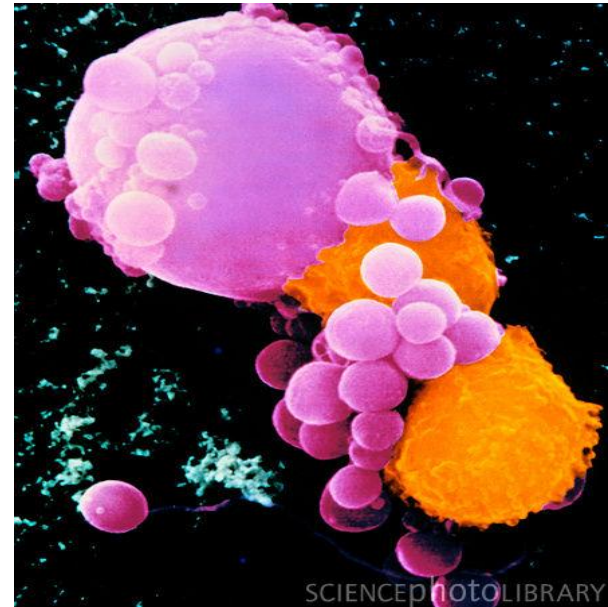


# APOPTOSIS

M.Kohutiar  
ÚLCHBCH 2.LF UK



Source: <http://www.sciencephoto.com/media/253985/enlarge>

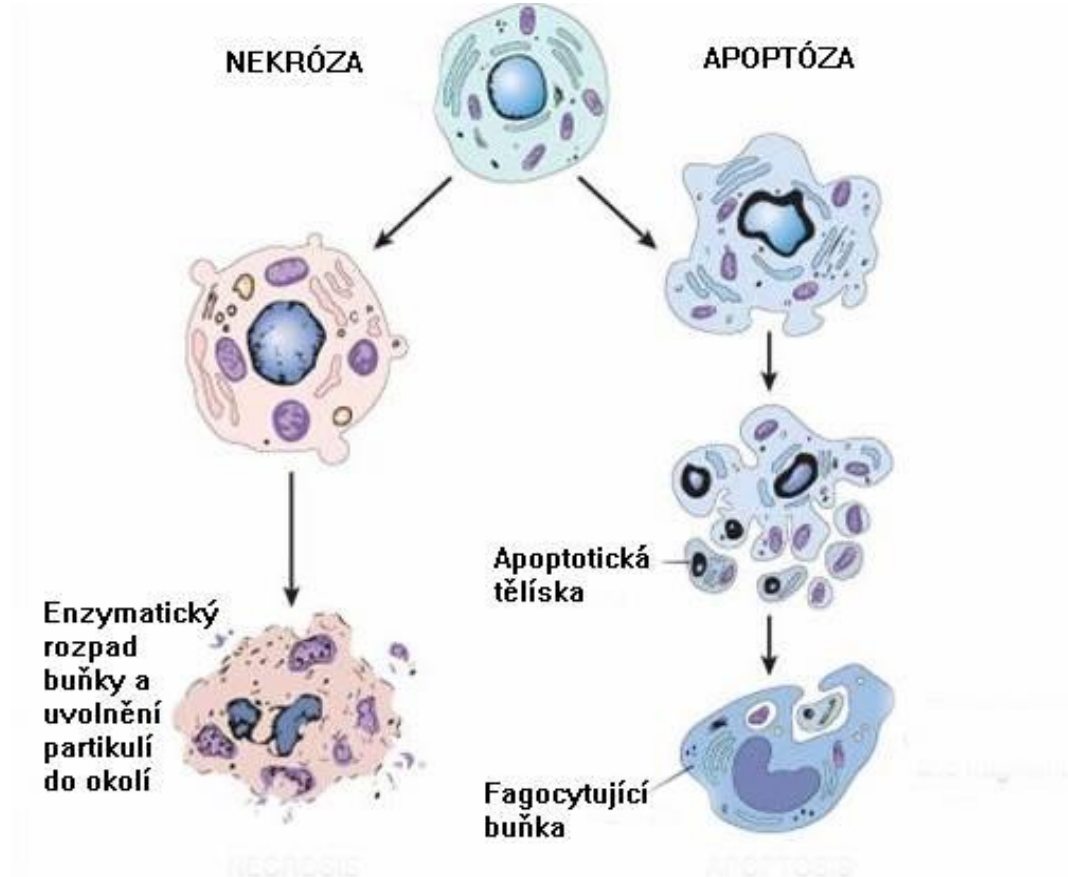
# Cell death

- **Toxic factors**

Irreversible damage of vital functions

- **Induced suicide** (Programmed Cell Death)

# Necrosis vs. apoptosis



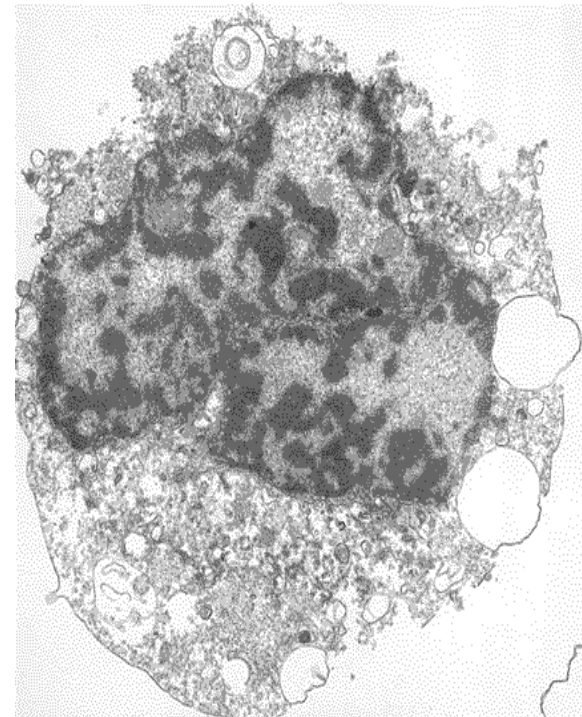
# The importance of apoptosis

- An essential factor for the organism development
- Elimination of potentially dangerous cells  
antitumor, antiviral

# Morphology of apoptosis

1. Occurrence: individual cells
2. Volume of cells: decreased
3. Cell membrane: Intact
4. Mitochondria: Intact
5. Core: condensation of chromatin
6. Integrity: apoptotic bodies
7. Blebbing of membrane
8. Failure of adherence

# Membrane blebbing

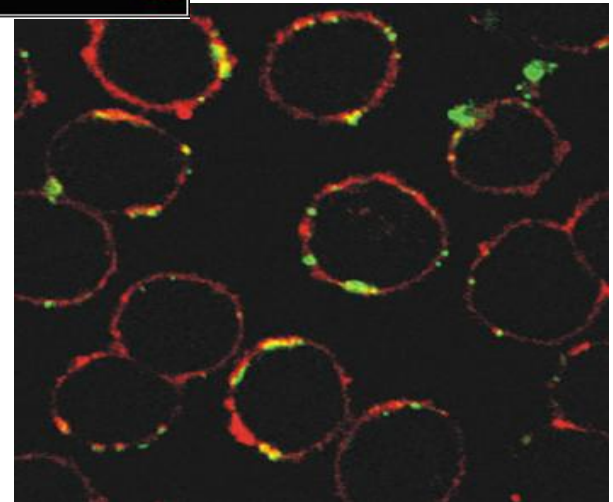
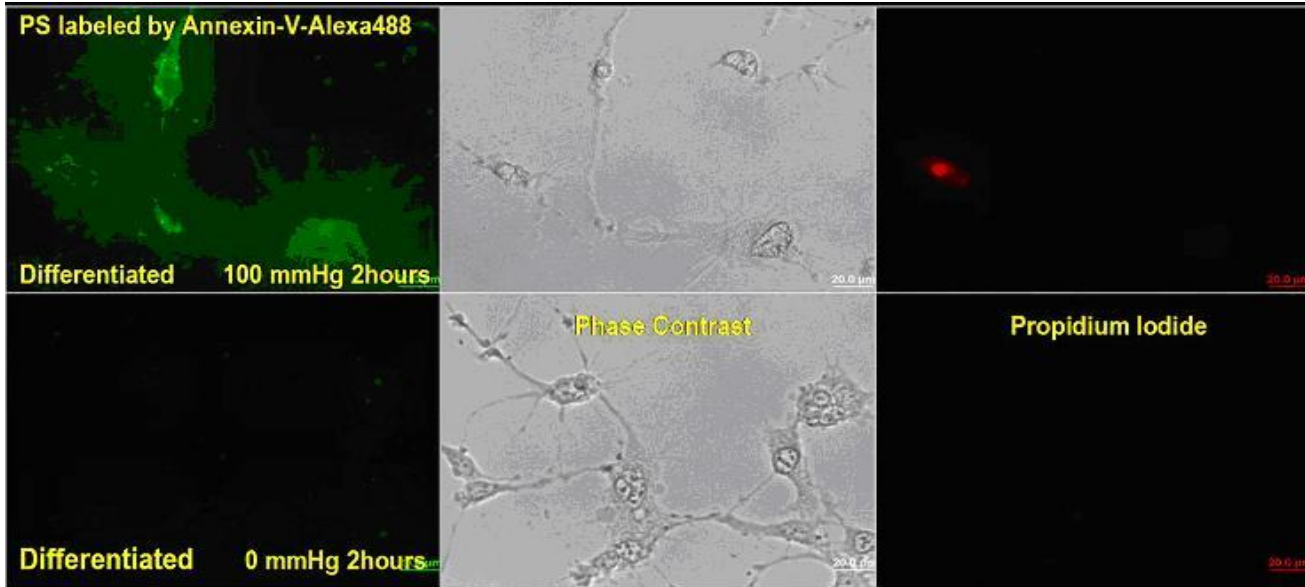


Source:

<http://sciencepark.mdanderson.org/fcores/flow/files/apoptosis.html>

<http://www.theitunurse.com/post/4603844767>

# Phosphatidylserine exposition



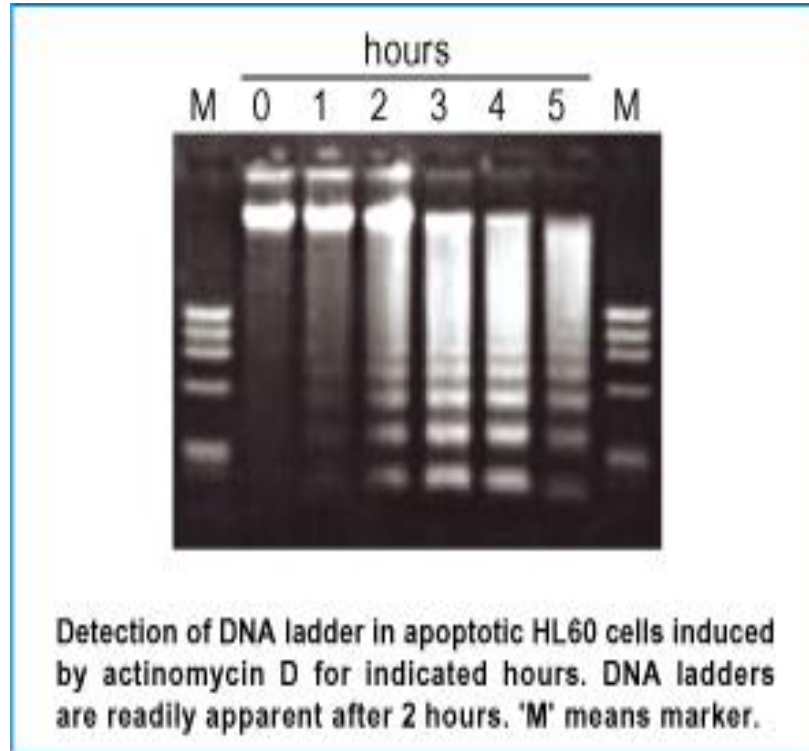
Source:

[http://www.cas.cz/o\\_avcr/zakladni\\_informace/dokumenty/anotace/2008/5\\_sekce\\_biologickych\\_a\\_lekarskych\\_ved.html](http://www.cas.cz/o_avcr/zakladni_informace/dokumenty/anotace/2008/5_sekce_biologickych_a_lekarskych_ved.html)

[http://nanostructure.usc.edu/research/CI\\_Stress.shtml](http://nanostructure.usc.edu/research/CI_Stress.shtml)

[http://nanostructure.usc.edu/research/CI\\_Stress.shtml](http://nanostructure.usc.edu/research/CI_Stress.shtml)

# DNA ladder



Source:

[http://www.itsbio.co.kr/main/goods\\_view.php?category2=60&no=129](http://www.itsbio.co.kr/main/goods_view.php?category2=60&no=129)



# Mechanisms of apoptosis

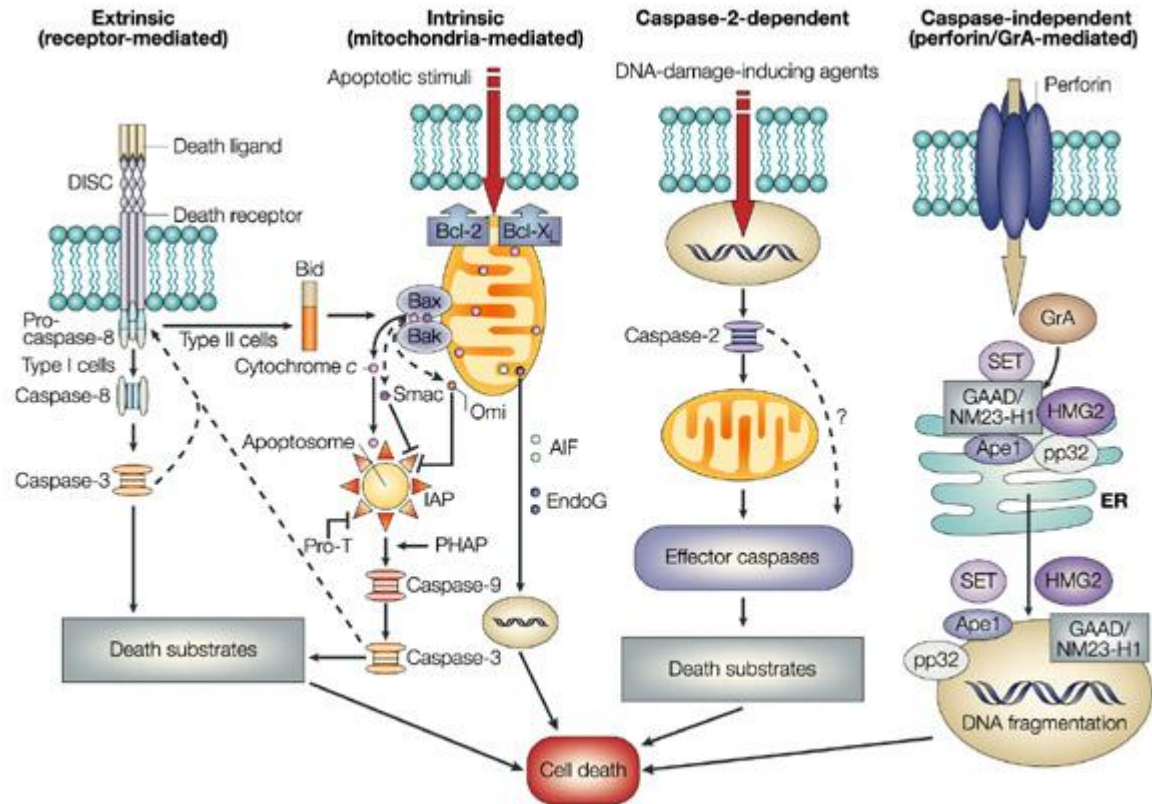
- **1. Intrinsic pathway**

Most of the signals derived primarily from mitochondria

- **2. Extrinsic pathway**

Activation of death domains of TNF-receptor family

# Apoptosis



Nature Reviews | Molecular Cell Biology

Source:

[http://www.nature.com/nrm/journal/v4/n7/box/nrm1150\\_BX1.html](http://www.nature.com/nrm/journal/v4/n7/box/nrm1150_BX1.html)

# Apoptotic signals

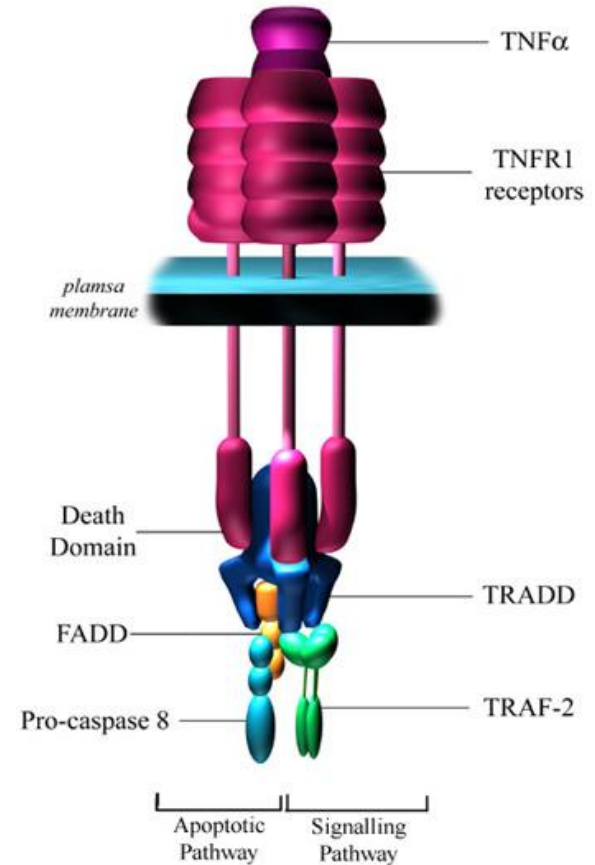
- **Endogenous:** p53
- **Exogenous:** apoptotic signal molecules

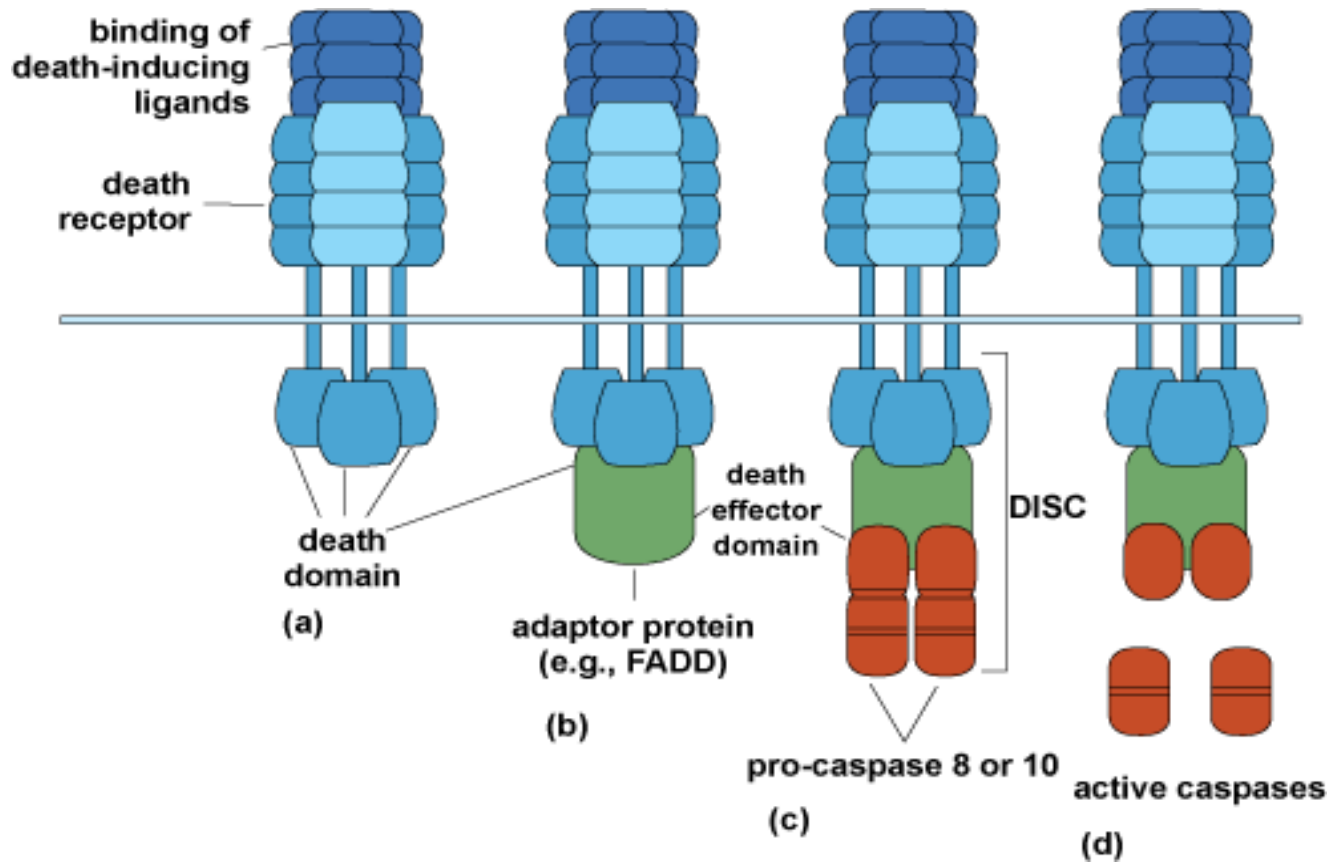
Glucocorticoids

Cytokines (IL-3, 4, 6)

# Ligands/Death receptors

- TNF family
- Fas-L/Fas (CD95)
- TNF $\alpha$ /TNFR1 a TNFR2
- Extra/intracellular domain (DD)





# Apoptosis-caspases

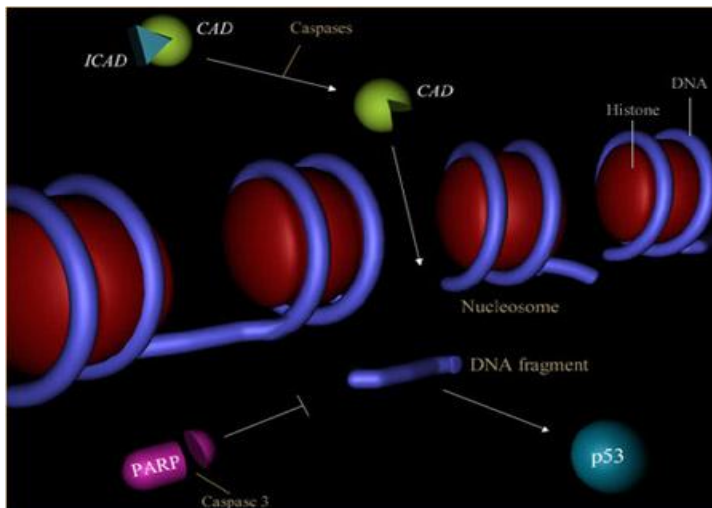
- Proteolysis of intracellular proteins
- **Caspases** (Cytosolic Aspartate-Specific cystein Proteases)
- Inactive form (procaspase)

# Target molecules

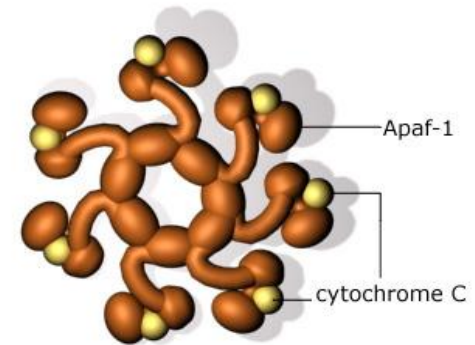
- Lamin
- Poly-ADP-ribose-polymerase (PARP)
- Actin
- Cytoskeletal proteins

# Alteration of mitochondrial membrane

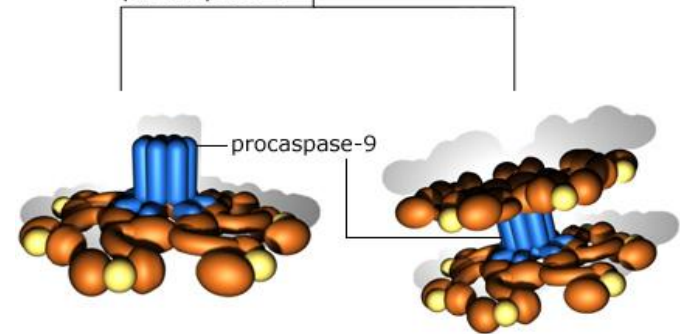
- Release of cytochrome c
- Binding on Apaf-1/pro-caspase 9 → apoptosome → activated caspase 9 → act. Caspase 3



First stage of apoptosome formation



Recruitment of procaspase-9

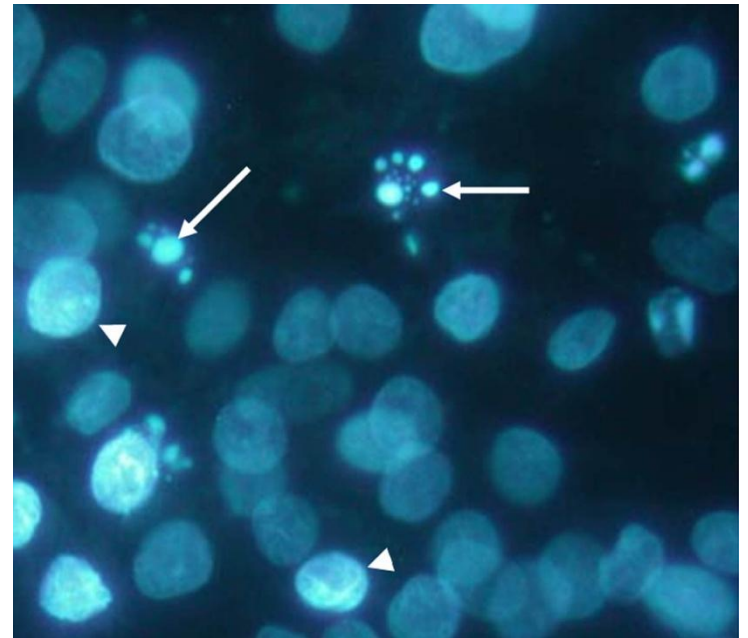
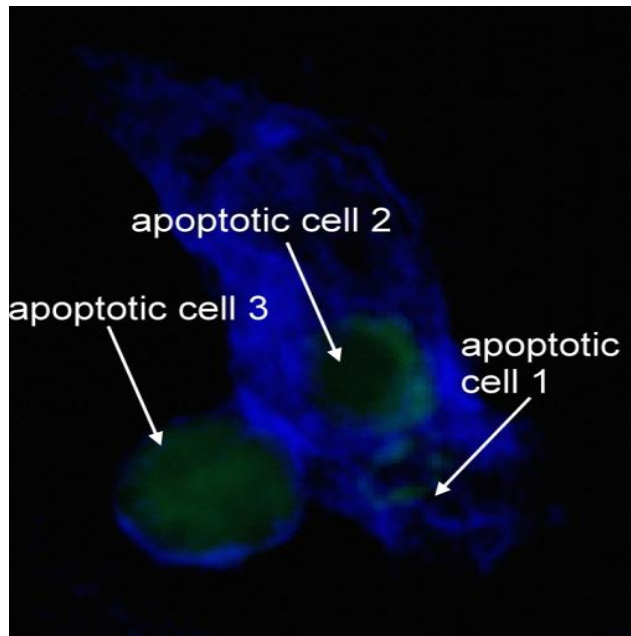


Caspase Activation



# Apoptotic bodies

- Phagocytosis
- **Without inflammation!**



# Regulation of apoptosis

- Pro-apoptotic genes and proteins
  - Bax
- Anti-apoptotic genes and proteins
  - Bcl-2
- p53

# Summary

- **1. Intrinsic mitochondrial pathway**

cyt c/Apaf-1/pro-caspase 9 → formation of apoptosome

- **2. Extrinsic pathway**

CD95/TNF-R1,2 → formation of DISC

# Literature

- MASOPUST, J. *Patobiochemie buňky.*
- KALOUSOVÁ, M. *Patobiochemie ve schématech.*
- VOET, VOET. *Principles of biochemistry.*
- DEVLIN. *Textbook of Biochemistry with Clinical Correlations.*