin release
Lysosome rupture
Cell Death

# Necrosis

**Necrotic process include a decrease in the availability of Caspases and intracellular ATP**

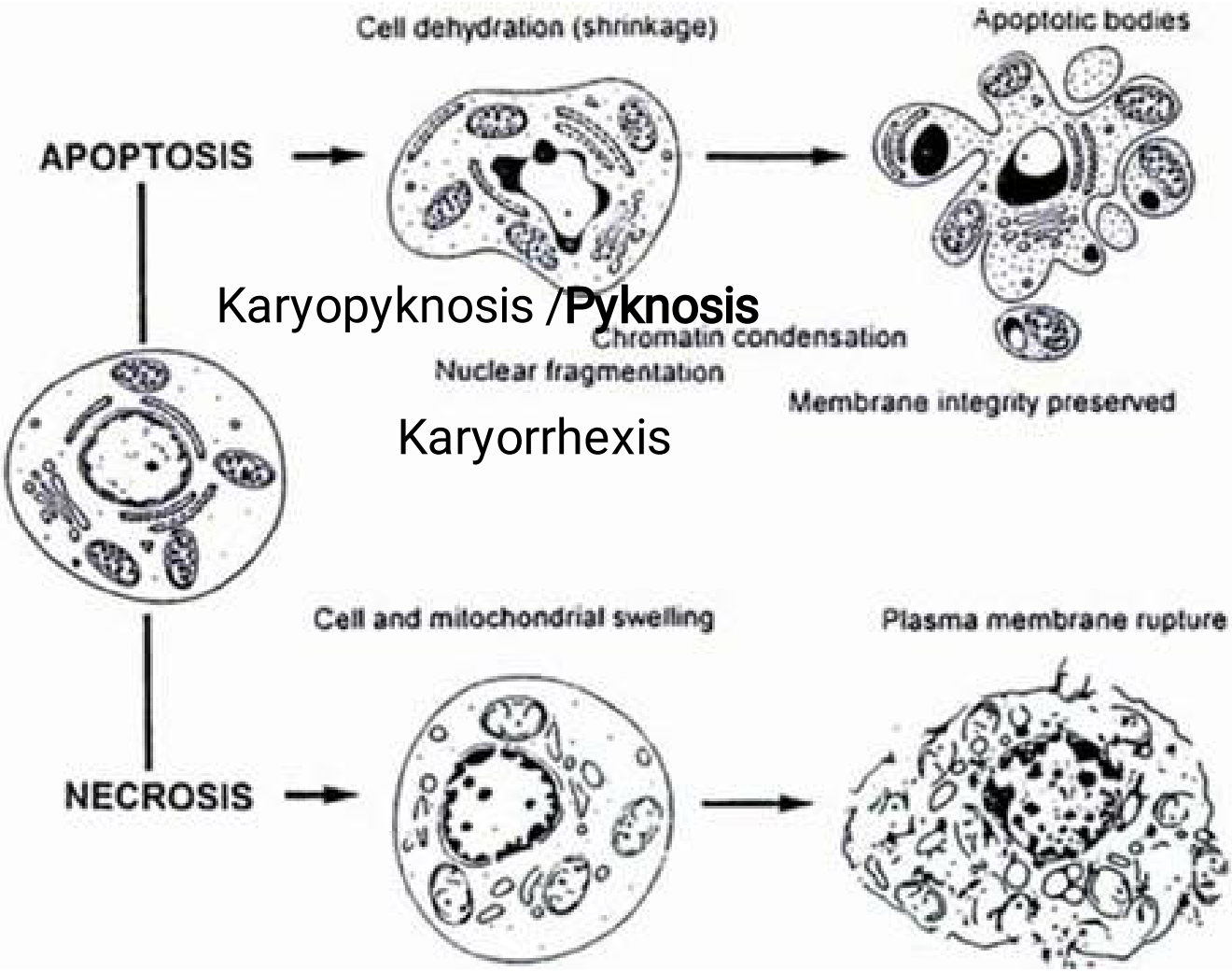
**Features includes**

- Cell swelling;
- Formation of cytoplasmic vacuoles;
- Distended endoplasmic reticulum;
- Formation of cytoplasmic blebs;
- Condensed, swollen or ruptured mitochondria;
- Disaggregation and detachment of ribosomes;
- Disrupted organelle membranes;
- Swollen and ruptured lysosomes;
- Disruption of the cell membrane

**loss of cell membrane integrity results in the release of the cytoplasmic contents into the surrounding tissue**

- sending chemotatic signals with eventual recruitment of inflammatory cells.

# Death by Injury vs. Death by Suicide (Necrosis vs. Apoptosis)



Comparison of morphological features of apoptosis and necrosis.

| Apoptosis | Necrosis |
|---|---|
| Single cells or small clusters of cells | Often contiguous cells |
| Cell shrinkage and convolution | Cell swelling |
| Pyknosis and karyorrhexis | Karyolysis, pyknosis, and karyorrhexis |
| Intact cell membrane | Disrupted cell membrane |
| Cytoplasm retained in apoptotic bodies | Cytoplasm released |
| No inflammation | Inflammation usually present |