

CELL SIGNALING

(American ENGLISH: cell signalling)

(9/11 2021)

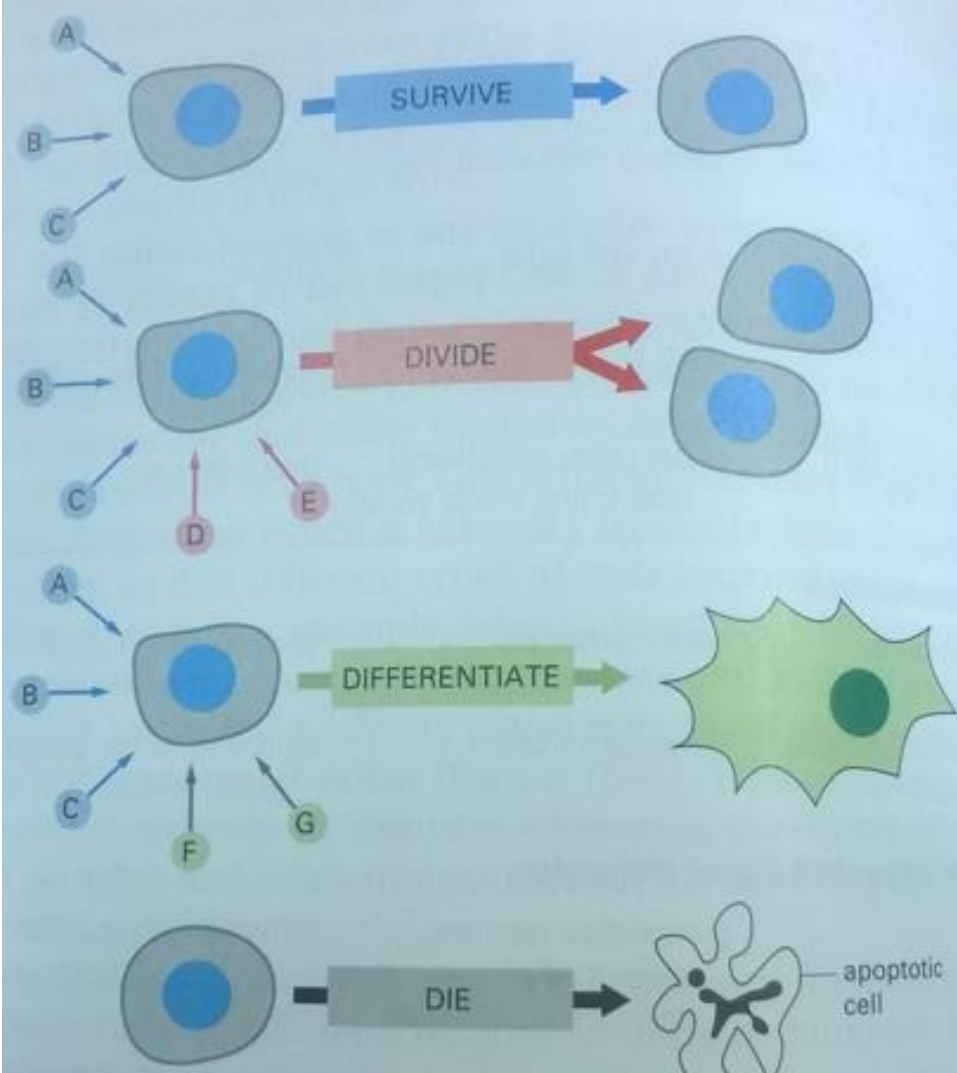
Cells respond to **signals** produced by

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, ...

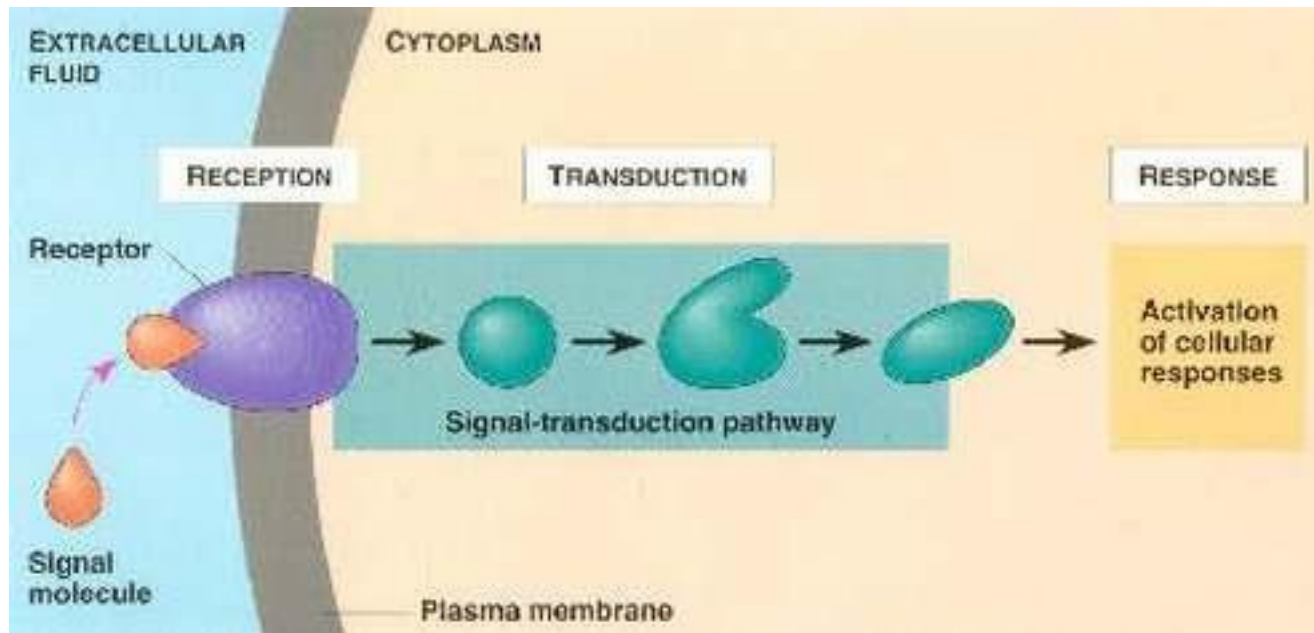
BIOLOGICAL SIGNAL

(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

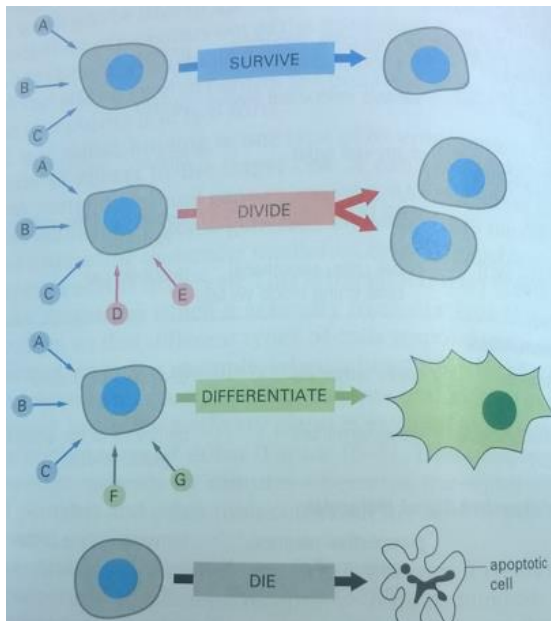
Heart muscle cells
= contraction of cytoskeleton

skeletal muscle cell
= contraction

Salivary gland cell
= secretion

RULE 3

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

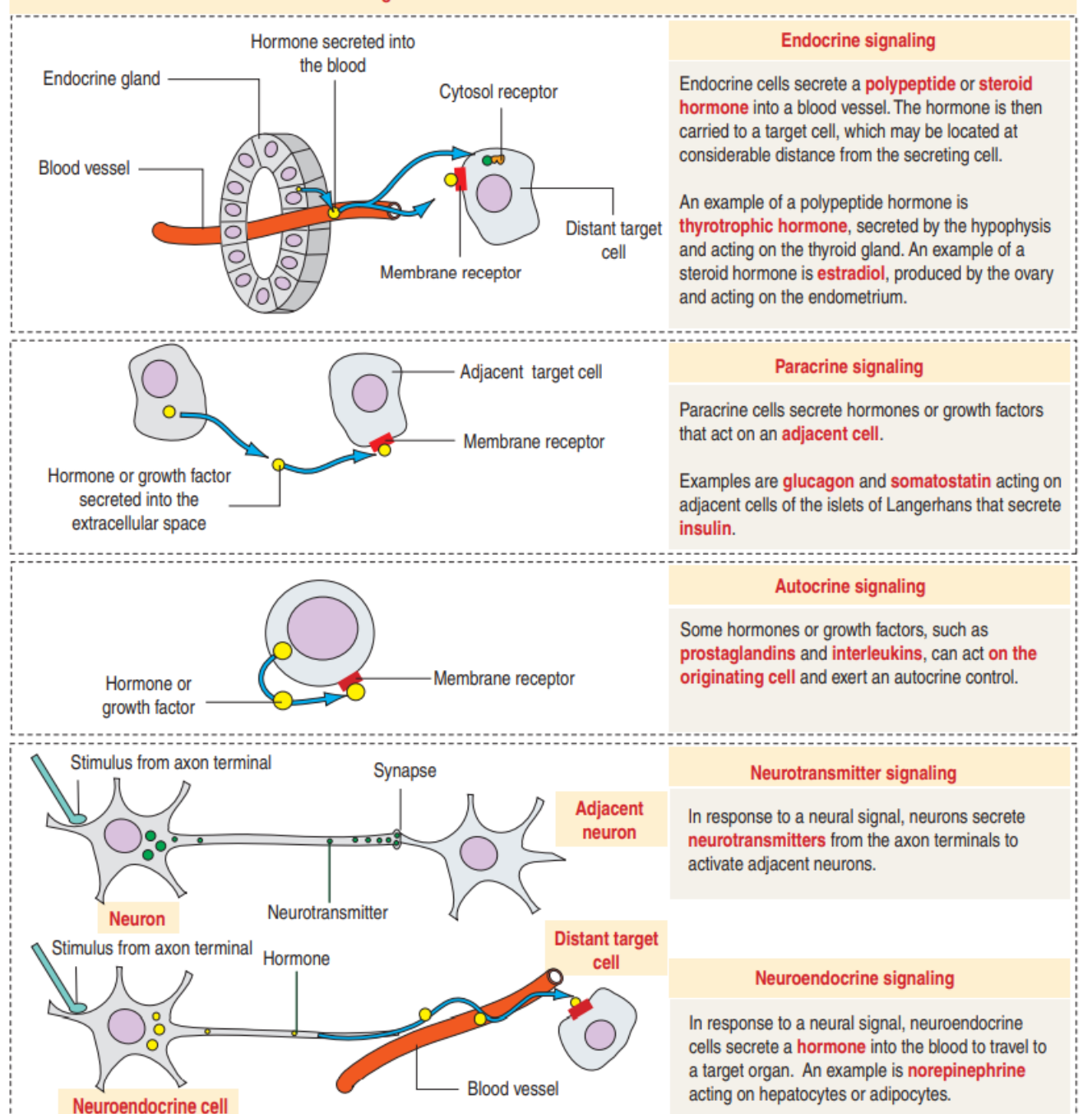


RULE 3

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

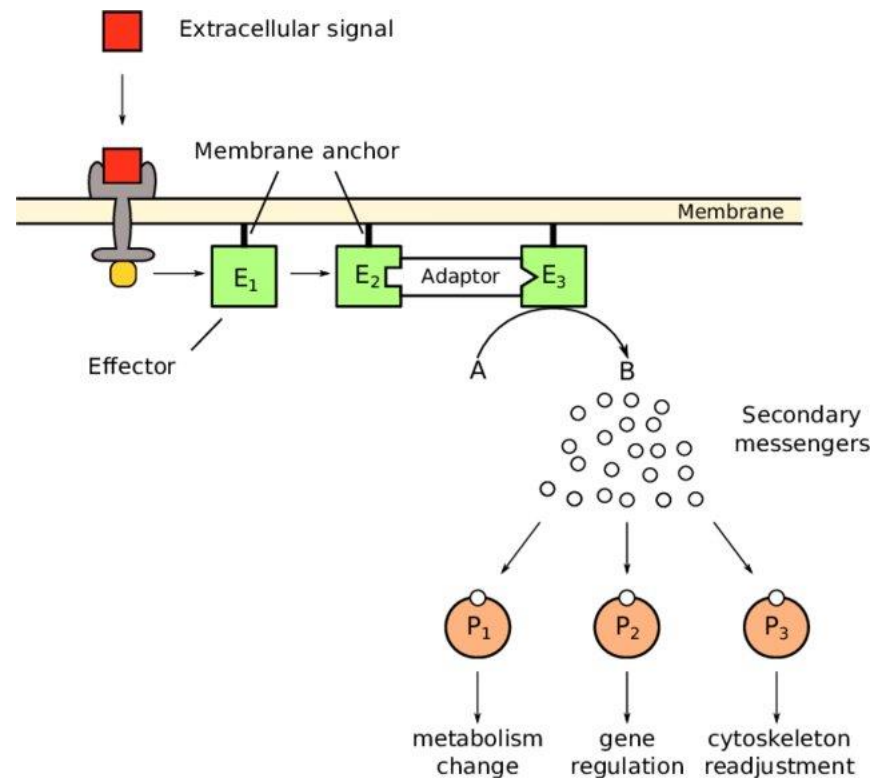
WE HAVE 4 FORMS OF INTERCELLULAR SIGNALING:

Figure 3-1. Mechanisms of hormone action



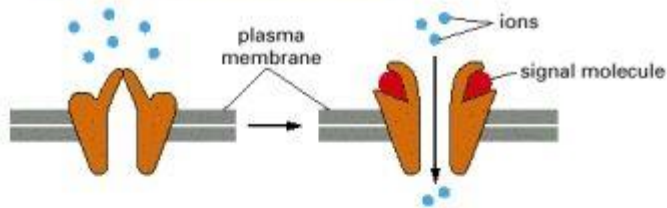
Internal machinery of signal molecule activity in the cells

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

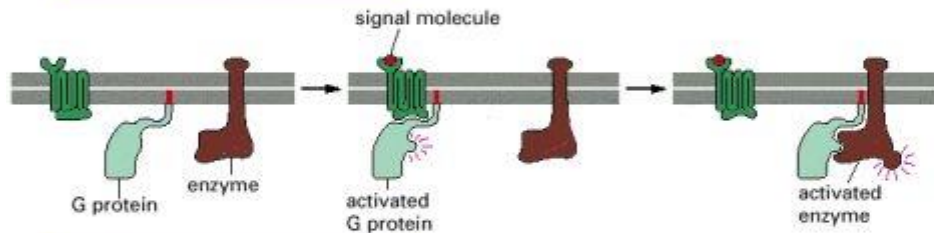


3 classes of surface receptors:

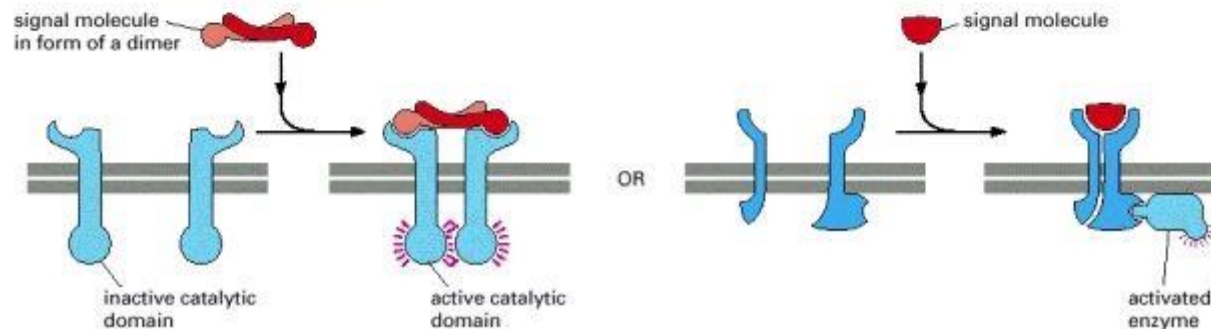
(A) ION-CHANNEL-LINKED RECEPTORS



(B) G-PROTEIN-LINKED RECEPTORS

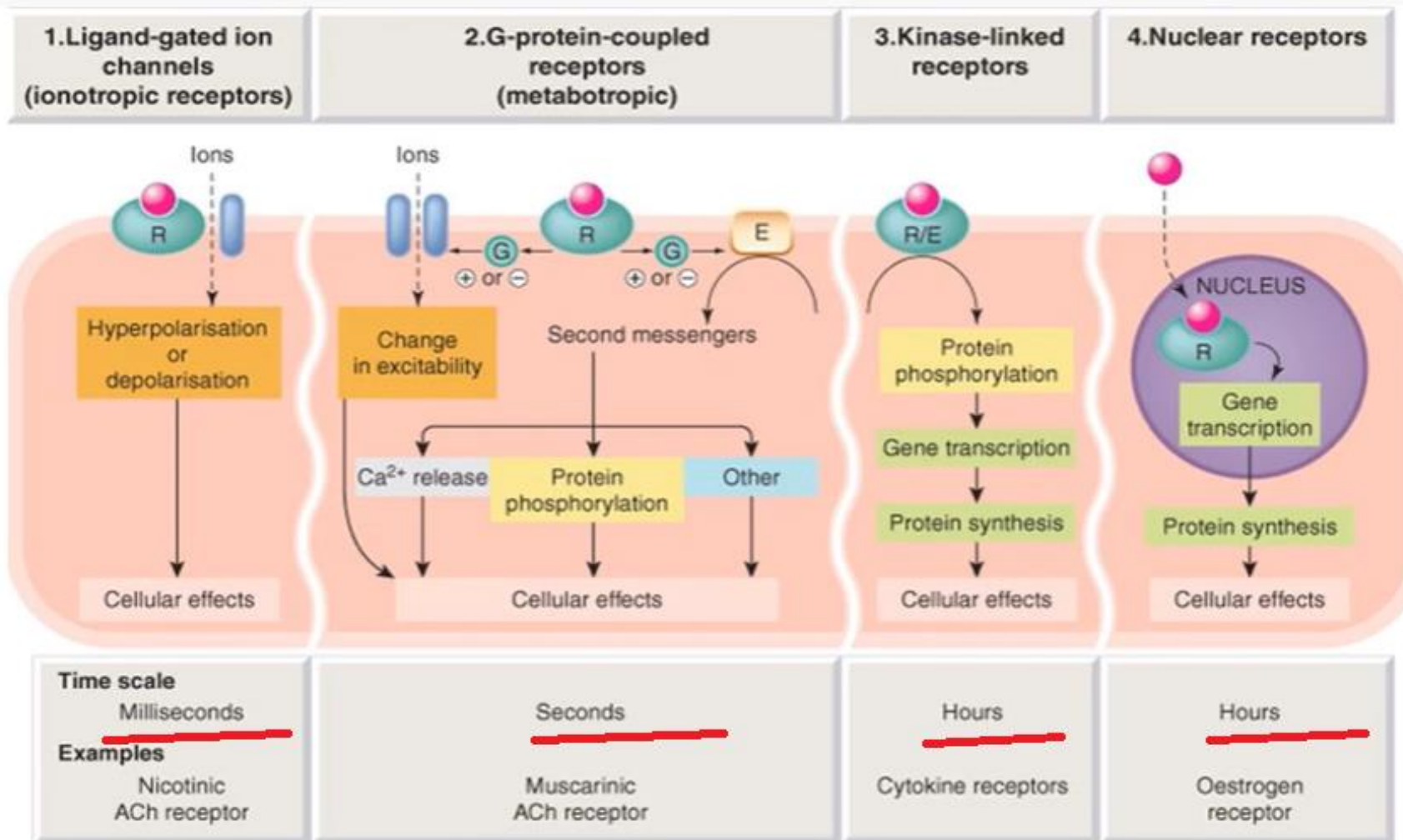


(C) ENZYME-LINKED RECEPTORS



Complex overview :

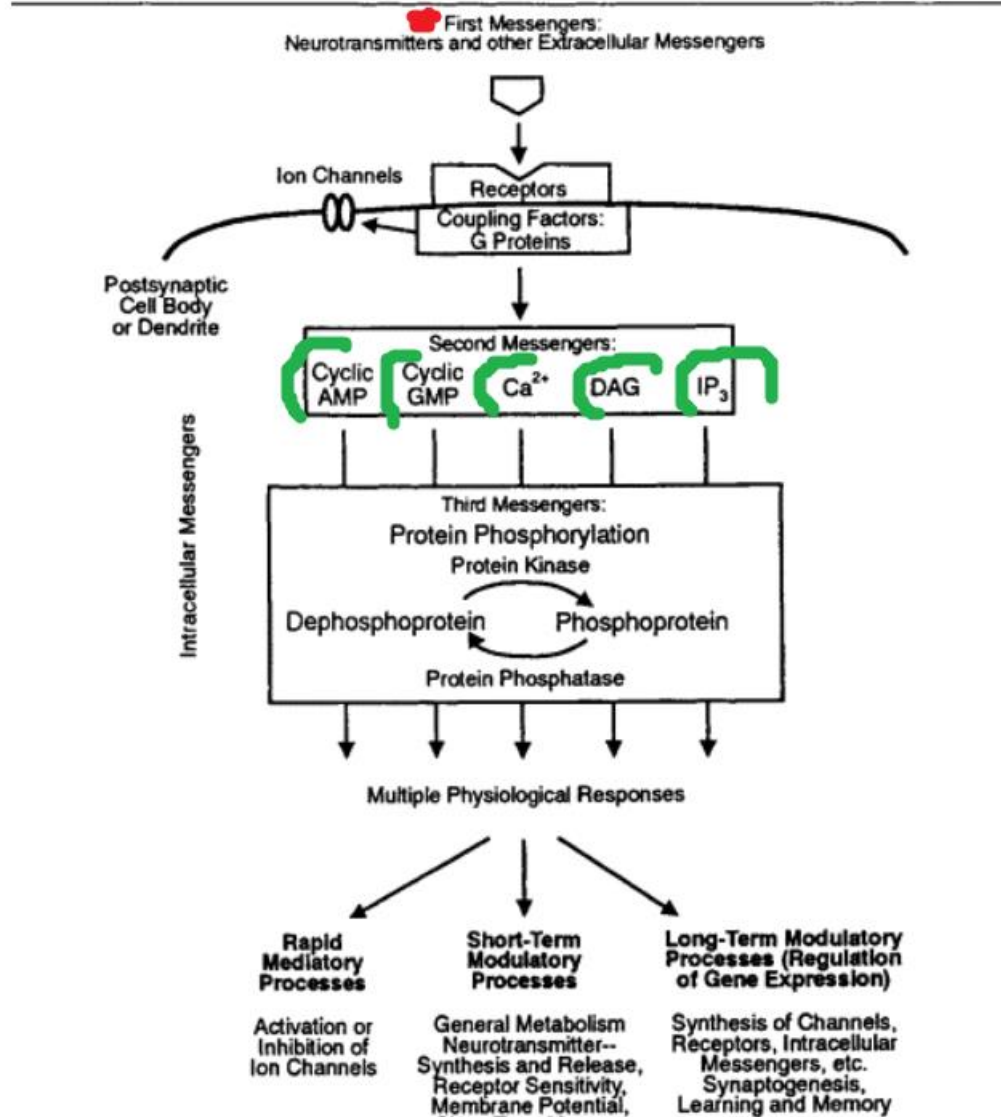
3 types of membrane receptors + nuclear.r.



FIRST messenger versus SECOND messenger

- **First messengers** are extracellular factors, often hormones or neurotransmitters, such as epinephrine, growth hormone, and serotonin. Because peptide hormones and neurotransmitters typically are biochemically hydrophilic molecules, these first messengers may not physically cross the phospholipid bilayer to initiate changes within the cell directly—unlike steroid hormones, which usually do.
- **Second messengers** are intracellular signaling molecules released by the cell in response to exposure to extracellular signaling molecules—the **first messengers**. (Intracellular signals, a non-local form or cell signaling)

...overview of second messenger



Examples of signal MOLECULES

- Alberts
Essential Cell Biology (chapter CELL SIGNAL)

Table 15-1 Some Examples of Signal Molecules

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

EXAMPLE 1 - pathology connected to cell signal machinery



Cholera



- Disease acquired by drinking contaminated water (w/human feces)
- Bacteria (*Vibrio cholerae*) colonizes lining of small intestine and produces toxin
- Toxin modifies G-protein involved in regulating salt & water secretion
- G protein stuck in active form → intestinal cells secrete salts, water
- Infected person develops profuse diarrhea and could die from loss of water and salts

EXAMPLE 2 - CANCER

- Papalazarou, V., Salmeron-Sanchez, M., and Machesky, L. M. (2018). Tissue engineering the cancer microenvironment—challenges and opportunities. *Biophys. Rev.* 10, 1695–1711. doi: 10.1007/s12551-018-0466-8

REC. LITERATURE

- Alberts (2004) Essential CELL Biology –
Chapter CELL COMMUNICATION

Cell signaling is important aspect for starting and of cell-death

for next lessons: please visit the pictures in article

The molecular machinery of regulated cell death

[Daolin Tang](#),^{#1,2} [Rui Kang](#),² [Tom Vanden Berghe](#),^{3,4,5} [Peter Vandenabeele](#),^{3,4,6} and [Guido Kroemer](#)

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6796845/>

Some advanced modern publication about important signal for cell (proliferation, differentiation, migration, cell death)

- **Stem cell proliferation is induced by apoptotic bodies from dying cells during epithelial tissue maintenance** [Courtney K. Brock](#), [Published: 05 March 2019](#)
- Engineered Biomaterials Control Differentiation and Proliferation of Human-Embryonic-Stem-Cell-Derived Cardiomyocytes via Timed Notch Activation Author links open overlay panel [Jason C. Tung¹](#) [Sharon L. Paige²](#)
- An engraved surface induces weak adherence and high proliferation of nonadherent cells and microorganisms during culture [Sunil Thomas](#)
Published Online: 12 Jun 2020 <https://doi.org/10.2144/btn-2020-0022>