

CELL SIGNALLING

(cell signaling)

British vs. Amer. English

- Why does CELL SIGNALLING exist in nature? All cells receive and respond to signals from their surroundings. **Even the simplest bacteria sense and swim toward high concentrations** of nutrients, such as glucose or amino acids. **Many unicellular eukaryotes also respond to signaling molecules secreted by other cells**, allowing cell-cell communication. Mating between yeast cells, for example, is signaled by peptides that are secreted by one cell and bind to receptors on the surface of another. It is in multicellular organisms, however, that cell-cell communication reaches its highest level of sophistication. **Whereas the cells of prokaryotes and unicellular eukaryotes are largely autonomous, the behavior of each individual cell in multicellular plants and animals must be carefully regulated to meet the needs** of the organism as a whole. This is accomplished by a variety of signaling molecules that are secreted or expressed on the surface of one cell and bind to receptors expressed by other cells, thereby integrating and coordinating the functions of the many individual cells that make up organisms as complex as human beings.
- The binding of most signaling molecules to their receptors initiates a series of intracellular reactions that regulate all aspects of cell behavior, including metabolism, movement, proliferation, survival, and differentiation. Understanding the molecular mechanisms responsible for these pathways of cell signaling has thus become a major area of active research (important for cytostatic and other anti-cancer drug, regeneration, anti-apoptotic drug, ...).

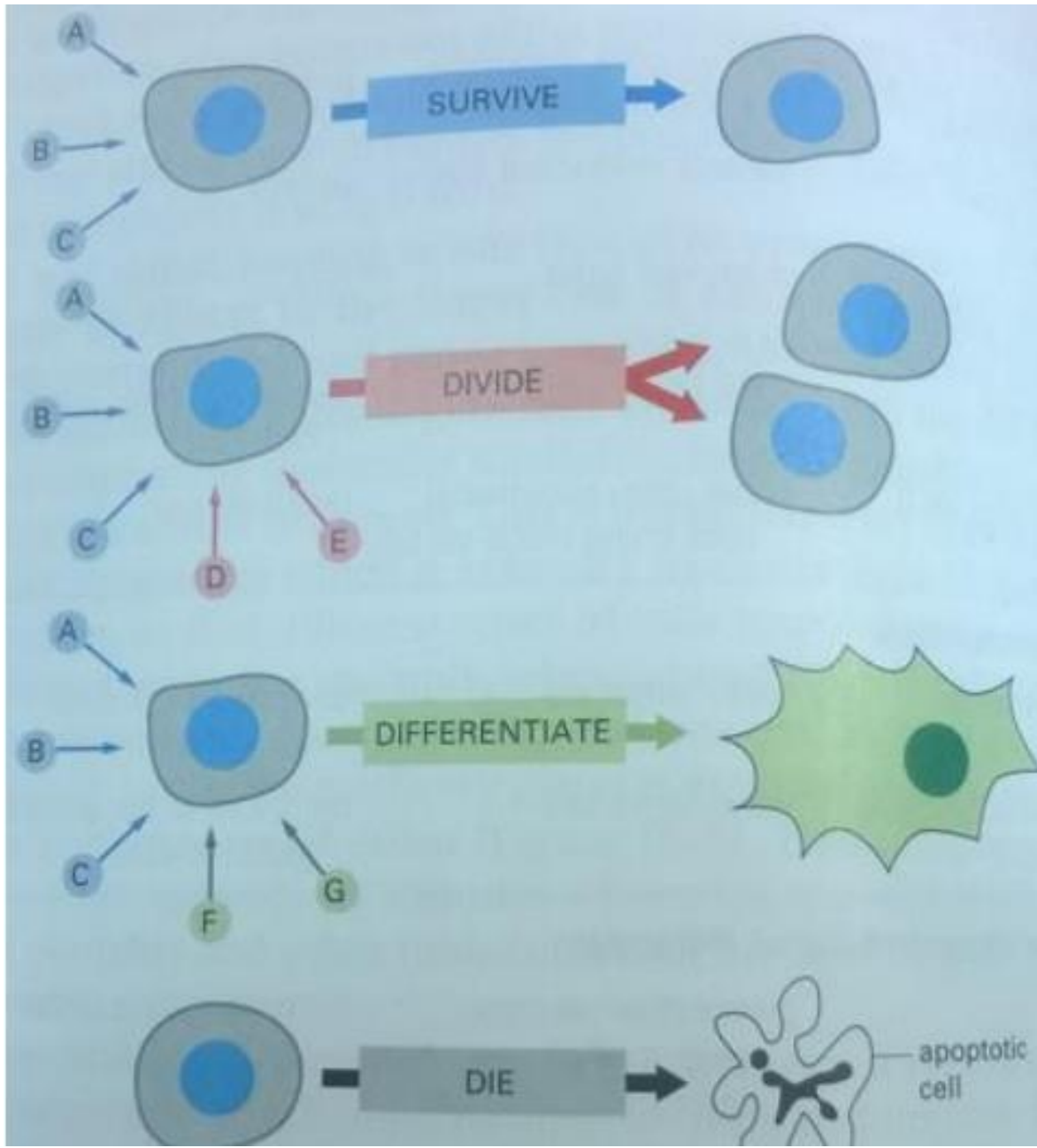
Cells respond to **signals** produced by

1) environment

2) other cells or by 3) themselves.

This mechanism, called **cell signaling**, allows cell-cell communication and is necessary for the functional regulation of single-cell organism and regulation and integration of multicellular organisms.

(NO SIGNAL = DEATH OF CELL)



ENVIROMENTAL SIGNAL

(pure physical signal)

Temperature, pressure, pH, roughness of surface, vibration, light, ...

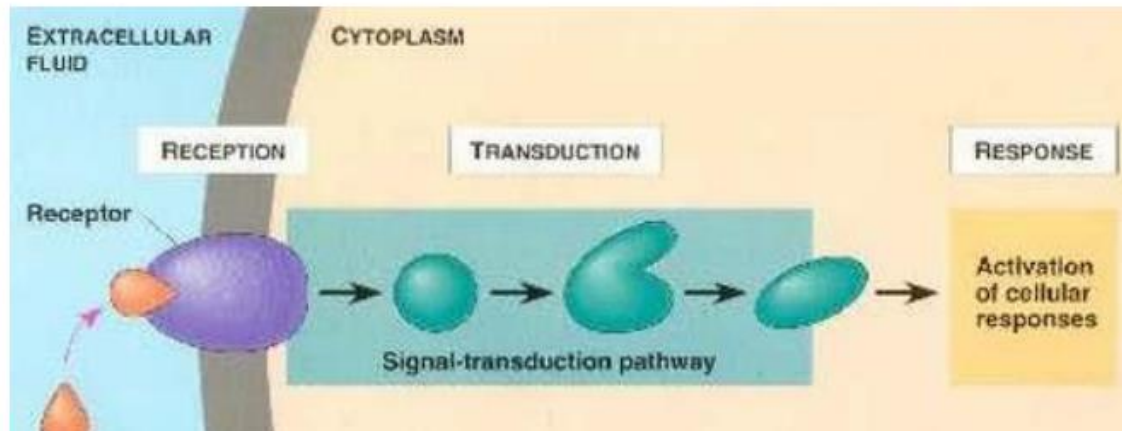
BIOLOGICAL SIGNAL

(mostly defined as: signaling by small molecules and macromolecules)

(for example: Nitric oxide, Adrenaline)

....We will focus in this lesson only to the biological signal:

Basic princip of signal molecule interaction with cell:



RULE 1

- Different cells have different reaction to the same signal molecule:

Example:

Acetylcholine

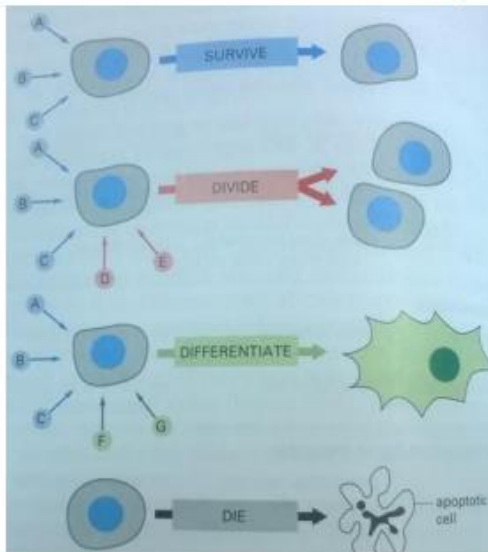
Heart muscle cells
= contraction of cytoskeleton

skeletal muscle cell
= contraction

Salivary gland cell
= secretion

Rule 2

- Some signals are based on one simple molecule, some other signals need „COMBINATION OF MOLECULES IN ONE TIME“ (or in following time)

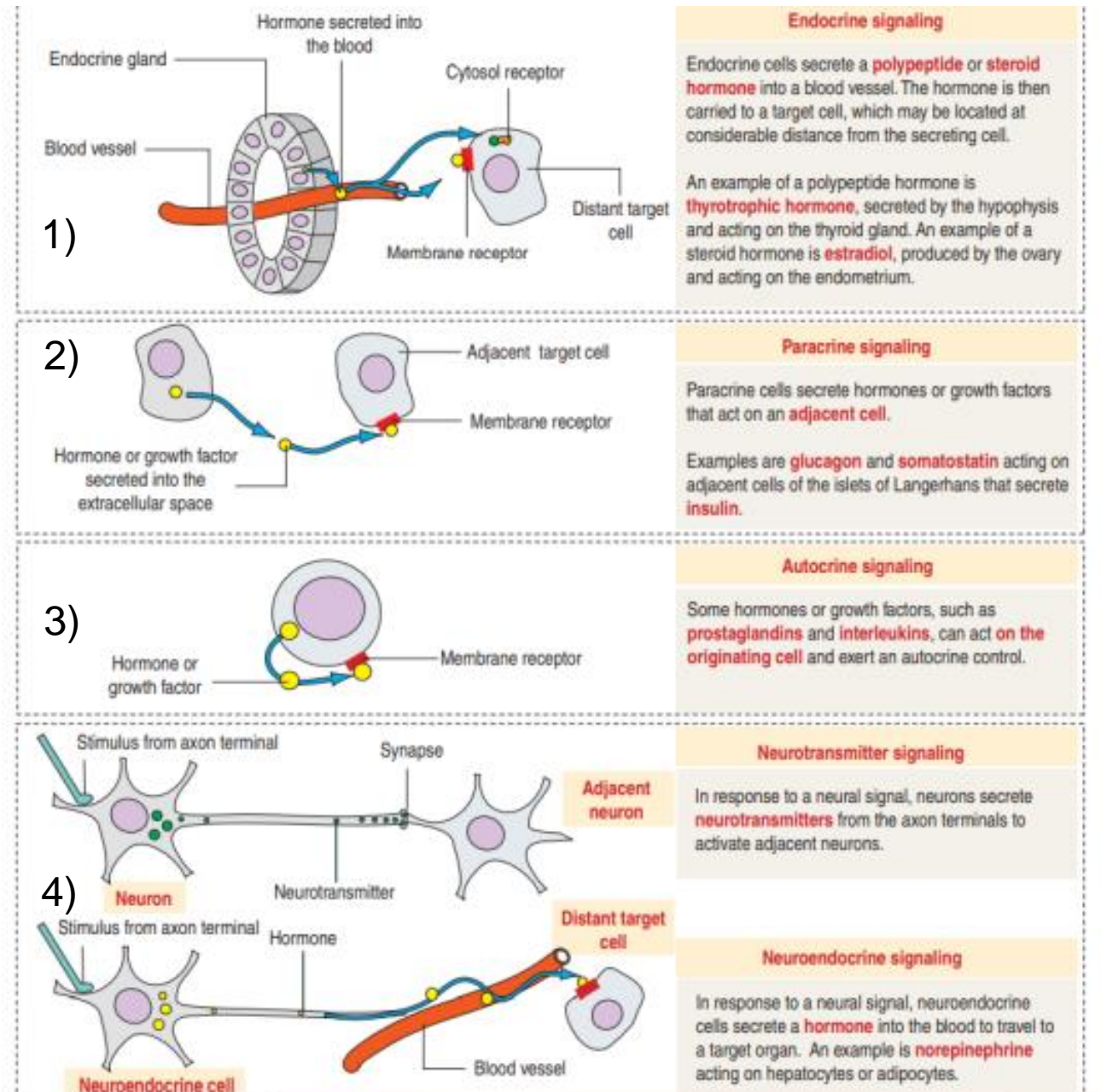


Rule 3

Some cells can be donated by signal from small distance some another from far location in the body.

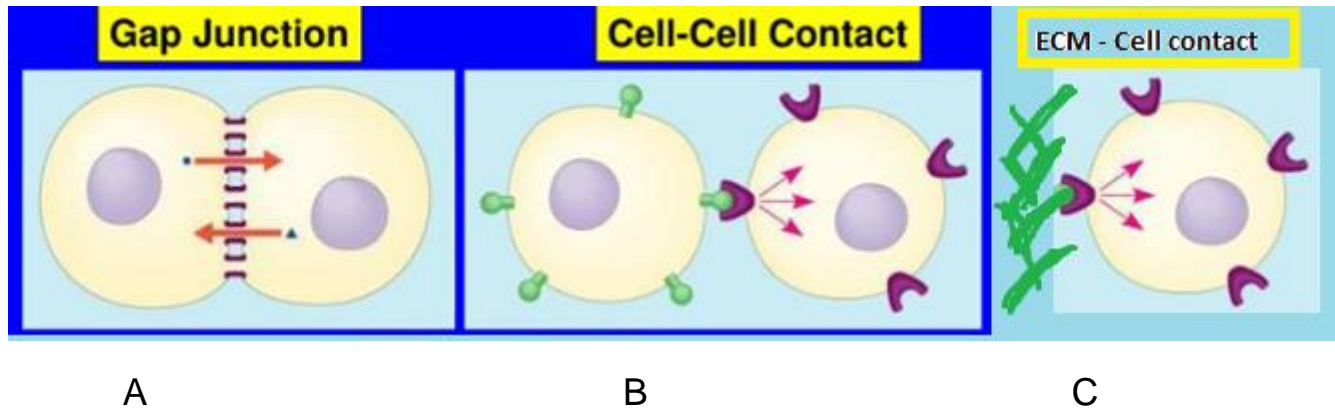
WE HAVE 5 FORMS OF INTERCELLULAR SIGNALING:

Learn the scheme!!!



5) ...and very specific JUXTACRINE cell-to-cell signaling

type of cell–cell or cell–extracellular matrix signaling in multicellular organisms that requires close contact. There are three subtypes:



A = communicating junction links the intracellular compartments of two adjacent cells, allowing transit of relatively small molecules.

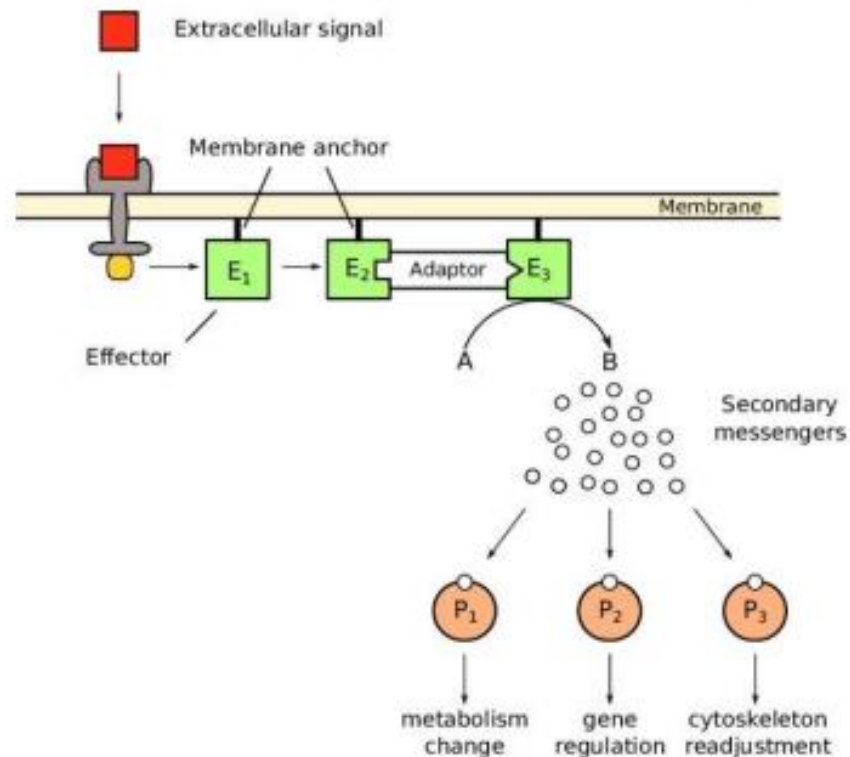
B = membrane ligand (protein, oligosaccharide, lipid) and a membrane protein of two adjacent cells interact.

C = **Extra**Cellular **m**atrix (ECM) such as glycoprotein and a membrane protein interact

Additionally, in unicellular organisms such as bacteria, juxtacrine signaling means interactions by membrane contact. Juxtacrine signaling has been observed for some growth factors, cytokine and chemokine cellular signals, playing an important role in the immune response.

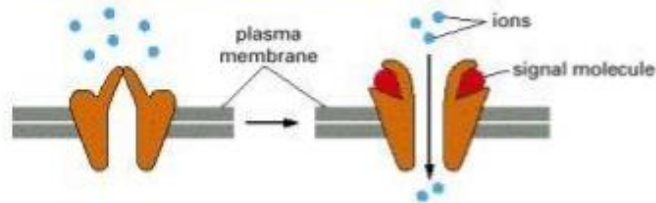
Mechanism of signaling

- !! Not all signal molecule had to induce change in DNA translation and gene delivery !!

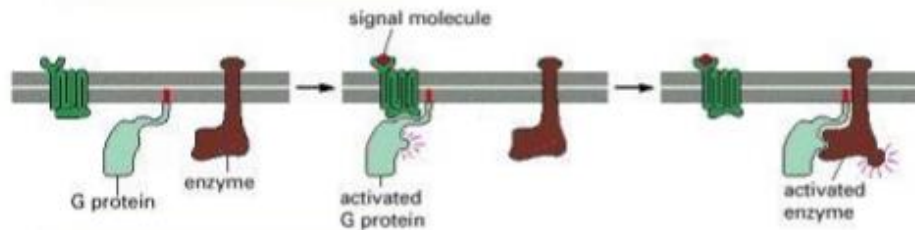


3 classes of surface receptors:

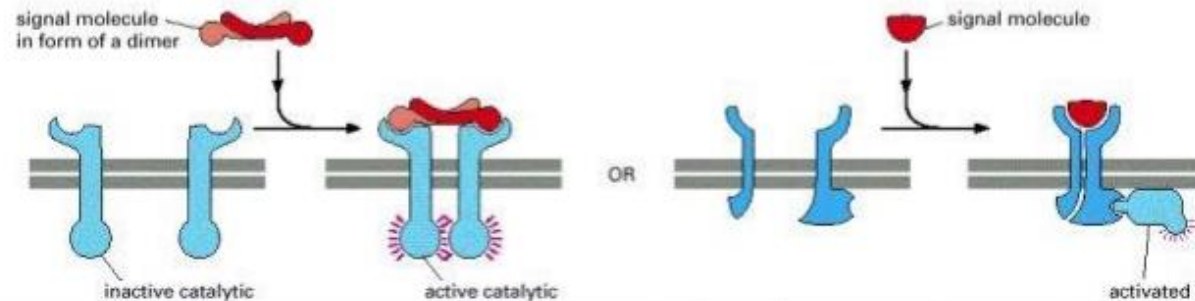
(A) ION-CHANNEL-LINKED RECEPTORS



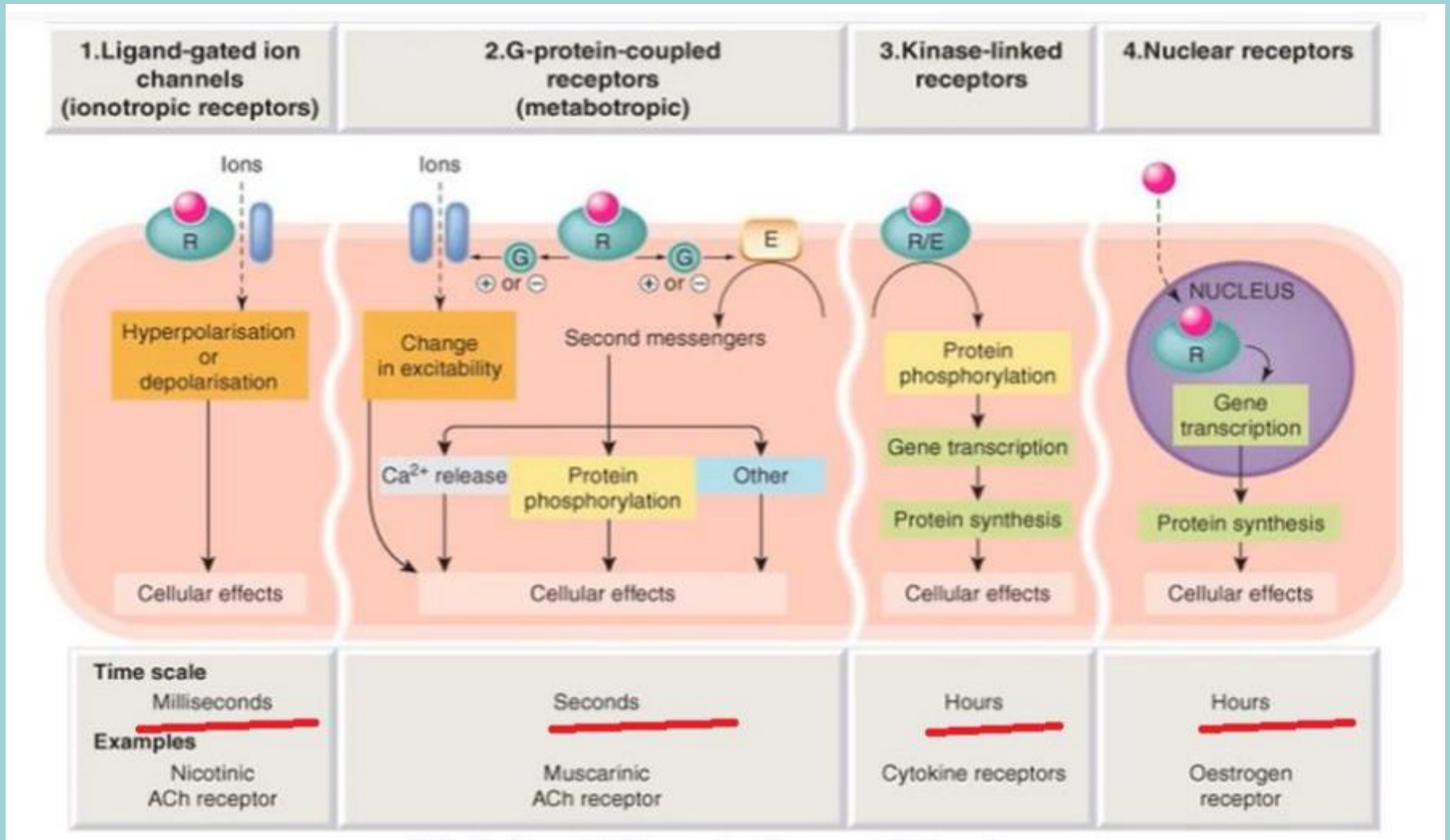
(B) G-PROTEIN-LINKED RECEPTORS



(C) ENZYME-LINKED RECEPTORS



Overview – signal net



Most important signal molecules in clinical pharmacology and experimental biology.

Please, learn
minimally
5 hormones
and
5 local mediators
And
2 neurotransmitter

(Name
Chemical nature
Action)

Table 16-1 Some Examples of Signal Molecules

SIGNAL MOLECULE	SITE OF ORIGIN	CHEMICAL NATURE	SOME ACTIONS
Hormones			
<i>Adrenaline (epinephrine)</i>	adrenal gland	derivative of the amino acid tyrosine	increases blood pressure, heart rate, and metabolism
<i>Cortisol</i>	adrenal gland	steroid (derivative of cholesterol)	affects metabolism of proteins, carbohydrates, and lipids in most tissues
<i>Estradiol</i>	ovary	steroid (derivative of cholesterol)	induces and maintains secondary female sexual characteristics
<i>Glucagon</i>	α cells of pancreas	peptide	stimulates glucose synthesis, glycogen breakdown, and lipid breakdown, e.g., in liver and fat cells
<i>Insulin</i>	β cells of pancreas	protein	stimulates glucose uptake, protein synthesis, and lipid synthesis, e.g., in liver cells
<i>Testosterone</i>	testis	steroid (derivative of cholesterol)	induces and maintains secondary male sexual characteristics
<i>Thyroid hormone (thyroxine)</i>	thyroid gland	derivative of the amino acid tyrosine	stimulates metabolism of many cell types
Local Mediators			
<i>Epidermal growth factor (EGF)</i>	various cells	protein	stimulates epidermal and many other cell types to proliferate
<i>Platelet-derived growth factor (PDGF)</i>	various cells, including blood platelets	protein	stimulates many cell types to proliferate
<i>Nerve growth factor (NGF)</i>	various innervated tissues	protein	promotes survival of certain classes of neurons; promotes growth of their axons
<i>Transforming growth factor-β (TGF-β)</i>	many cell types	protein	inhibits cell proliferation; stimulates extracellular matrix production
<i>Histamine</i>	mast cells	derivative of the amino acid histidine	causes blood vessels to dilate and become leaky, helping to cause inflammation
<i>Nitric oxide (NO)</i>	nerve cells; endothelial cells lining blood vessels	dissolved gas	causes smooth muscle cells to relax; regulates nerve cell activity
Neurotransmitters			
<i>Acetylcholine</i>	nerve terminals	derivative of choline	excitatory neurotransmitter at many nerve-muscle synapses and in central nervous system
<i>γ-Aminobutyric acid (GABA)</i>	nerve terminals	derivative of the amino acid glutamic acid	inhibitory neurotransmitter in central nervous system

Signaling is important for

a) CELL CYCLE

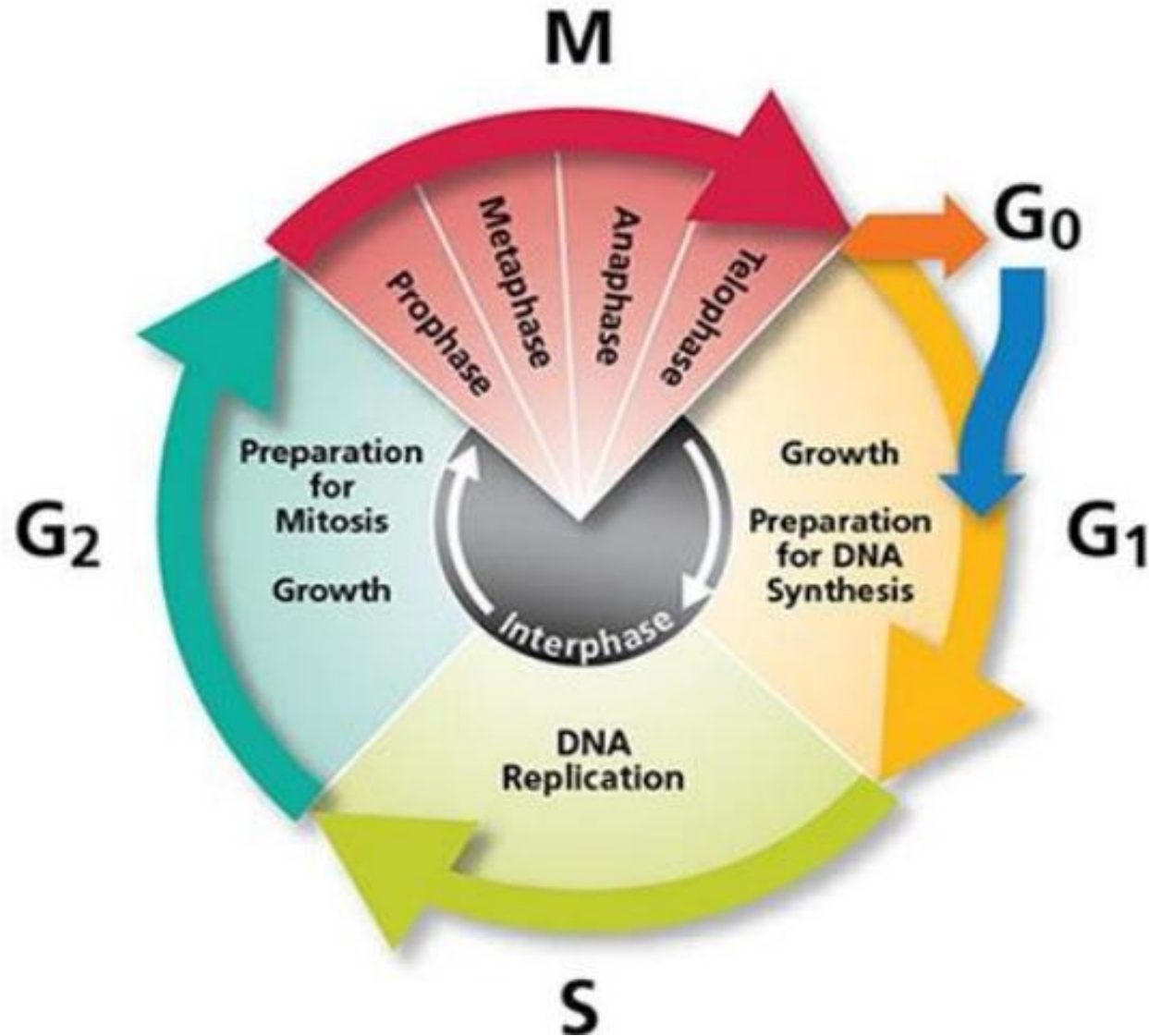
b) APOPTOSIS

c) NON-apoptotic death

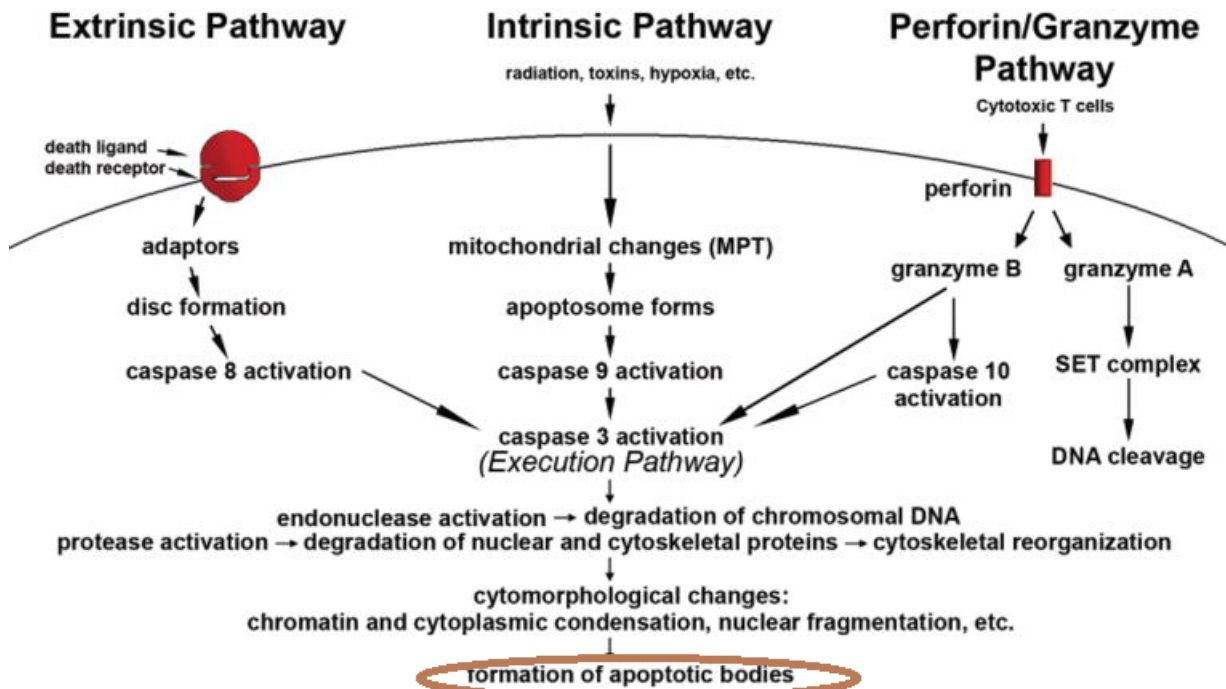
- (note: **necrosis** is very fast and unprogramed death, where injury or toxic enviroment prevent apoptosis or another non-apoptotic death, cell is lysed and solution is dangerous for near cells in tissue)



a) Cell cycle



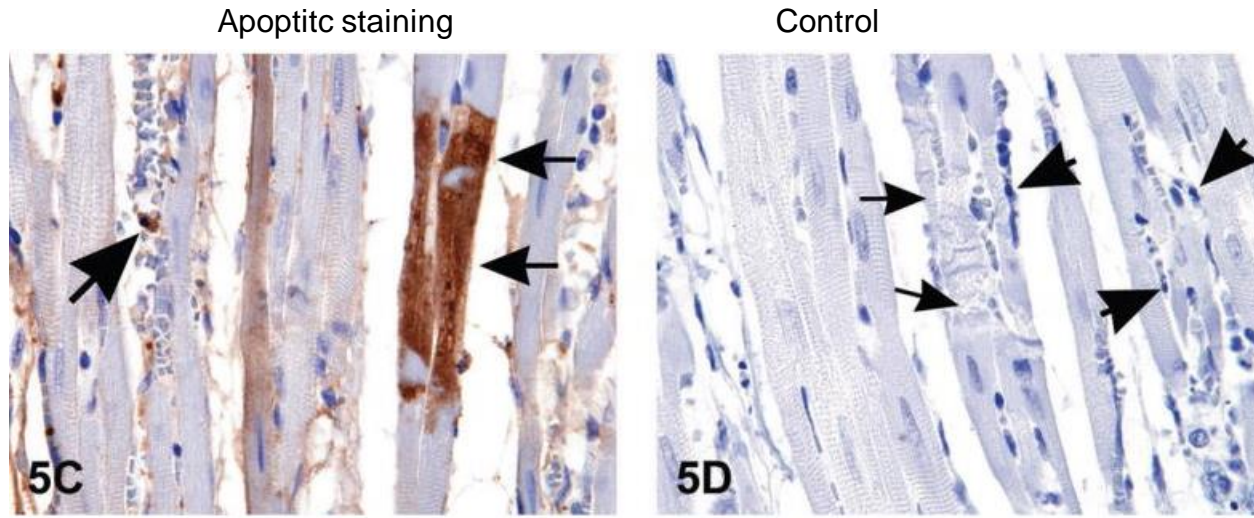
b) Apoptosis



apoptosis

- microscopical view to tissue

Example of apoptosis in rat heart (infarction of myocardium)



- Figure 5C illustrates **cleaved caspase-3 staining for** apoptosis revealing the presence of intracytoplasmic positive myofibers (small arrows) located in the interventricular septum; large arrow indicates an **apoptotic body**. Figure 5D is a negative control of the same heart demonstrated in 5C. The small arrows demonstrate degenerating myofibers; large arrows indicate apoptotic bodies.

(note: This proteolytic cascade, in which one caspase can activate other caspases, amplifies the apoptotic signaling pathway and thus leads to rapid cell death)

apoptosis

**Some advanced article for future study (not in exam)
(apoptosis is important curative factro in ancer, infarcted region, neurodageneratie d.)**

Inhibiting the inhibitors: Targeting anti-apoptotic proteins in cancer and therapy resistance

[Nir Shahar](#)¹, [Sarit Larisch](#)²

Abstract The cytotoxic effect of anti-cancer drugs relies on their ability to induce programmed cell death known as apoptosis. Evading apoptosis is a common characteristic of cancer cells and it is linked to both carcinogenesis and anticancer drug resistance.

Revisiting miRNA-21 as a Therapeutic Strategy for Myocardial Infarction:

A Systematic Review

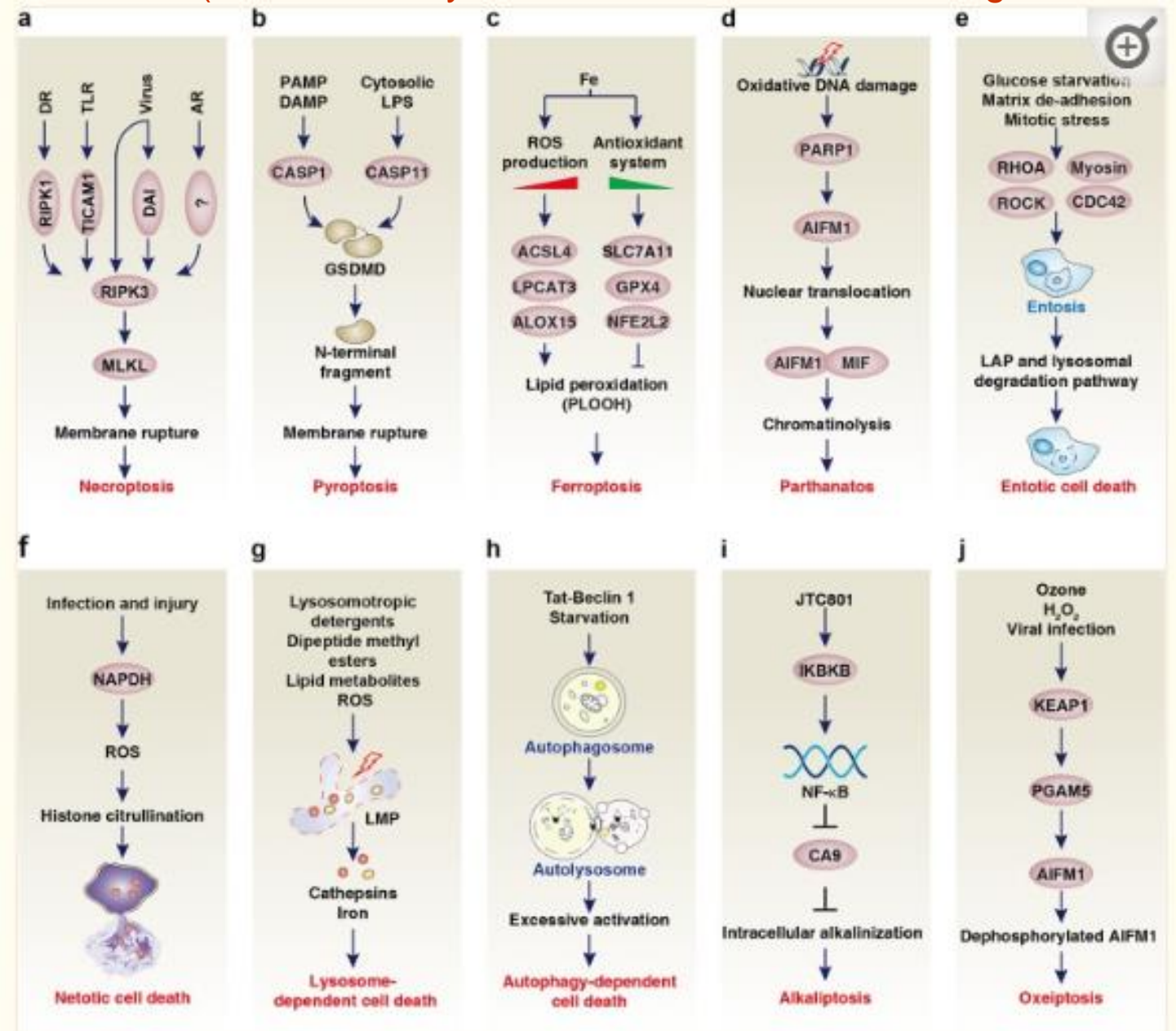
V Sothivelr, MY Hasan, S Mohd Saffian... - Journal of ..., 2022

Studies described thecardioprotective effects of miR-21 to reduce infarct size by improving angiogenesis, antiapoptotic...

An overview of investigational antiapoptotic drugs with potential application for the treatment of neurodegenerative disorders

A. Camins, F. Sureda, +4 authors M. Pallàs, 2010

c) NON-apoptotic death (learn minimally 5 death-names and 5 initial signal molecule)



Advanced publication: