Apoptosis

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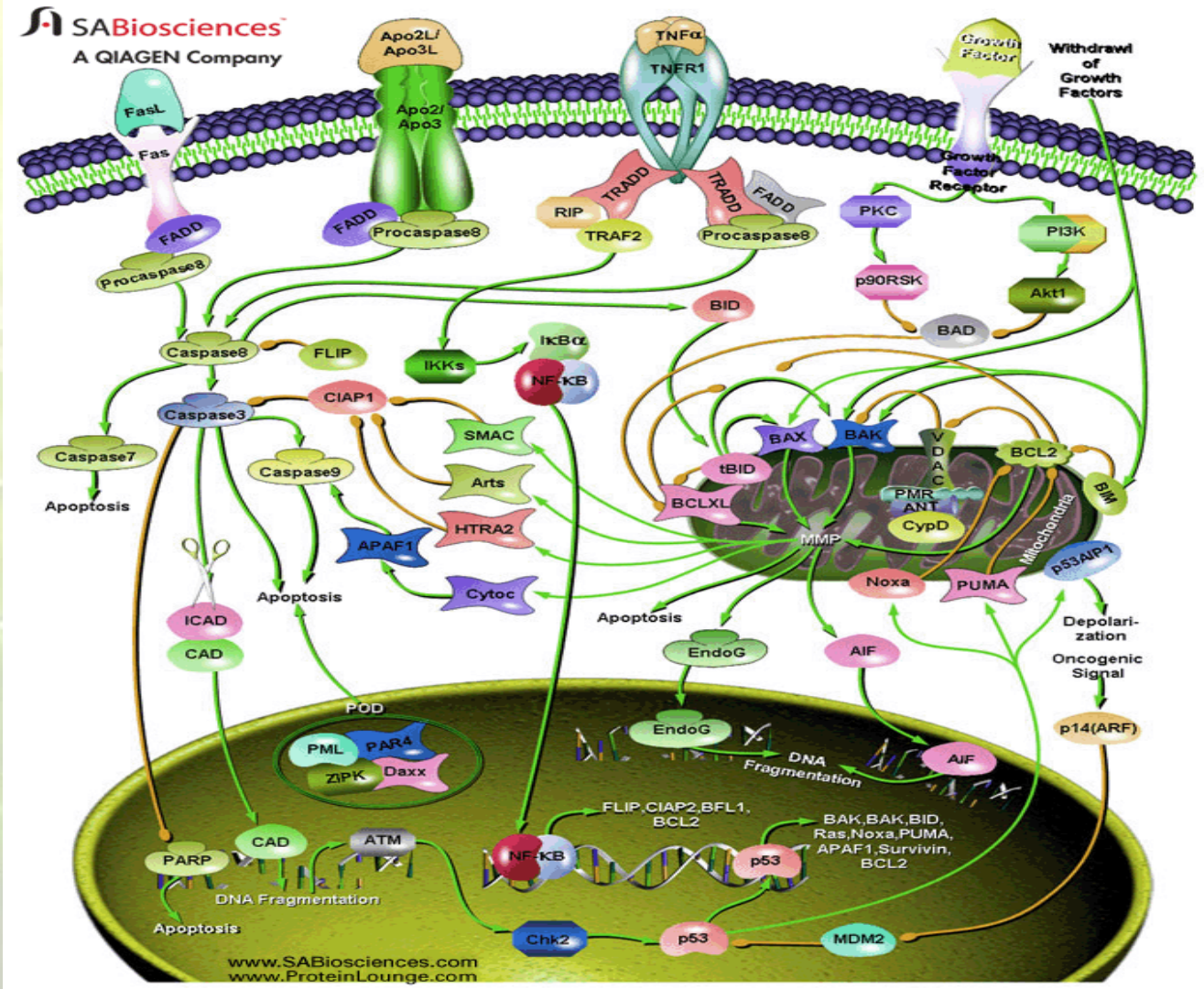


“In a healthy adult human, billions of cells die in the bone marrow and intestine every hour.”

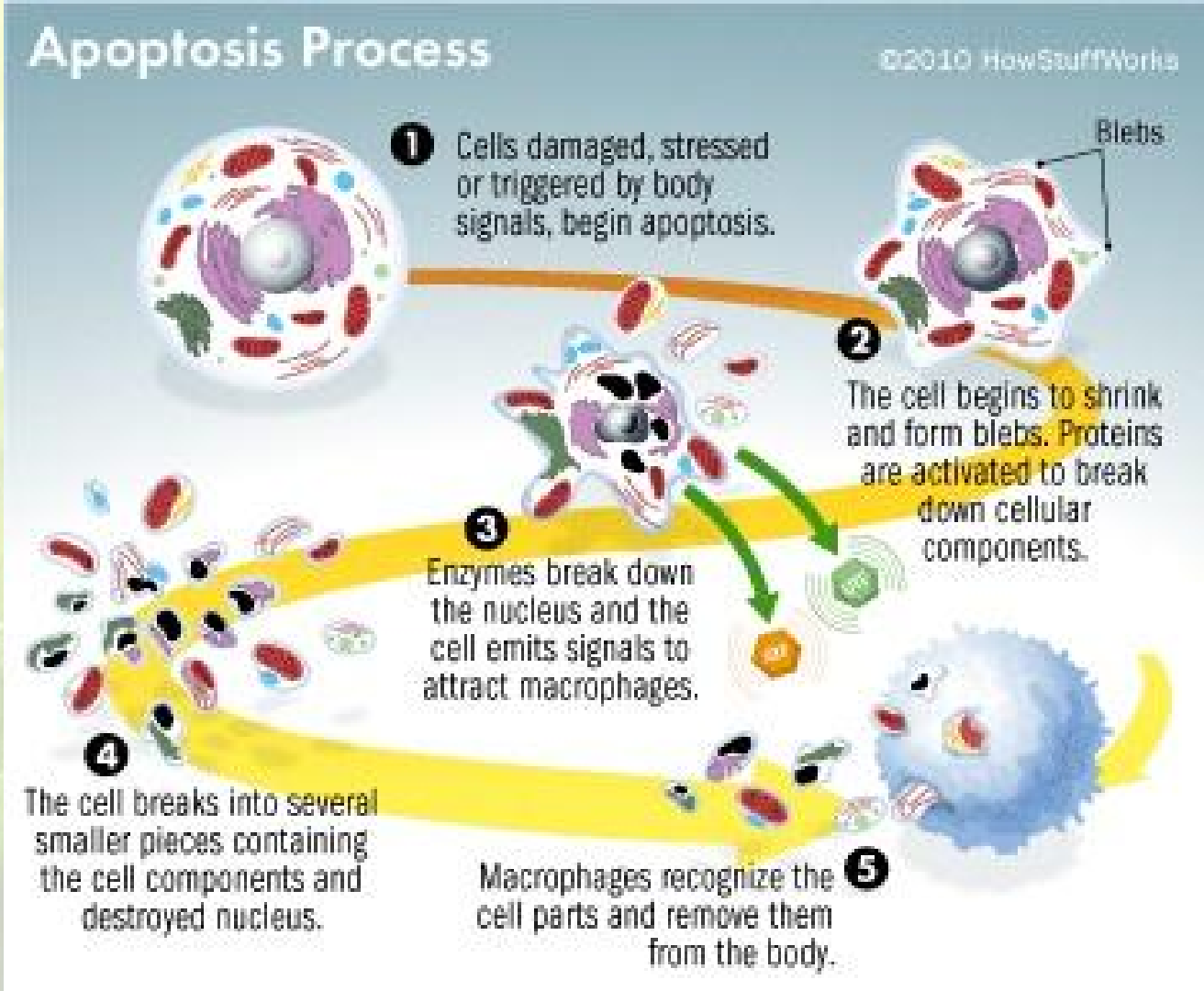
-Alberts et al. (2002).

Today's topics:

- Mechanisms of apoptosis
- Triggers of apoptosis
- Role in human development
- Role in disease

Mechanism

How does it work?

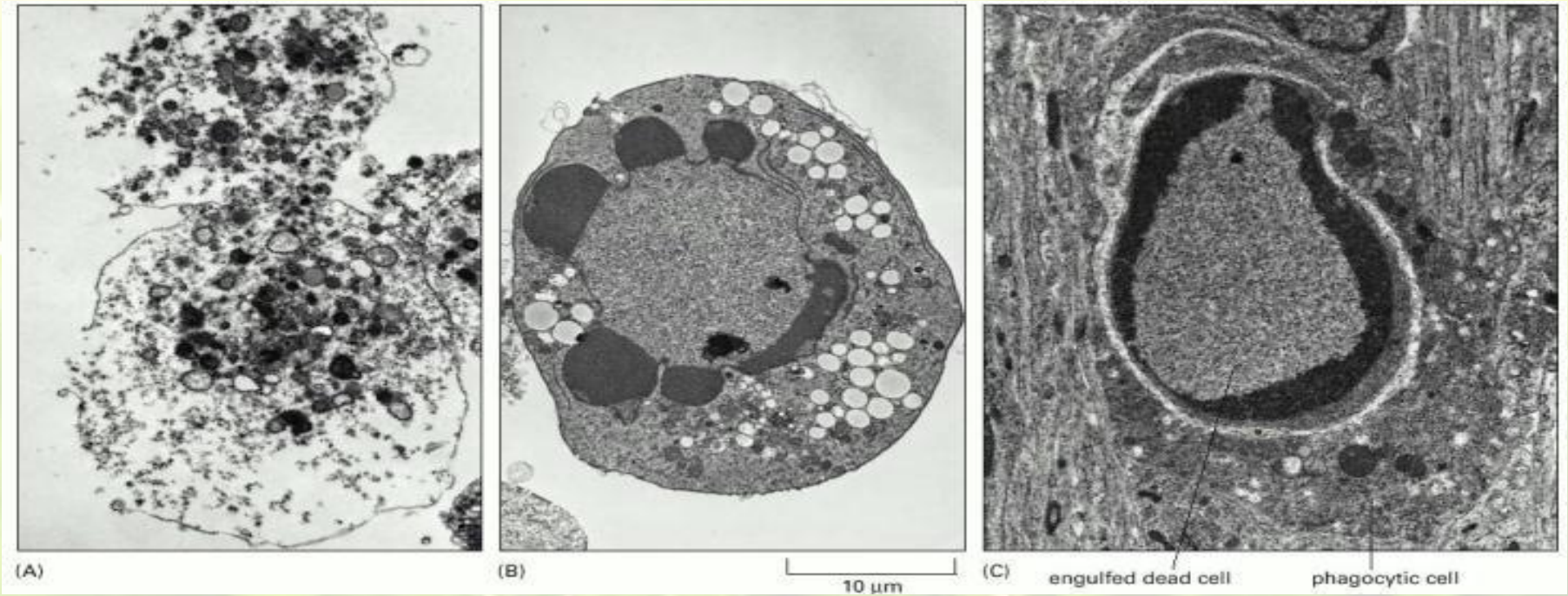


Edmonds (2010)

Mechanism continued...

- Caspases activated
- Cleave/activate cascade effect
- Cytoskeleton collapses
- Nuclear lamins cleaved
- DNA-ase activated
- DNA is taken apart
- Alters cell surface to signal macrophage

(ALSA. 2010)



A) Necrosis

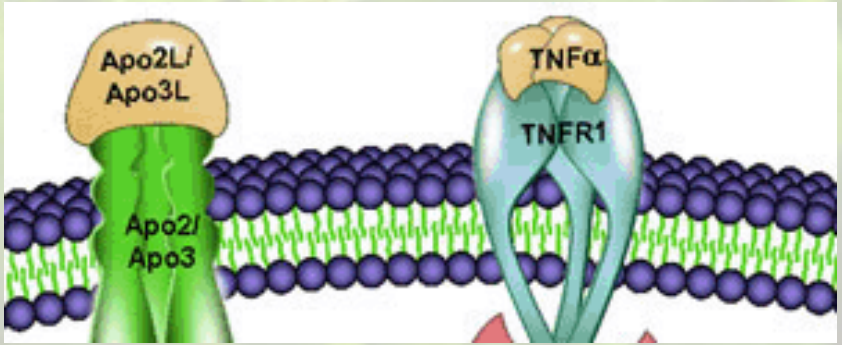
B) Apoptosis

C) Phagocyte after Apoptosis

Alberts et al. (2002).

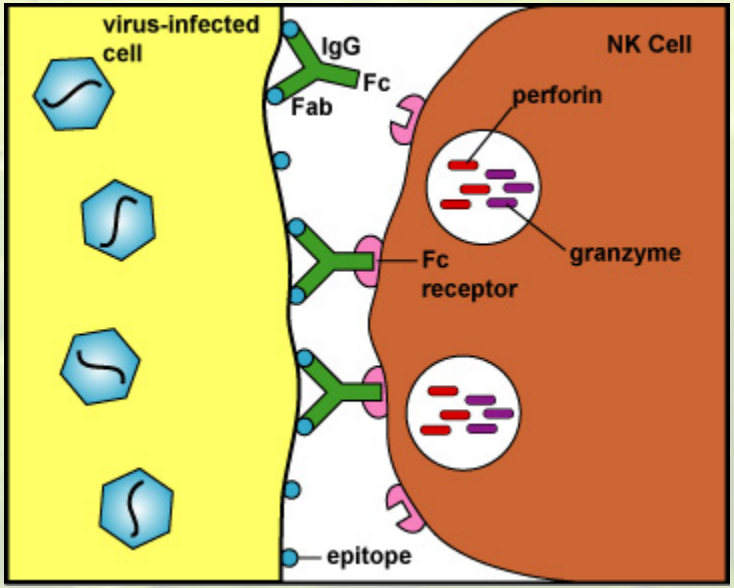
Triggers - Extrinsic

- These triggers arise when the extracellular space surrounding the cell decides that the cell needs to die
- Activated by “Death Ligans”
- “Death Receptors”



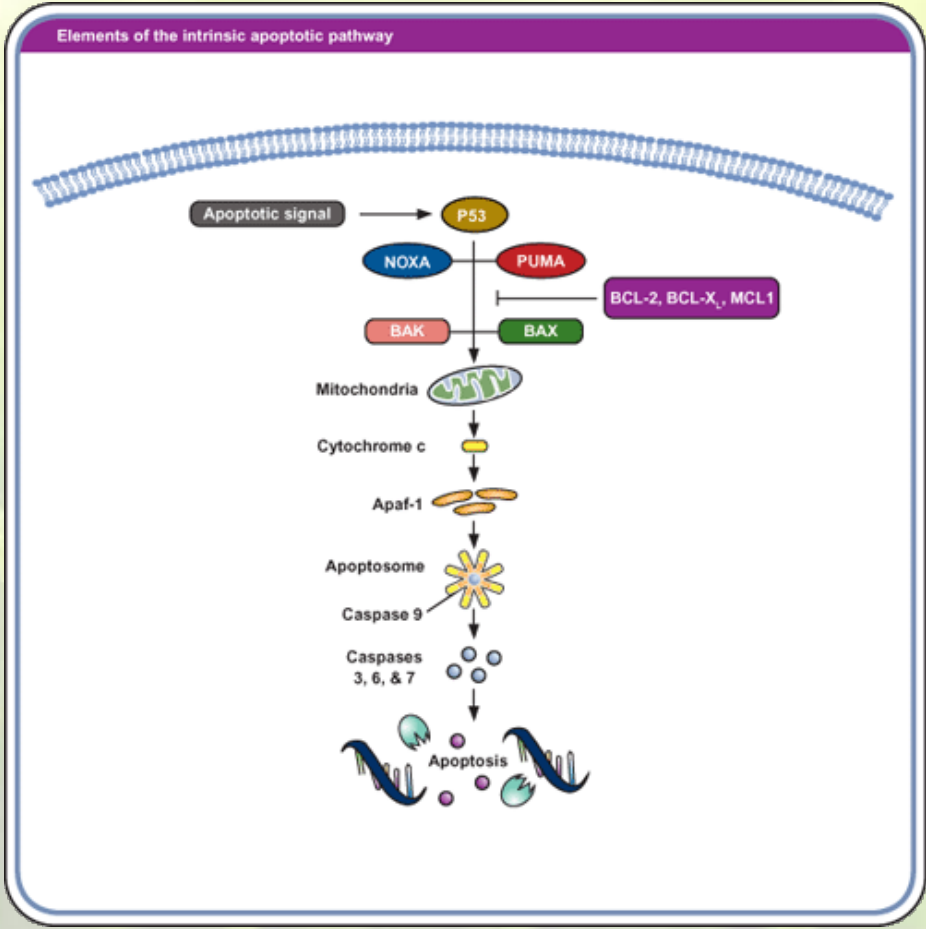
Triggers - NK Cells

- NK cell uses apoptosis
- Immunity
- Antibodies



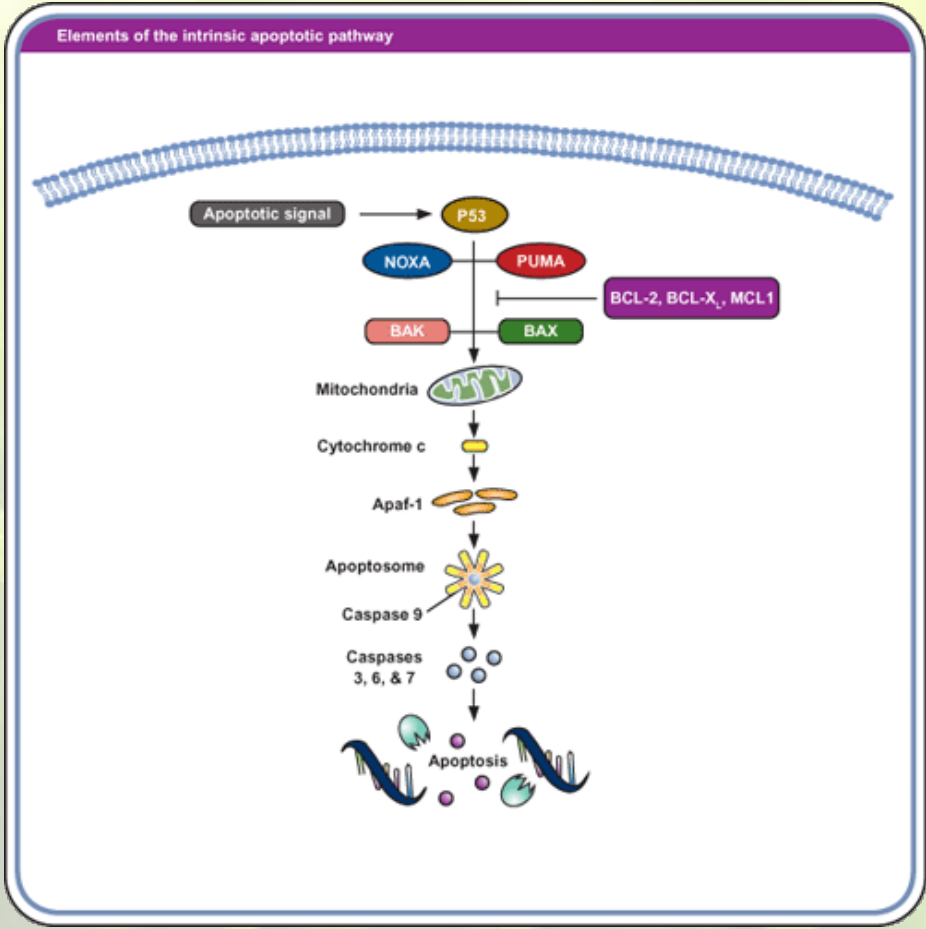
Triggers - Intrinsic

- Protein P53



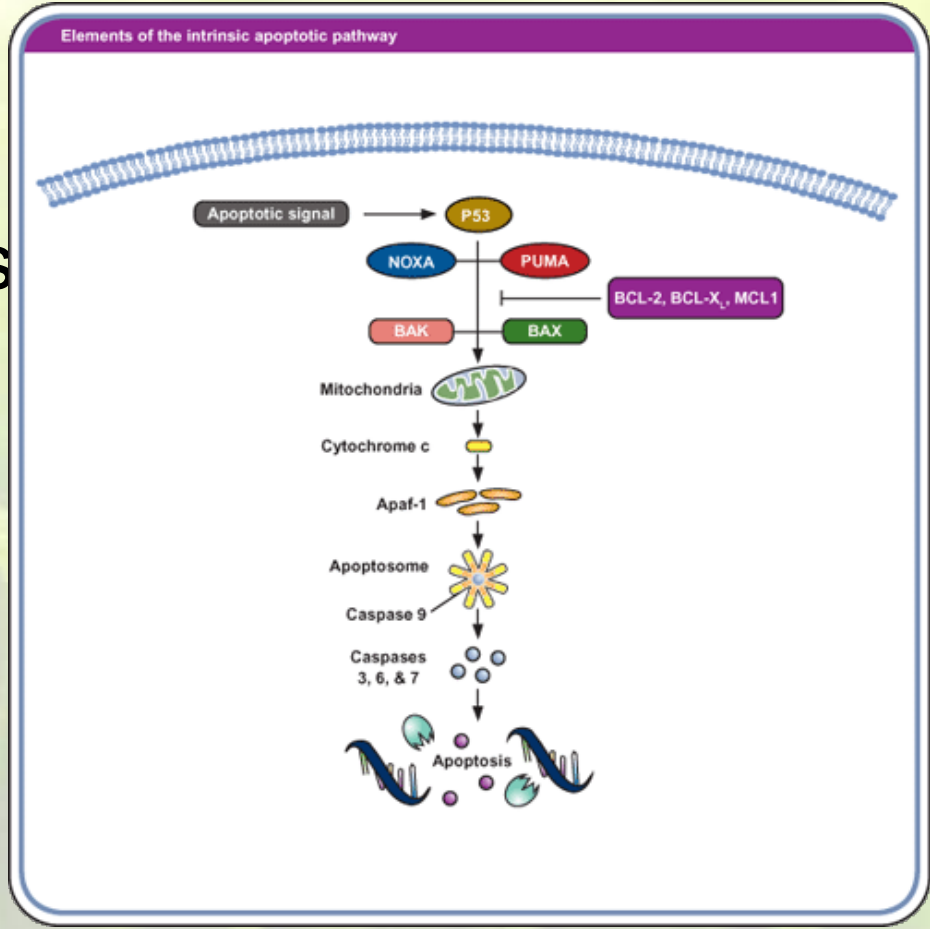
Triggers - Intrinsic

- Pro-apoptotic proteins
  - Bcl-10
  - Bax
  - Bak
  - Bid
  - Bad
  - Bim
  - Bik
  - Blk



Triggers - Intrinsic

- Anti-apoptotic proteins
  - Bcl-2
  - Bcl-x
  - Bcl-xL
  - Bcl-Xs
  - Bcl-w
  - BAG



Role In Development

- Apoptosis is responsible for removing webbing between the fingers and toes of the fetus around week 16 of Gestation.

- Any residual webbing is called syndactyly

Role in Development

Syndactyly is more common in Amish populations

There are over 6 diseases associated with webbed toes, however most of the world has some residual webbing.

- Downs Syndrome
- Apert Syndrome
- Carpenter Syndrome
- Hydantoin (medication) taken during pregnancy

Role in Development

Current research suggests...

- Varying levels of zinc reduces the completion of apoptosis in fingers and toes
- Low levels of Choline in the mother's diet stunts apoptosis

Role in Development

- The average child (8-14)
  - 20-30 billion cells die a day
- The average adult
  - 60-70 billion cells die a day

The Apoptosis Role in Disease

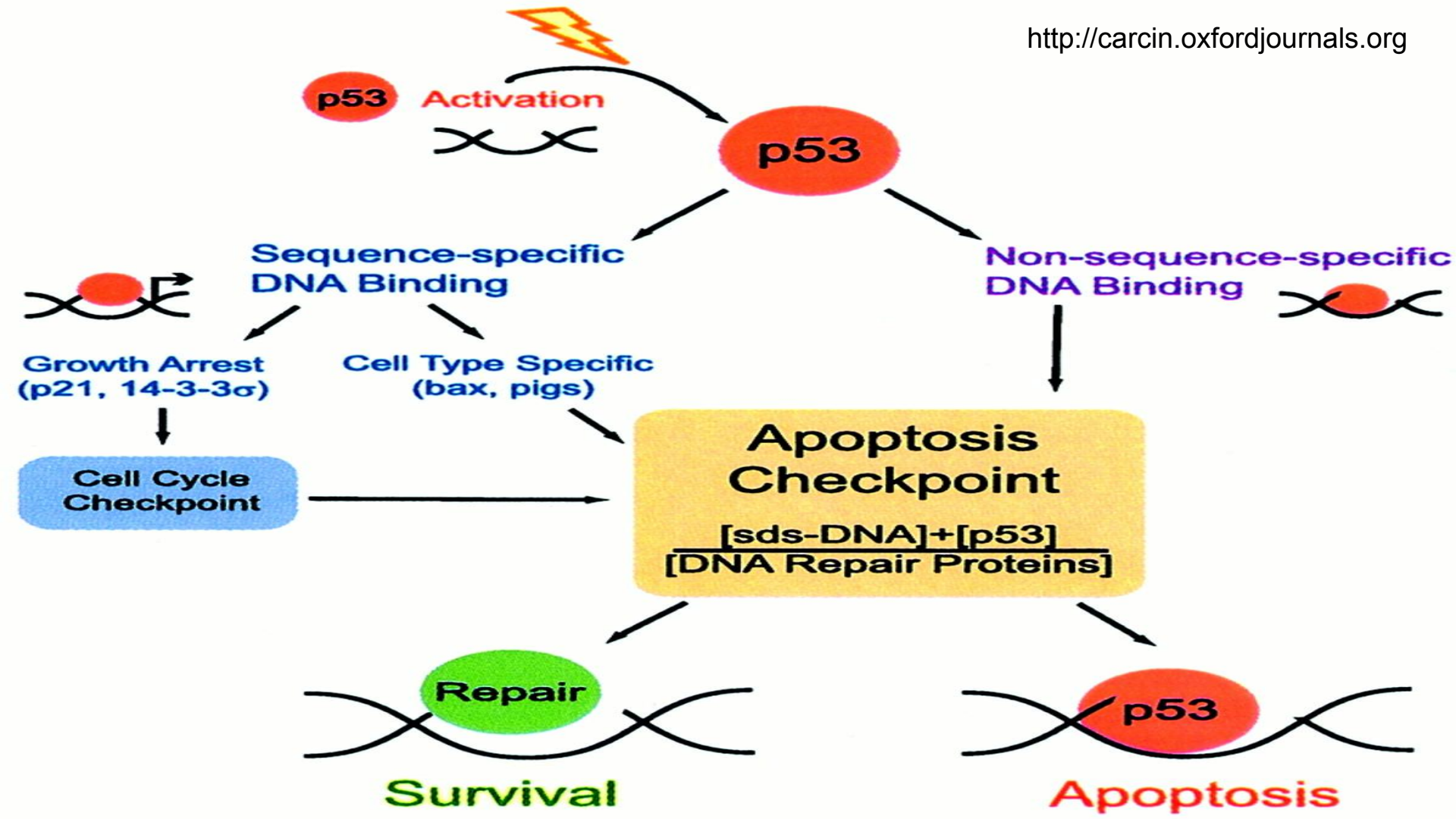
Apoptosis plays a role in disease in three ways:

1. **It is beneficial when it destroys cells with damaged DNA.**

2. **It is involved in disease when:**
    A. **Apoptosis is evaded.**
    B. **Apoptosis is mistakenly triggered.**

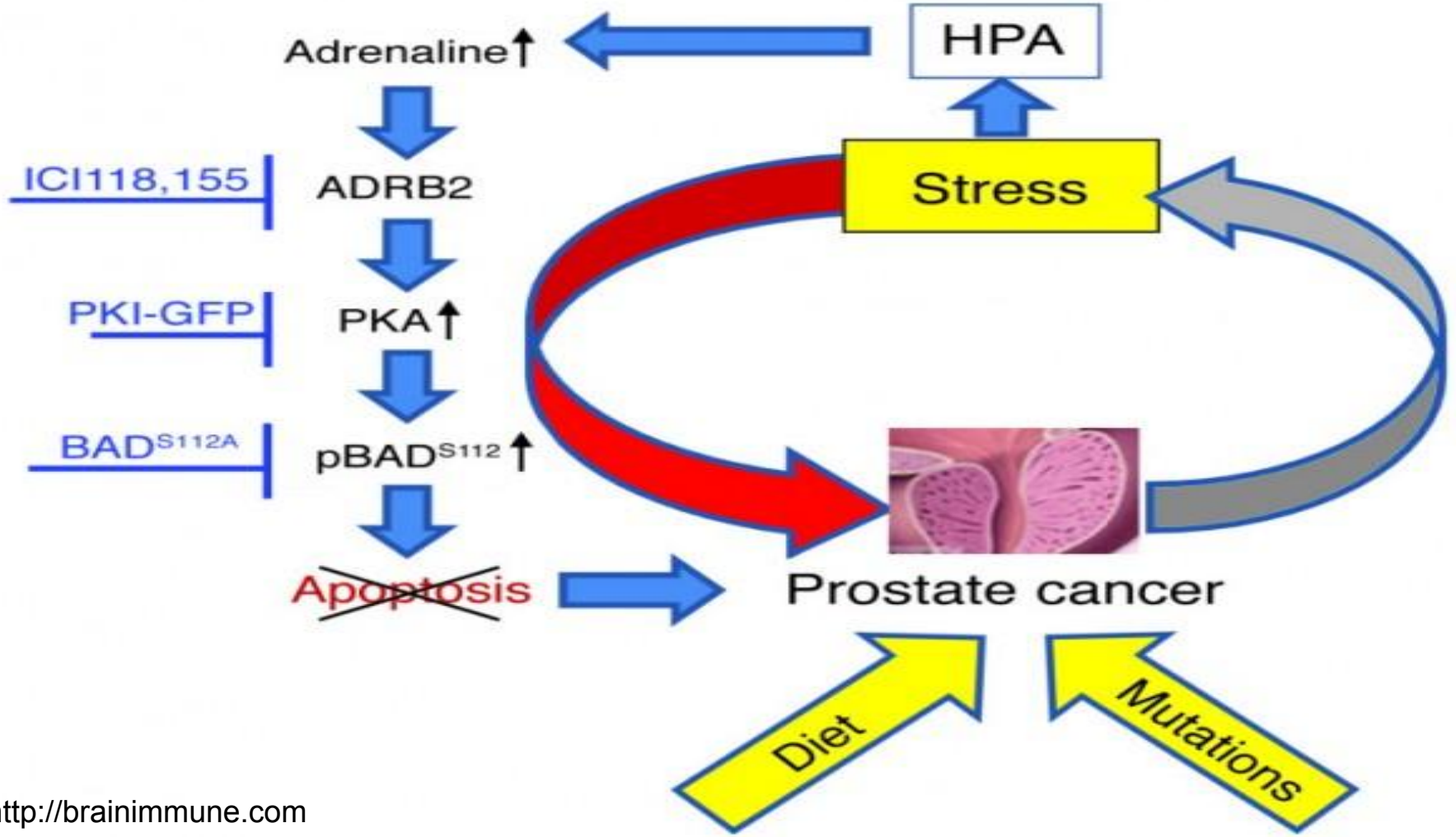
Rubin, 2012

http://carcin.oxfordjournals.org



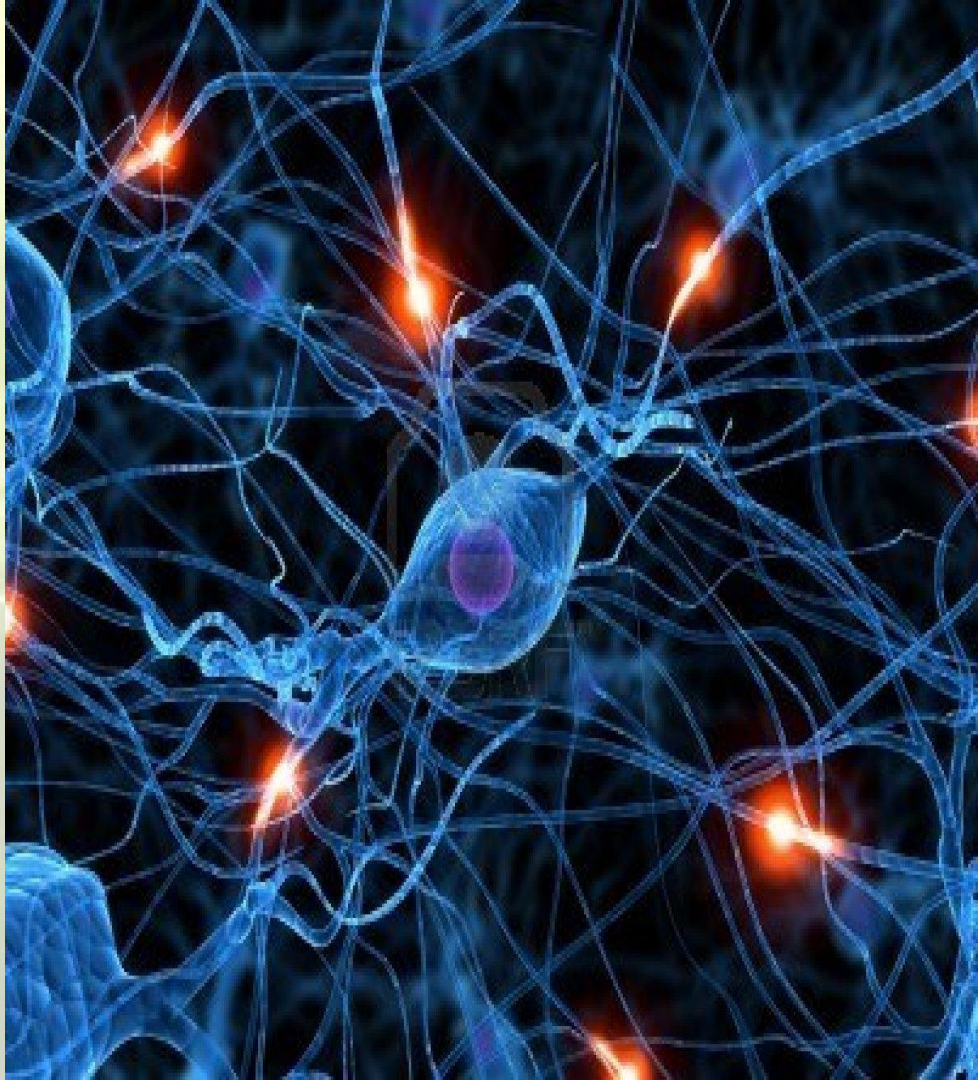
Cancer, HIV and some other diseases occur when a virus is able to interrupt the apoptosis process.

Rubin, 2012


Adrenaline↑
HPA
ICI118,155
ADRB2
Stress
PKI-GFP
PKA↑
BADS112A
pBADS112↑
Apoptosis
Prostate cancer
Diet
Mutations

Apoptosis is Mistakenly Triggered

- Nerve cells do not reproduce
- It’s important that Nerve cells don’t undergo apoptosis because they can’t be replaced.
- Unusually severe cell stresses sometimes induce nerve cells to undergo apoptosis.



Apoptosis is Mistakenly Triggered

Apoptosis in nerve cells contributes to the following neurodegenerative diseases.

1. Amyotrophic Lateral Sclerosis (ALS, Lou Gehrigs disease)
2. Alzheimer's disease
3. Huntingtons disease
4. Parkinson’s disease

Rubin, 2012

Conclusions

1. The mechanisms of apoptosis
    - Proteins cascade then cell is eaten by macrophage
2. The triggers of apoptosis
    - Are induced by extrinsic or intrinsic factors
    - Vital for immunity
3. Apoptosis occurs at week 16 of gestation.
    - Failure is called syndactyly.
4. Apoptosis plays the following roles in disease: (1) Prevents viral propagation (2) In nerve cells, causes neurodegeneration (3) When interrupted, contributes to cancer.

Apoptosis is important because we each have 10’s of billions of cells in our body dying every day!

Thank you

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Mechanism

What is the difference between apoptosis and necrosis?

A. Apoptosis never happens to just lone one cell.
B. Necrosis is a group of cells attacking other cells. Apoptosis acts alone.
C. Apoptosis signals macrophages to clean up scrap cell parts. Necrosis does not.
D. Your presentation was a very effective sleep inducing agent.
E. Necrosis is two cells stuck together.

Rubin, 2012

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Triggers

More Pro-apoptotic proteins inside the cell will lead to?

A. Apoptosis
B. Cell regeneration
C. Myofibril inflammation
D. Cooties
E. Anti-apoptotic proteins

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Development

In what week of gestation is apoptosis responsible for removing the webbing between fingers and toes?

A. week 8
B. week 32
C. week 16
D. week 23

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Disease

Which disease process involves apoptosis?

A. Preventing viral propagation
B. Neurodegeneration
C. Heart disease
D. Cancer development
E. Answers A, B and D

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Questions?