بسم الله الرحمن الرحيم

السلام عليكم ورحمة الله وبركاته

Endocrine System Introduction

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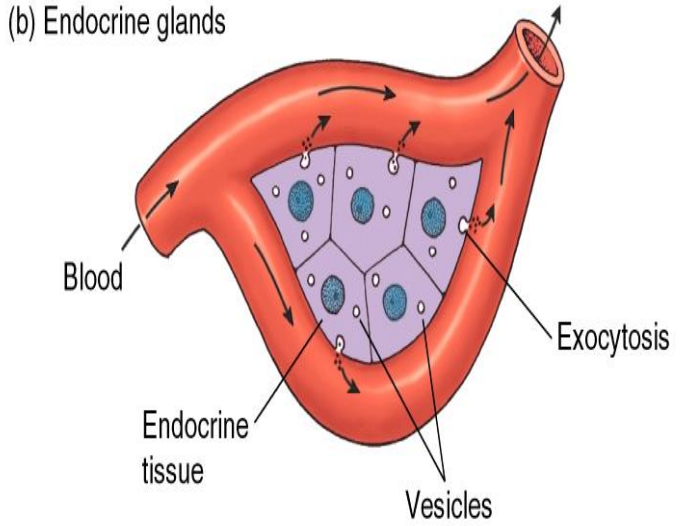
Objectives

- Difference between endocrine & exocrine glands
- Chemical messengers
- Major endocrine organs
- Hormone
  - What is the hormone?
  - Types of stimuli
  - What are target cells?
  - Chemical structure
  - Transport
- Mechanism of action
  - Receptors, down-regulation & up-regulation
  - Intracellular signaling
  - Second messenger (cAMP, IP3 & tyrosine kinase)
  - Hormones interactions at target cells
  - Clearance of hormones

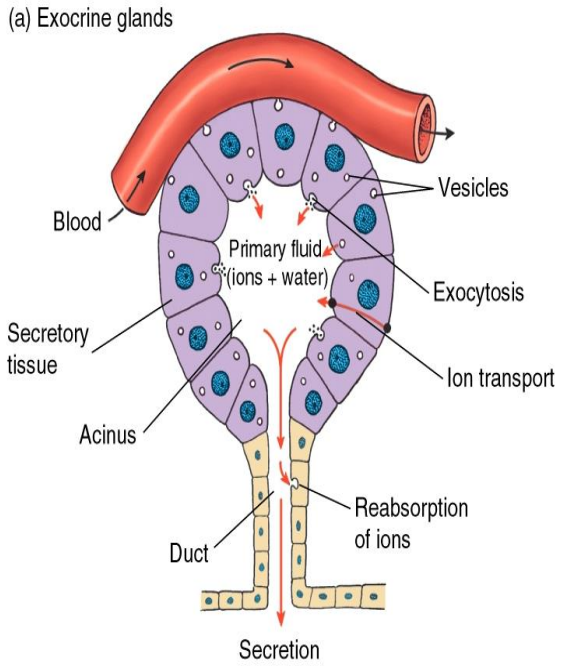
The endocrine glands

They are ductless glands that produce hormones released directly into the blood.



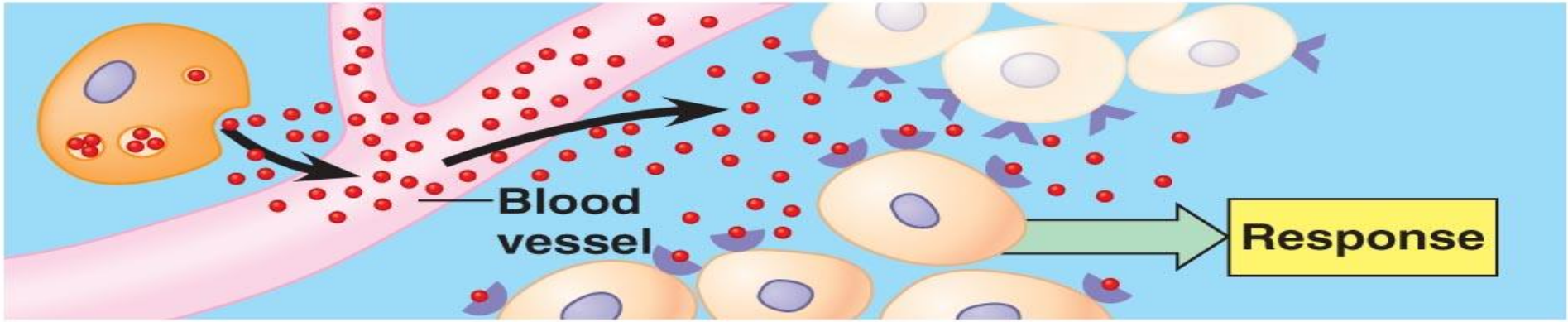
The exocrine glands

Release their products at the body's surface or into body cavities through ducts.

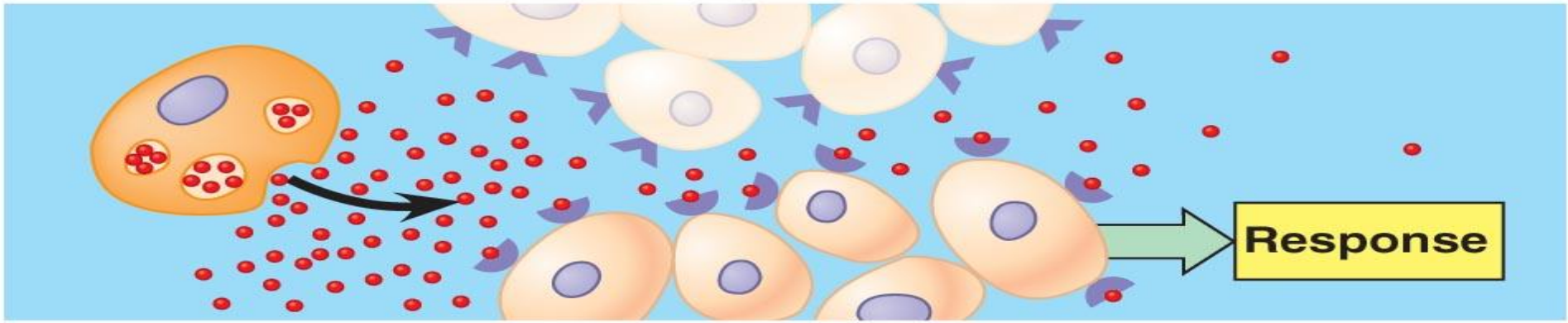


Chemical messengers

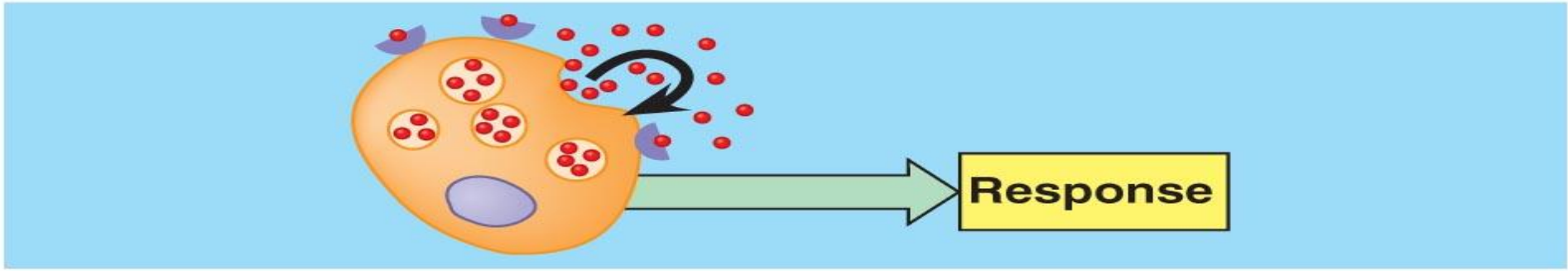
- The activities of cells, tissues and organs are coordinated by the interplay of several types of chemical messenger systems:
  - Endocrine hormones
  - Paracrines
  - Autocrines
  - Neurotransmitters
  - Neuroendocrine hormones
  - Cytokines: peptides secreted by cells into ECF and function as autocrines, paracrines, or endocrine hormones and act on other cells (e.g., leptin & interleukins)



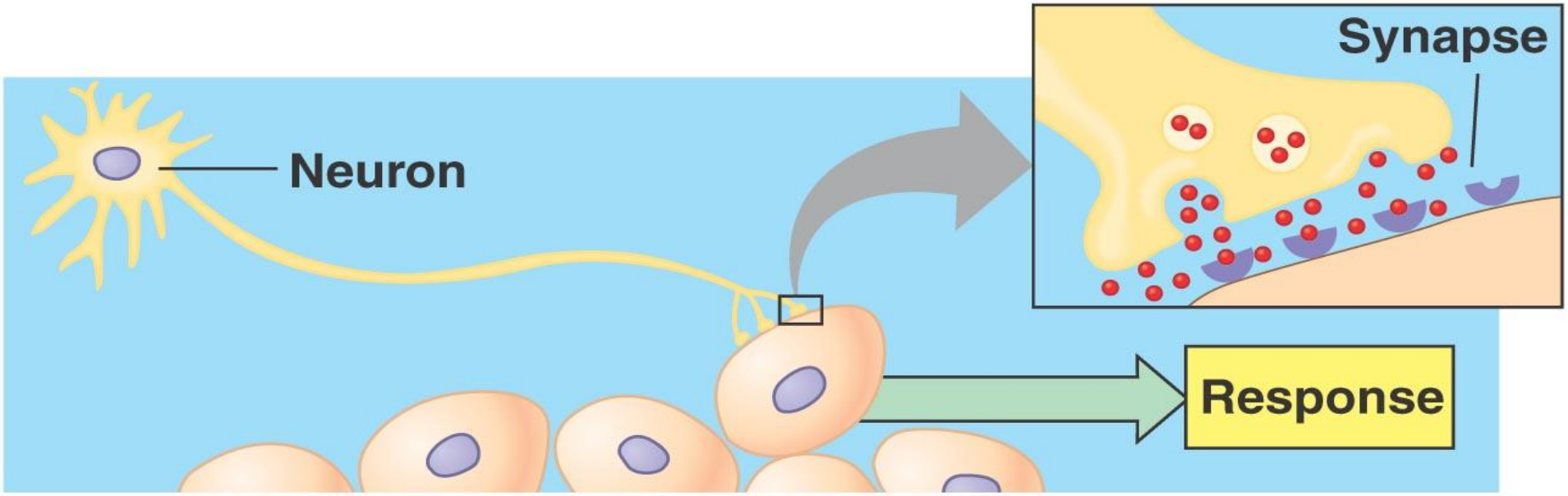
(a) Endocrine signaling:Released by glands into blood and influence the function of other cells.



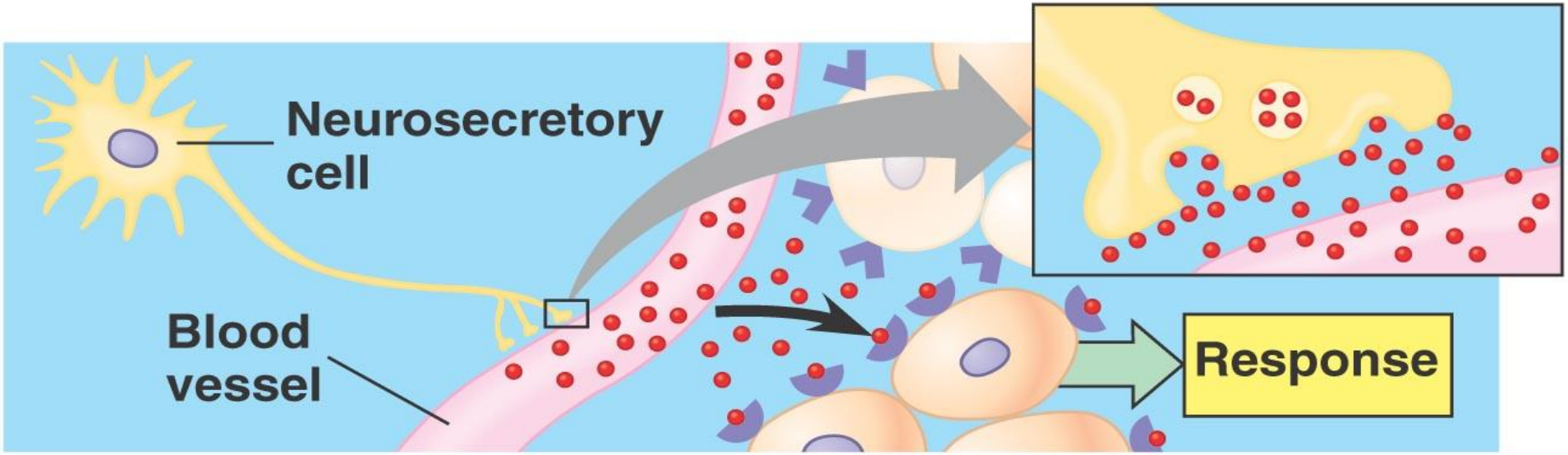
(b) Paracrine signaling **:Secreted by cells into ECF and affect neighboring cells of a different type.**



(c) Autocrine signaling **:Secreted by cells into ECF and affect the function of the same cells.**



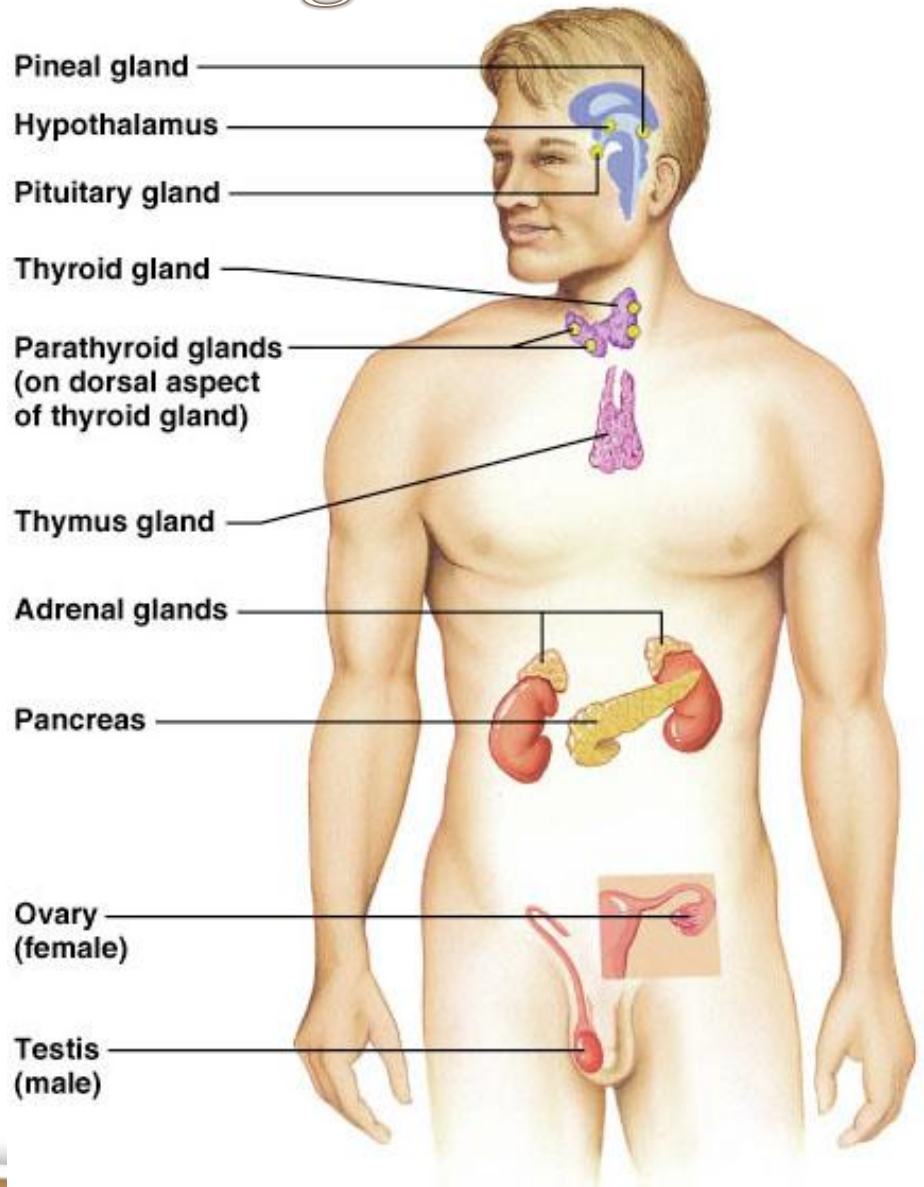
(d) Synaptic signaling (Neurotransmitters): are released by axon terminals of neurons into synaptic junctions and act locally to control nerve cell functions.

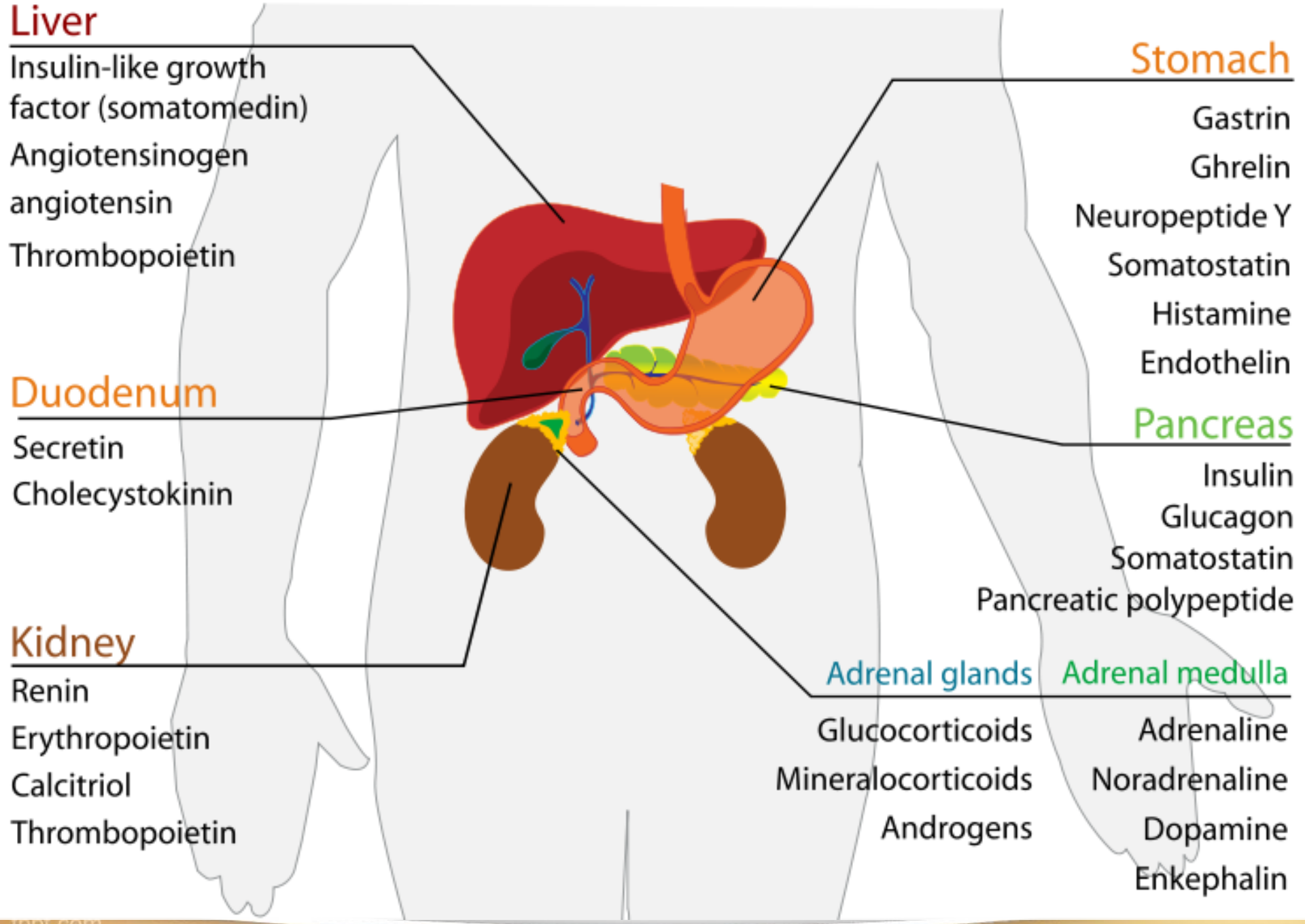


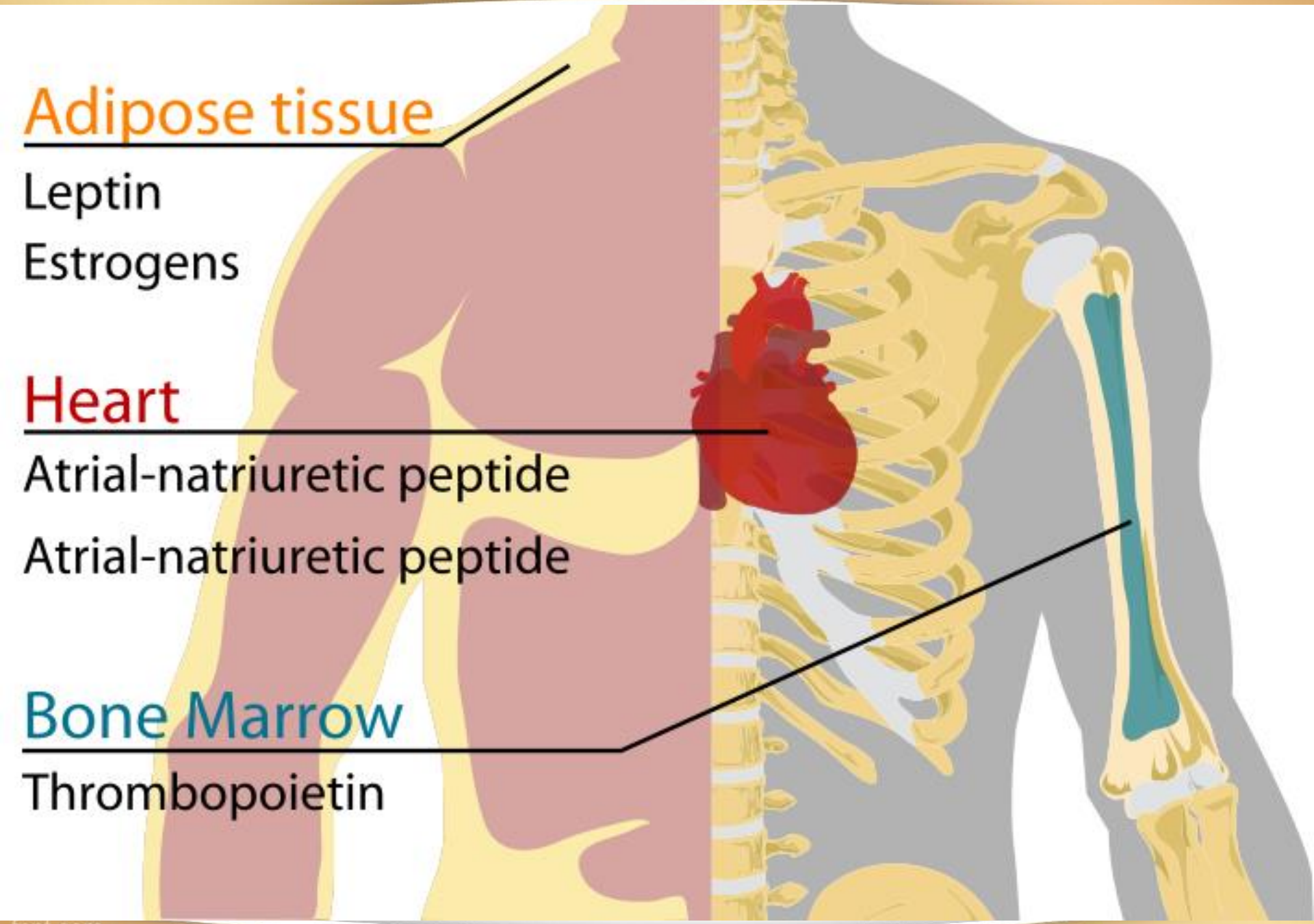
(e) Neuroendocrine signaling Secreted by neurons into blood and influence the function of other cells

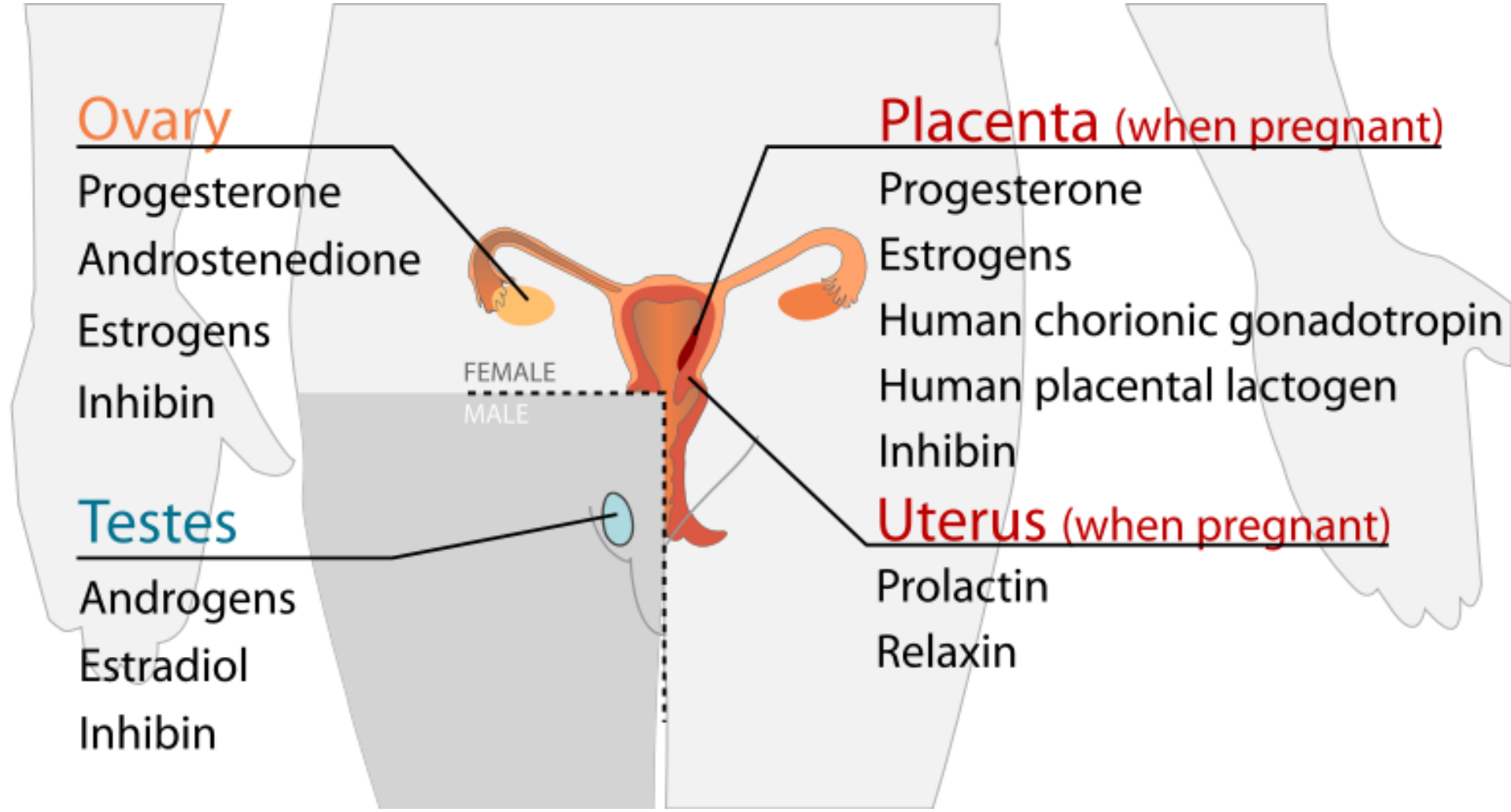
Major endocrine organs

- The pituitary, thyroid, parathyroid, adrenal, the pancreas and the gonads (ovaries and testes).
- The hypothalamus, which is part of the nervous system, is also considered as a major endocrine organ.




Liver
Insulin-like growth factor (somatomedin)
Angiotensinogen
angiotensin
Thrombopoietin
Duodenum
Secretin
Cholecystokinin
Kidney
Renin
Erythropoietin
Calcitriol
Thrombopoietin
Stomach
Gastrin
Ghrelin
Neuropeptide Y
Somatostatin
Histamine
Endothelin
Pancreas
Insulin
Glucagon
Somatostatin
Pancreatic polypeptide
Adrenal glands
Glucocorticoids
Mineralocorticoids
Androgens
Adrenal medulla
Adrenaline
Noradrenaline
Dopamine
Enkephalin


Adipose tissue
Leptin
Estrogens
Heart
Atrial-natriuretic peptide
Atrial-natriuretic peptide
Bone Marrow
Thrombopoietin


Ovary
Progesterone
Androstenedione
Estrogens
Inhibin
Testes
Androgens
Estradiol
Inhibin
FEMALE
MALE
Placenta (when pregnant)
Progesterone
Estrogens
Human chorionic gonadotropin
Human placental lactogen
Inhibin
Uterus (when pregnant)
Prolactin
Relaxin

Hormones

The multiple hormone systems play a key role in regulating almost all body functions:

1. Metabolism
2. Growth and development
3. Water and electrolyte balance
4. Reproduction
5. Behavior

What is the hormone?

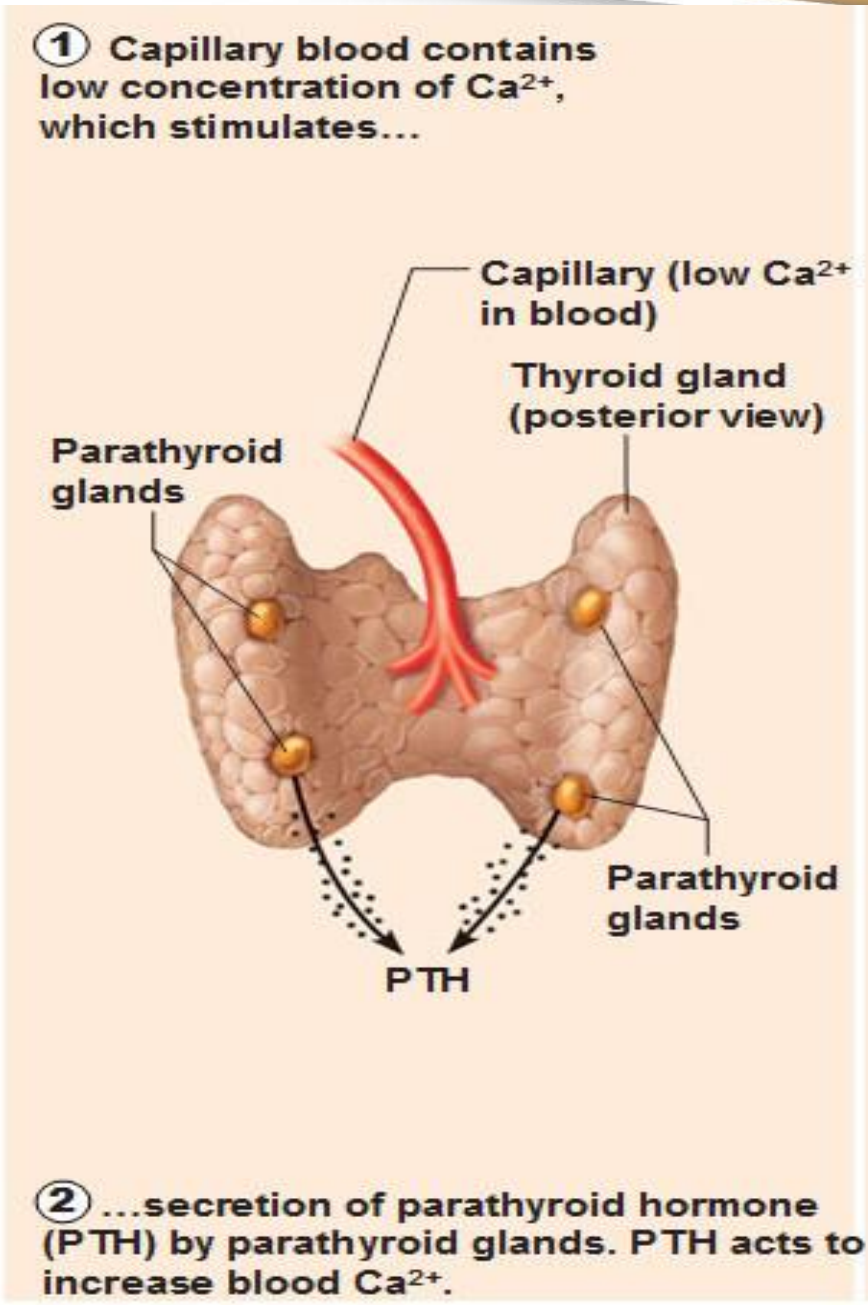
- Chemical substance secreted in a small amount from endocrine gland directly to the blood stream in response to stimulus to cause physiological responses at other type of cells (target cells).
- Hormone can affect many different types of target cells (e.g. GH and Thyroxin)
- Hormone can affect only specific target cells (e.g. ACTH and estrogen)

Classification of stimuli

- Humoral Stimuli
- Neural Stimuli
- Hormonal Stimuli

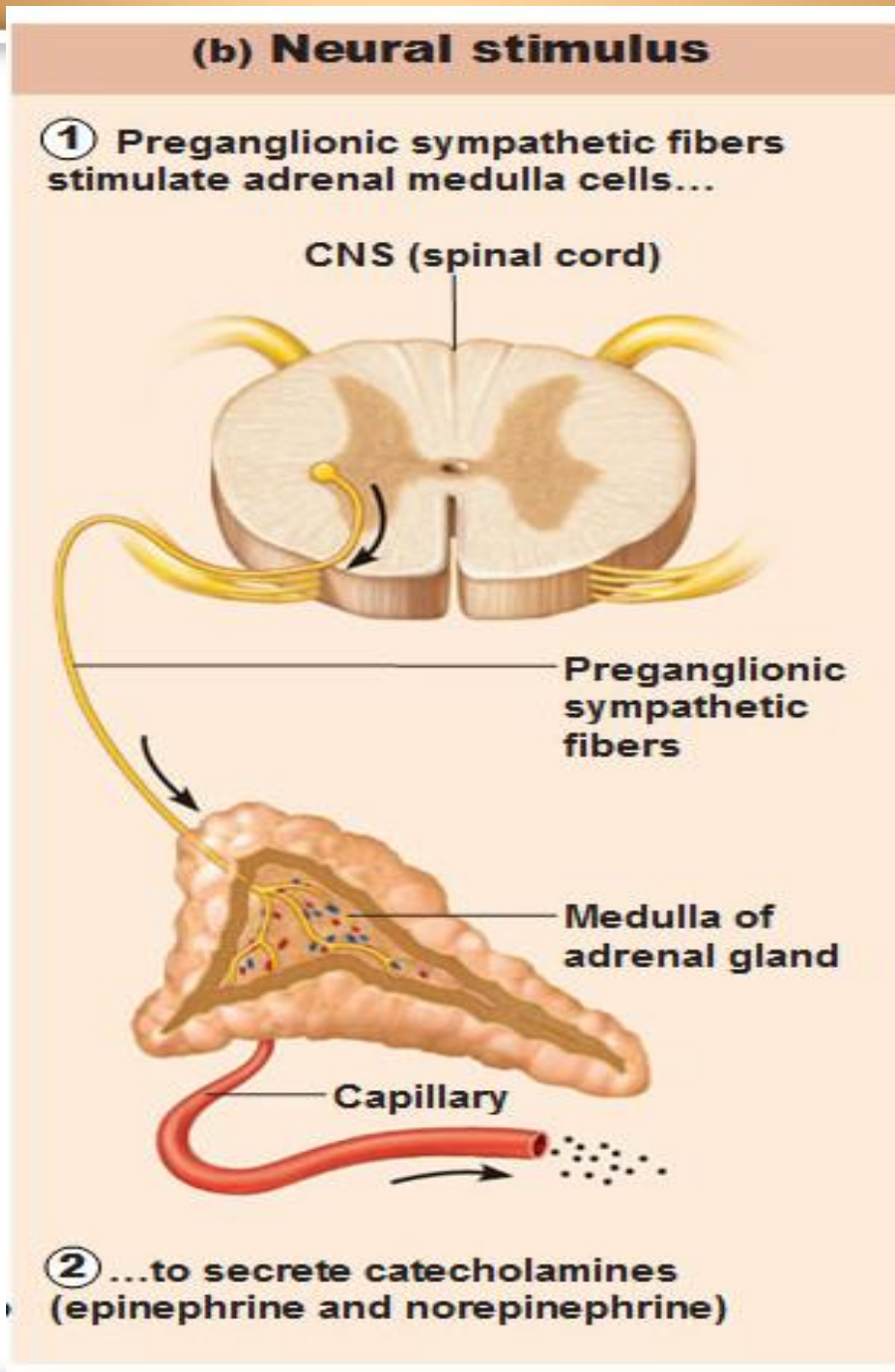
Humoral Stimuli:

Secretion of hormones in direct response to changing in blood levels of ions and nutrients



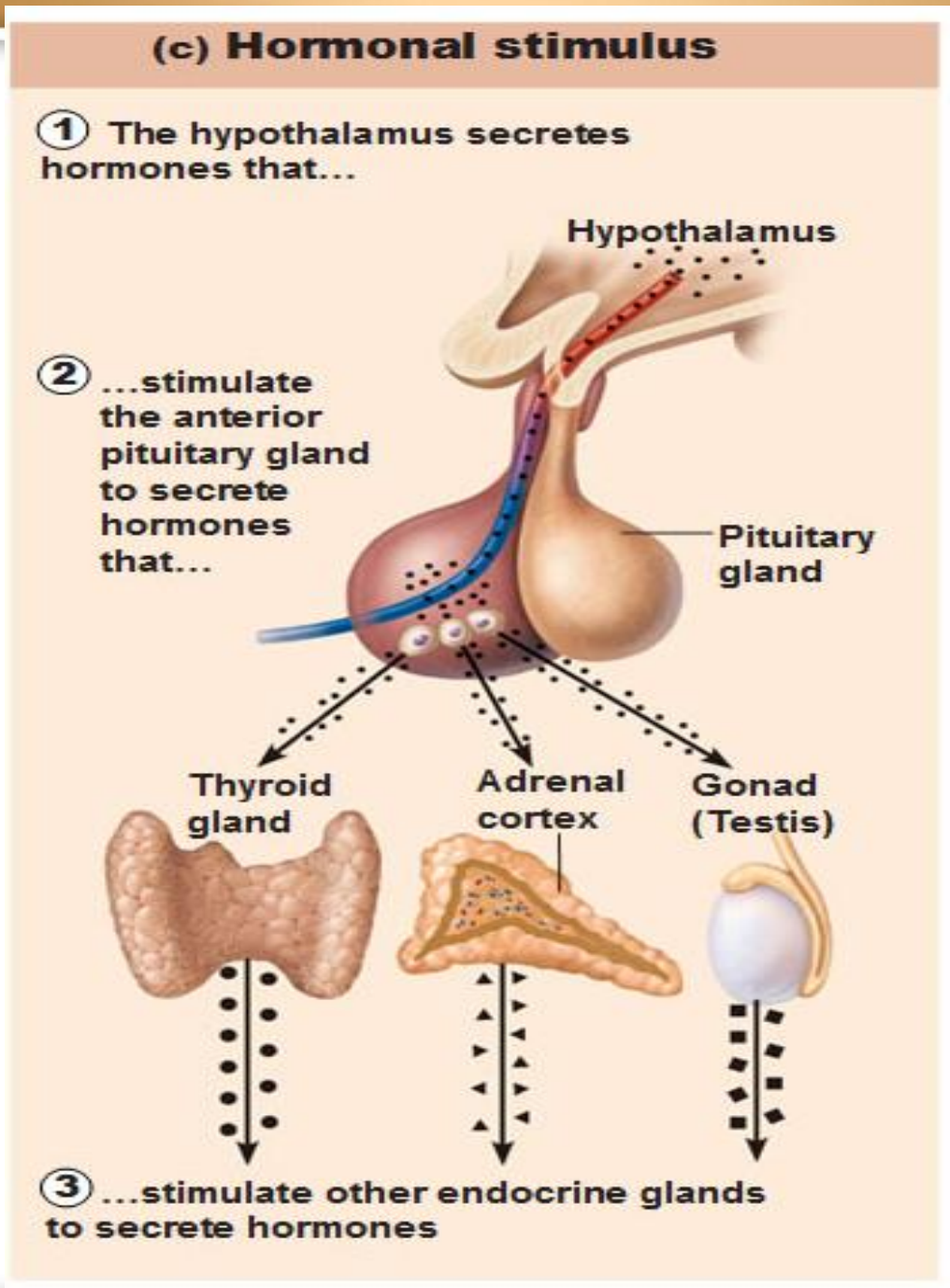
Neural Stimuli:

Nerve signals stimulate hormone release.



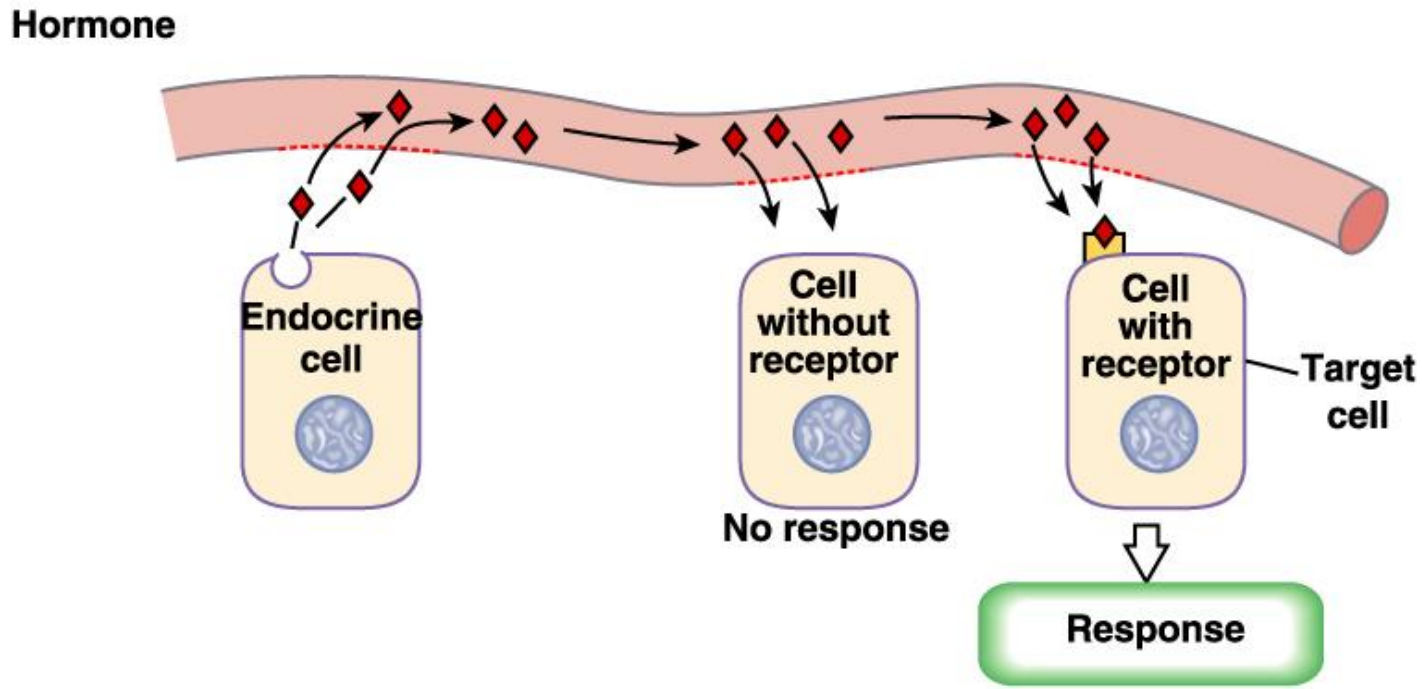
Hormonal Stimuli:

Release of hormones in response to hormones produced by other endocrine gland.



What are target cells?

Target cells refer to cells that contain specific receptors (binding sites) for a particular hormone.



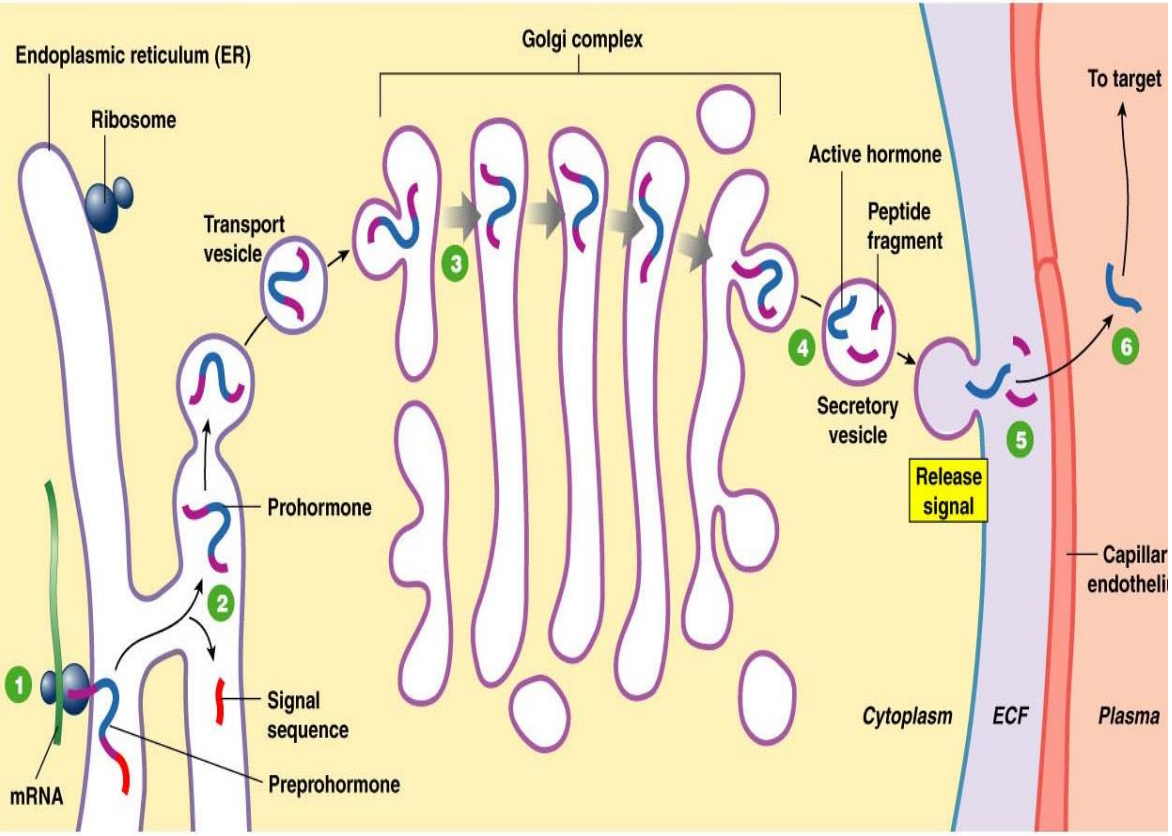
Chemical structure of hormones

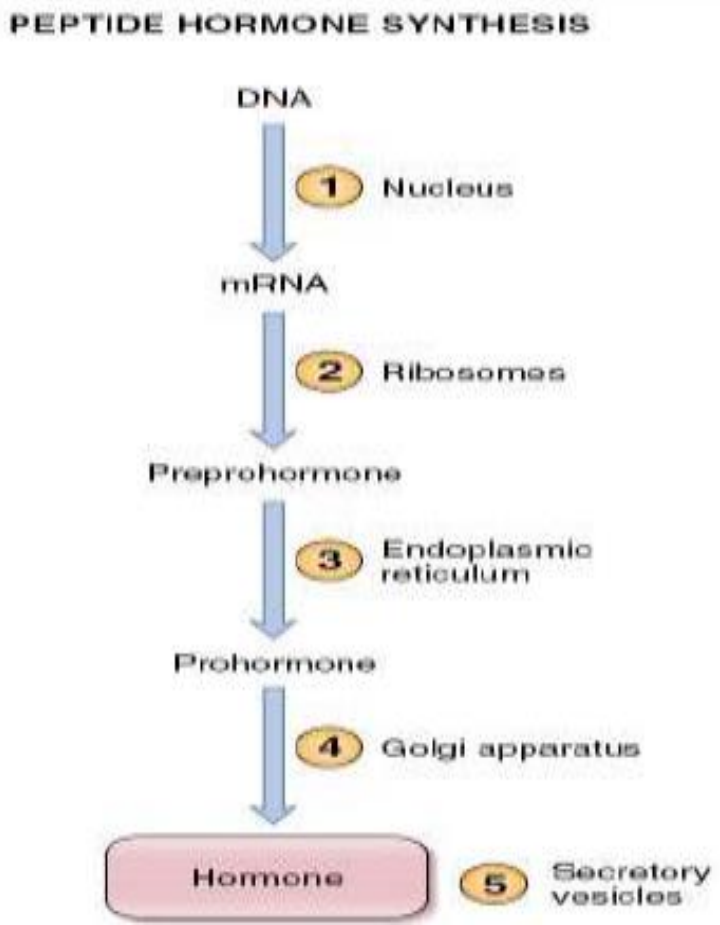
Three general classes of hormones:

- Proteins and polypeptides (anterior and posterior pituitary, pancreatic and parathyroid hormones) stored in vesicles until needed
- Steroids (adrenocortical, ovarian and testicular hormones) diffuse across the cell membrane
- Derivatives of amino acid tyrosine (thyroid hormones and catecholamines)

Peptide (Protein) Hormones

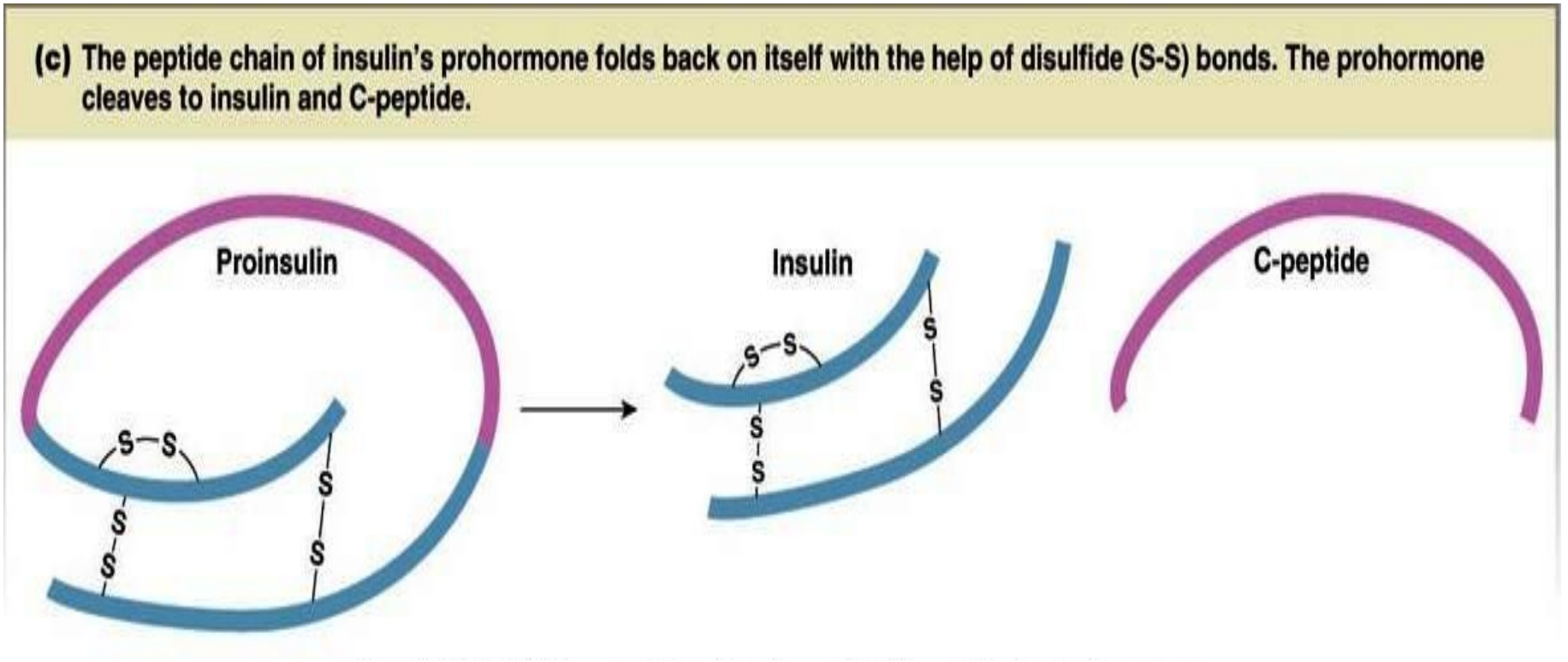
Synthesized as preprohormone → post-translational modification to prohormone → then hormone





Example of protein hormone

- Insulin



Steroid Hormones

- Derived from cholesterol (lipophilic)
- Secreted by gonads, adrenal cortex, placenta
- On-demand synthesis (SER)
- Cross membranes (no storage)
- Usually bound to carrier proteins

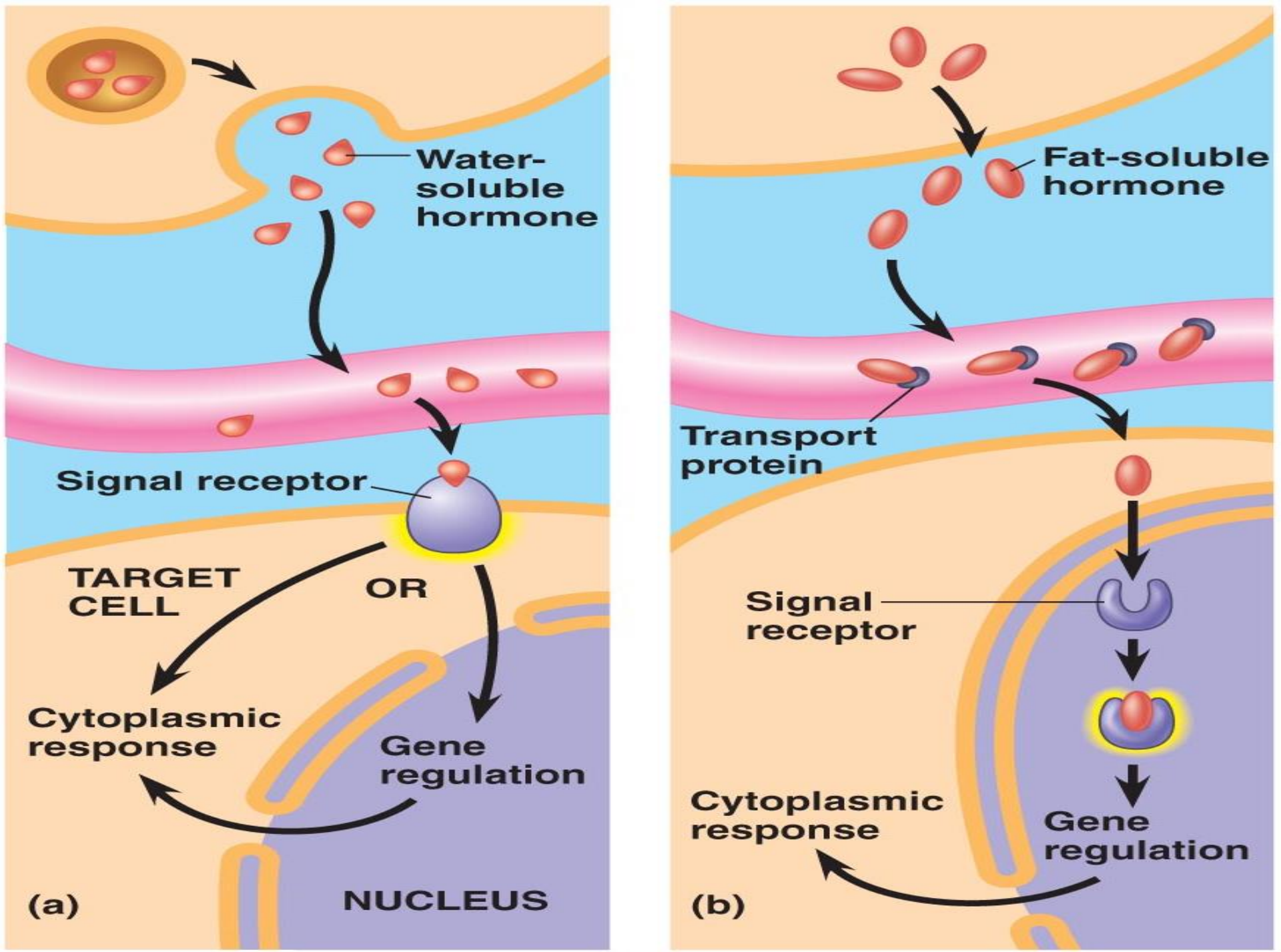
Amine Hormones

- Derived from tyrosine or tryptophan
- 3 groups
  - Tyrosine ⇒ Catecholamines
    Behave like peptide hormones
  - Tyrosine ⇒ Thyroid hormones
    Behave like steroid hormones
  - Tryptophan ⇒ Melatonin

Transport of hormones

- Water soluble hormones (hydrophilic): peptides & catecholamines dissolved in plasma
- Fat soluble hormones (hydrophobic): Steroids and thyroid hormones transported bound to plasma proteins (90%).

  Binding to plasma proteins helps to:
  - Provide reservoirs
  - Slow hormones clearance


Water-soluble hormone
Signal receptor
TARGET CELL
OR
Cytoplasmic response
Gene regulation
(a)
NUCLEUS
Fat-soluble hormone
Transport protein
Signal receptor
Cytoplasmic response
Gene regulation
(b)

Mechanism of hormone action

- In order for a target cell to respond to a hormone, specific protein receptors must be present on its plasma membrane or in its interior to which that hormone can attach.
- Only when this binding occurs can the hormone influence the working of the cell:-
  - Hormone-receptor interaction (1st messenger)
  - Enzyme activation
  - Release of the second messenger
  - Effects on cellular function

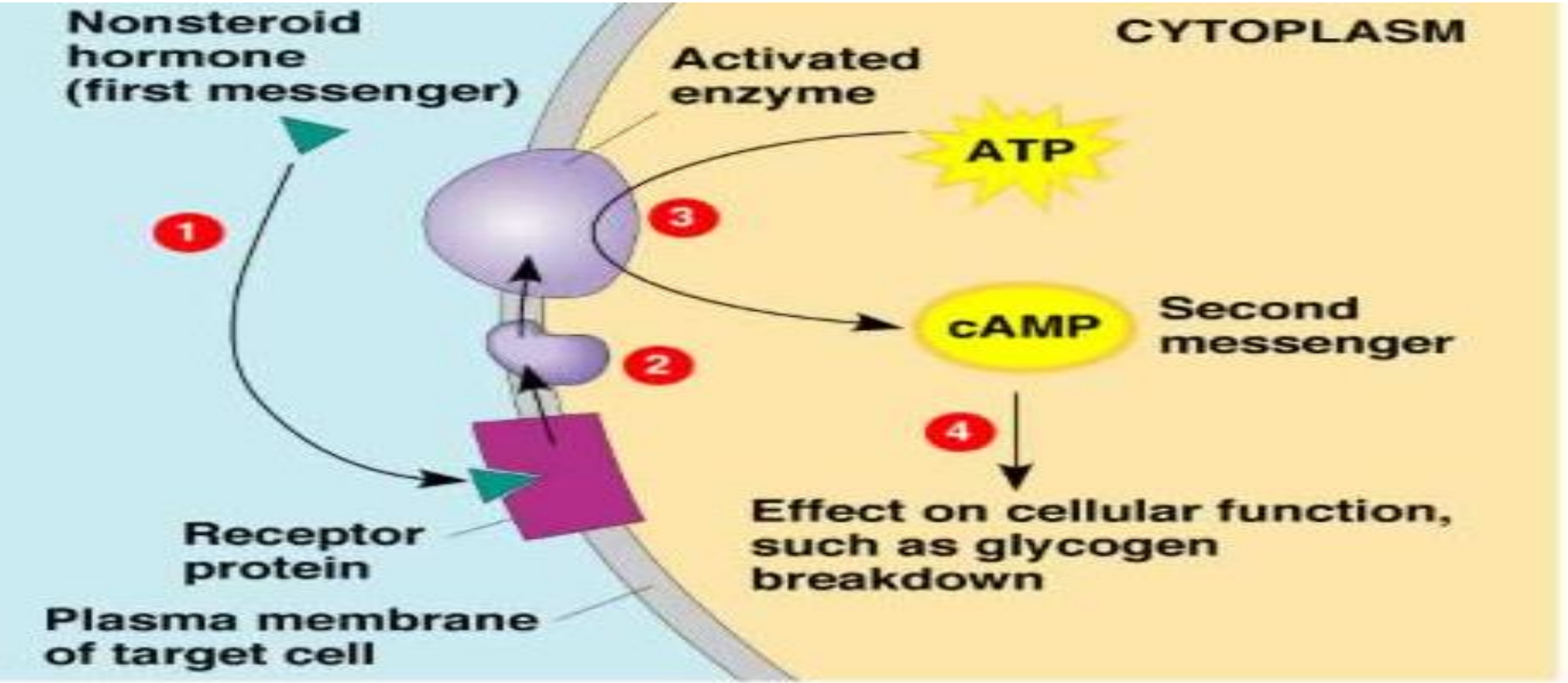
Hormone receptors

- Hormonal receptors are large proteins
- 2000-100,000 receptors/cell
- Receptors are highly specific for a single hormone
- Receptor's location:
  - On the surface of cell membrane (proteins, peptides and catecholamines)
  - In the cell cytoplasm (Steroids)
  - In the cell nucleus (thyroid hormones)

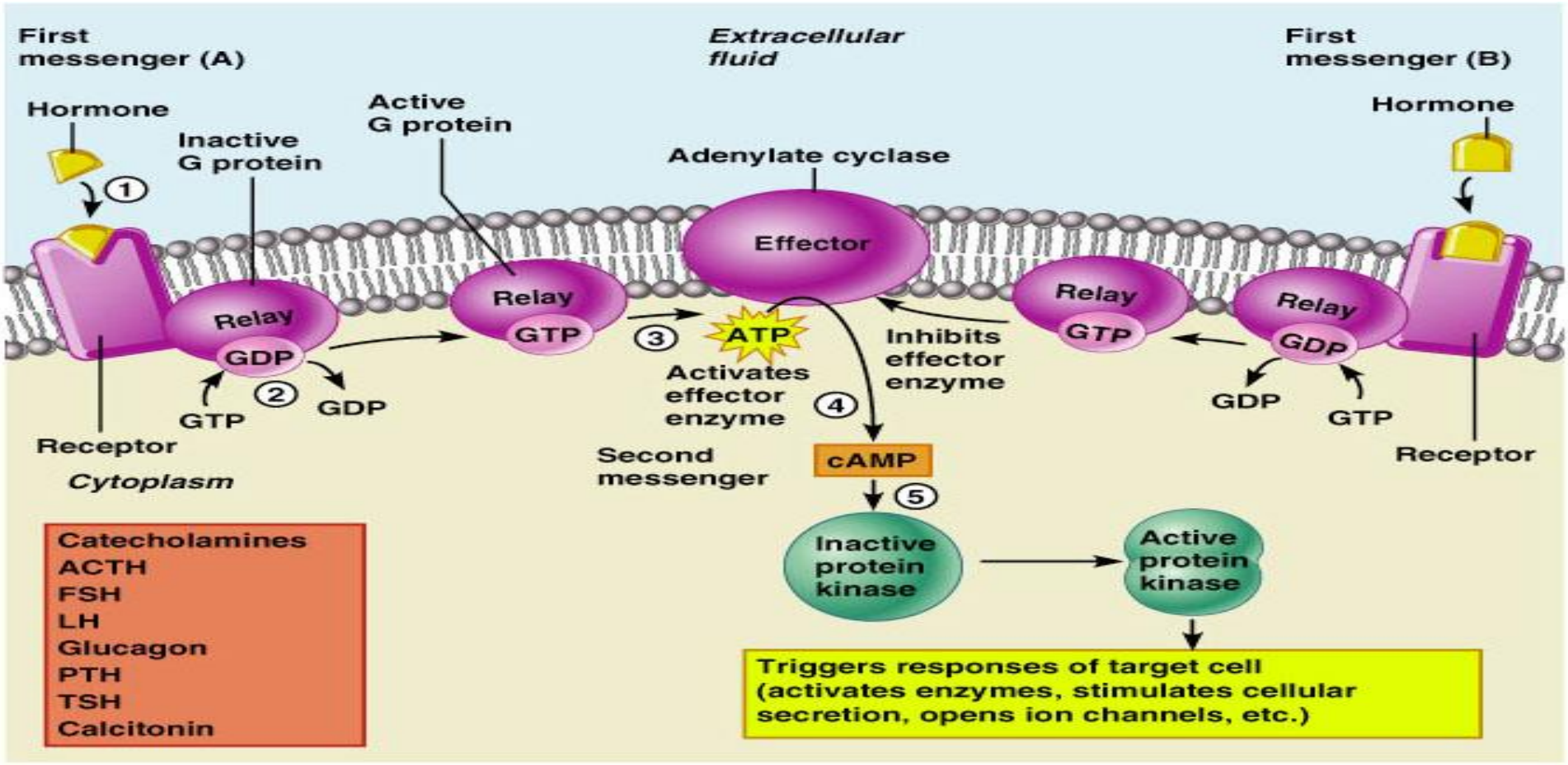
Protein and peptide hormones

Receptor on the cell membrane

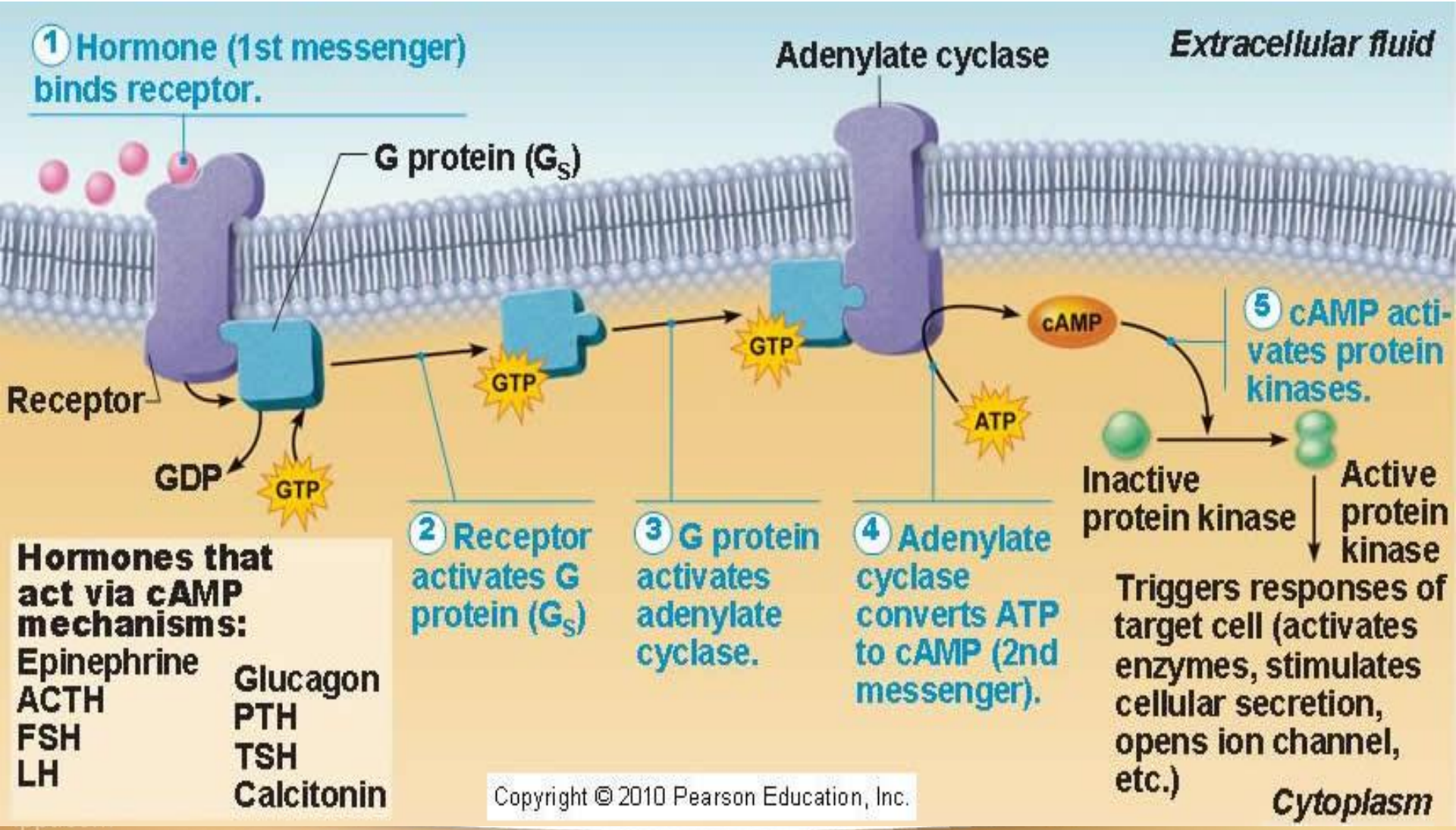
The means by which hormones exert intracellular actions is to stimulate formation of the second messenger inside the cell. The second messenger does the rest.

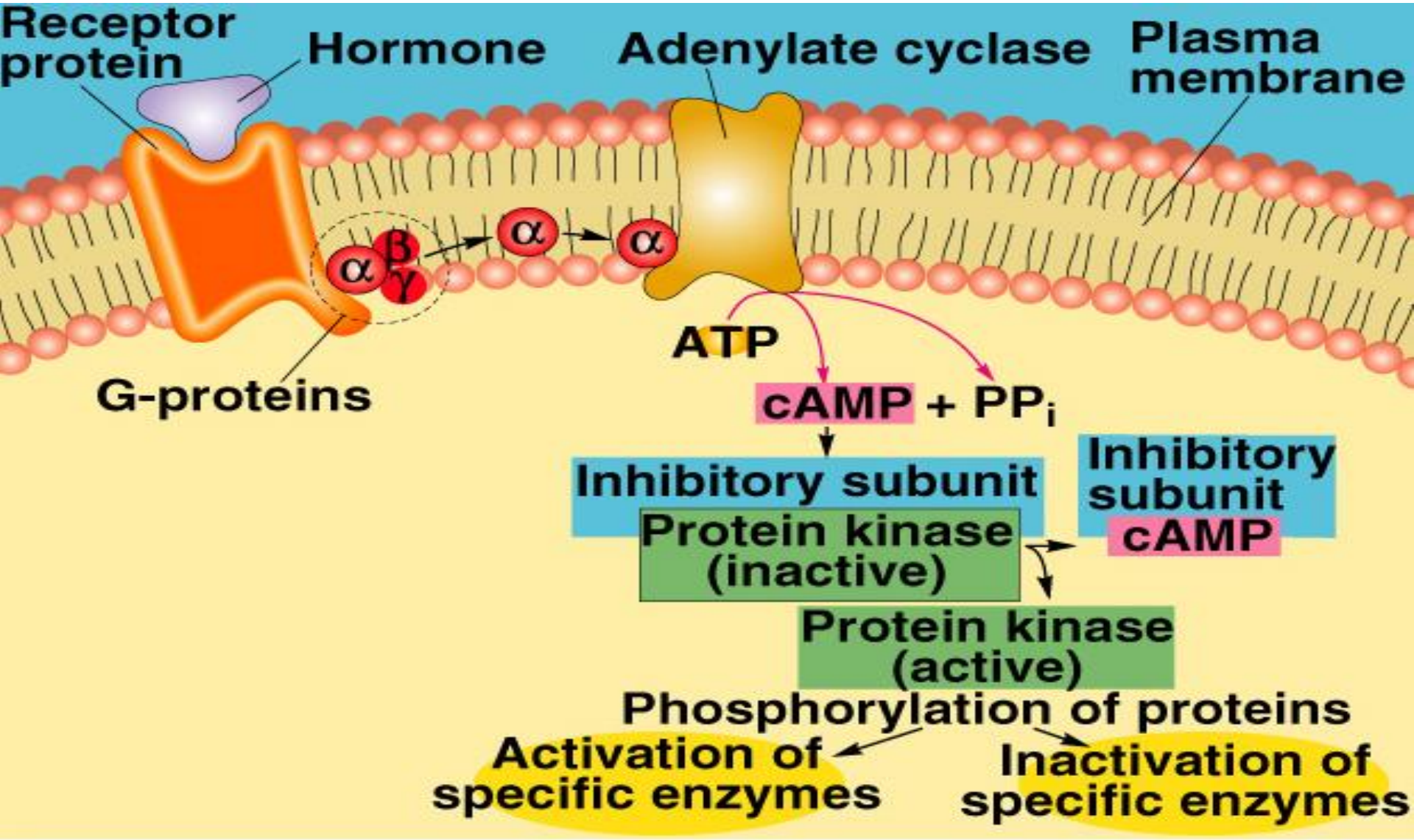


Mechanism of action (peptides and protein hormones)

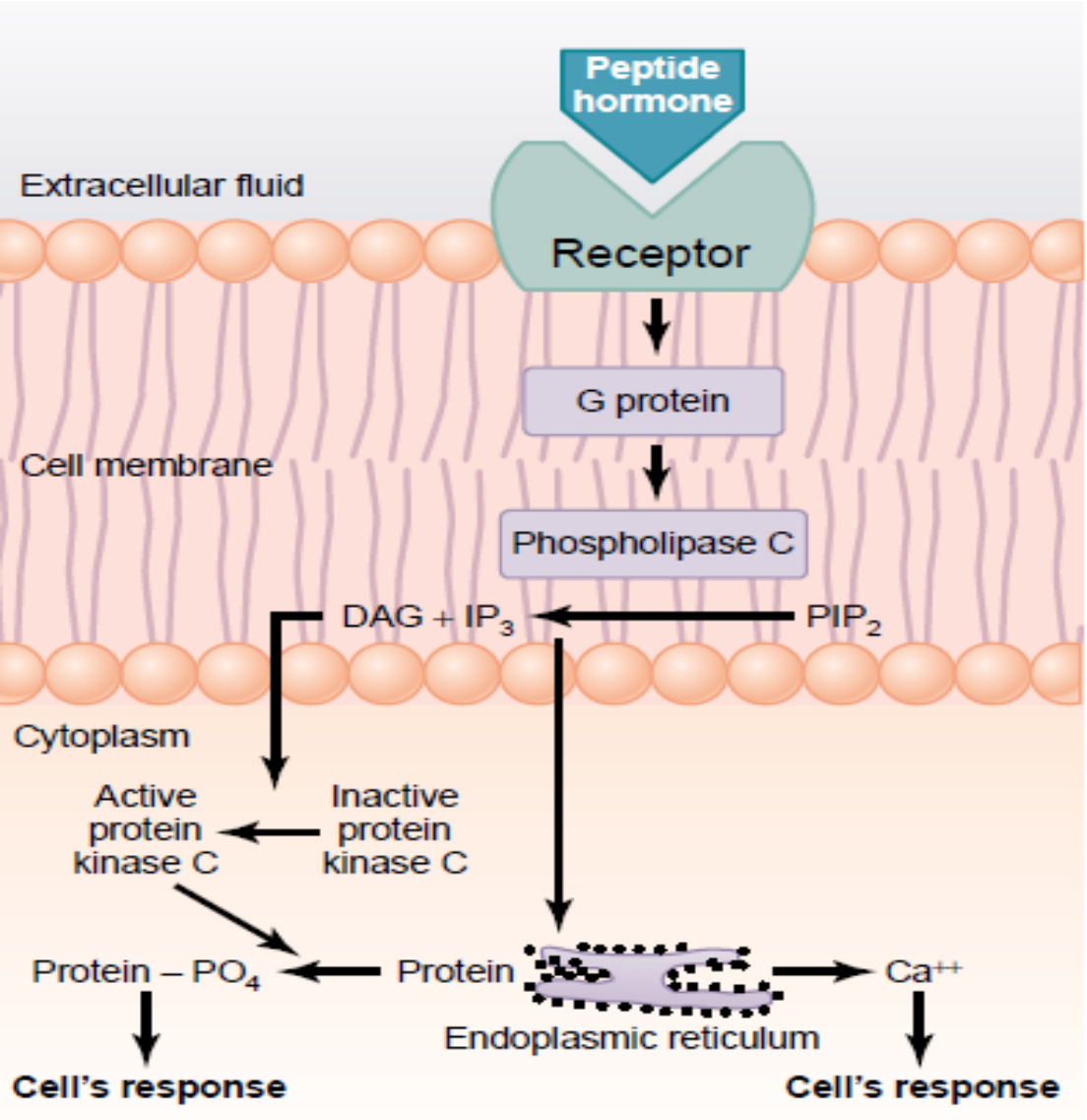


Second Messenger
(Adynylate Cyclase – cAMP system)



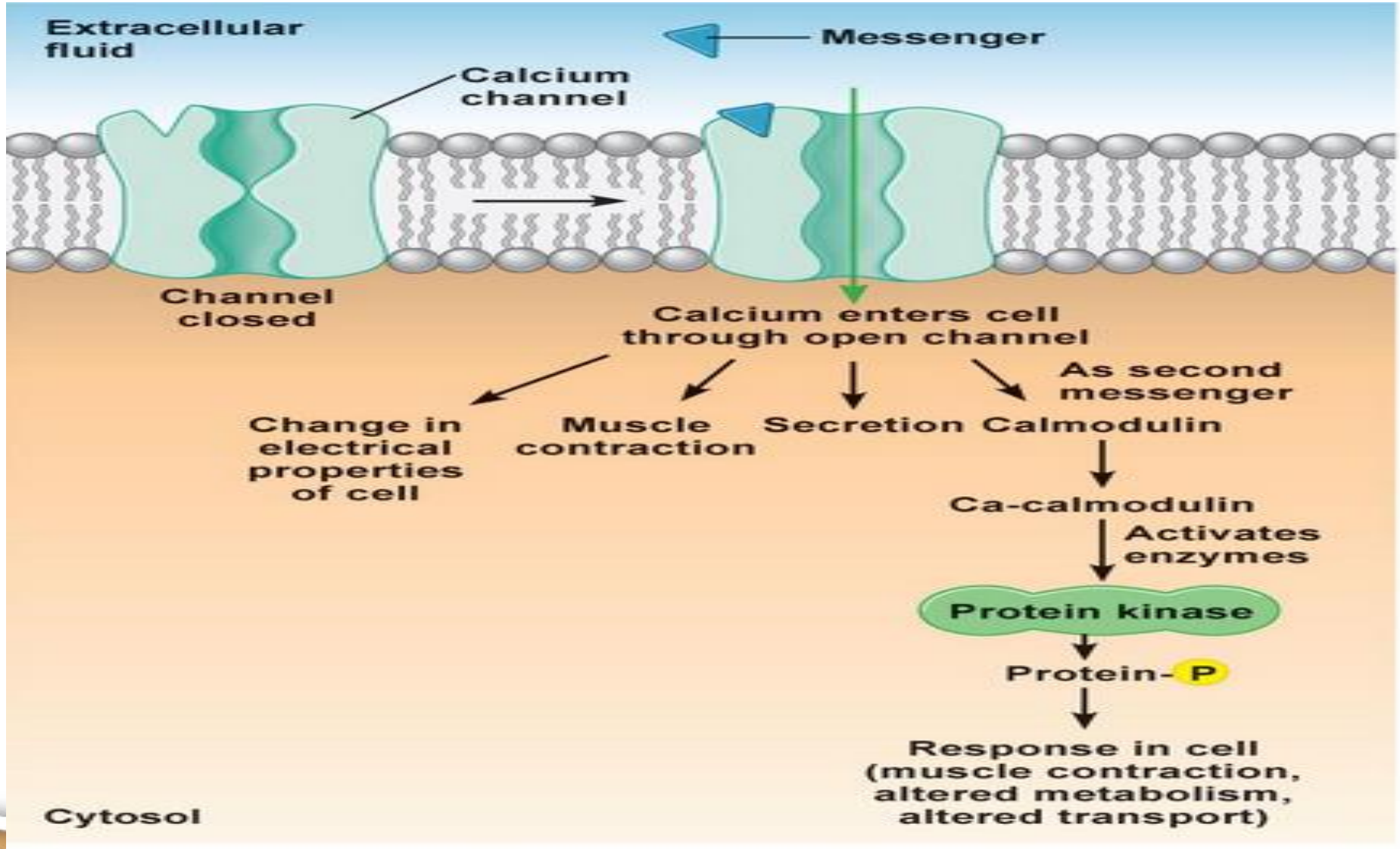

Receptor protein
Hormone
Adenylate cyclase
Plasma membrane
α
β
γ
α
α
G-proteins
ATP
cAMP + PPi
Inhibitory subunit
Protein kinase (inactive)
Inhibitory subunit
cAMP
Protein kinase (active)
Phosphorylation of proteins
Activation of specific enzymes
Inactivation of specific enzymes

Second Messenger (Phospholipase C - IP3 system)

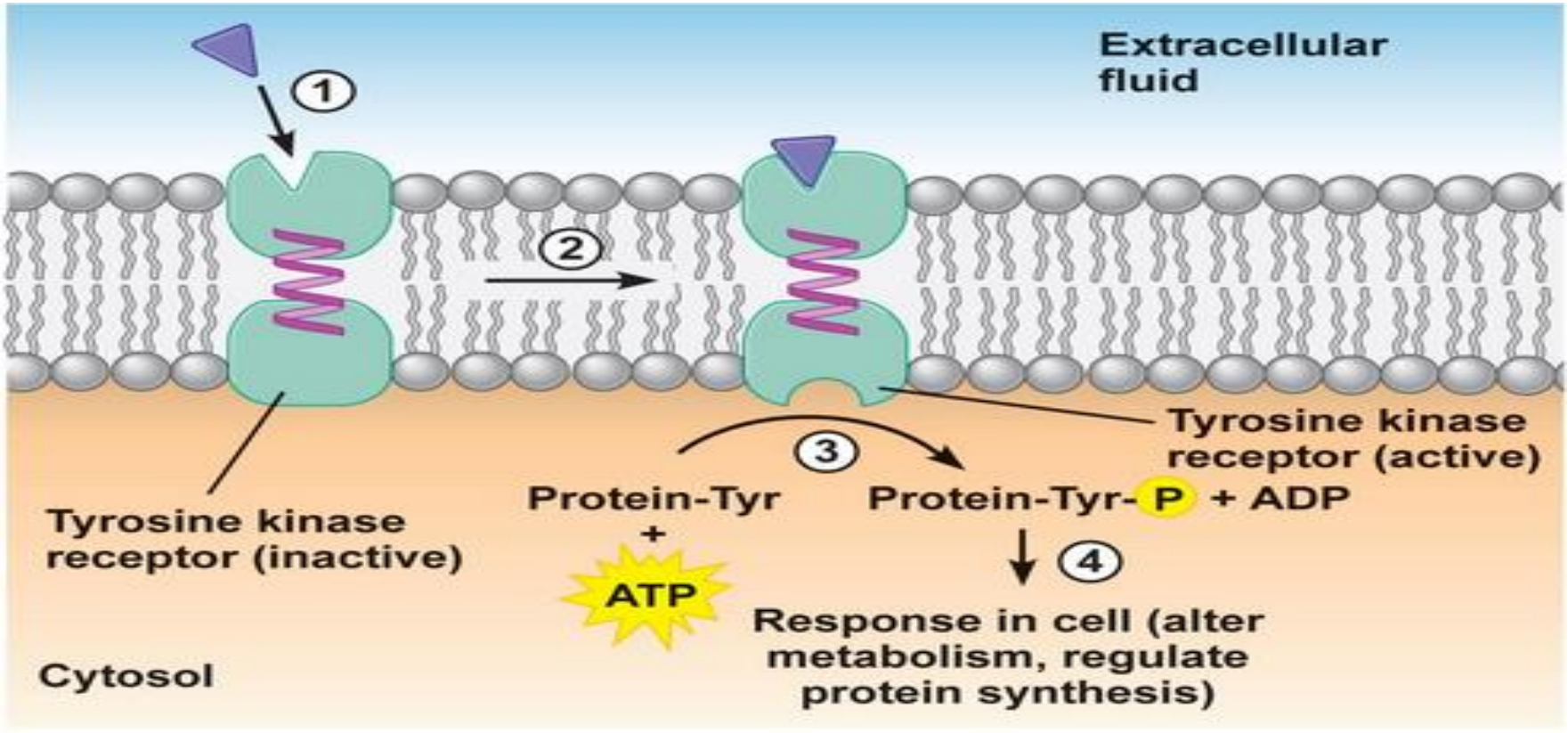


Some Hormones that use the phospholipase C second messenger system:
-Angiotensin II (vascular smooth muscle)
-Catecholamines (a receptors)
-Gonadotropin-releasing hormone (GnRH)
-Growth hormone–releasing hormone (GHRH)
-Oxytocin
-Thyroid-releasing hormone (TRH)
-Vasopressin (V1 receptor, vascular smooth muscle)

Second Messenger
(Calcium-calmodulin system)



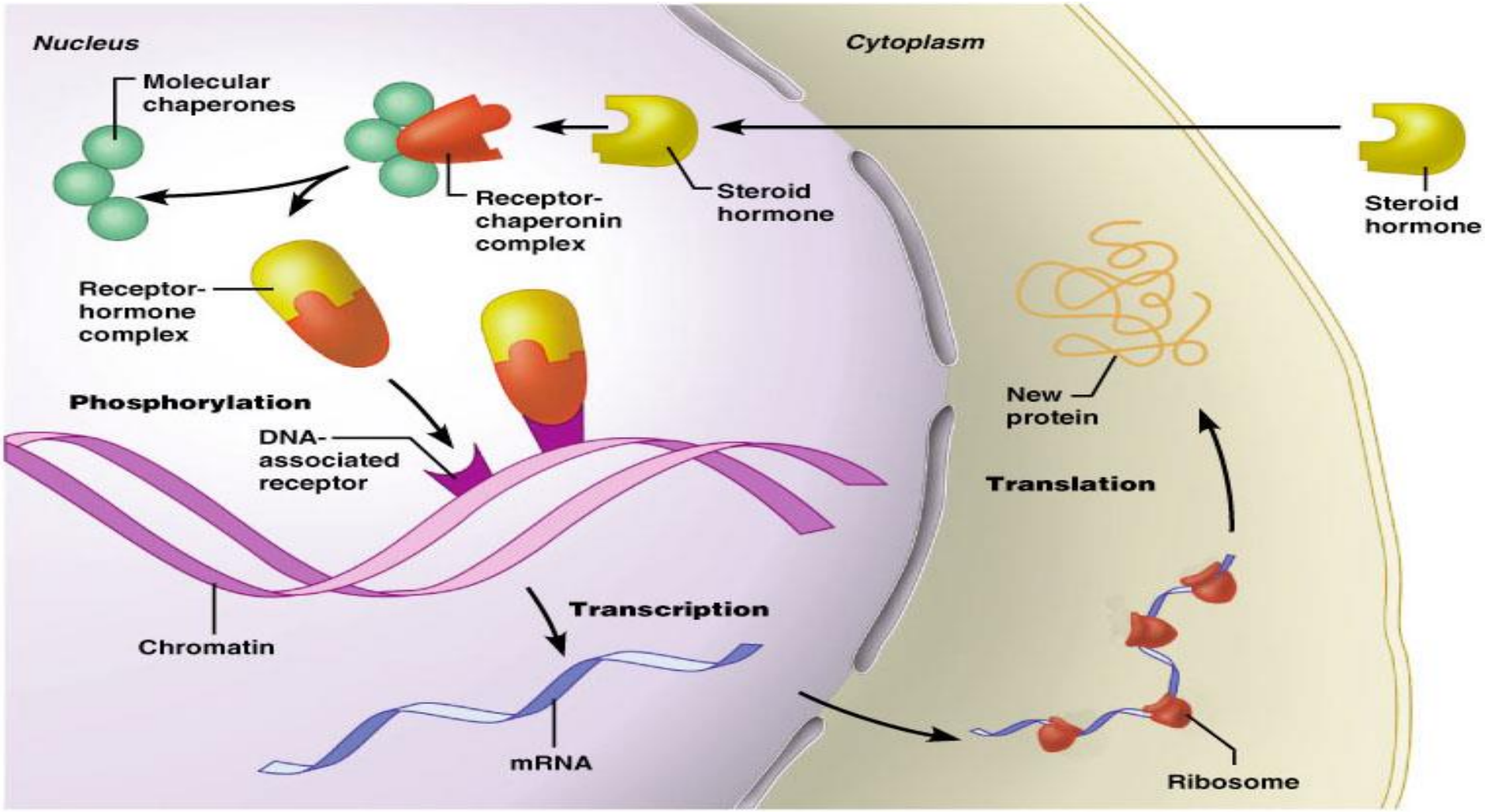
Second Messenger (Tyrosine Kinase System)



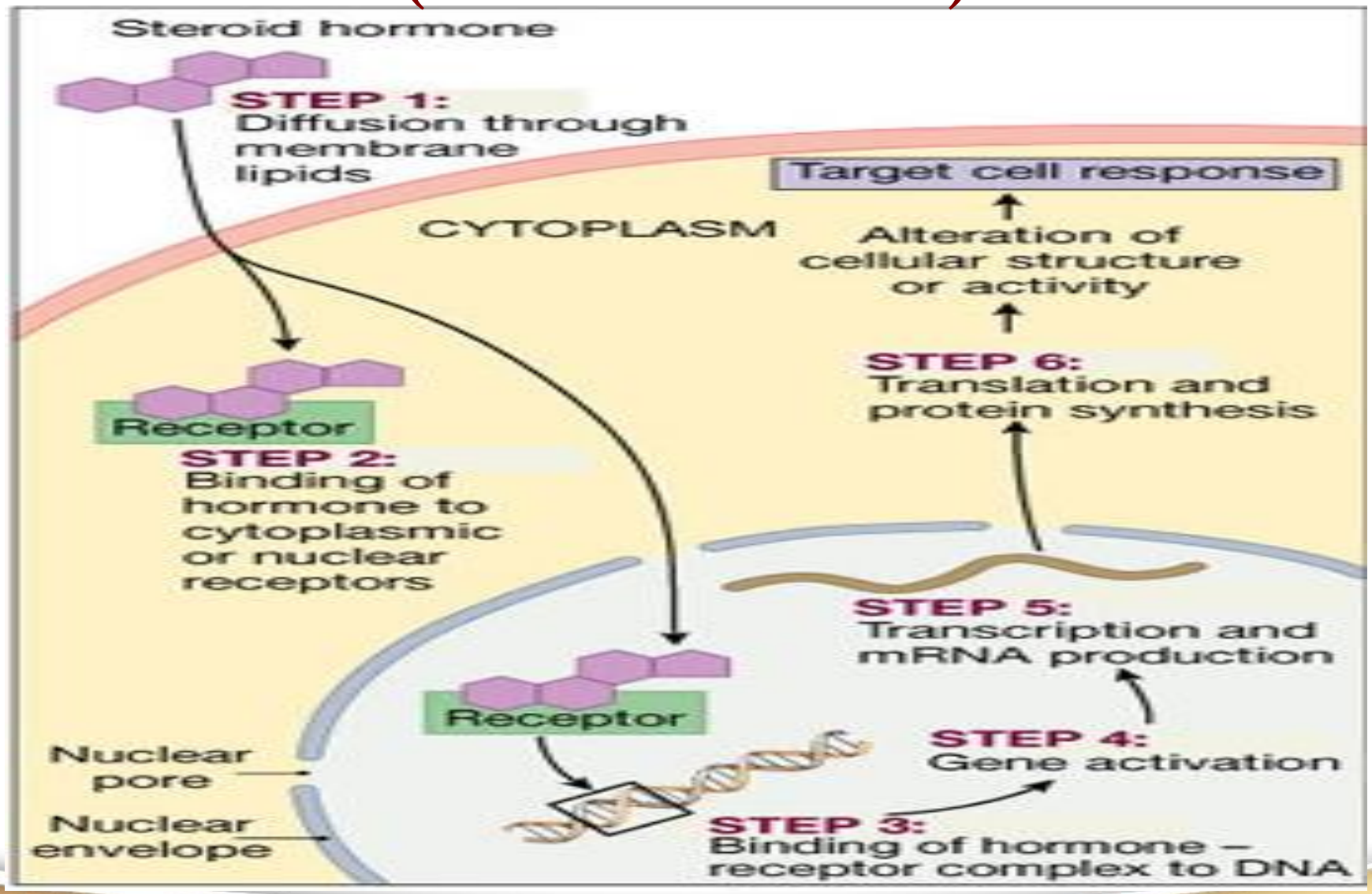
An important hormone that exerts its effects through tyrosine kinase is **insulin**.

Steroid hormones, Thyroid hormones

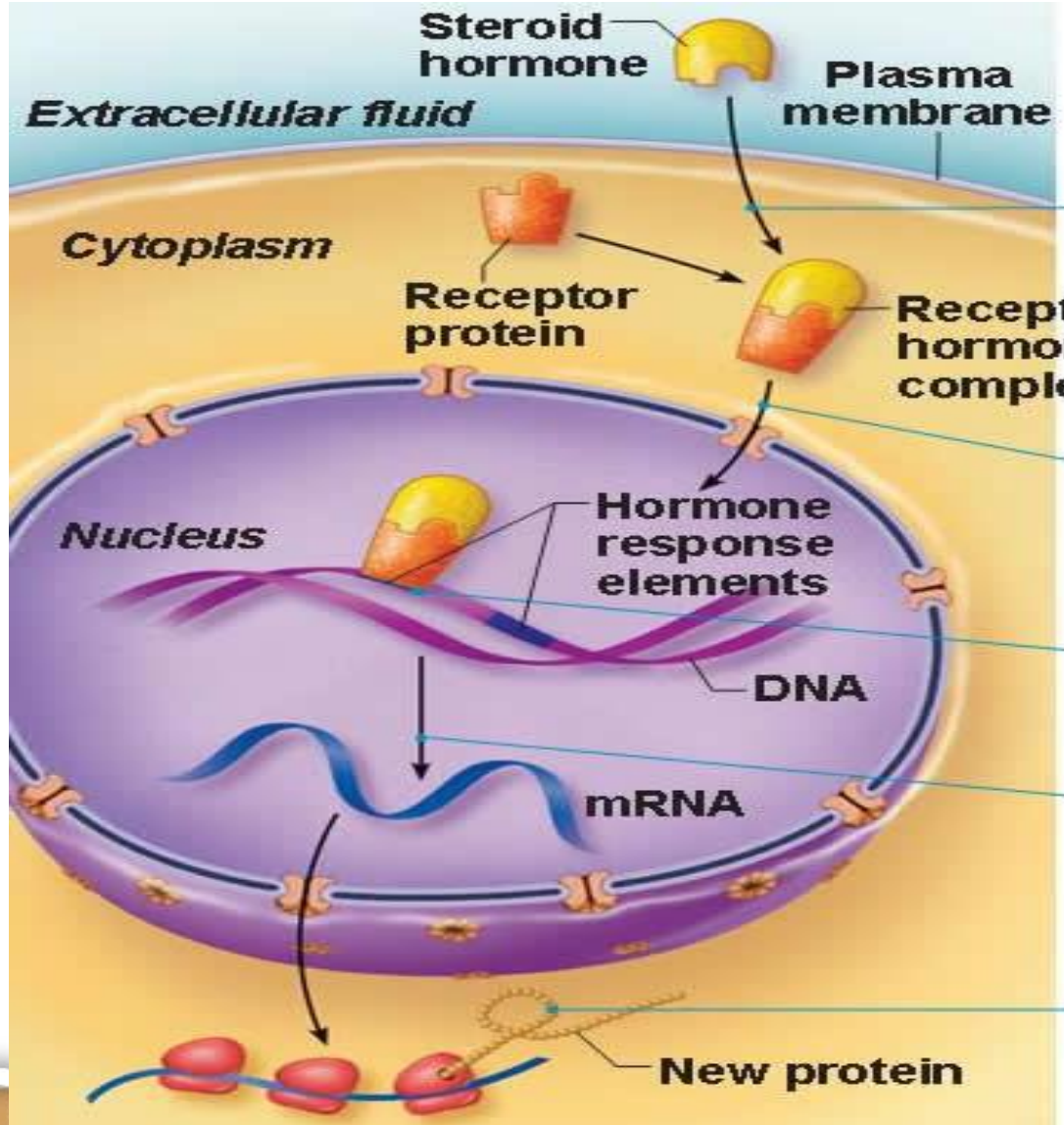
Receptor inside the cell: direct gene activation



Mechanism of action (Steroid Hormones)



Mechanism of action (Steroid Hormones)



1. The steroid hormone diffuses through the plasma membrane and binds an intracellular receptor.
2. The receptor-hormone complex enters the nucleus.
3. The receptor- hormone complex binds a hormone response element (a specific DNA sequence).
4. Binding initiates transcription of the gene to mRNA.
5. The mRNA directs protein synthesis.

Regulation of hormonal receptors

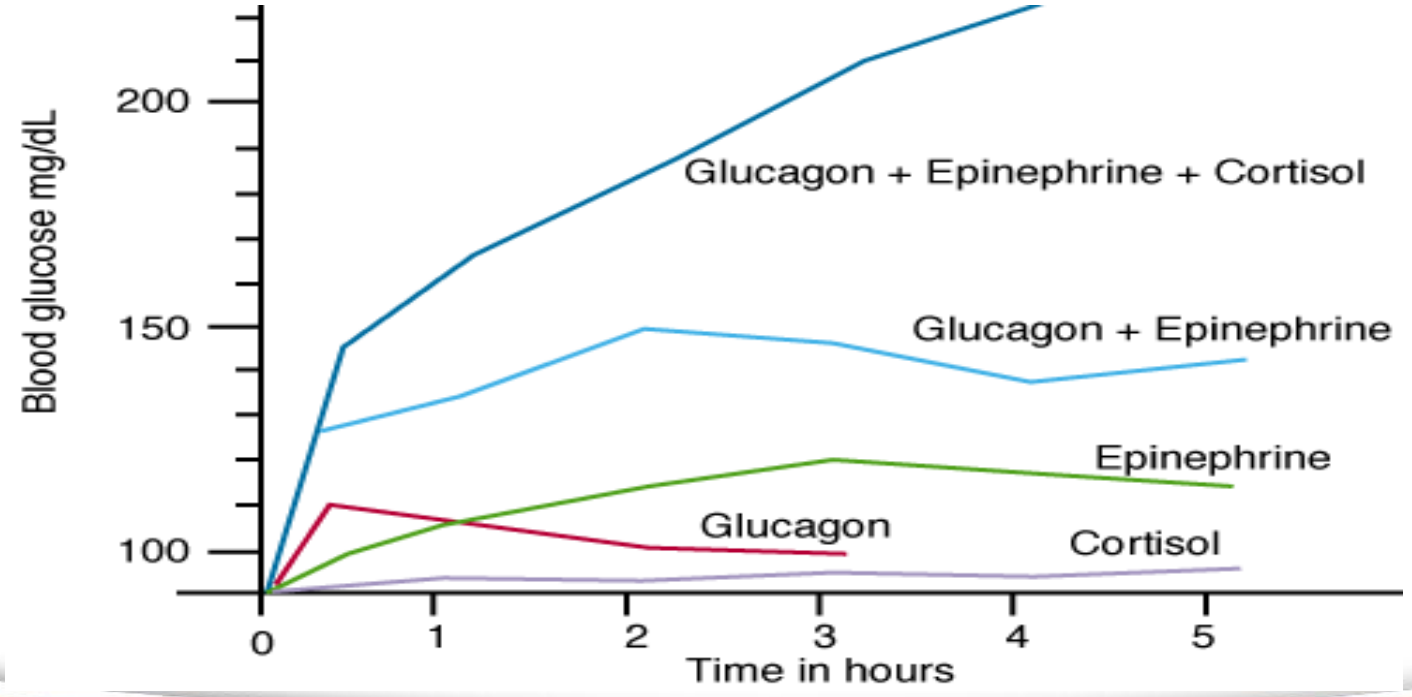
- Receptors does not remain constant
  - Inactivated or destroyed
  - Reactivated or manufactured
  - Dose-response relationship.
  - Sensitivity.
  - Number.
  - Affinity.
- Down-regulation
  - Increase hormone concentration leads to decrease in the number of active receptors
  - Most peptide hormones have pulsatile secretion which prevents down regulation
- Up-regulation
  - The hormone induces greater than normal formation of a receptor or intracellular signaling proteins

Hormones interactions at target cells

- Multiple hormones can affect a single target simultaneously
- Three types of hormone interactions:
  1. **Synergism**
  2. **Permissiveness**
  3. **Antagonism**

Synergism

- Combined action of hormones is more than just additive!
- Example: Synergistic effects of glucagon, cortisol and epinephrine on blood glucose levels.



Permissiveness

- One hormone allows another hormone to have its full effect
  - Especially during growth
- Example
  - Thyroid hormone have permissive effect on growth hormone action
  - Deficiency of thyroid hormone in infants leads to dwarfism.

Antagonism

- Antagonistic hormones have opposing physiological actions
  - Certain hormone diminishes the effect of other hormone
- Example
  - Glucagon antagonizes the action of insulin

Clearance of hormones

- Two factors control the concentration of a hormone in the blood:
  - The rate of its secretion
  - The rate of its removal (metabolic clearance)
- Hormones are cleared by:
  - Metabolic destruction by tissues
  - Binding with tissues
  - Excretion by the liver into bile
  - Excretion by the kidney into urine
- Clearance of protein bound hormones is slower than clearance of peptide hormones