Life and Health Science

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Chapter 11: Cell Communication

An In-Depth Exploration of Cellular Communication and Signalling Mechanisms

Cell Communication

- Cell-to-cell communication is essential for multi cellular organisms.
- Biologists have discovrered some universal mechanismas of cellular regulations

Introduction to cell communication

Think !!!

- If your cells are just simple building blocks, unconscious and static as bricks in a wall?
- Cells can detect what's going on around them, and they can respond in real-time to cues from their neighbours and environment.
- At this very moment, your cells are sending and receiving millions of messages in the form of chemical signalling molecules!

Definition

Any of several ways in which living cells of an organism communicate with one another, whether by direct contact between cells or by means of chemical signals carried by neurotransmitter substances, hormones and cyclic AMP.

- Cell communication is essential for coordinating cellular functions.
- Enables processes like growth, immune response, and maintaining balance.
- Involves a series of signals and responses that keep multicellular organisms organized.

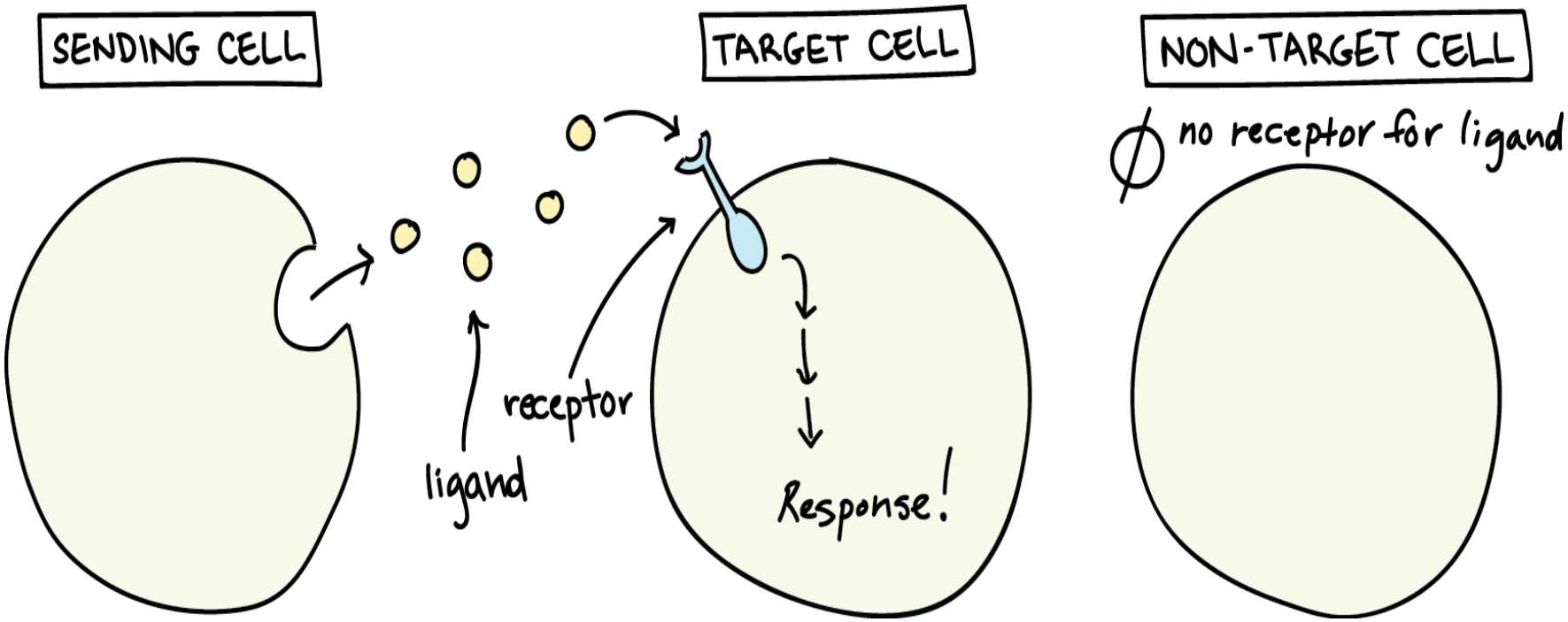
DO CELLS COMMUNICATE AND WHY?

- **Cells** can also **communicate** directly with one another and change their own internal working in response by way a variety of chemical and mechanical signals.
- In multi-cellular organisms, cell signalling allows for the specialisation of a group of **cells**.
- This **communication** is essential for functions like growth, immune response, tissue repair, and homeostasis.

Overview of cell signalling

- Cells typically communicate using chemical signals.
- These chemical signals, which are proteins or other molecules produced by a **sending cell**, are often secreted from the cell and released into the extracellular space.
- There, they can float – like messages in a bottle – over to neighbouring cells.

Overview of cell signaling



Importance of Cell Communication

- Ensures cells can respond to environmental changes.
- Maintains homeostasis by regulating internal cellular activities.
- Essential for tissue repair, growth, and adaptation to external stimuli.

Cell signalling in Prokaryotes and Eukaryotes

Cell Signalling in Prokaryotes

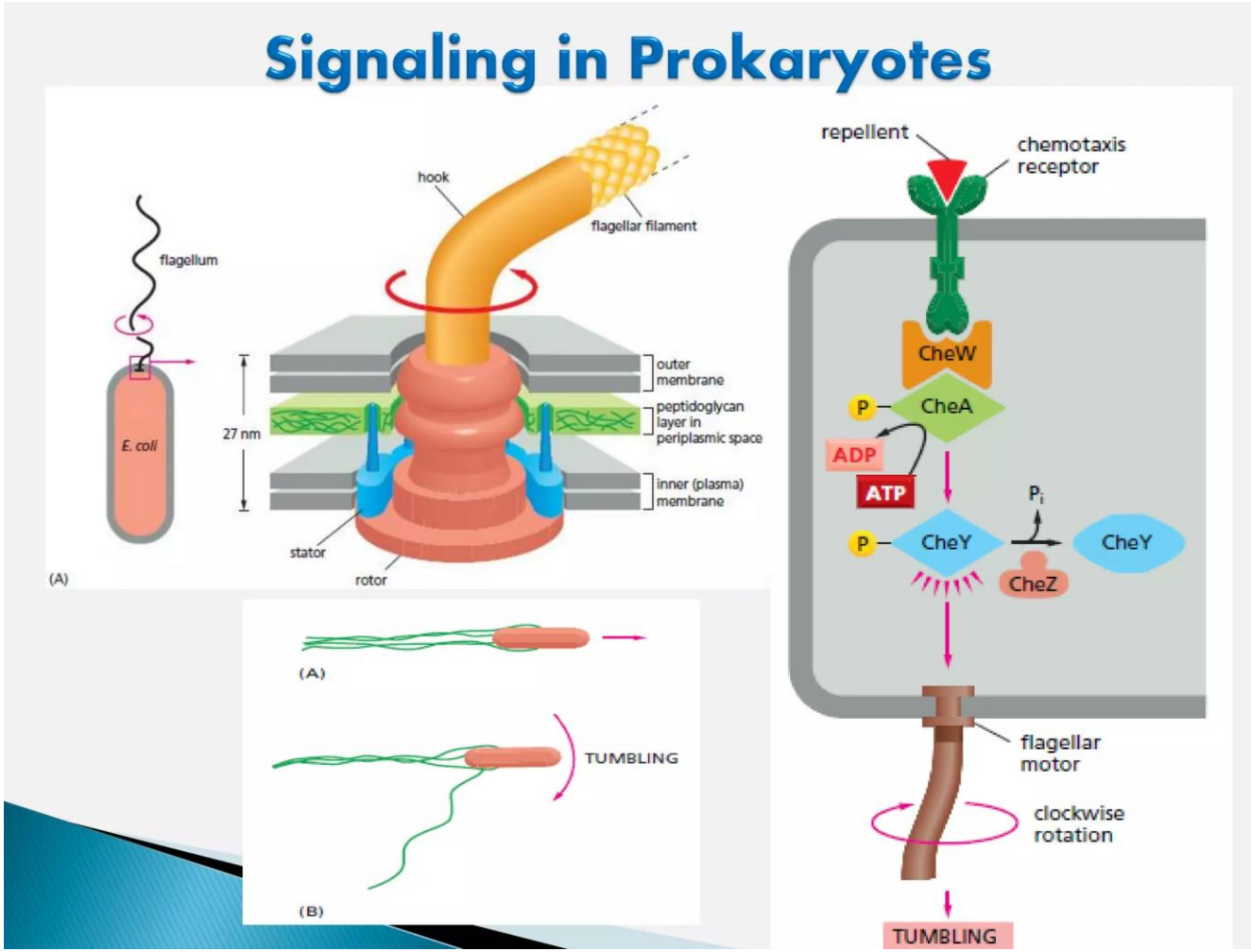
- *Korman et al.* (1979) reported on the relationship between the degree of chemotactic activity in *Escherichia coli*.
- They concluded: the response of the bacterial flagella was proportional to the amount of a specific receptor on its cell surface.
- Regulation of Flagella movement by histidine kinase - a good example of prokaryote signaling
- Also an evidence of evolution of Signaling mechanism from prokaryote to eukaryote
- Clock wise and anticlockwise movement of flagella regulated by signaling- determines its swimming pattern

Cell signalling in Prokaryotes

Example:1

- Many bacteria respond to chemical signals secreted by their neighbours and increase in concentration with increasing population density. This process called quorum sensing.
- Allows to bacteria to coordinate their behaviour including their motility, antibiotic production, spore formation and sexual conjugation.
- Promotes survival and saves from danger.

Signaling in Prokaryotes

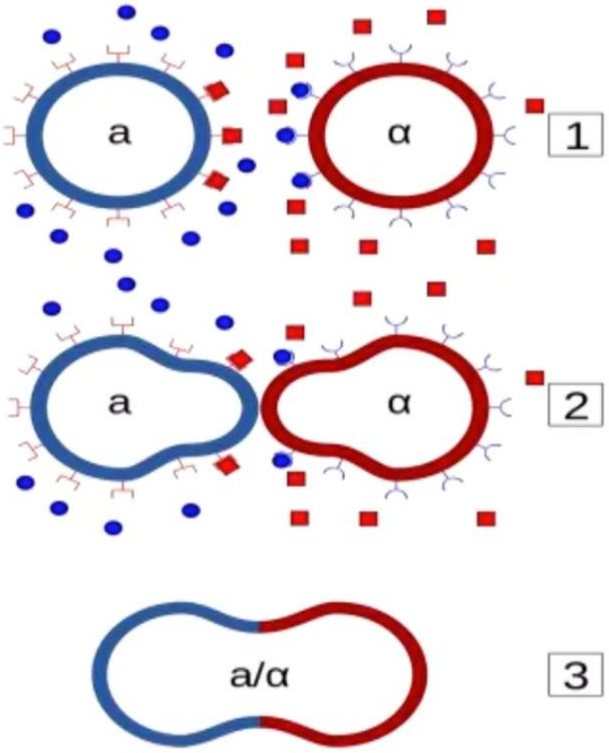


Cell Signalling in Prokaryotes

Example:1

- Similarly, budding yeast *S.Cerevisiae* communicate with one another in preparation for mating.

- A haploid individual, ready to mate, secrets a peptide called mating factor that signals cells of the opposite mating type to stop proliferation and prepare for mating



CELL SIGNALLING IN EUKARYOTES

- Eukaryotic signaling systems are much more elaborate than those in yeasts or bacteria.
- More than 1500 genes encode different receptor proteins in human.
- Flies, worms and mammals all use essentially similar machinery for cell communication.

CELL SIGNALLING IN EUKARYOTES

- In plants, as in animals, cells are in constant communication with one another.
- Plant cells communicate to coordinate their activities in response to the changing conditions of light, dark, temperature, which guide the plants growth, flowering and fruiting.
- Plants use different signaling molecules and receptors than animals

Communication of cells

❖ Two main kinds of communication

1. Intercellular signalling (Signaling between the cells)

   (a) Paracrine signaling

2. Intracellular signalling (Signalling inside the cell)

   (b) Autocrine signaling
   (c) Endocrine signaling
   (d) Direct cell-cell contact signaling

Classification if Signaling Pathway

There are four basic categories of chemical signaling found multicellular organisms:

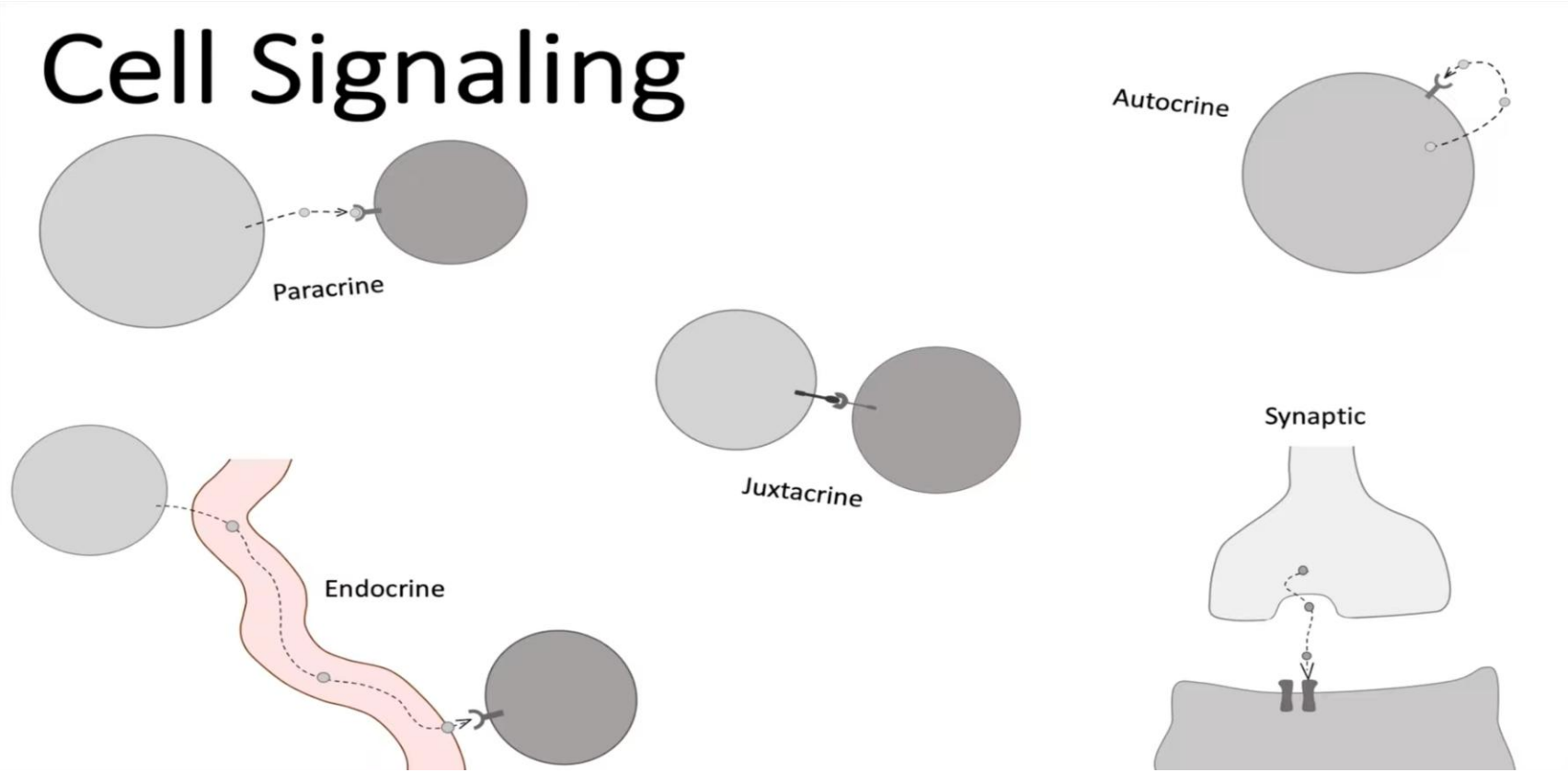
(a) Paracrine: Signals act on nearby cells (e.g., growth factors).

(b) Autocrine: Signals affect the cell that releases them.

(c) Endocrine: Hormones act over long distances via the bloodstream.

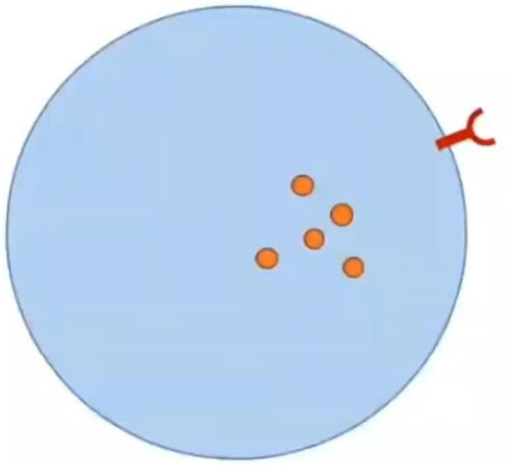
(d) Juxtacrine: Direct cell-to-cell contact, important in immune responses.

Different cell signalling mechanisms



Autocrine Signalling

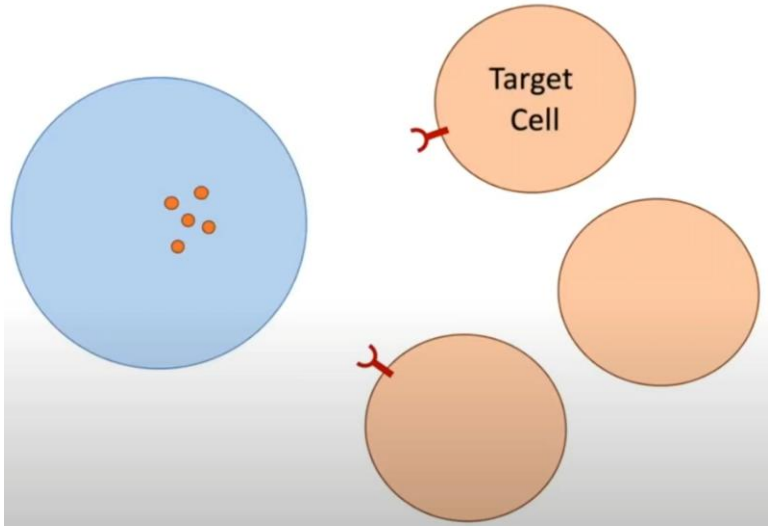
- Cells respond to signaling molecules that they themselves produce (response of the immune system to foreign antigens, and cancer cells).
- Cells respond to signals they release themselves, common in immune response.



Paracrine Signalling

- Signals are released to act on nearby cells, often used in tissue repair.

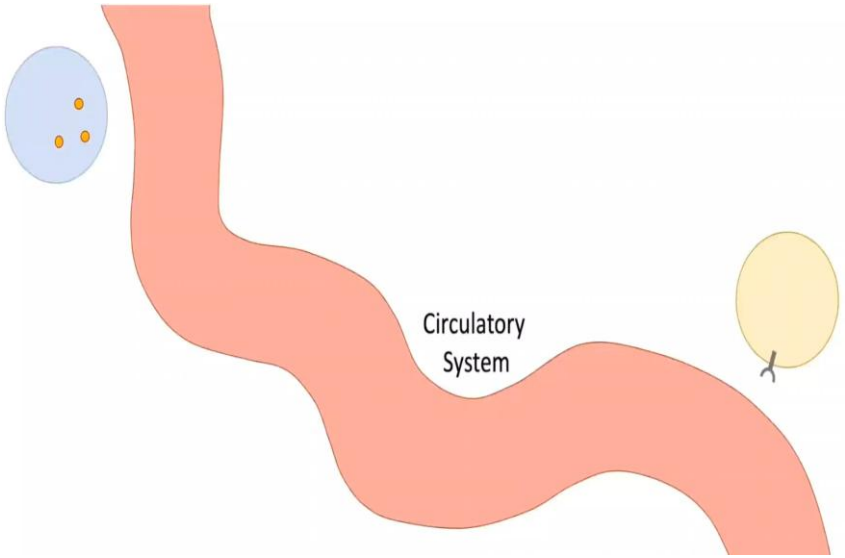
- The signaling molecules released by one cell act on neighboring target cells (neurotransmitters).



Endocrine Signalling

- Hormones travel through the bloodstream to act on distant cells.

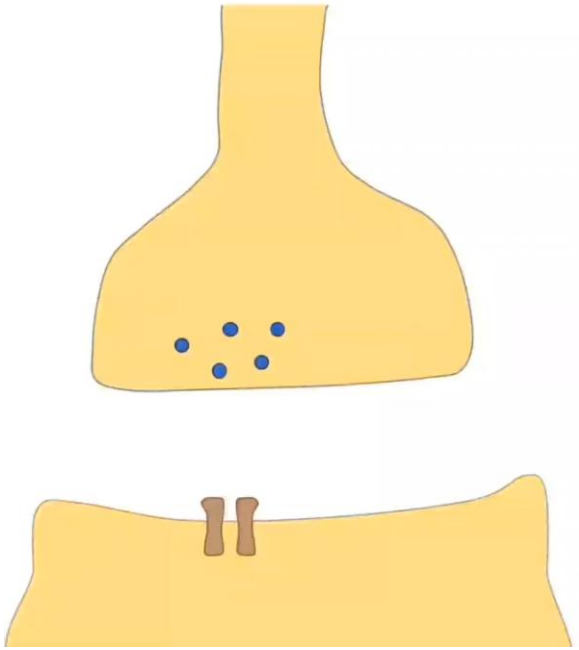
- The signaling molecules are hormones secreted by endocrine cells and carried through the circulation system to act on target cells at distant body sites.



Synaptic Signalling

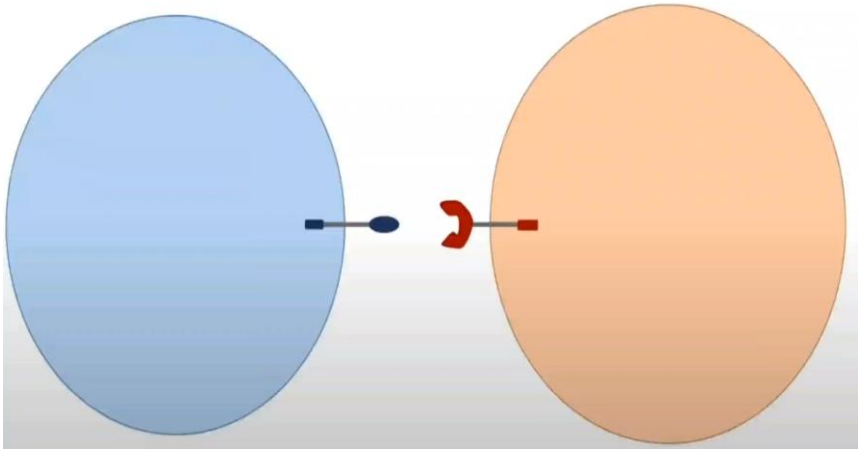
- The process by which neurons communicate with each other at specialized junctions called synapses.

- Neurons release neurotransmitters across synapses to communicate.



Juxtacrine Signaling

- A type of cell communication that occurs when cells are in direct contact with each other and signaling molecules act locally on adjacent target cells.



- Also known as direct-contact signaling.

Key Components of Cell Signalling

- **Host Cells** : The cells producing Ligands
- **Signaling Molecules (Ligands):** Chemical messengers like hormones and proteins.
- **Receptors:** Protein molecules that bind ligands, either on the cell surface or within the cell.
- **Intracellular messengers:** Secondary messengers - Intermediate compounds carriers the cell to the intracellular sensors.

Key Components of Cell Signalling

- **Target cell:** Cell that receives a chemical signal from a signaling cell and responds by binding to a specific receptor protein.
- **Signal Transduction Pathways**: Relay signals inside the cell, often amplifying response.
- **Cellular Responses:** Changes in gene expression, metabolism, or cell behaviour.

Types of Signaling molecules

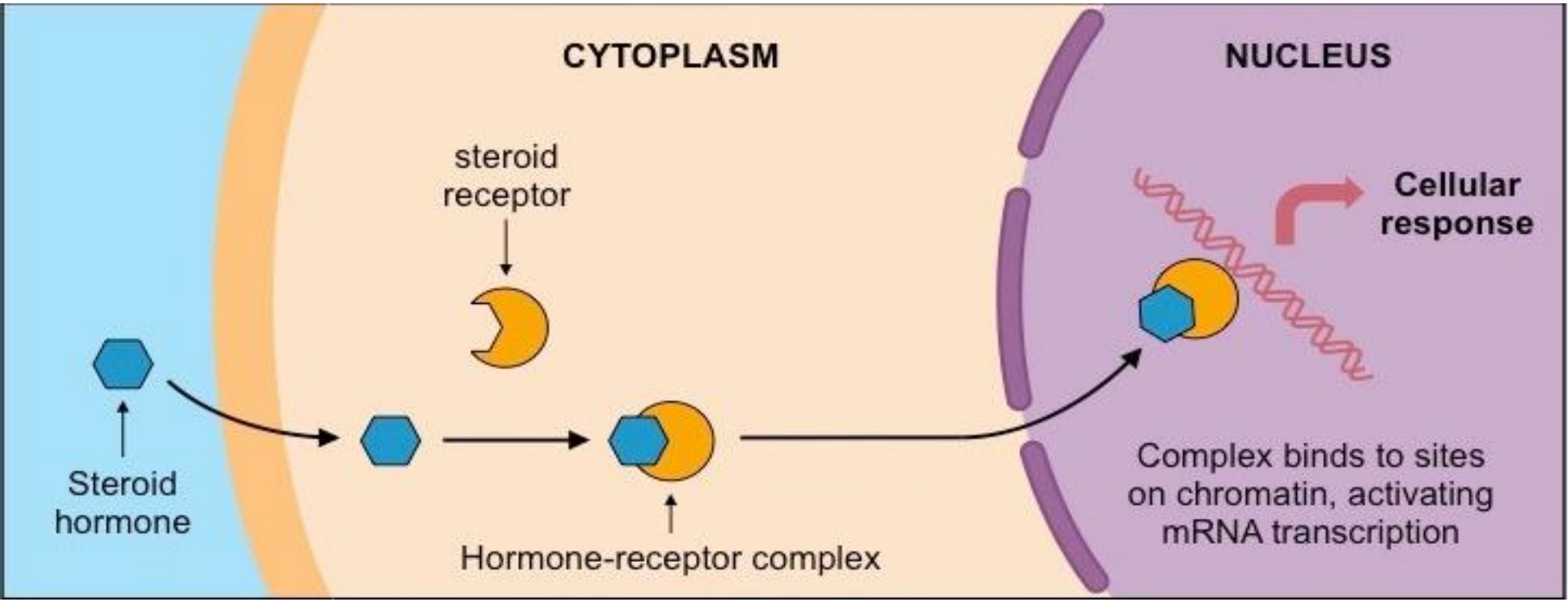
1) Hormone

2) Neurotransmitter

3) Cytokines

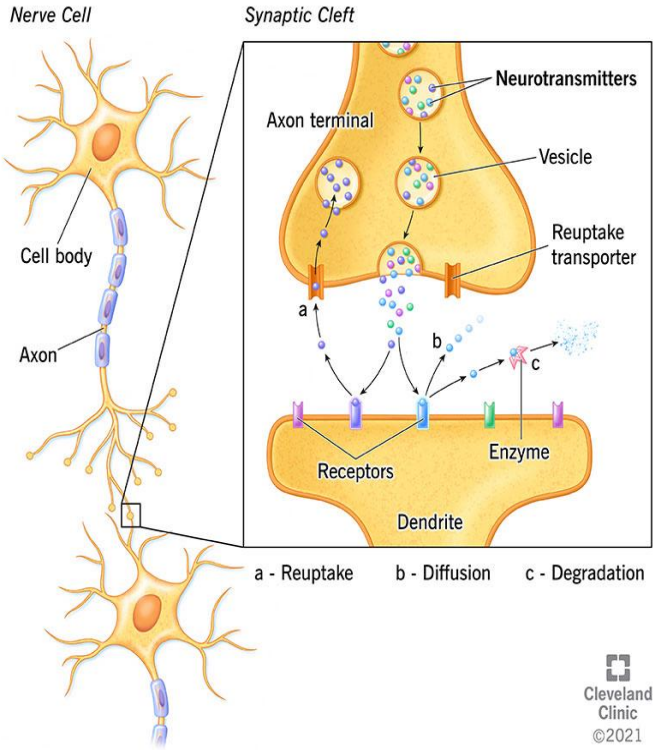
Hormones

- A class of signaling molecules produced by glands in multicellular organisms.
- Transported by the circulatory system to target distant organs to regulate physiology and behaviour.



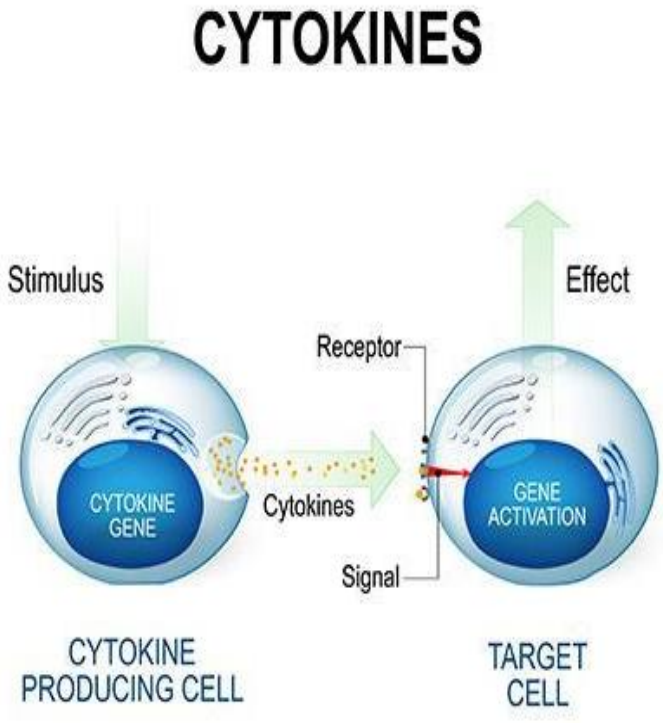
Neurotransmitters

- Endogenous chemicals that transmit signals across a synapse from one neuron to another “target” neuron.
- Released from synaptic vesicles from synapses into the synaptic ceft, where recived by receptors on other synapses.



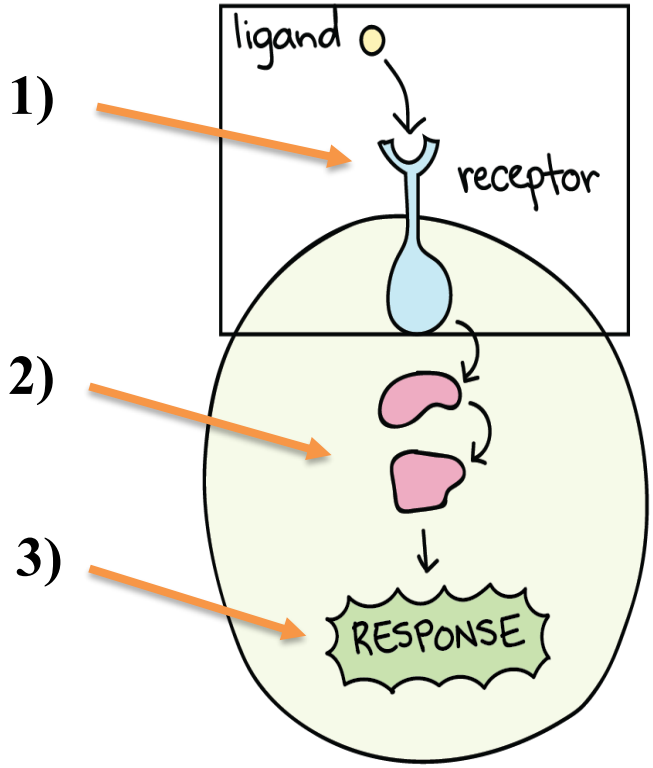
Cytokines

- They are signalling molecule of immune system.
- Cytokines represent a diverse group of molecules that transmit intercellular signals.
- These signals may either be autocrine (where the same cell both produces the cytokine and responds to it) or paracrine (where the cytokine is made by one cell and acts on another).



How Cell Signalling occurs

1. Ligand binds to the specific receptor.
2. The receptor undergoes changes in its size and activity.
3. Finally, the approprite response is generated.



The three stages of cell signaling

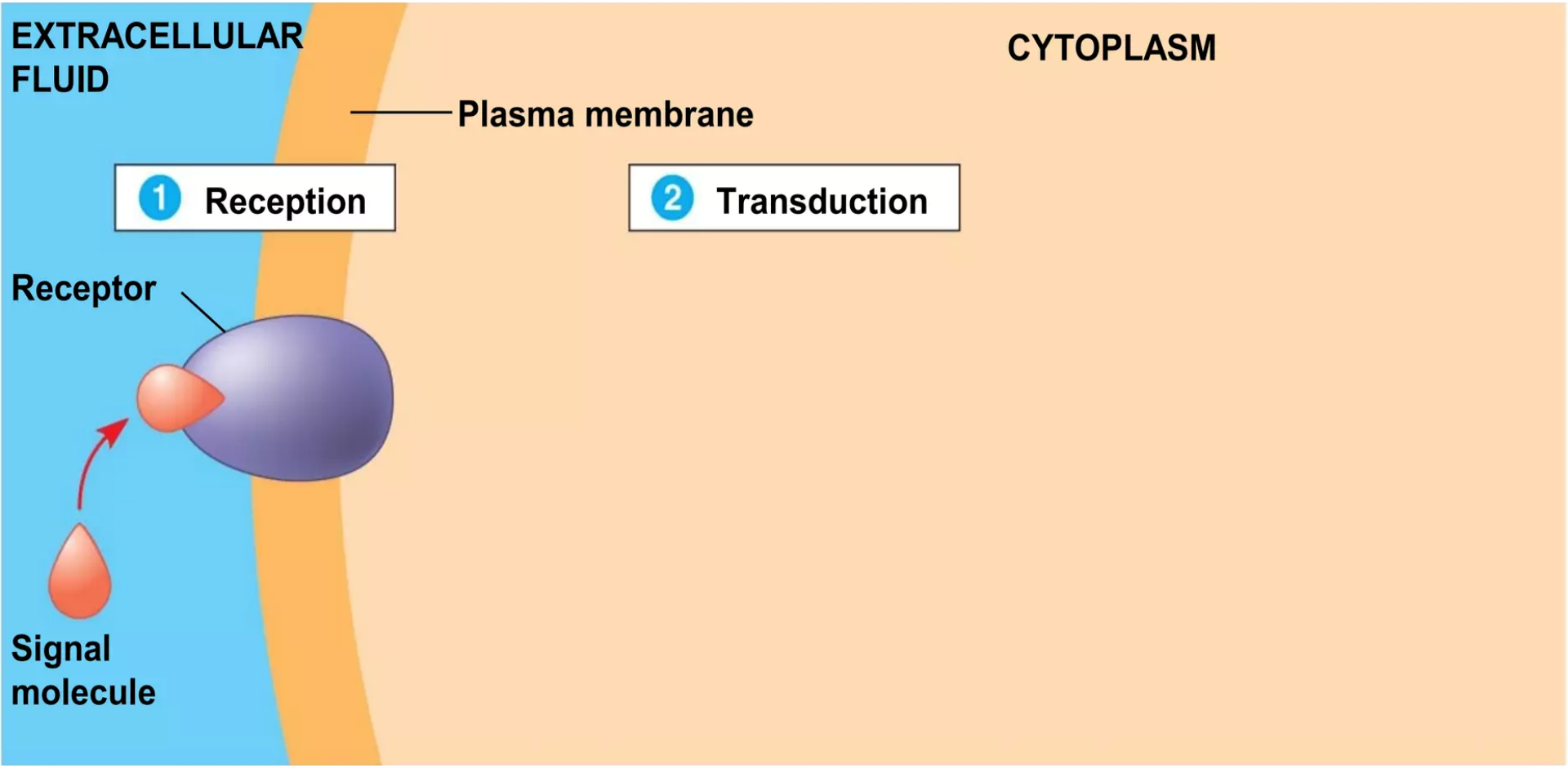
- Earl W.Sutherland dicovered how the hormones epinephrine acts on cells.
- Sutherland suggested that cells receving signals went through three processes.

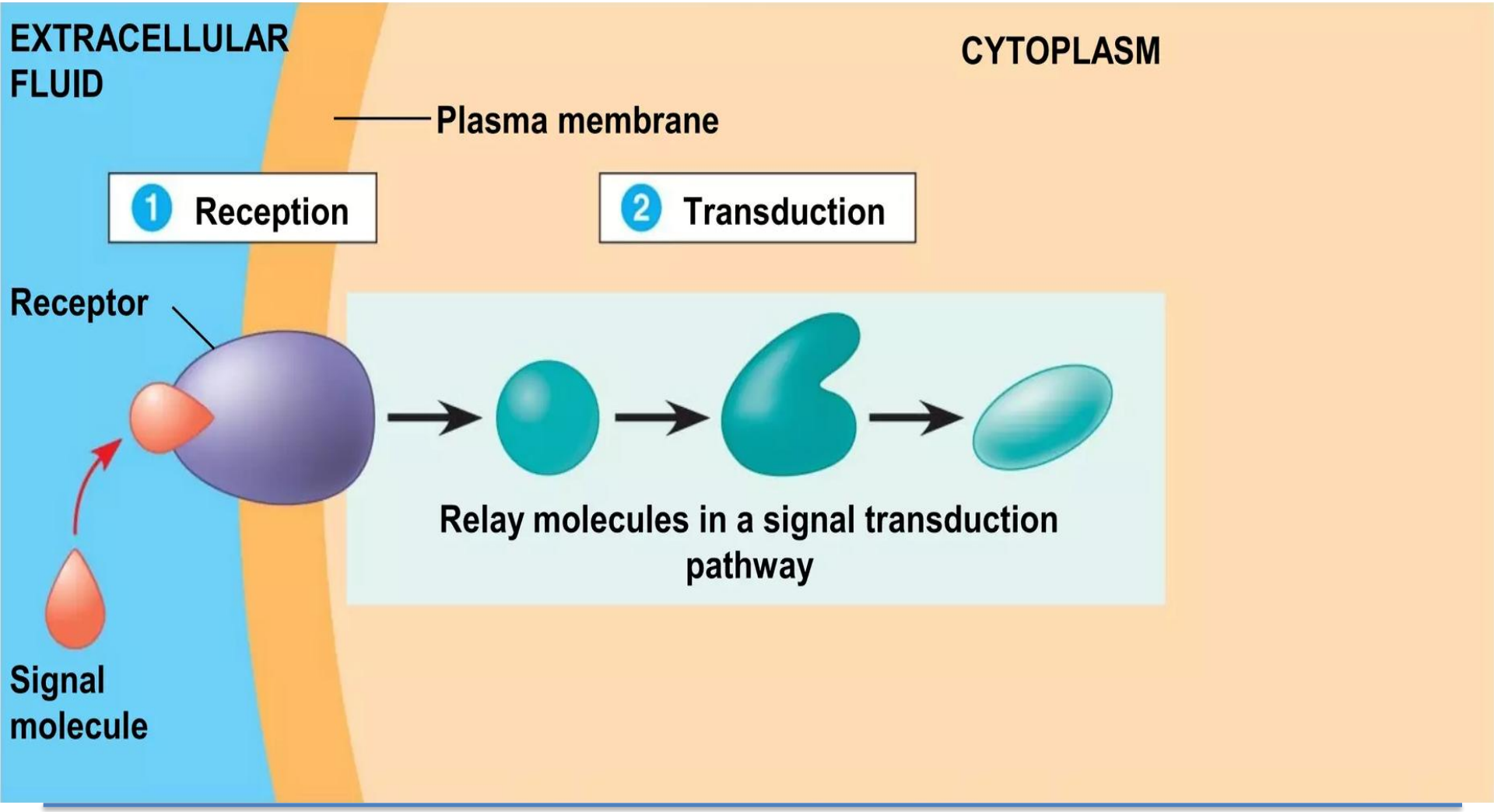
1)Reception

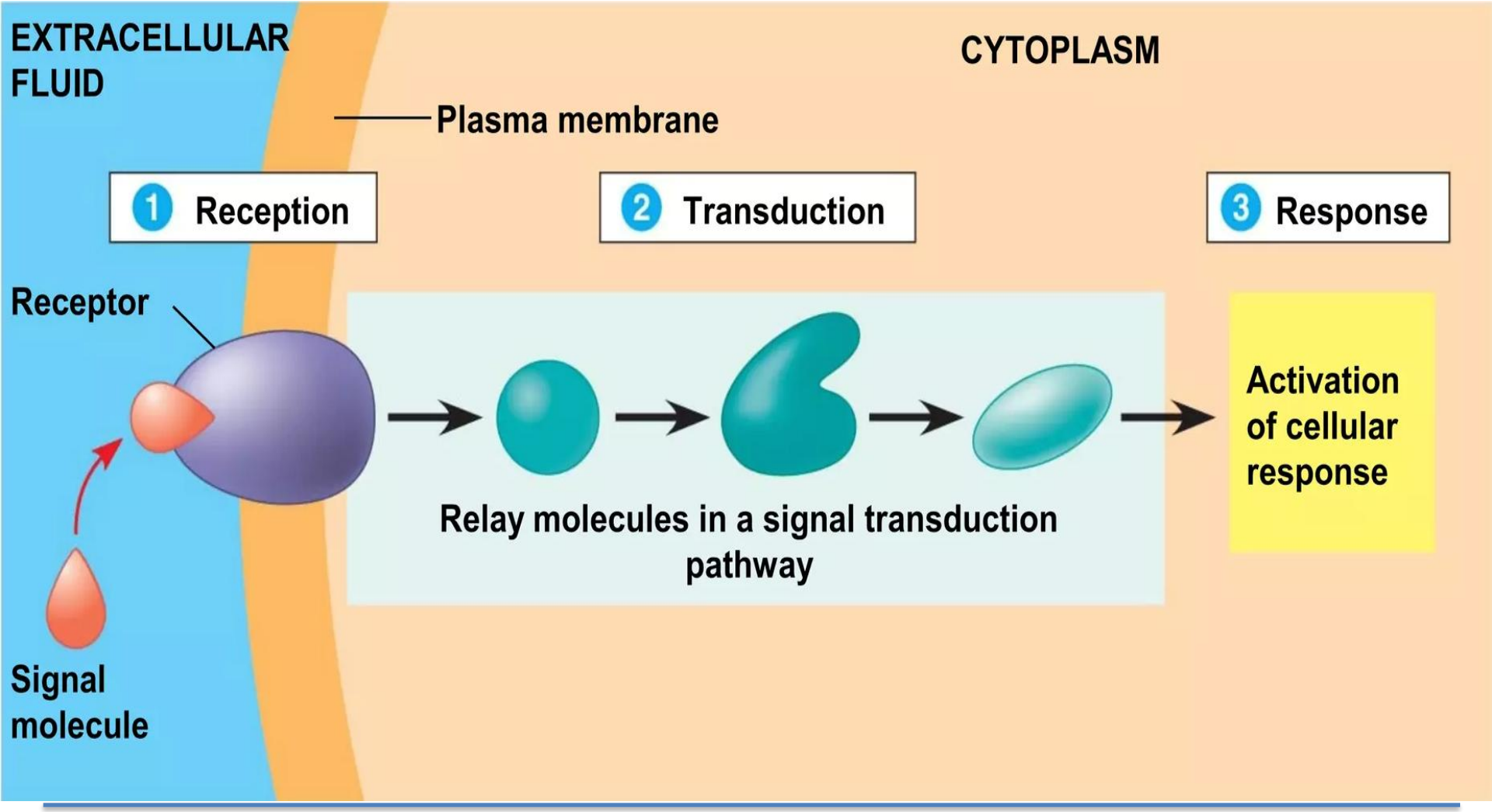
2)Transduction

3)Response

Usually, two molecules are involved: 1) Ligand 2) Receptor




EXTRACELLULAR FLUID
CYTOPLASM
Plasma membrane
1 Reception
2 Transduction
Receptor
Relay molecules in a signal transduction pathway
Signal molecule


EXTRACELLULAR FLUID
CYTOPLASM
Plasma membrane
1 Reception
2 Transduction
3 Response
Receptor
Activation of cellular response
Relay molecules in a signal transduction pathway
Signal molecule

Reception

- A signal molecule binds to a receptor protein, causing it to change shape.
- The binding between a signal molecule (ligand) and receptor is highly specific.
- A conformational change in a receptor is often the initial transduction of the signal.
- Most signal receptors are plasma membrane proteins.

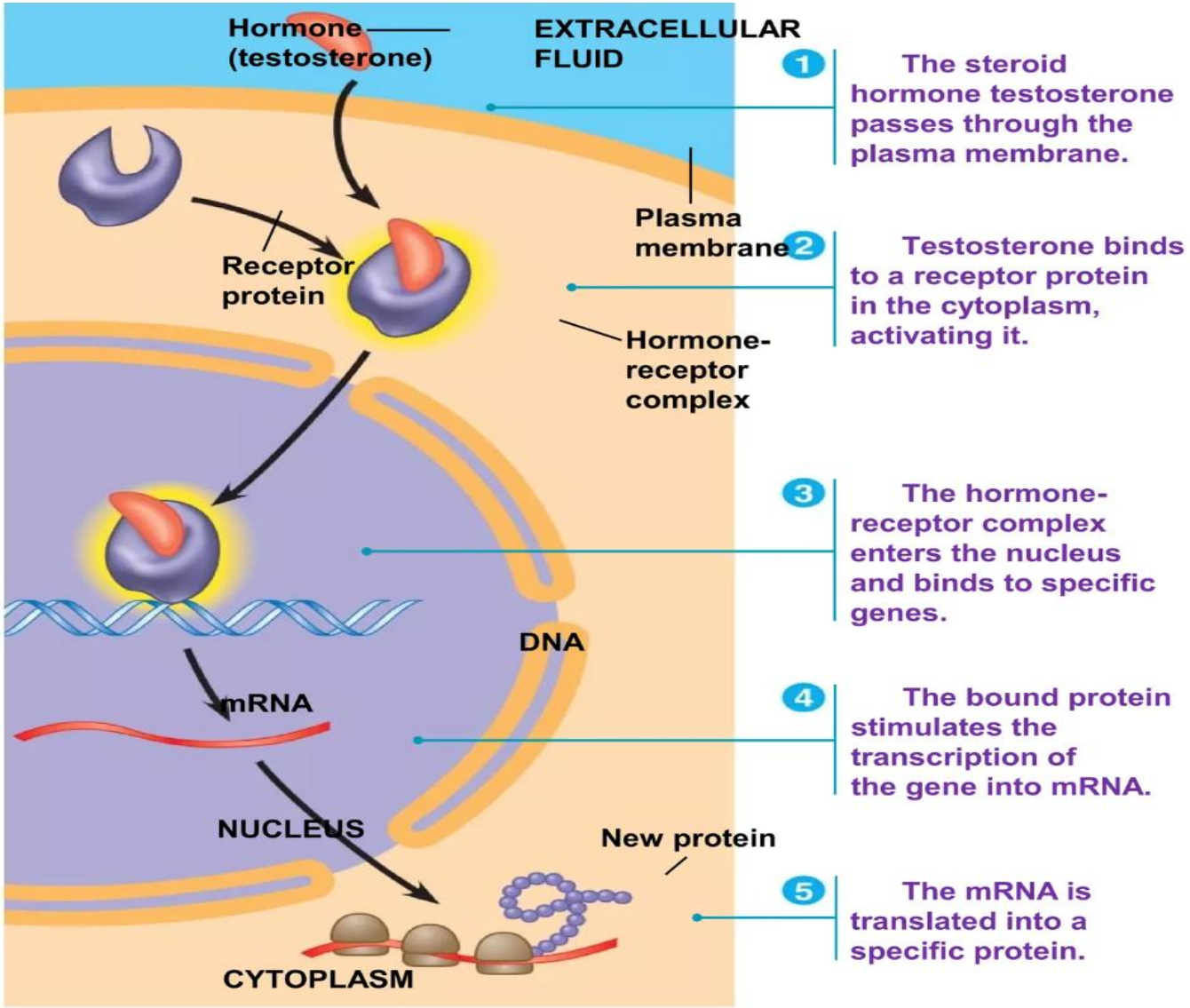
Intracellular receptors

• Some receptor proteins are intracellular, found in the cytosol or nucleus of target cells.

• Small or hydrophobic chemical messengers can readily cross the membrane and activate receptors.

• Examples of hydrophobic messengers are the steroid and thyroid hormones of animals.

• An activated hormone-receptor complex can act as a transcription factor, turning on specific genes.


Hormone (testosterone)
EXTRACELLULAR FLUID
1 The steroid hormone testosterone passes through the plasma membrane.
Plasma membrane
Receptor protein
2 Testosterone binds to a receptor protein in the cytoplasm, activating it.
Hormone-receptor complex
3 The hormone-receptor complex enters the nucleus and binds to specific genes.
DNA
mRNA
4 The bound protein stimulates the transcription of the gene into mRNA.
NUCLEUS
New protein
5 The mRNA is translated into a specific protein.
CYTOPLASM

Receptors in the Plasma membrane

- Most water-soluble signal molecules bind to specific sites on receptor proteins in the plasma membrane.

- There are three main types of membrane receptors:

1)G-protein-linked receptors

2)Receptor tyrosine kinases

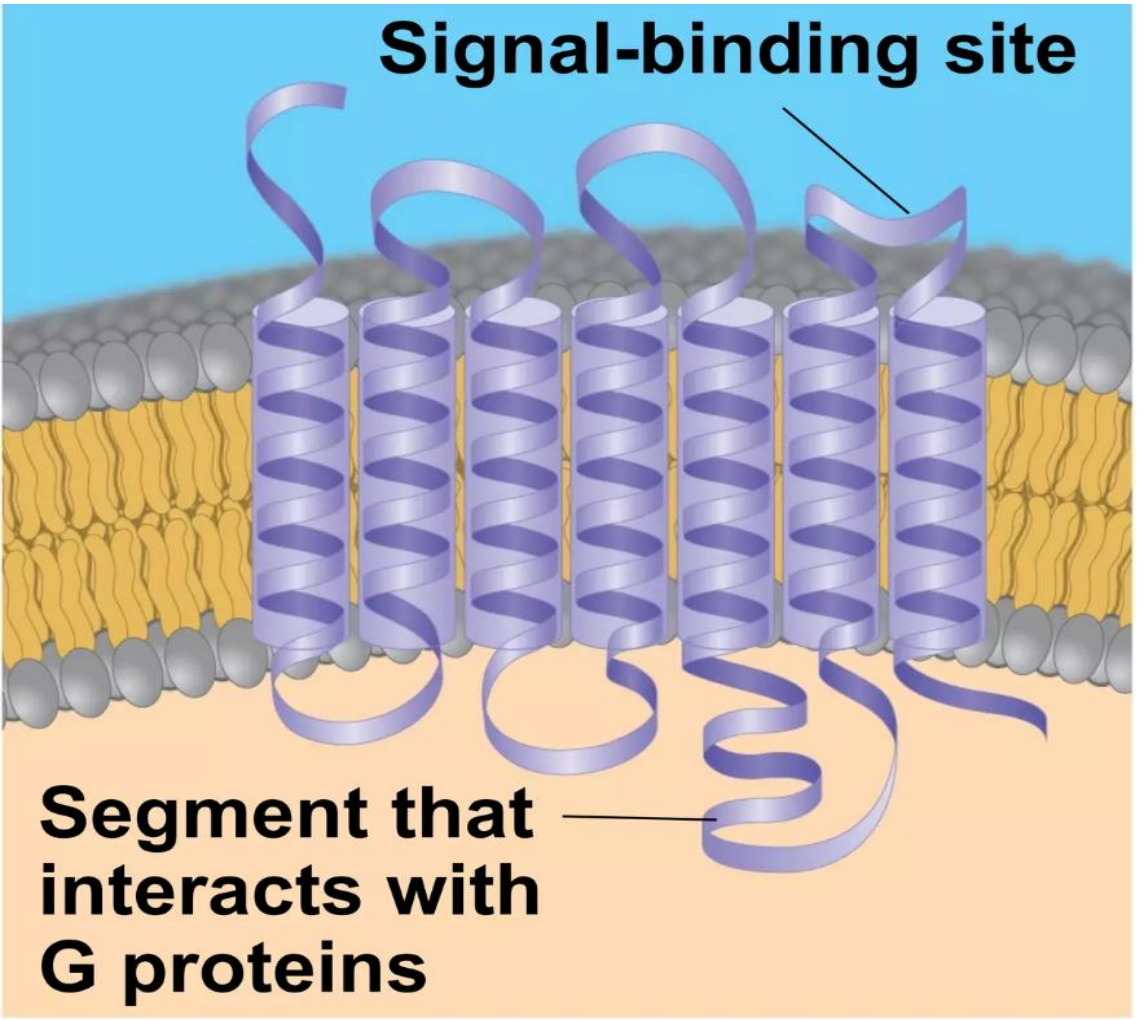
3)Ion channel receptors

G-protein-linked receptors

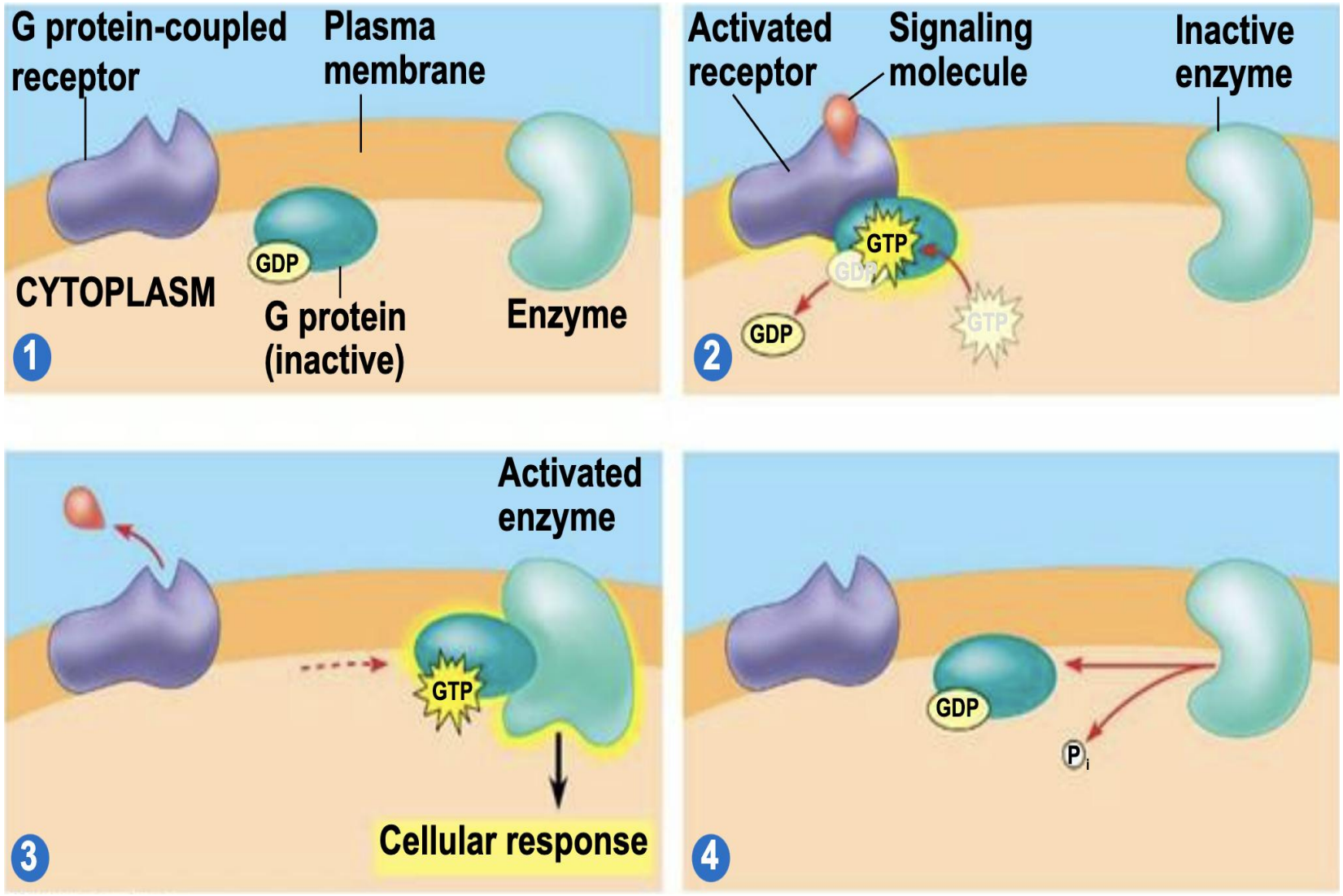
What are G-protein-linked receptors?

- A G-protein-linked receptor is a plasma membrane receptor that works with the help of a G protein.
- The G-protein acts as an on/off switch: If GDP is bound to the G protein, the G protein is inactive

G-protien linked receptor



G-protien Function: “On” and “Off”

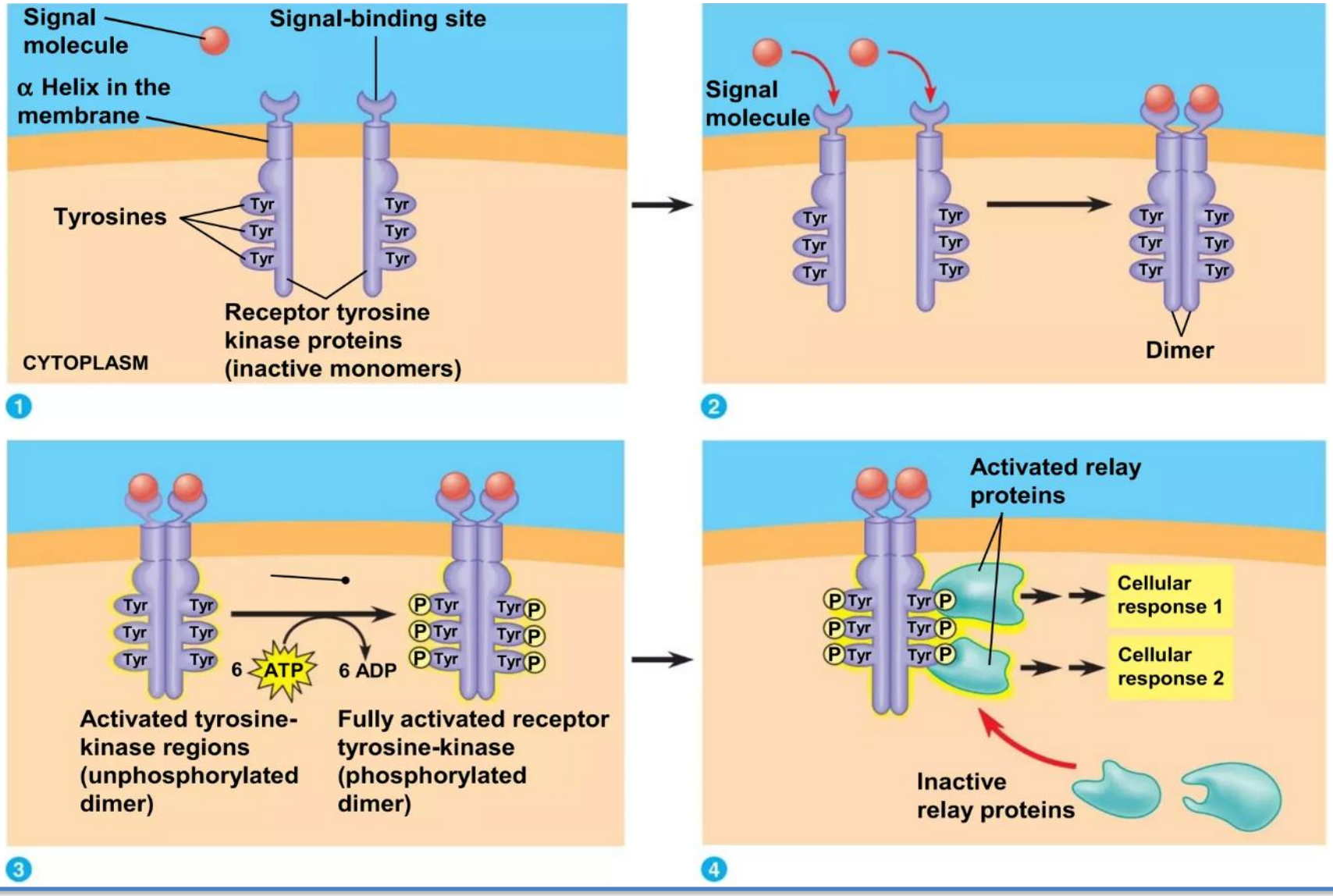


Receptor tyrosine kinases

What is receptor tyrosine kinases?

- Receptor tyrosine kinases are membrane receptors that attach phosphates to tyrosine.
- A receptor tyrosine kinase can trigger multiple signal transduction pathways at once.

Receptor tyrosine kinases

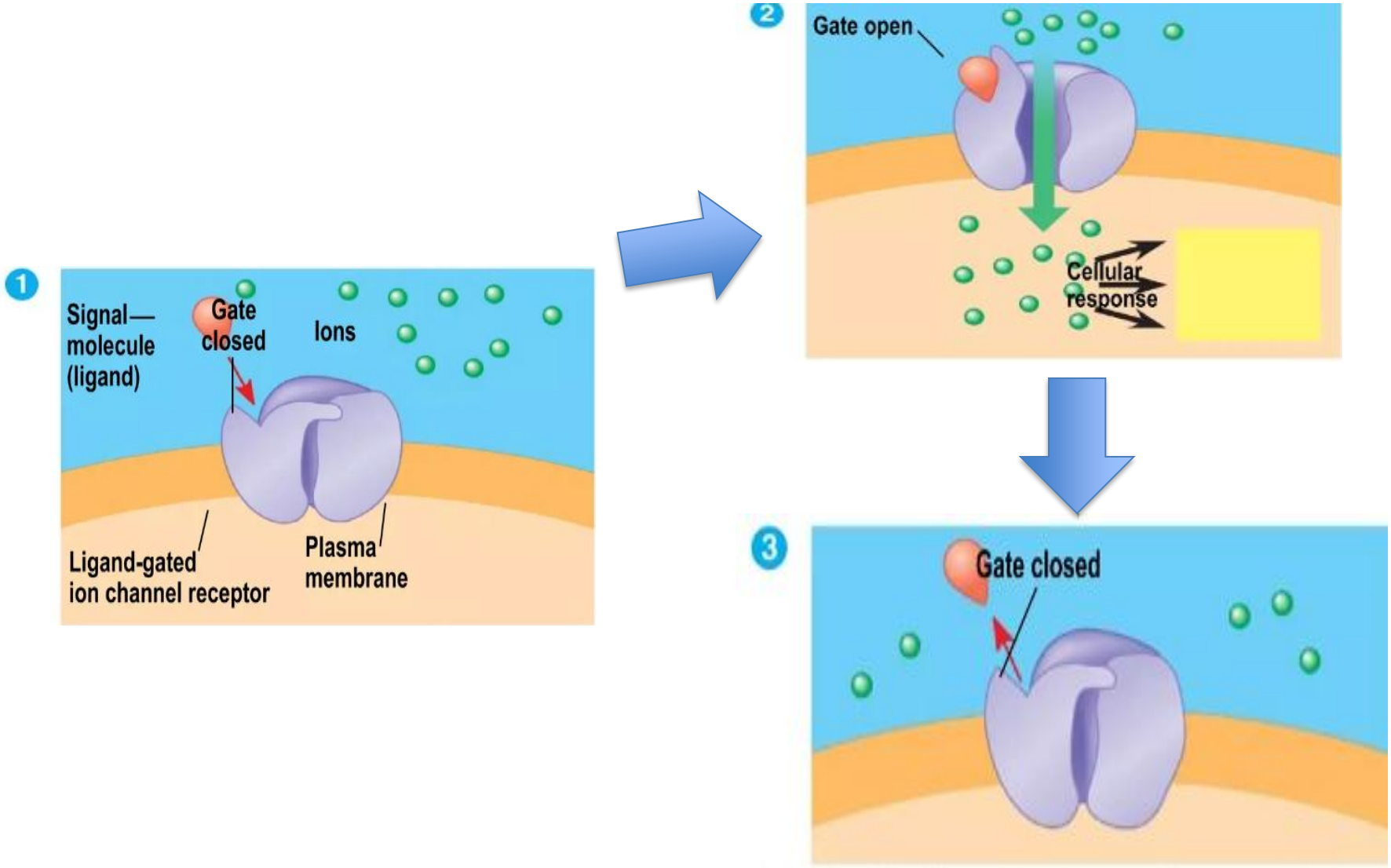


Ion channel receptors

What is Ion channel receptors?

- An ion channel receptor acts as a gate when the receptor changes shape.
- When a signal molecule binds as a ligand to the receptor, the gate allows specific ions, such as Na^+ or Ca^{2+} , through a channel in the receptor.

Ion channel receptors



Transduction

Transduction: Cascadas of molecular interaction relay signals from receptors to target molecules in the cell.

Transduction usually involves multiple steps.

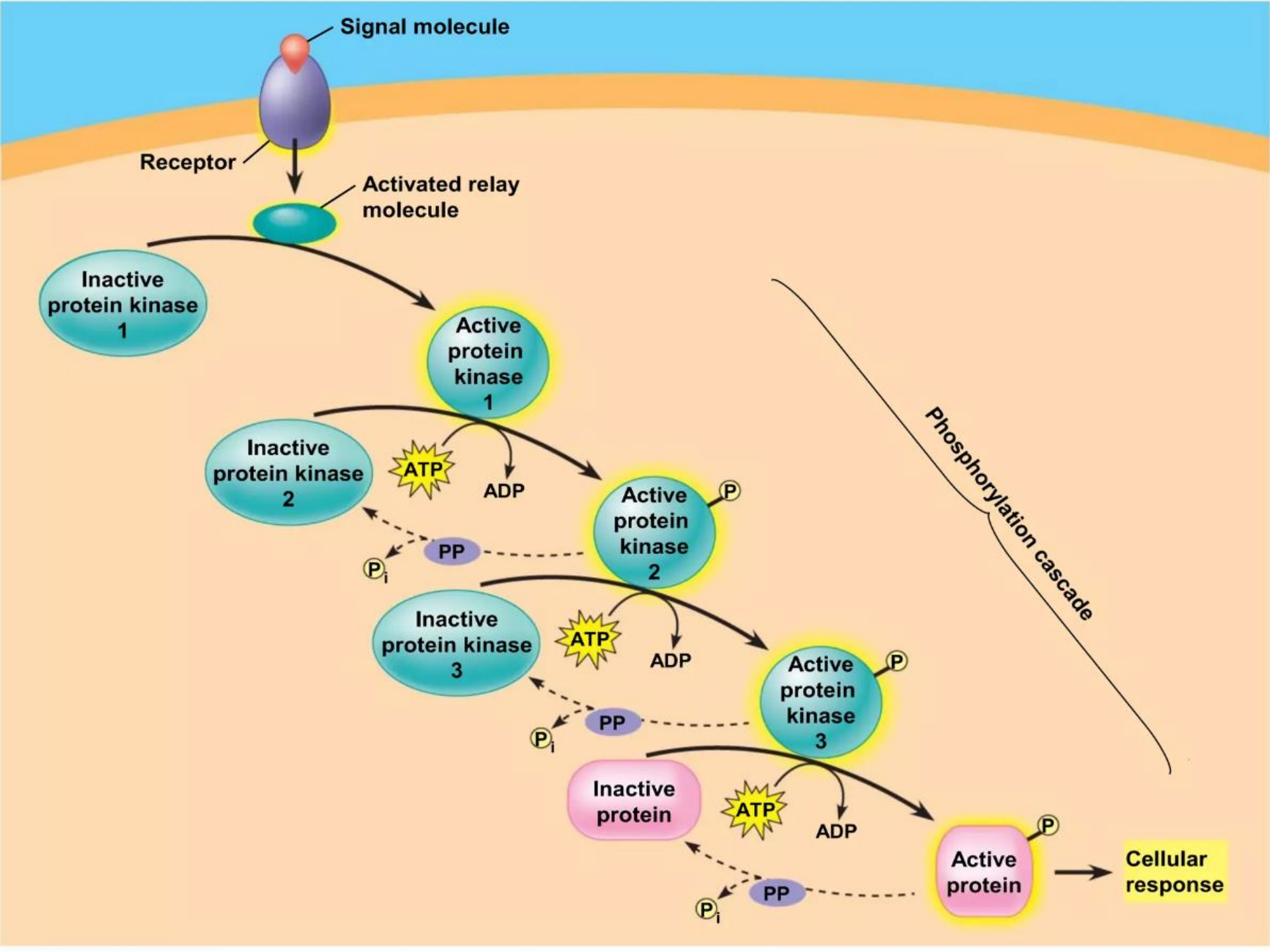
- **Multistep pathways can amplify a signal:** A few molecules can produce a large cellular response.
- Multistep pathways provide more opportunities for coordination and regulation.

Signal Transduction Pathway

- The molecules that relay a signal from receptor to response are mostly proteins.
- Like falling dominoes, the receptor activates another protein, which activates another, and so on, until the protein producing the response is activated.
- At each step, the signal is transduced into a different form, usually a conformational change.

Protien Phosphorylation and Dephosphorylation

- In many pathways, the signal is transmitted by a cascade of protein phosphorylations.
- Phosphatase enzymes remove the phosphates.
- This phosphorylation and dephosphorylation system acts as a molecular switch, turning activities on and off.


Signal molecule
Receptor
Activated relay molecule
Inactive protein kinase 1
Active protein kinase 1
Inactive protein kinase 2
ATP
ADP
Active protein kinase 2
P
PP
Pi
Inactive protein kinase 3
ATP
ADP
Active protein kinase 3
P
PP
Pi
Inactive protein
ATP
ADP
Active protein
P
PP
Pi
Cellular response
Phosphorylation cascade

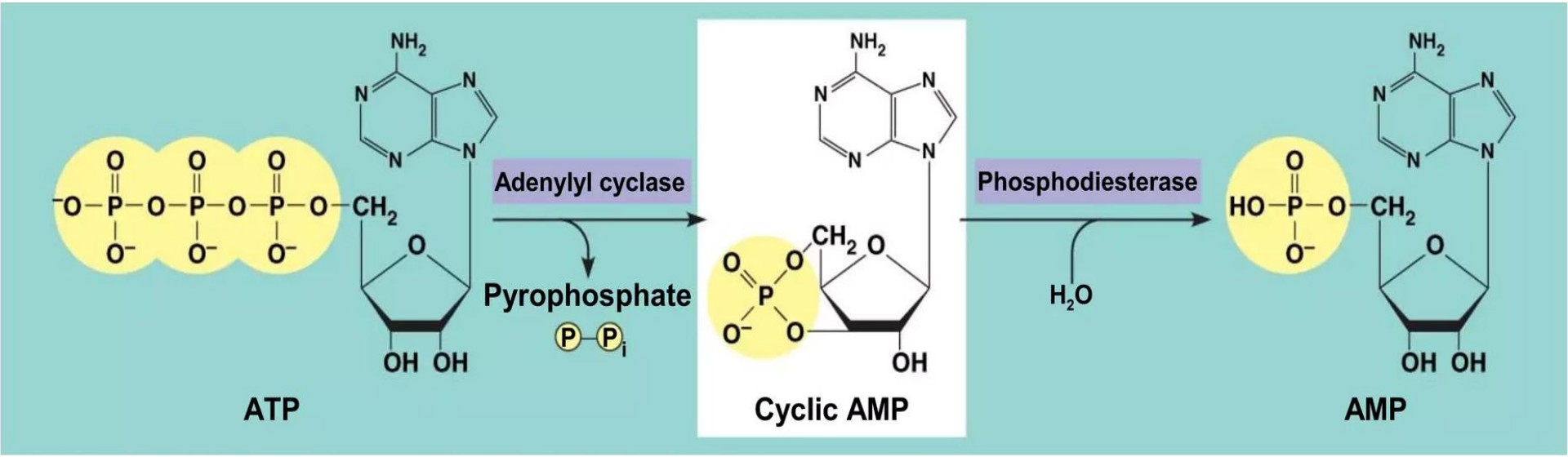
Small Molecules and Ions Exchange

- Second messengers are small, nonprotein, water-soluble molecules or ions.
- The extracellular signal molecule that binds to the membrane is a pathway's "first messenger".
- Second messengers can readily spread throughout cells by diffusion.
- Second messengers participate in pathways initiated by G-protein-linked receptors and receptor tyrosine kinases.

Cyclic AMP

- Cyclic AMP (cAMP) is one of the most widely used second messengers.
- Adenylyl cyclase, an enzyme in the plasma membrane, converts ATP to cAMP in response to an extracellular signal.

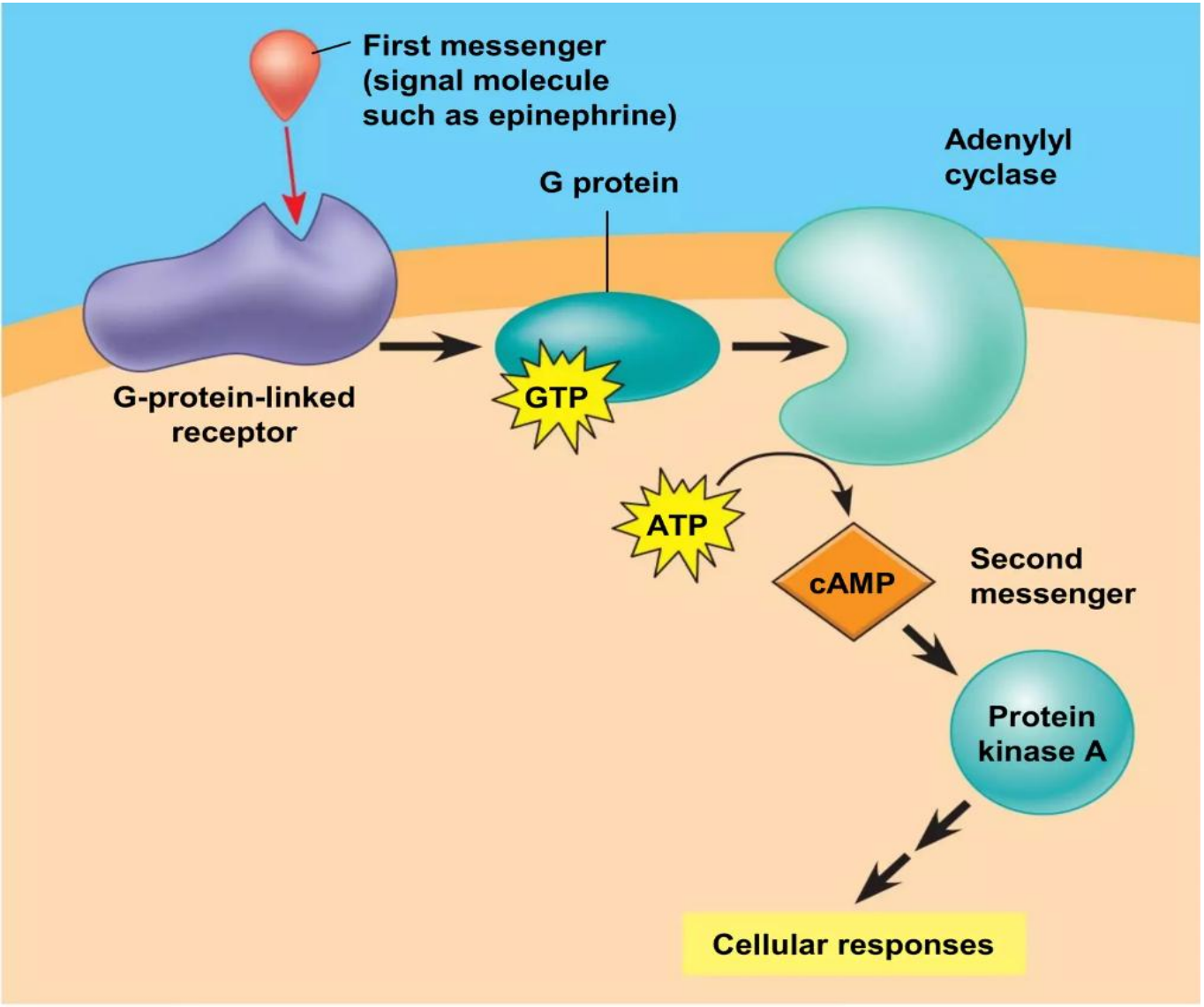
Cyclic AMP


Adenylyl cyclase
Pyrophosphate
Phosphodiesterase
H_2O
ATP
Cyclic AMP
AMP

G-protein-linked receptors

- Many signal molecules trigger formation of cAMP.
- Other components of cAMP pathways are G proteins, G-protein-linked receptors, and protein kinases.
- cAMP usually activates protein kinase A, which phosphorylates various other proteins.
- Further regulation of cell metabolism is provided by G-protein systems that inhibit adenylyl cyclase.

G-protein-linked receptors

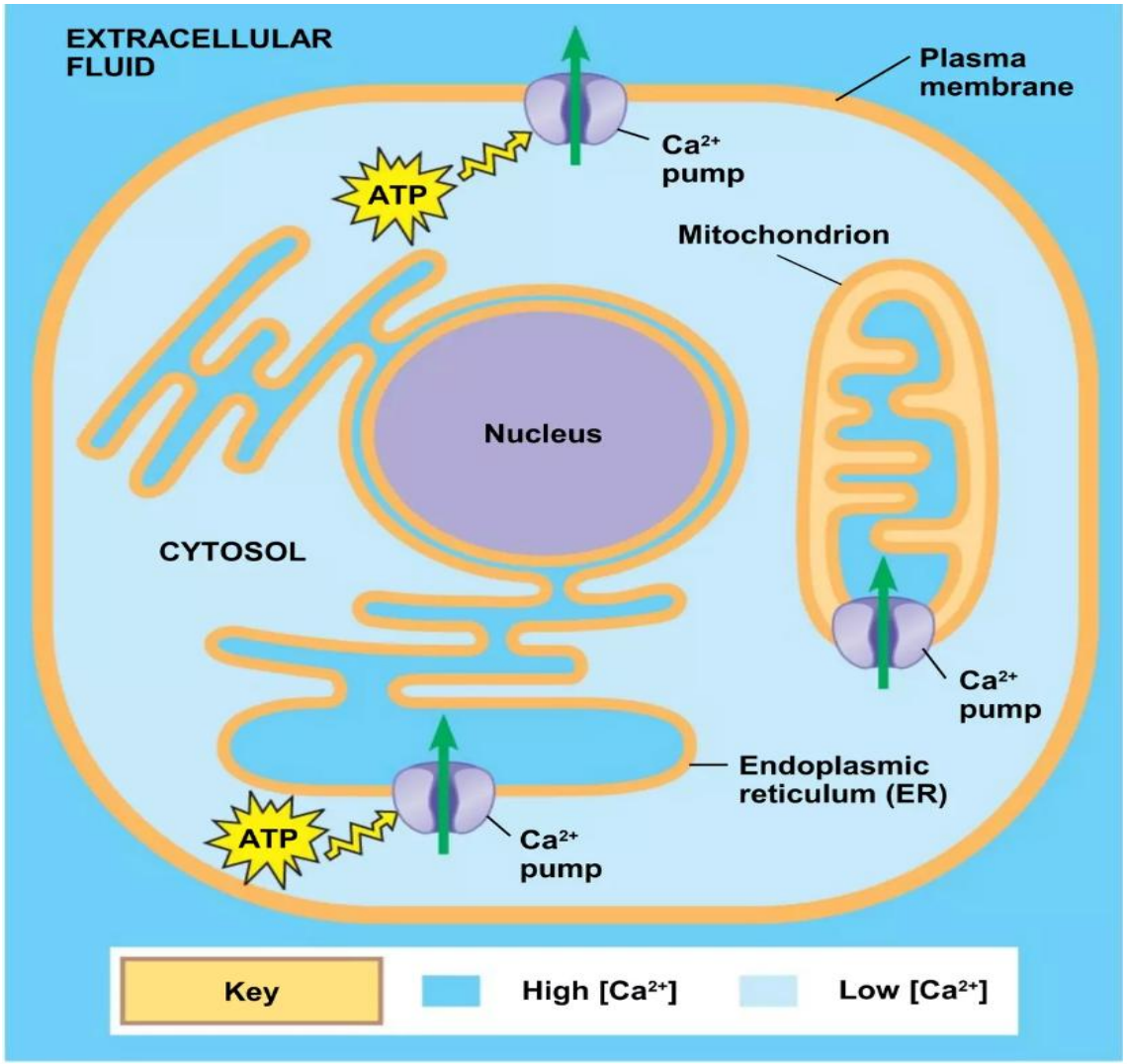


Calcium ions

- Calcium ions (Ca^{2+}) act as a second messenger in many pathways.

- Ca^{2+} ions help transmit signals within cells by acting as a second messenger, often in response to extracellular signals like hormones or neurotransmitters, and triggering various cellular responses, such as muscle contraction, secretion, and cell division.

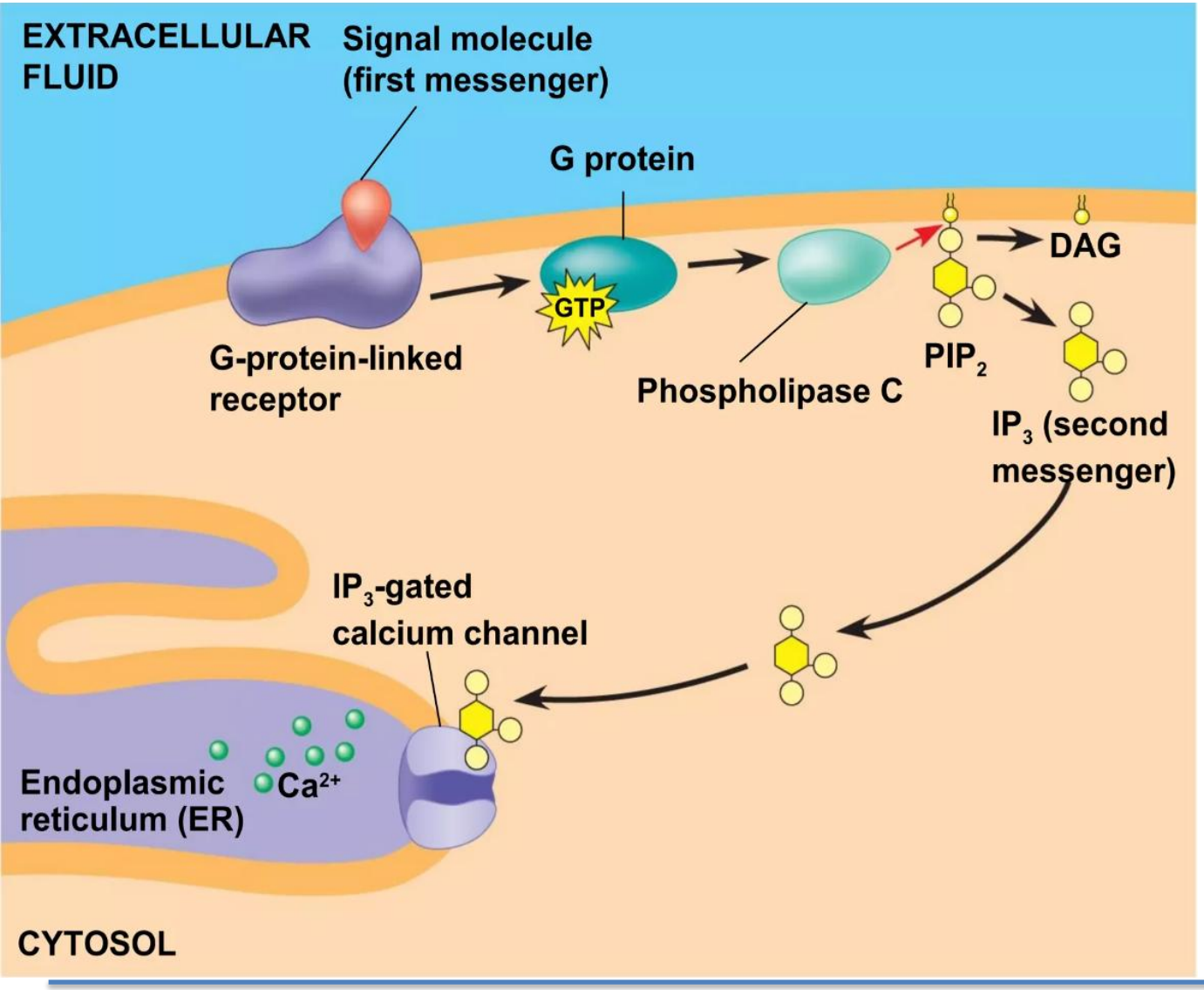
Calcium ions



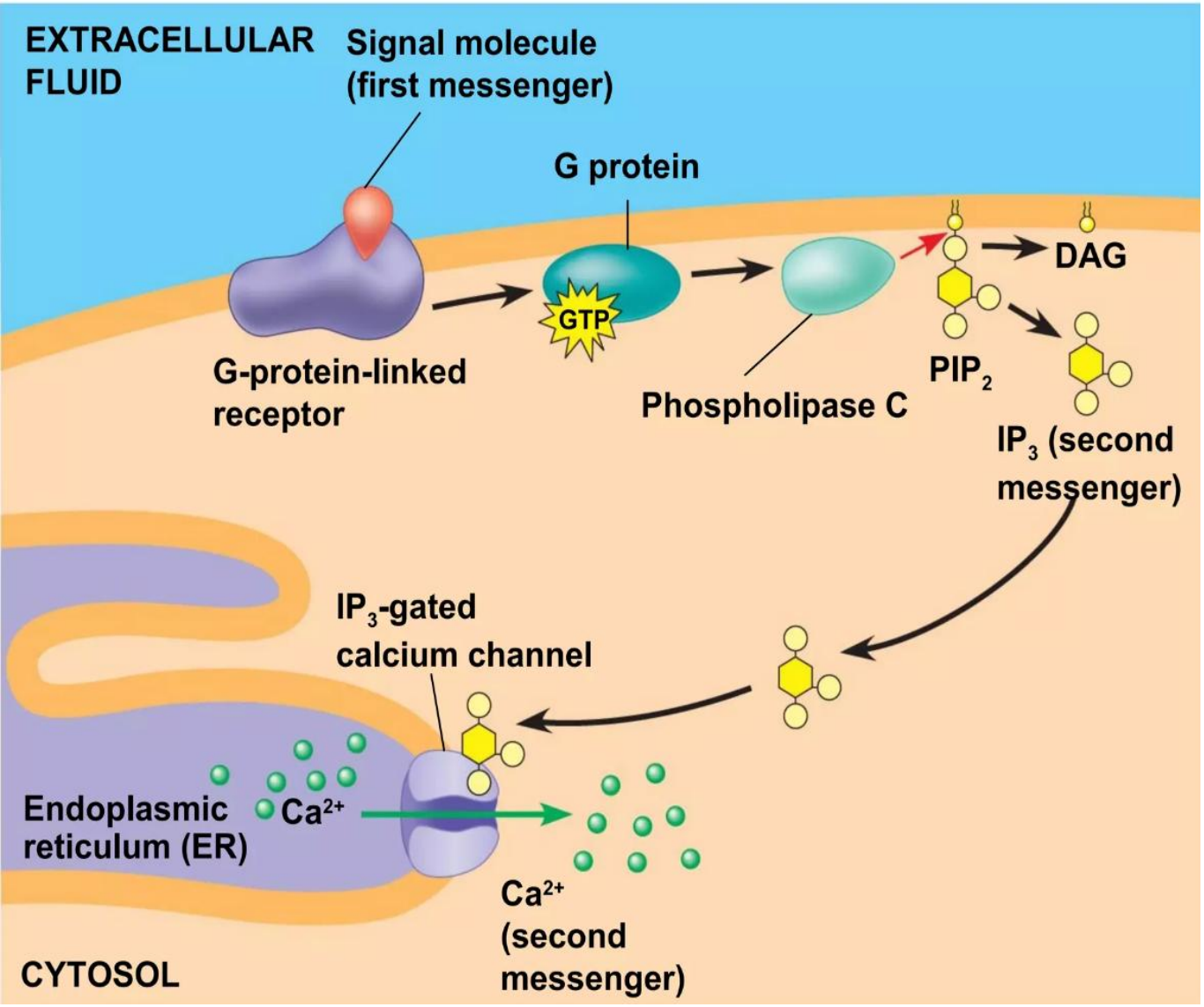
Inositol Triphoshate (IP_3)

- A signal relayed by a signal transduction pathway may trigger an increase in calcium in the cytosol.
- Pathways leading to the release of calcium involve inositol triphosphate (IP3) and diacylglycerol (DAG) as second messengers

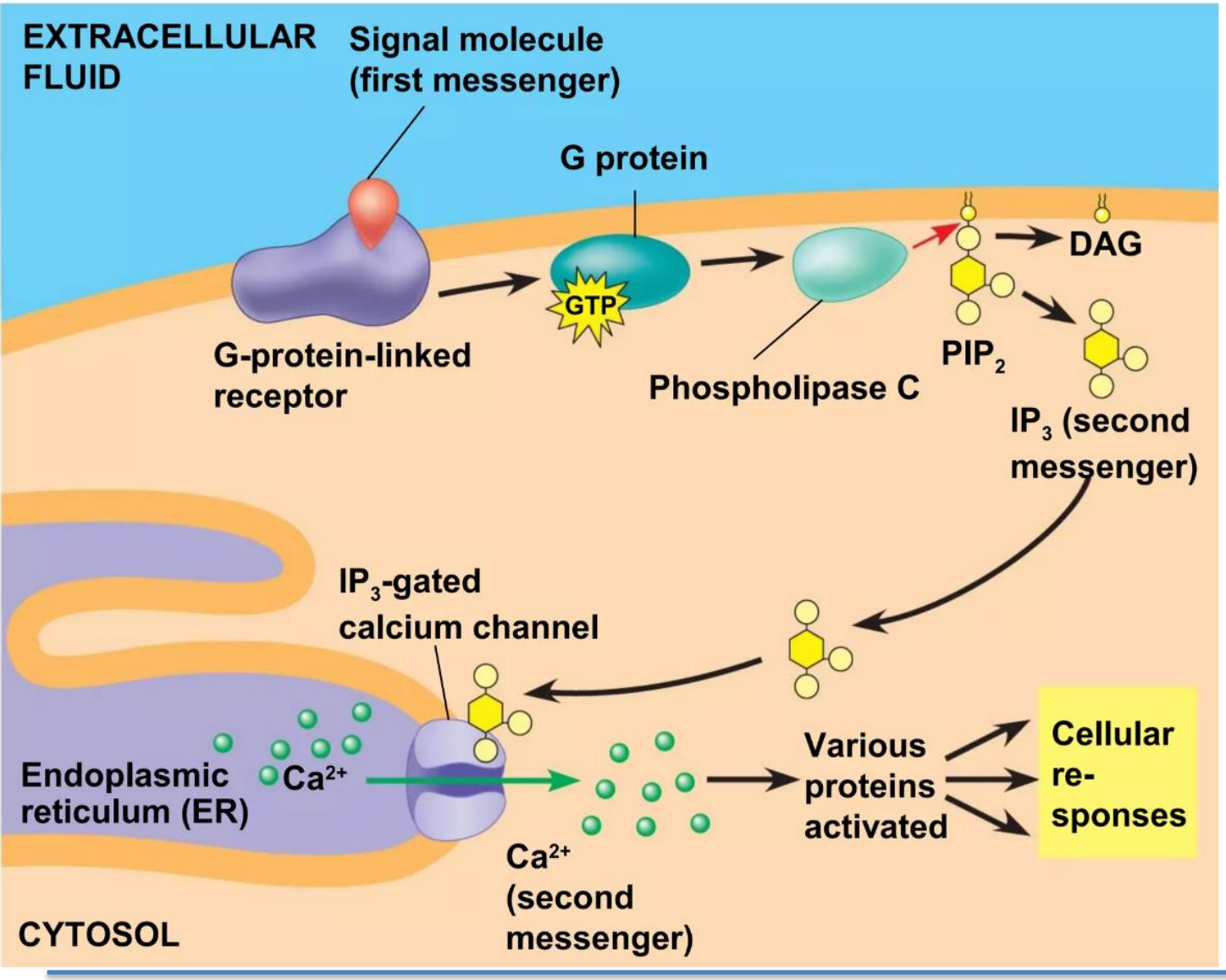
Inositol Triphoshate (IP_3)



Inositol Triphoshate (IP_3)



Inositol Triphoshate (IP_3)



Response

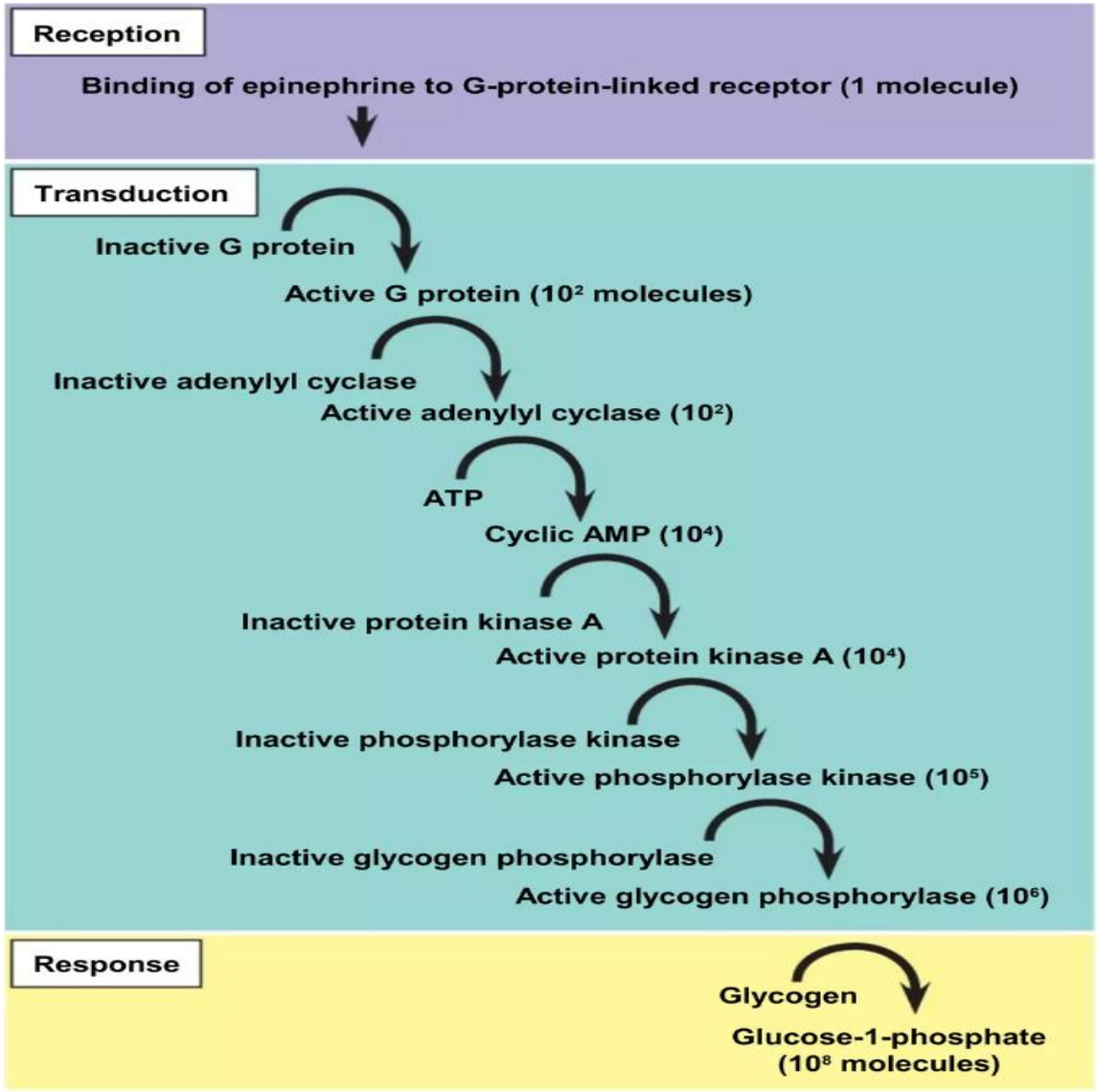
Response: Cells signaling leads to regulation of cytoplasmic activities or transcription.

- The cells response to an extracellular signal is sometimes called the “output response”

Cytoplasmic and Nuclear Response

- Ultimately, a signal transduction pathway leads to regulation of one or more cellular activities.
- The response may occur in the cytoplasm or may involve action in the nucleus.
- Many pathways regulate the activity of enzymes.

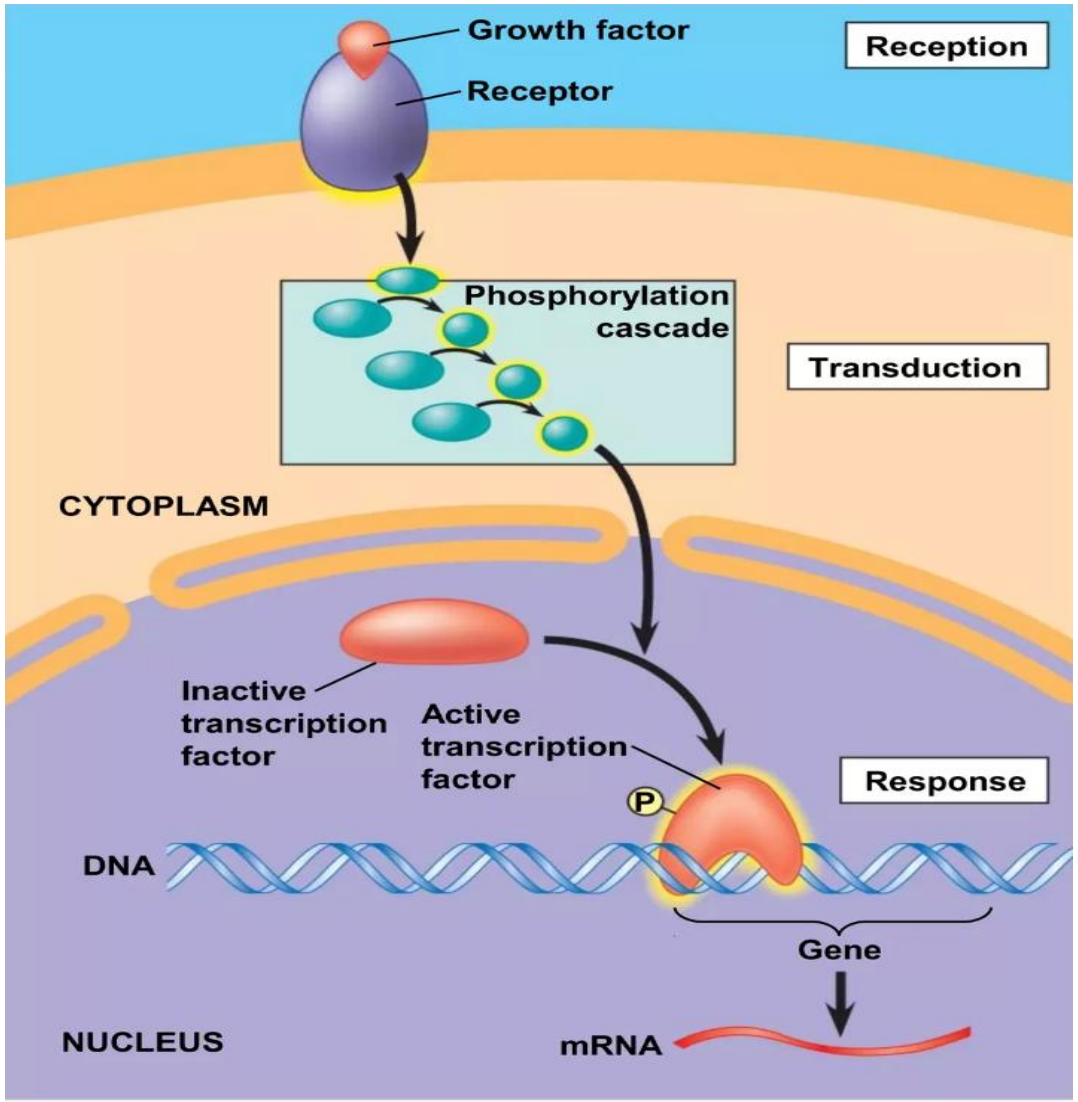
Schemitic of signaling



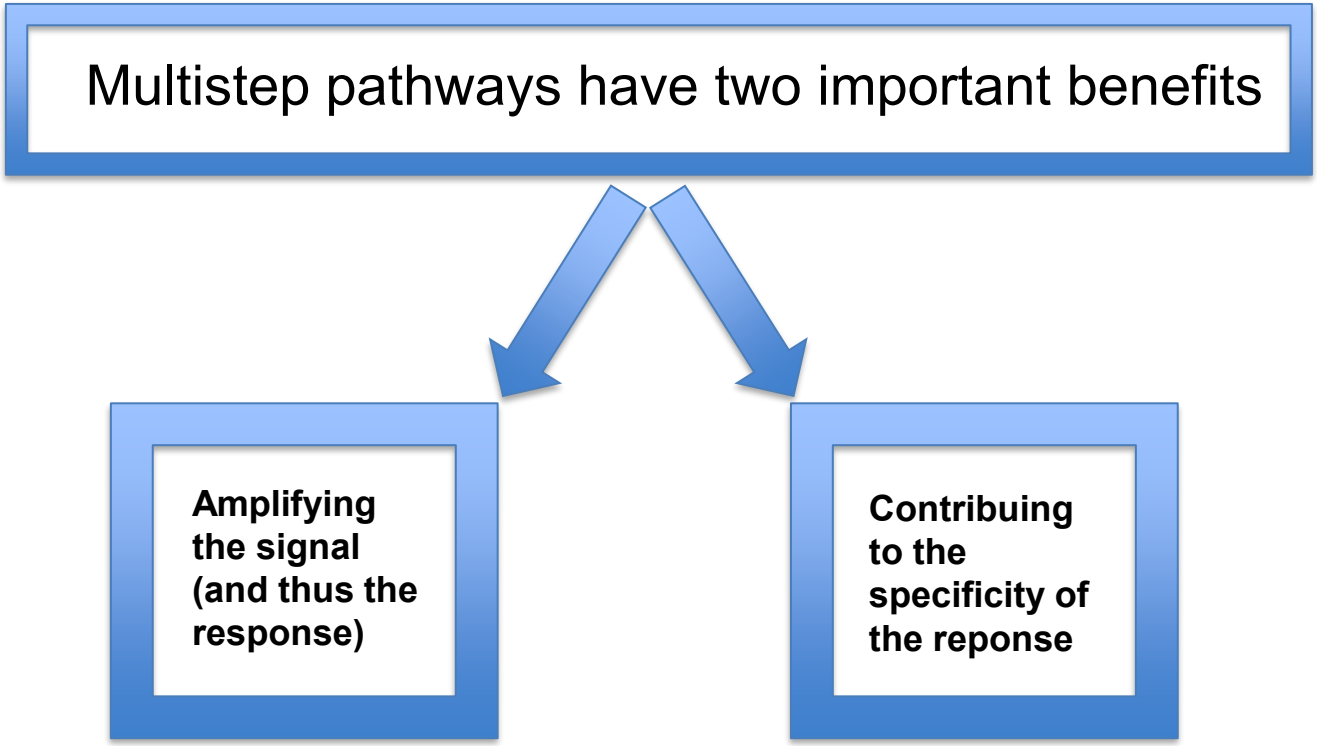
Nuclear Response

- Many other signaling pathway regulate the synthesis of enzymes or other proteins, usually by turning genes on or off in the nucles.
- The final activated molecule may function as a transcription factor.

Nuclear Response



Fine-Tuning of the Response



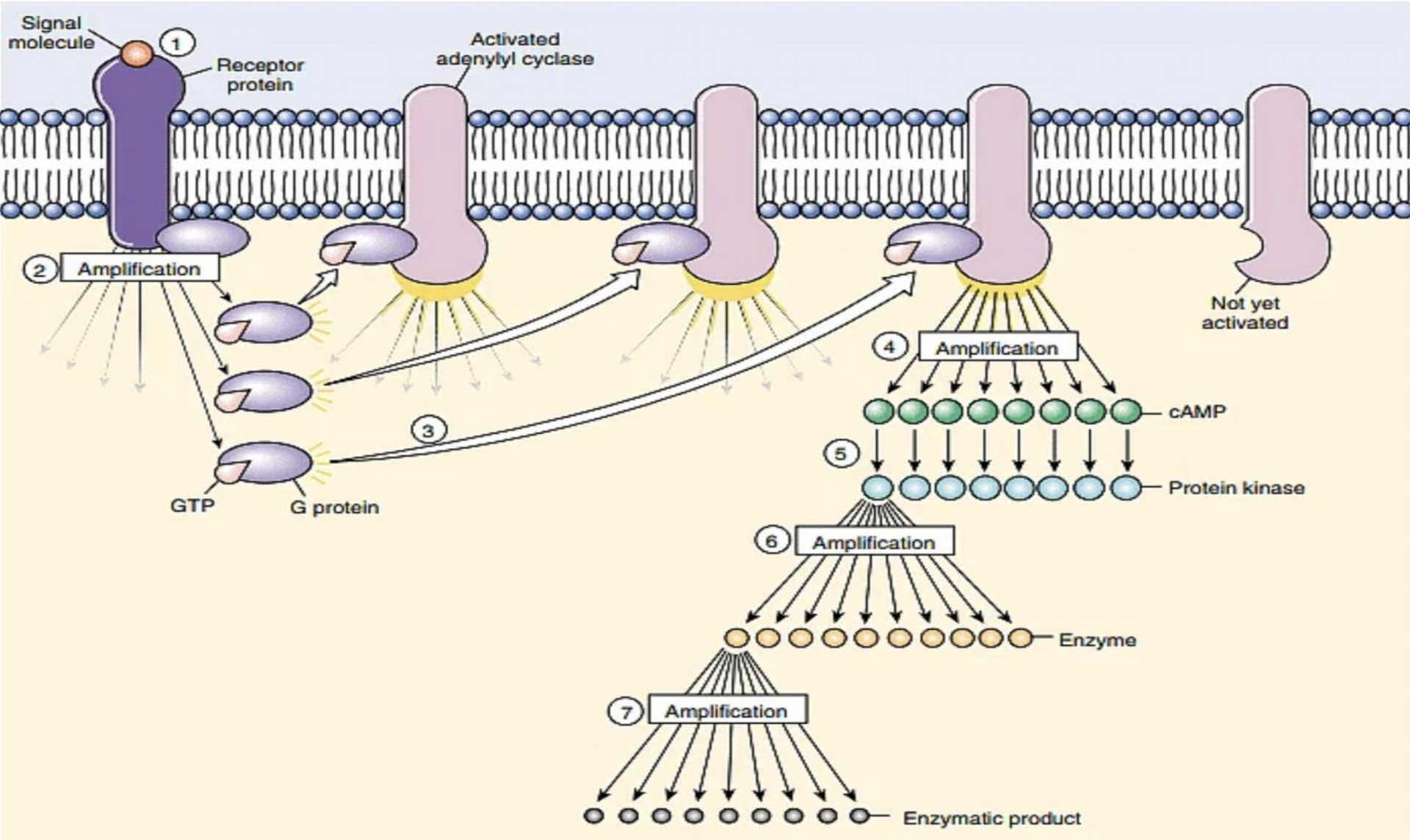
Signal Amplifications

Signal Cascade: Amplification occurs through a cascade of molecular events where each activated molecule can, in turn, activate multiple downstream targets, allowing a small initial signal to produce a large response.

Enzyme Activation: Commonly, enzymes like kinases are involved in these cascades, where each enzyme activates numerous other molecules, rapidly amplifying the signal across the cell.

Response Magnitude: This amplification mechanism ensures that even low concentrations of a signaling molecule can lead to a significant cellular response, increasing the sensitivity and efficiency of the cell's response to its environment.

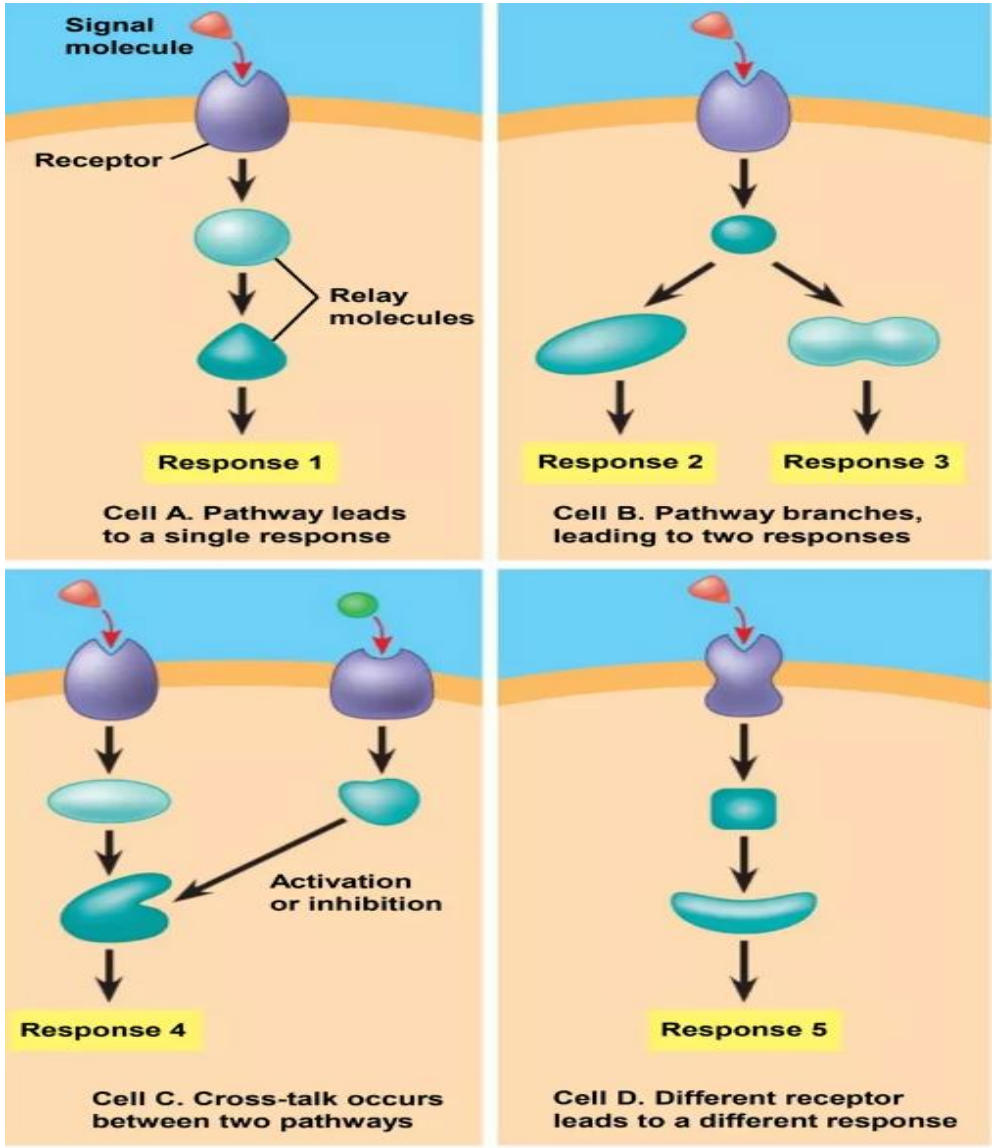
Signal Amplifications



The Specificity of Cells Signaling

- Different kinds of cells have different collections of proteins.
- These differences in proteins give each kind of cell specificity in detecting and responding to signals.
- The response of a cell to a signal depends on the cell's particular collection of proteins.
- Pathway branching and "cross-talk" further help the cell coordinate incoming signals.

Multistep pathways

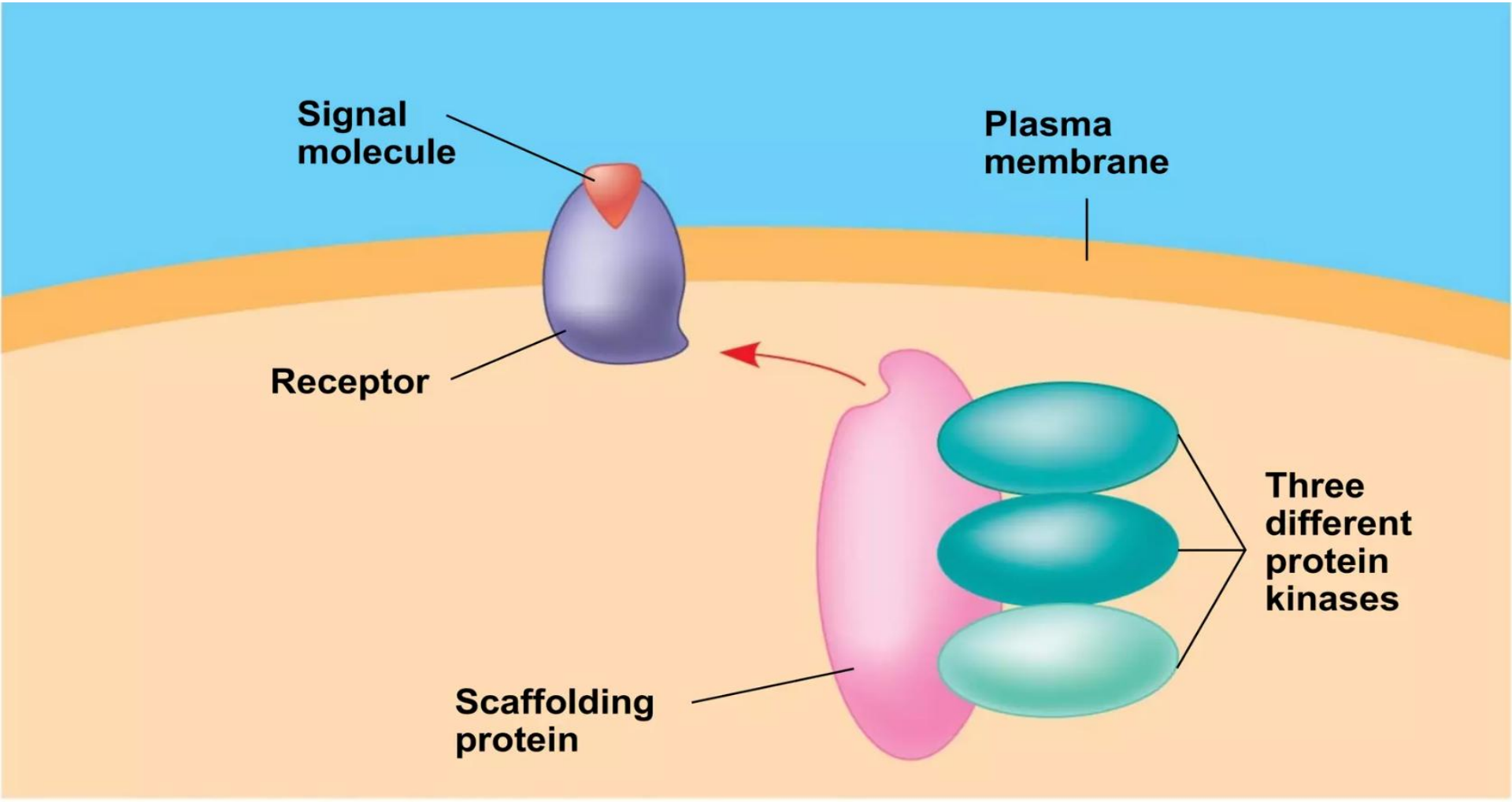


Signaling Efficiency

Signaling Efficiency: Scaffolding Proteins and Signaling Complexes.

- Scaffolding proteins are large relay proteins to which other relay proteins are attached.
- Scaffolding proteins can increase the signal transduction efficiency

Signaling Efficiency

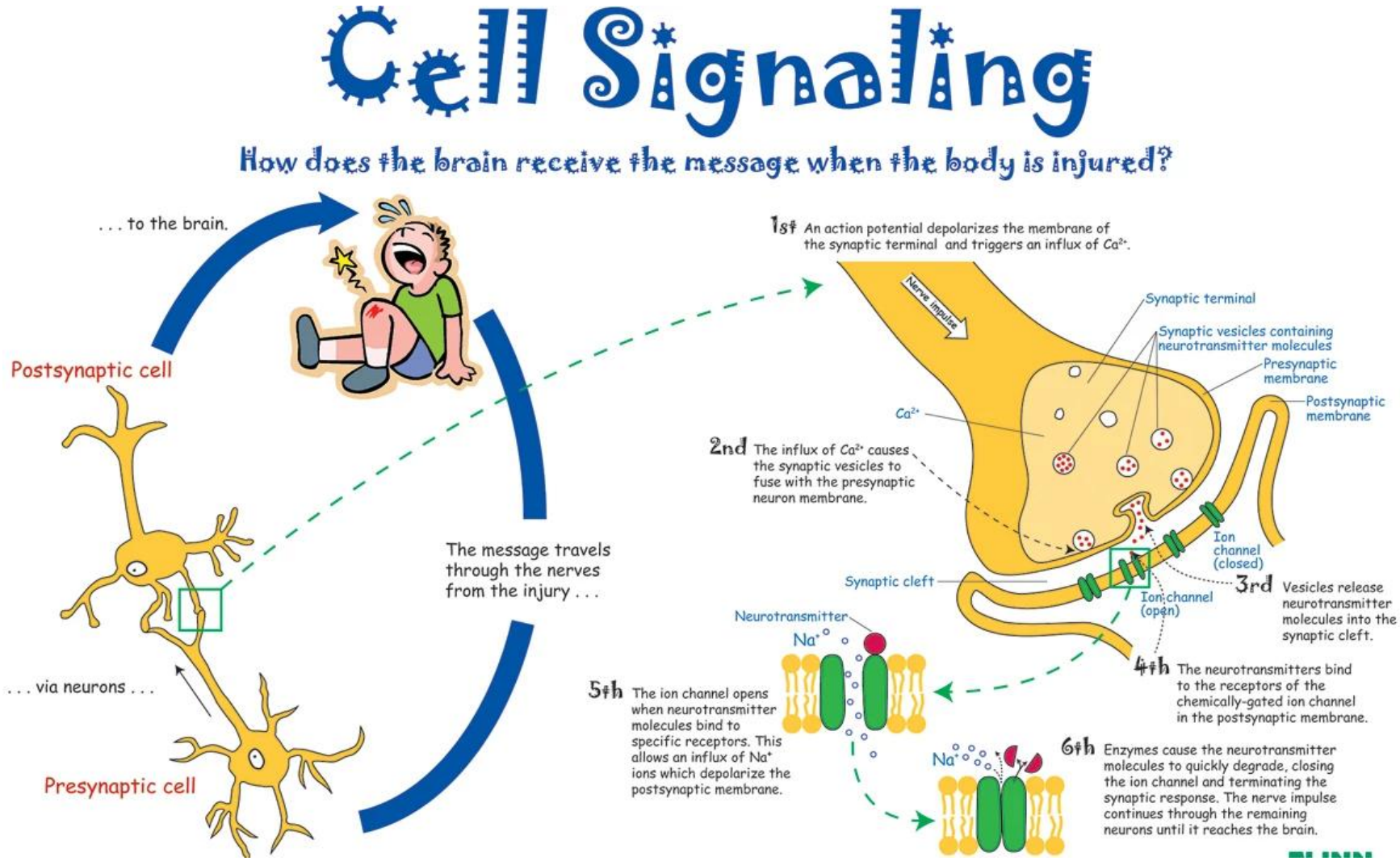


Cell Signallig in Specific System

Cell signaling in nervous system

- Synaptic signaling: Communication between neurons via neurotransmitters.
- Neurotransmitter release at synapse triggers receptor binding.
- Types of receptors: Ionotropic (direct) and metabotropic (indirect via GPCR).
- Fast, precise signaling essential for reflexes, perception, and coordination.

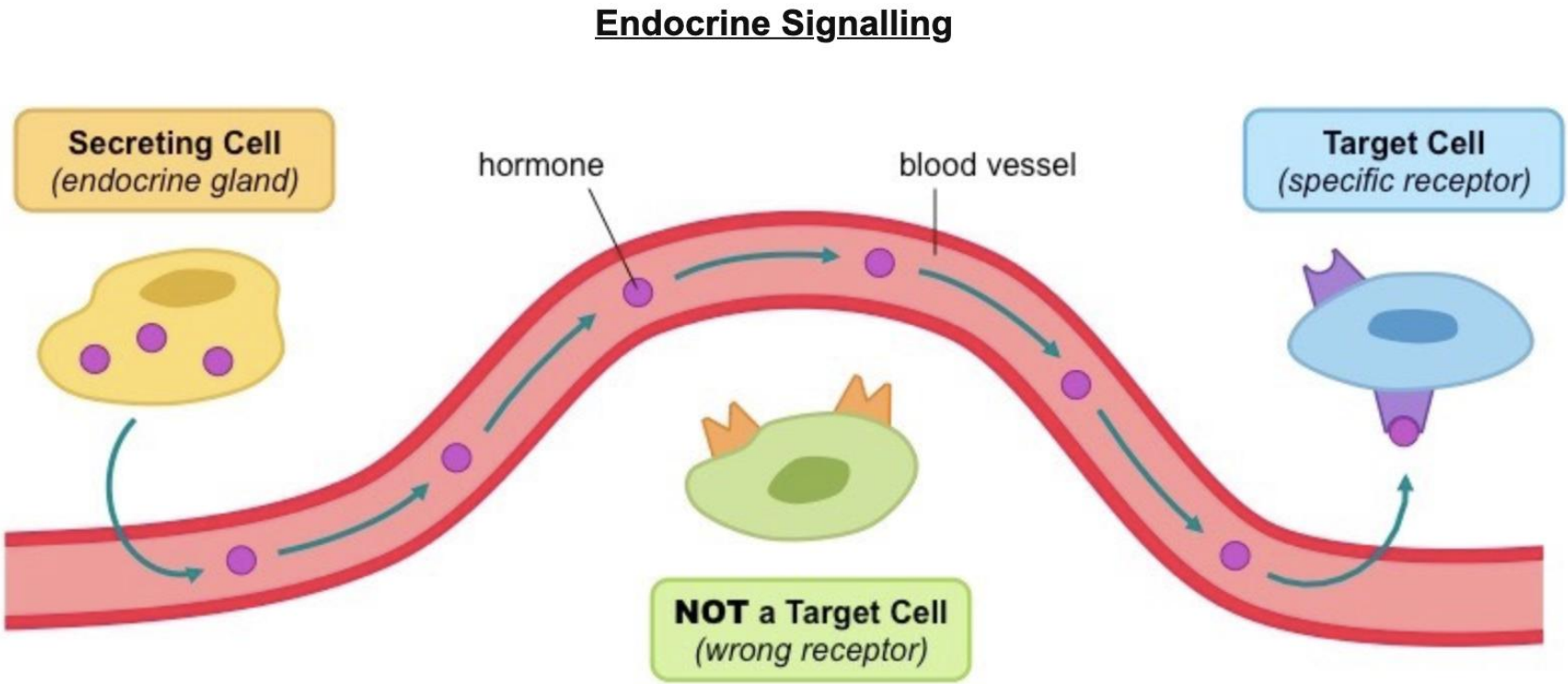
Cell signaling in nervous system



Endocrine system signaling

- Hormonal signaling for long-distance communication in the body.
- Hormones (e.g., insulin, adrenaline) travel through bloodstream to target cells.
- Receptors on target cells respond to specific hormones.
- Slower but sustained effects regulate metabolism, growth, and homeostasis.

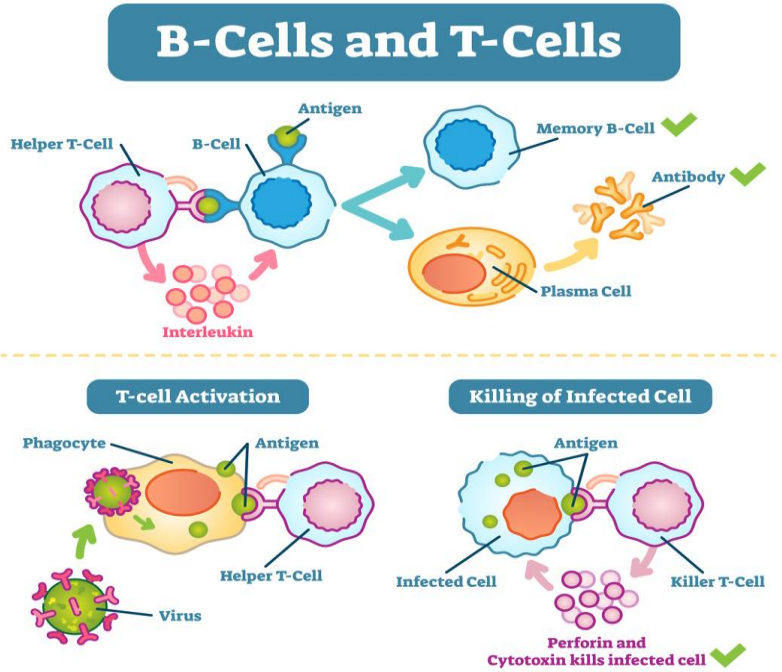
Endocrine system signaling

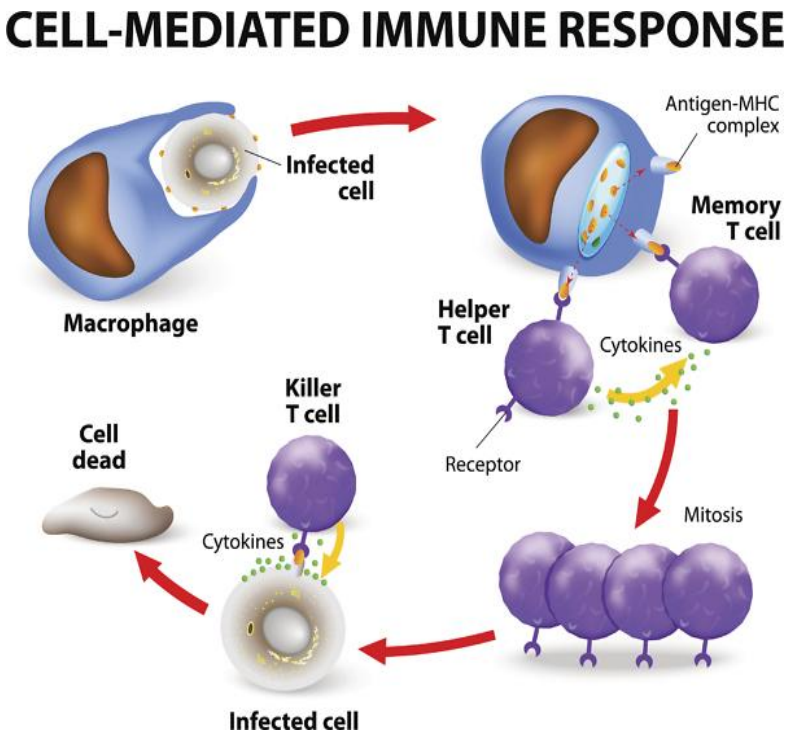


Immune System Signaling

- Cytokines mediate immune cell communication and coordination.
- Released by immune cells to direct responses (e.g., inflammation).
- T and B cells recognize antigens and trigger immune defenses.
- Enables precise pathogen targeting while avoiding self-reactivity.

Immune System Signaling





Complications

When Cell Communication Goes Wrong?

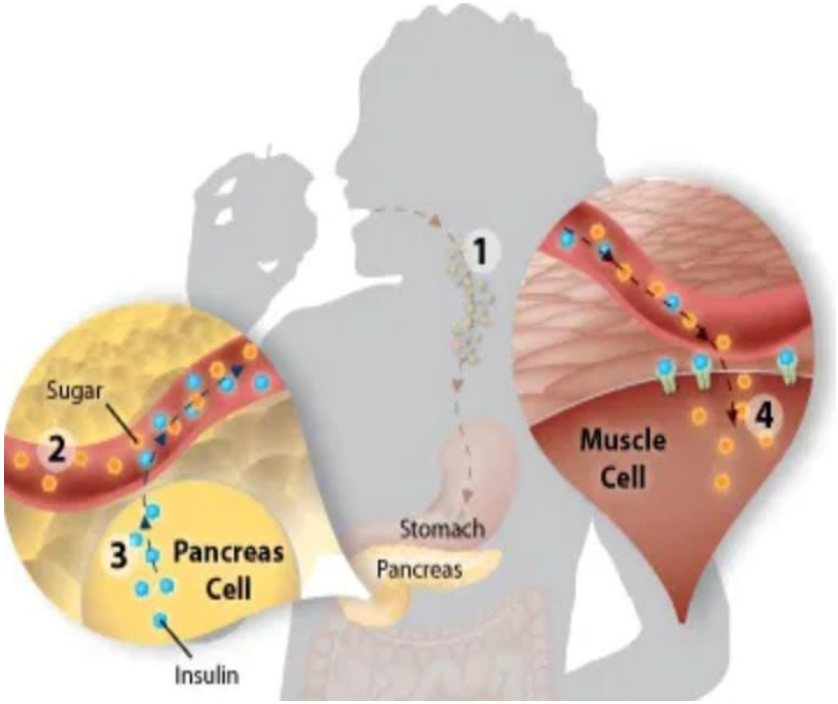
- The cells in our bodies are constantly sending out and receiving signals.
- But what if a cell fails to send out a signal at the proper time?
- Or what if a signal doesn't reach its target?
- What if a target cell does not respond to a signal, or a cell responds even though it has not received a signal?

Losing the signal

- Normally, cells in the pancreas release a signal, called insulin, that tells your liver, muscle and fat cells to store this sugar for later use.

- In type I diabetes, the pancreatic cells that produce insulin are lost. Consequently, the insulin signal is also lost.

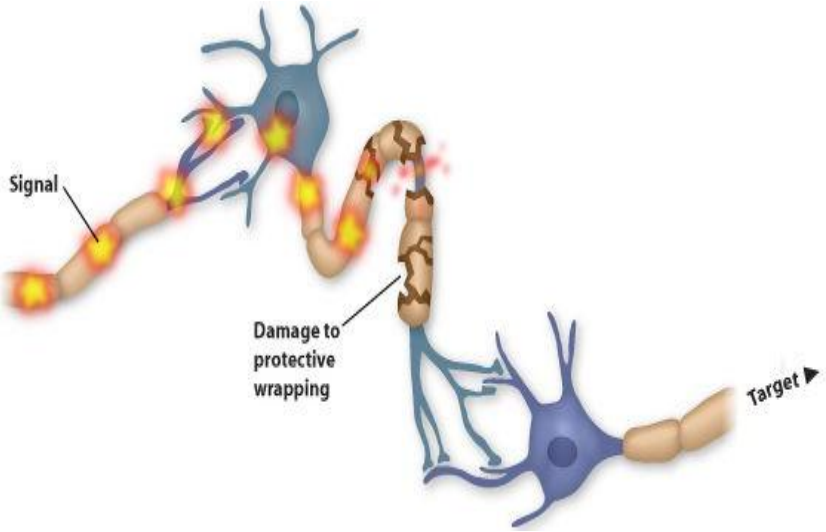
- As a result, sugar accumulates to toxic levels in the blood.



When a Signal Doesn't Reach Its Target

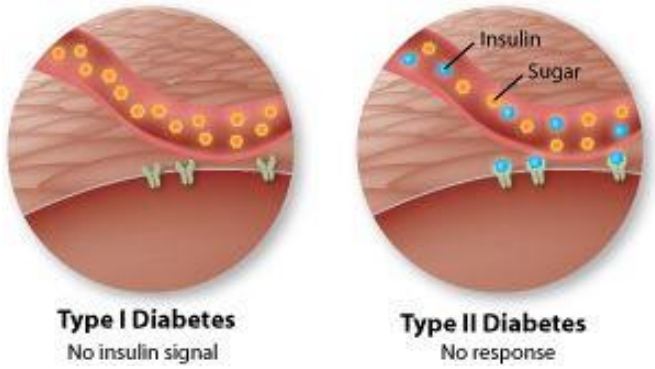
- Multiple sclerosis is a disease in which the protective wrappings around nerve cells in the brain and spinal cord are destroyed.

- The affected nerve cells can no longer transmit signals from one area of the brain to another.



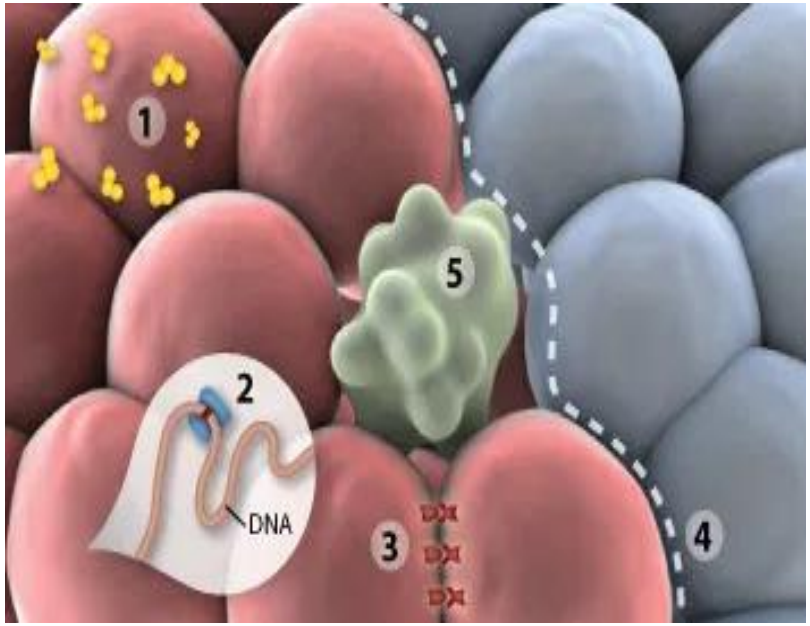
When the Target Ignores the Signal

- Type I and type II diabetes have very similar symptoms, but they have different causes.
- People who have type I diabetes are unable to produce the insulin signal, those with type II diabetes do produce insulin.
- The cells of type II diabetics have lost the ability to respond to insulin.
- The end result is the same: blood sugar levels become dangerously high.



Multiple Breakdowns

Cell growth and division is such an important process that it is under tight control with many checks and balances. But even so, cell communication can break down. The result is uncontrolled cell growth, often leading to cancer.



Many mechanisms maintain appropriate cell growth: Cell division occurs in response to external signals (1). Enzymes repair damaged DNA (2). Cells make connections with their neighbours (3). If these connections suddenly change, neighbouring cells send out an alert. Cells respect and stay within tissue boundaries (4). If a cell is beyond repair, it initiates its own death (5).

Treatment

Treatment of diesese cause by cell signaling problems

- Just as cell signaling can go wrong resulting in disease, many disease treatments rely on cell communication.
- If you think of disease as a roadblock in cell signaling, treatment is an alternate route.
- The first step is to locate the problem.
- The second step is to find a way around the problem. Sometimes it's easy.
- For example: The treatment for type I diabetes is to inject insulin into the blood stream.

Significance of cell signaling

- Cell signaling is basis of Prokaryote and Eukaryote life.
- For normal functioning coordination of every signaling pathway is necessary.
- Altered signaling pathways may lead to diseases.
- Defect can be in any component of signalling ultimately leading to the disease development.
- Cell signaling has been identified in Cancer, Cardiovascular diseases, Alzheimer's disease, and many other disorders.
- Cell Signaling is an important area of research for drug discovery.