ENDOCRINOLOGY (INTRODUCTION)

Dr. Hana Alzamil
King Saud University

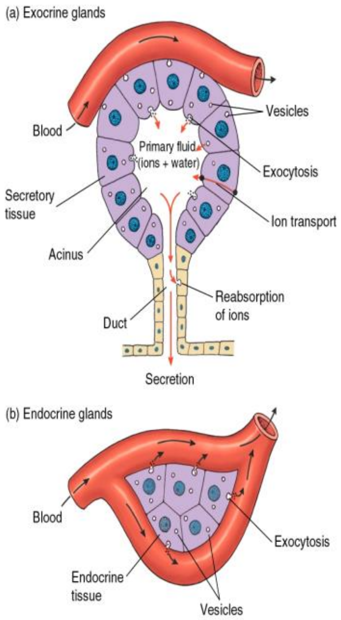
INTRODUCTION

- Endocrine vs exocrine gland
- Chemical messengers
- Hormone
  - Definition
  - Chemical structure
  - Paracrine, autocrine, endocrine, neuroendocrine
  - Transport and clearance
- Mechanism of action
  - Receptors, down-regulation and up-regulation
  - Intracellular signaling
  - Second messenger (cAMP, IP3)

INTRODUCTION

A. **Exocrine gland**
   - Ducts
   - Lumen and surfaces

B. **Endocrine gland**
   - Chemical messengers
   - Blood stream

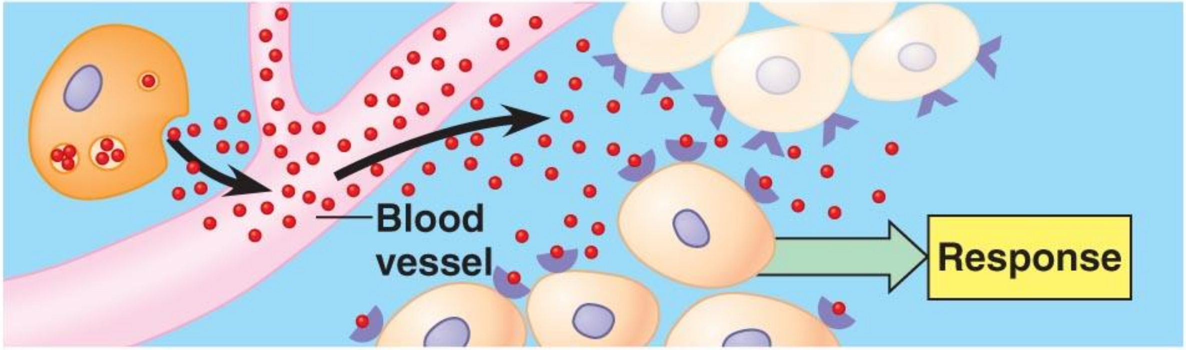


CHEMICAL MESSENGERS

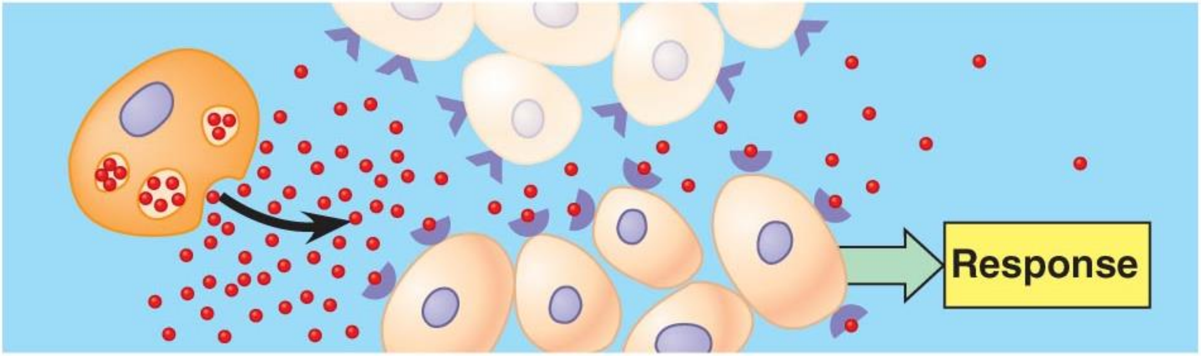
- The activities of cells, tissues and organs are coordinated by chemical messengers
  - Neurotransmitters
  - Endocrine hormones
  - Neuroendocrine hormones
  - Paracrines
  - Autocrines
  - Cytokines

SMALL GROUP ACTIVITY

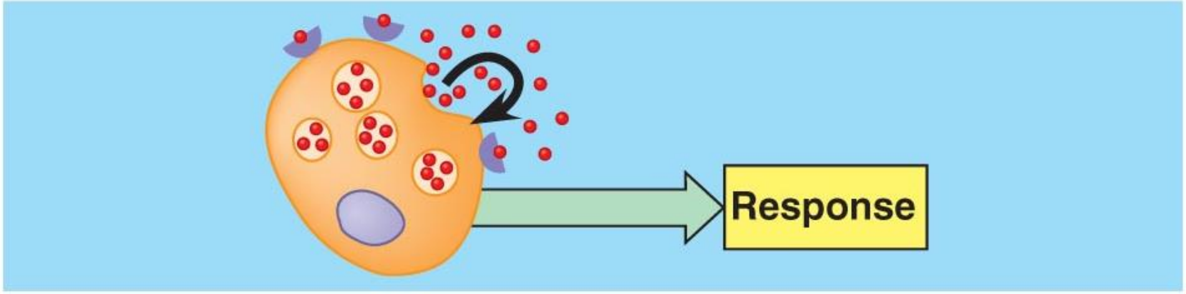
- Divide into 6 groups
- Explain
  - Neurotransmitter
  - Neurondocrine
  - Endocrine
  - Paracrine
  - Autocrine
  - Cytokines



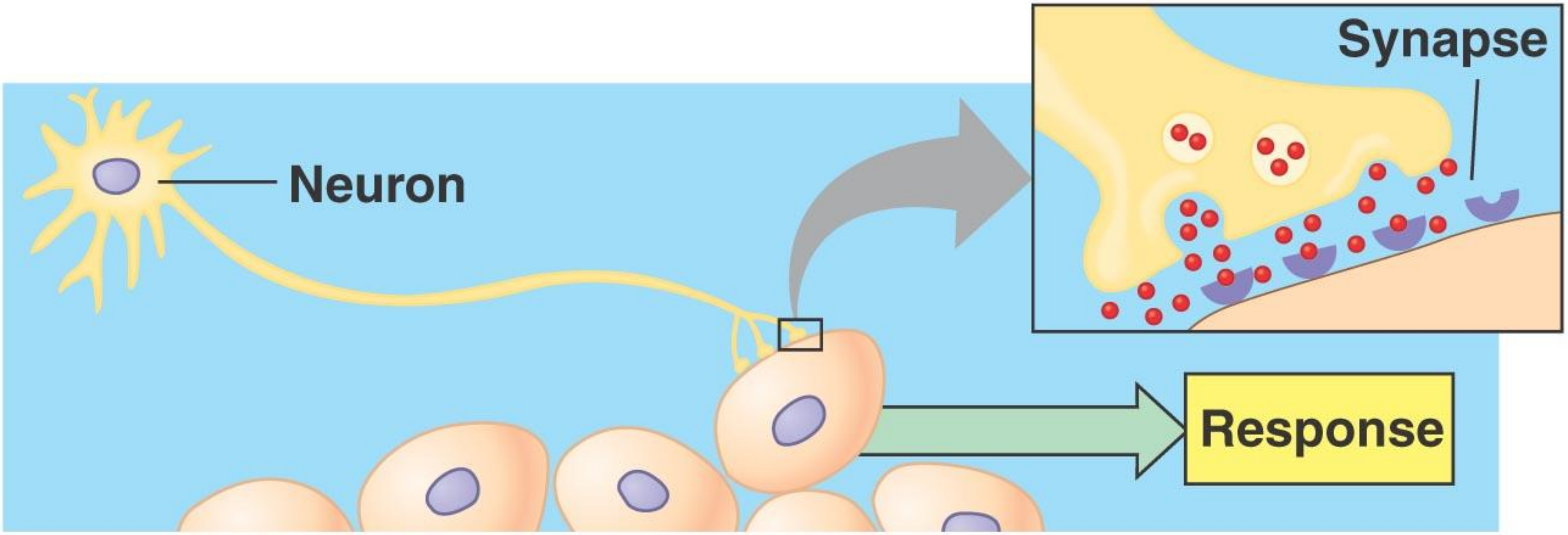
(a) Endocrine signaling



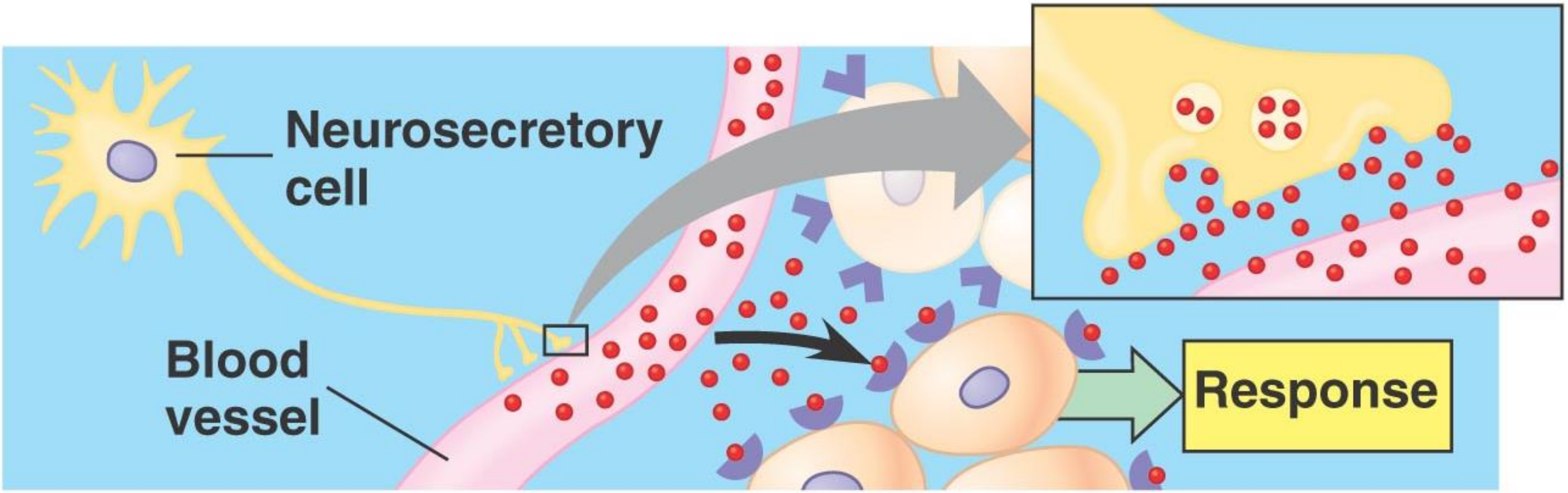
(b) Paracrine signaling



(c) Autocrine signaling



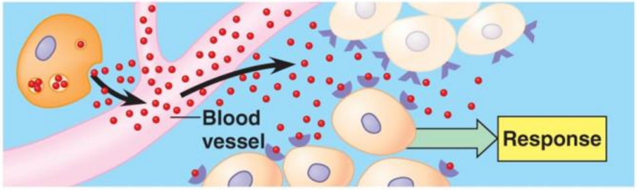
(d) Synaptic signaling



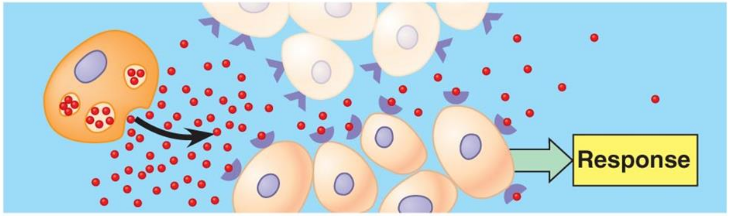
(e) Neuroendocrine signaling

CYTOKINES

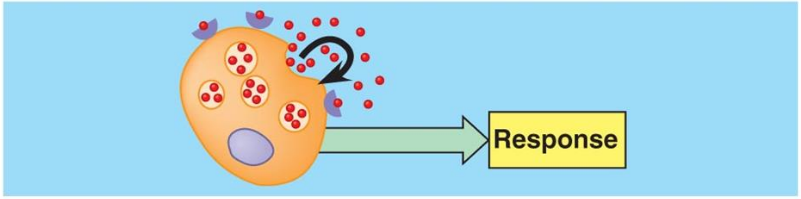
- Peptides (interleukins, lymphokines, adipokines)
- Secreted by cells into extracellular fluid.
- Can function as



(a) Endocrine signaling



(b) Paracrine signaling



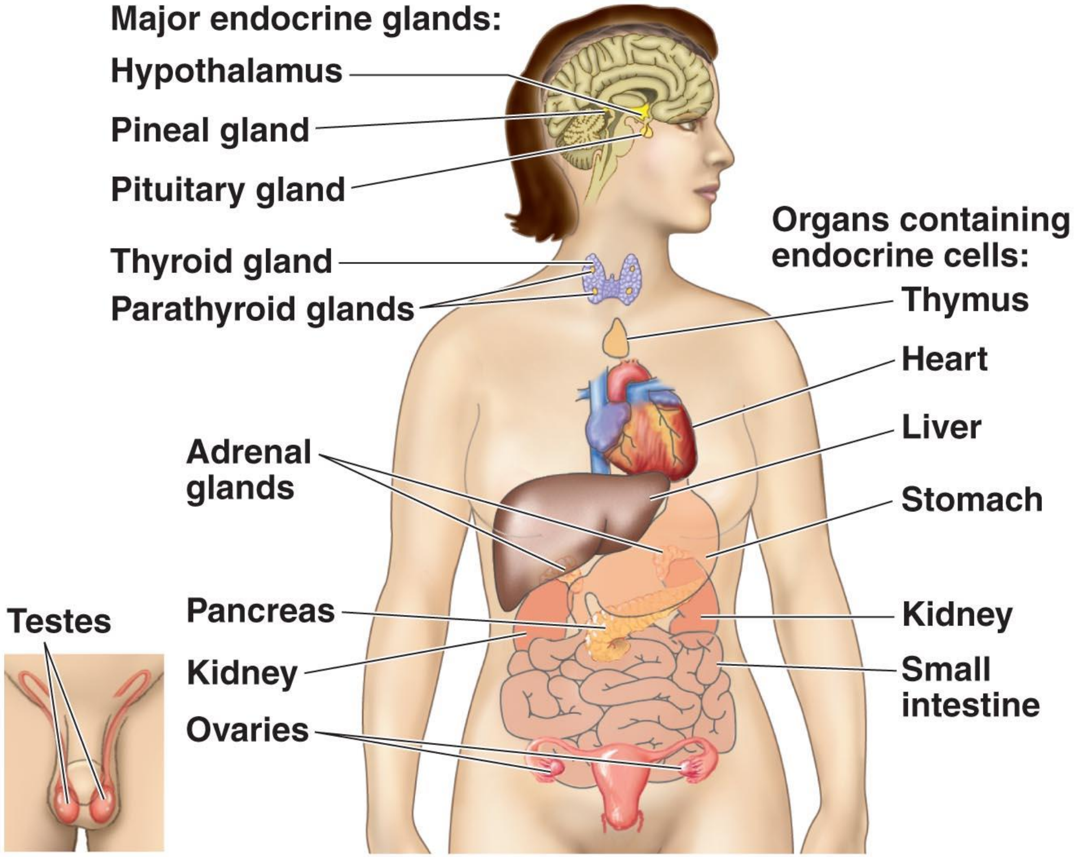
(c) Autocrine signaling

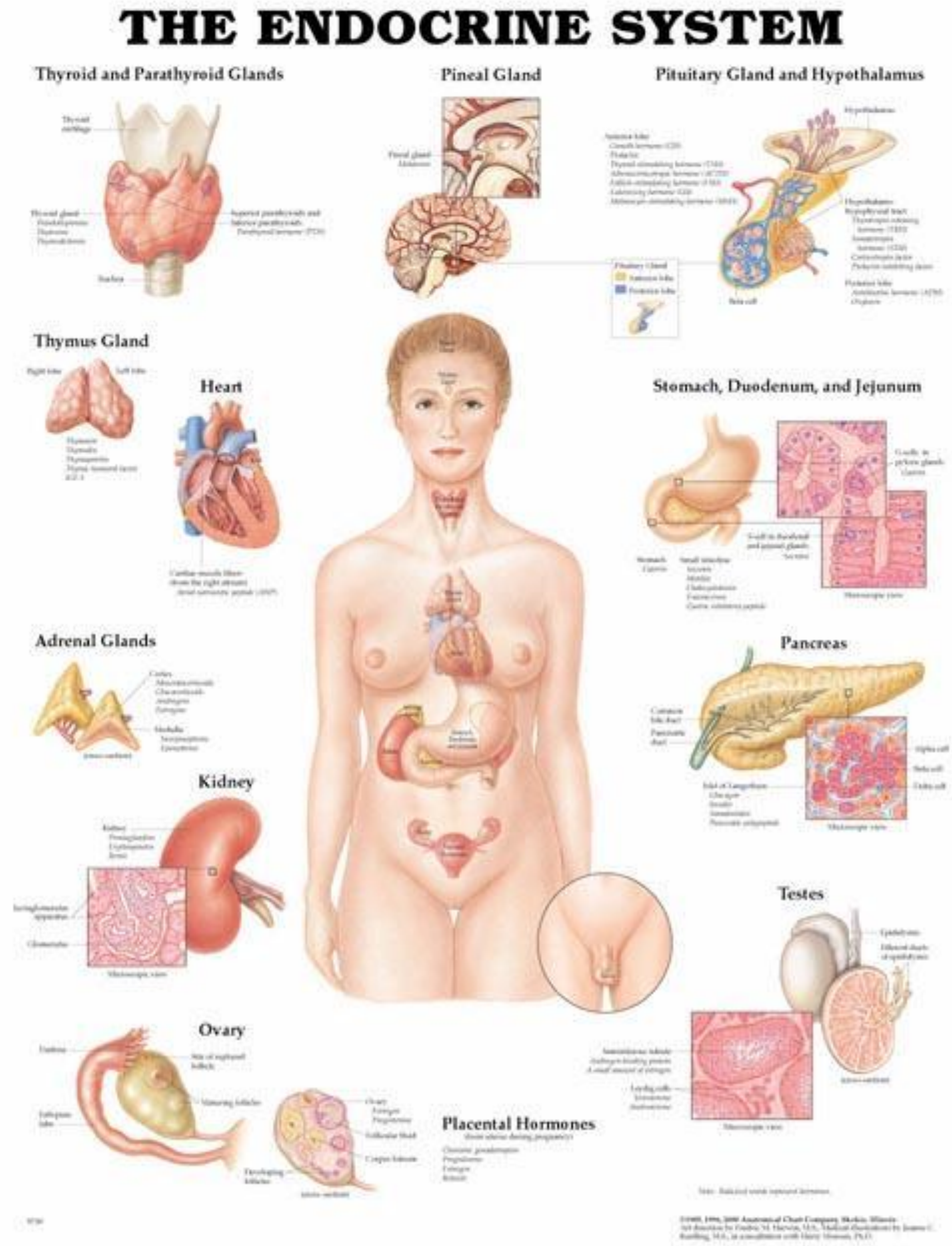
LARGE GROUP ACTIVITY

- List the endocrine glands.

INTRODUCTION

- Endocrine glands:
  - Pituitary
  - Thyroid
  - Parathyroid
  - Adrenal
  - Pancreas
  - Ovaries
  - Testes




THE ENDOCRINE SYSTEM
Thyroid and Parathyroid Glands
Pineal Gland
Pituitary Gland and Hypothalamus
Thymus Gland
Heart
Stomach, Duodenum, and Jejunum
Adrenal Glands
Pancreas
Kidney
Testes
Ovary
Placental Hormones

INTRODUCTION

- The multiple hormone systems play a key role in regulating almost all body functions:
  - Metabolism
  - Growth and development
  - Water and electrolyte balance
  - Reproduction
  - Behavior

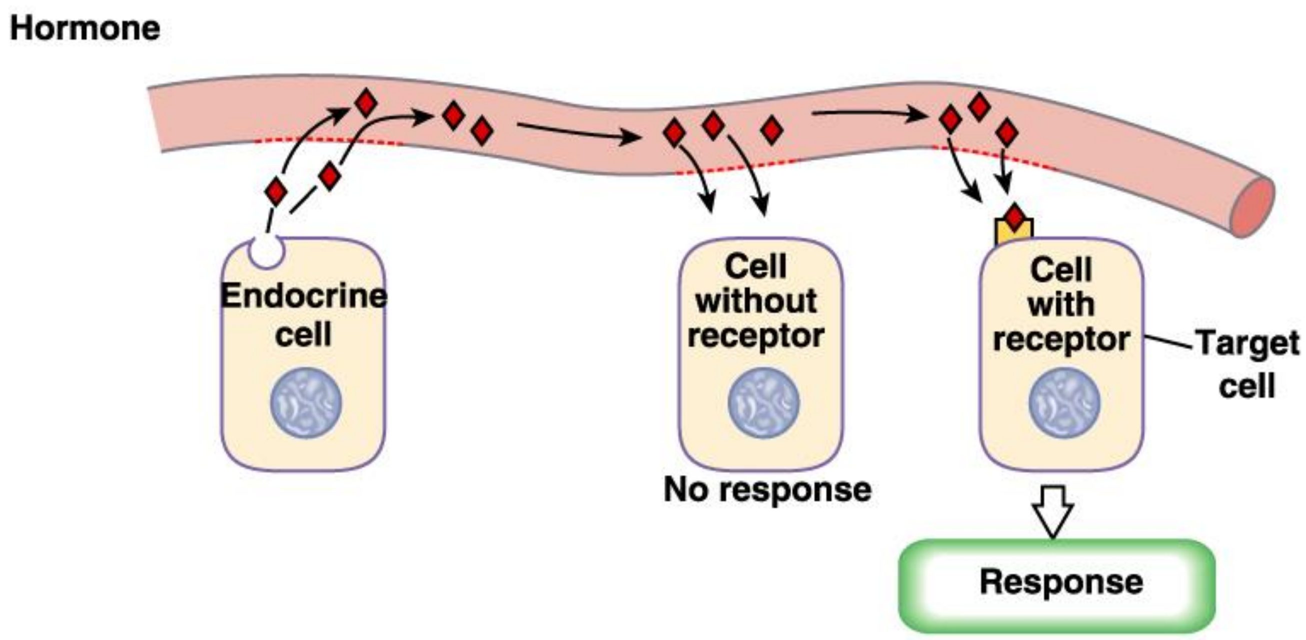
INTRODUCTION

- Definition :
  - Hormone is a chemical substance released by group of cells to control the function of other type of cells.
- Types of hormones
  - Affect many different types of cells (eg. GH and Thyroxin)
  - Affect only specific target cells (eg. ACTH and estrogen)

INTRODUCTION

- What are target cells?

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



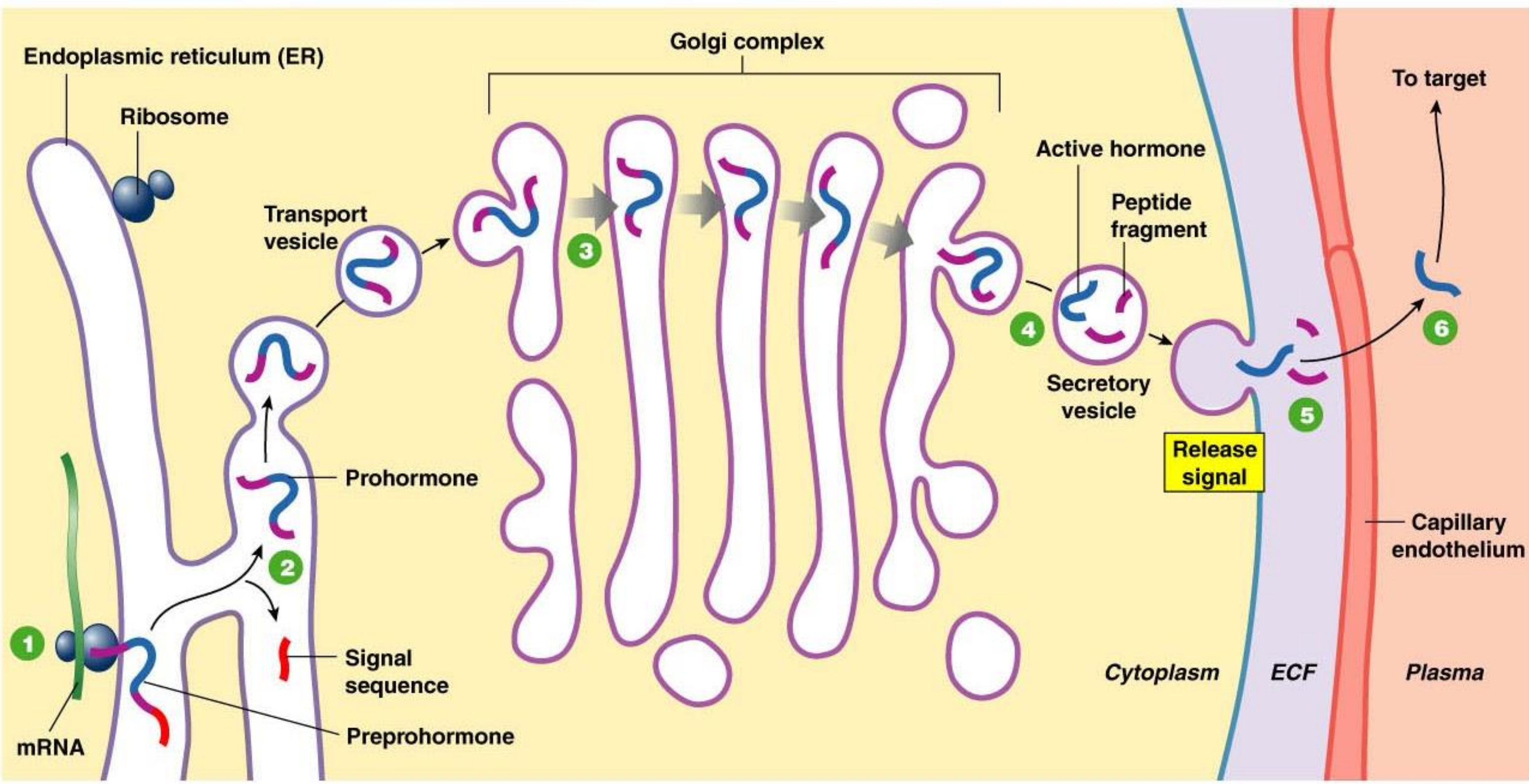
Silverthorn, Human Physiology, 3rd edition Figure 6-1&2

INTRODUCTION

- Chemical structure of hormones
  - Three general classes of hormones:
    - Proteins and polypeptides (anterior and posterior pituitary, pancreas and parathyroid hormones) stored in vesicles until needed
    - Steroids (adrenal cortex, ovarian and testicular hormones) diffuse across the cell membrane
    - Derivatives of amino acid tyrosine (thyroid hormones and catecholamines)

PEPTIDE (PROTEIN) HORMONES

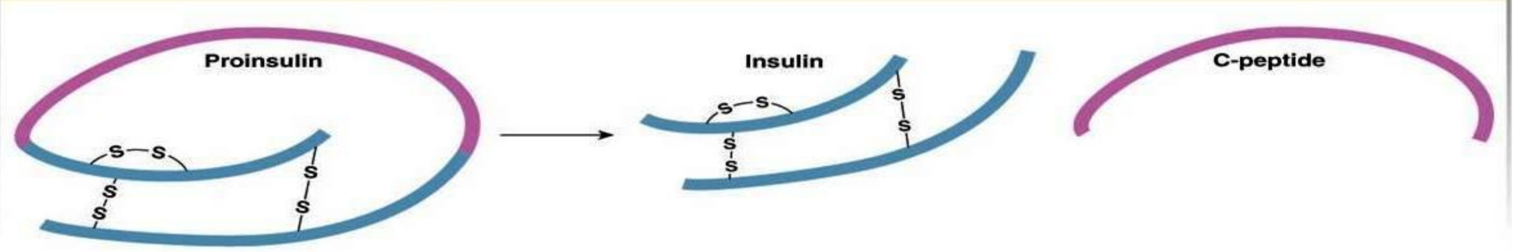
- Synthesized as preprohormone → post-translational modification to prohormone → then hormone



PEPTIDE (PROTEIN) HORMONES

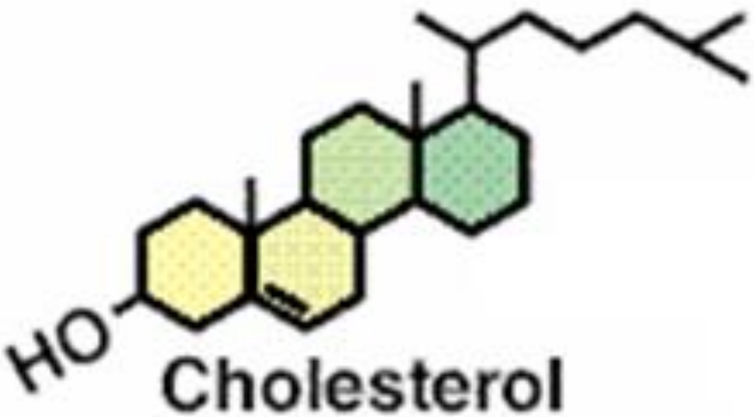
- Example of protein hormone
  - Insulin

(c) **The peptide chain of insulin's prohormone folds back on itself with the help of disulfide (S-S) bonds. The prohormone cleaves to insulin and C-peptide.**



STEROID HORMONES

- Secreted by gonads, adrenals, placenta
- Derived from cholesterol (lipophilic)
  - Cross membranes (no storage)
- On-demand synthesis (SER)
- Usually Bound to Carrier proteins



AMINE HORMONES

- Derived from tyrosine or tryptophan
- 3 groups
  - Tryptophan ⇒ Melatonin
  - Tyrosine ⇒ Catecholamines

    behave like peptide hormones
  - Tyrosine ⇒ Thyroid hormones

    behave like steroid hormones

TRANSPORT OF HORMONES

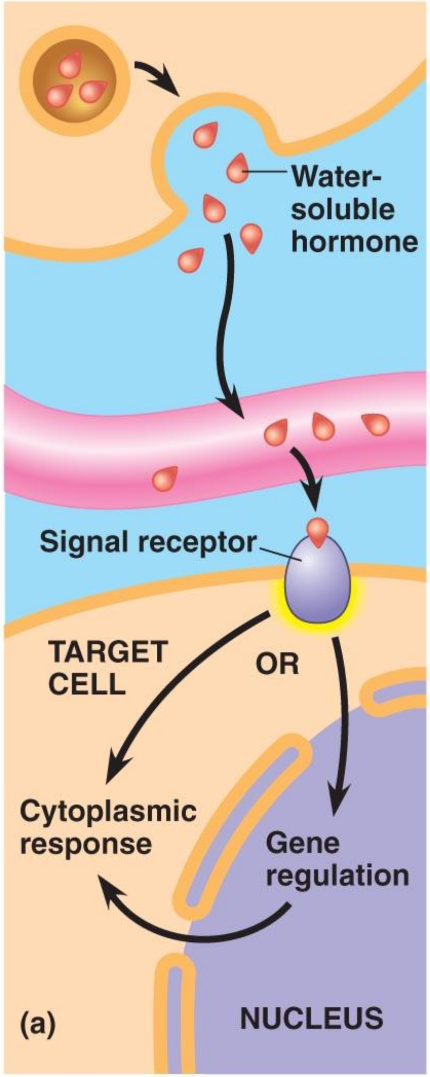
- Water soluble hormones- hydrophilic (peptides & catecholamines) dissolved in plasma

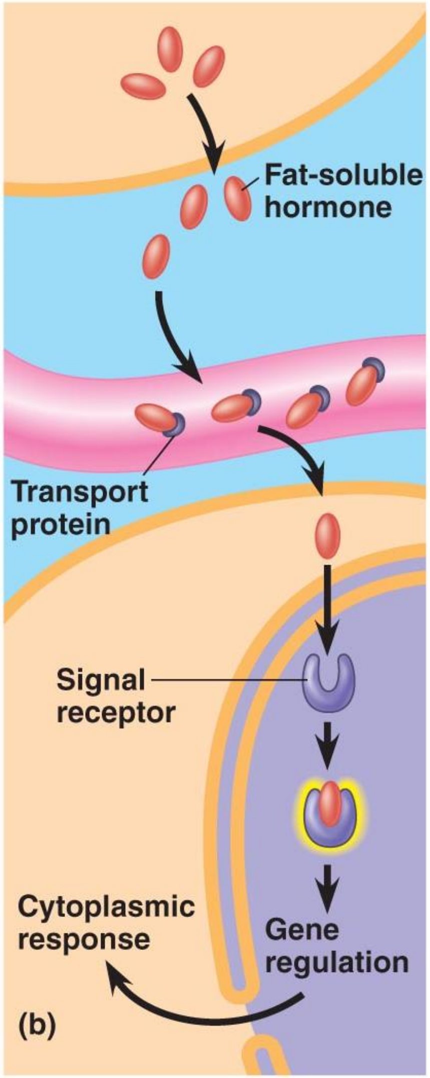
- Fat soluble hormones – hydrophobic Steroids and thyroid hormones transported bound to plasma proteins (90%),

  binding to proteins helps to

  - Provide reservoirs
  - Slow hormones clearance

DIFFERENCES BETWEEN WATER AND FAT SOLUBLE HORMONES





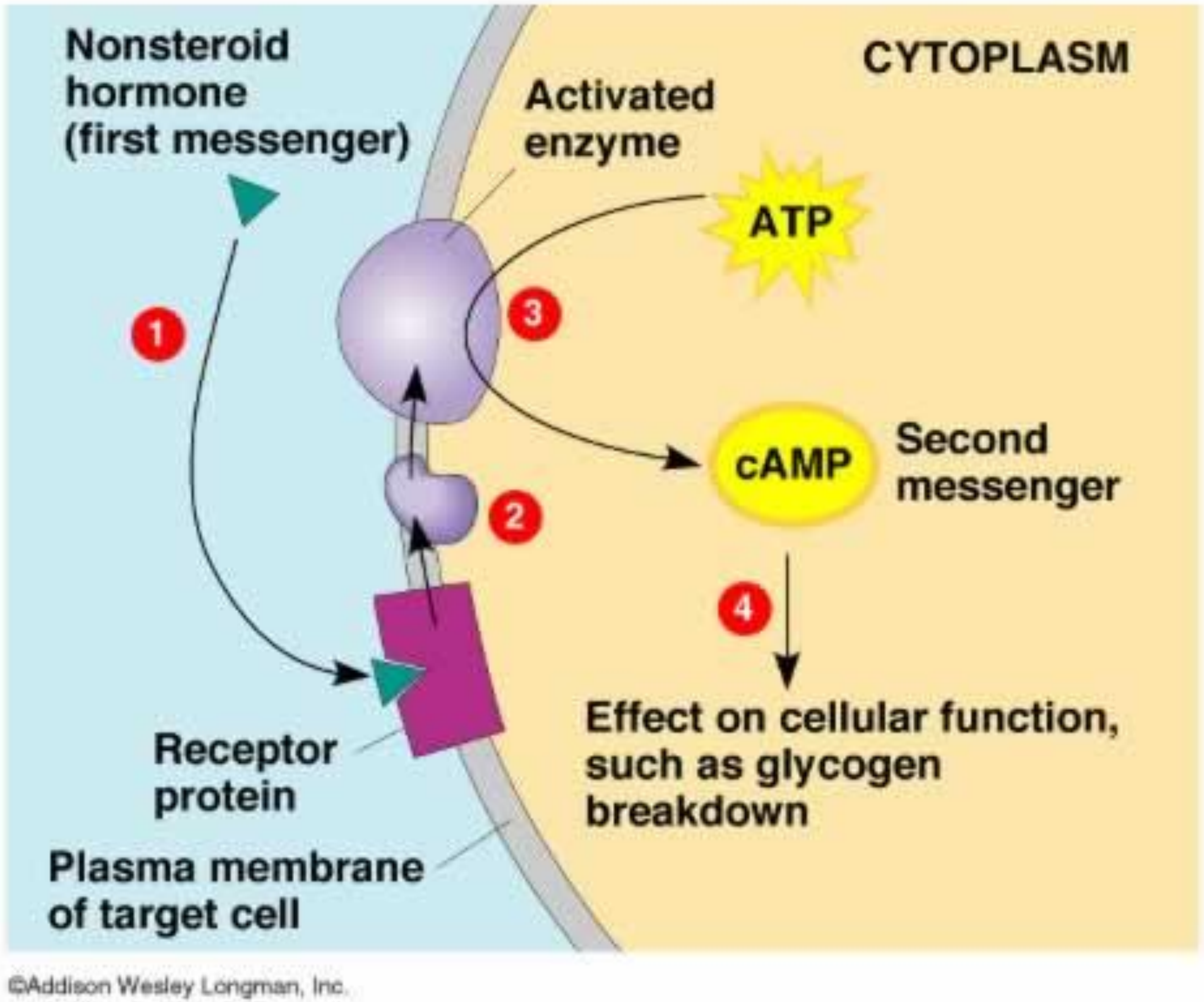
MECHANISM OF ACTION OF HORMONES

- Mechanism of action :
  1. Hormone-receptor interaction (1^{st} messenger)
  2. Enzyme activation
  3. Release of the second messenger
  4. Effects on cellular function

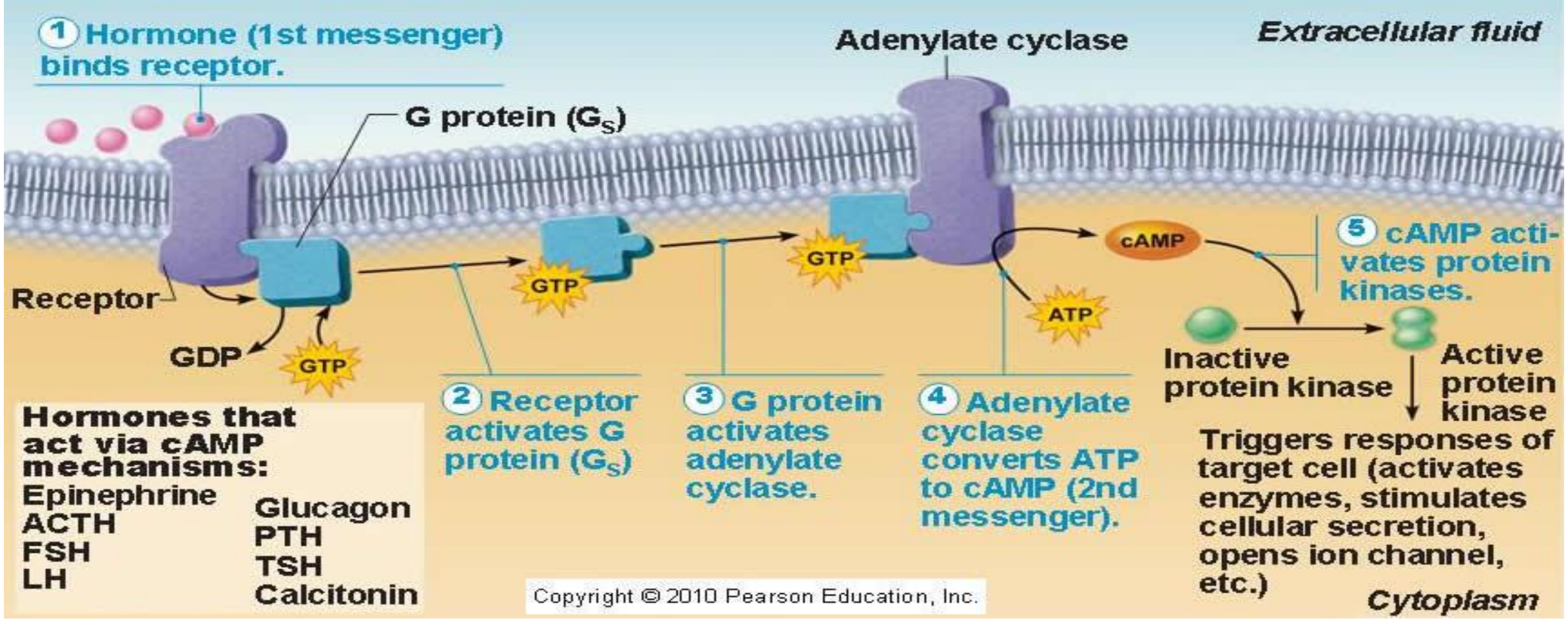
HORMONES & RECEPTORS

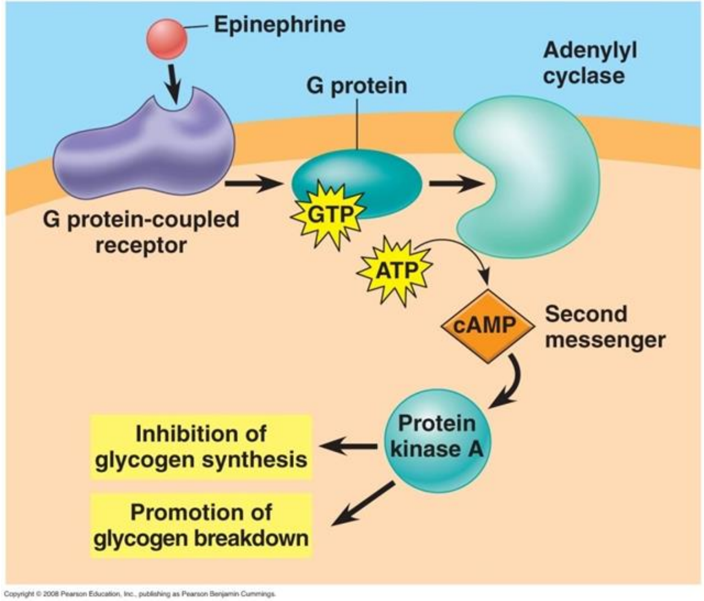
- Receptors:
  - Hormonal receptors are large proteins
  - 2000-100,000 receptors/cell
  - Receptors are highly specific for a single hormone
- Receptor's Location:
  - On the surface of cell membrane (proteins, peptides and catecholamines)
  - In the cell cytoplasm (Steroids)
  - In the cell nucleus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

MECHANISM OF ACTION (PEPTIDES AND PROTEIN HORMONES)

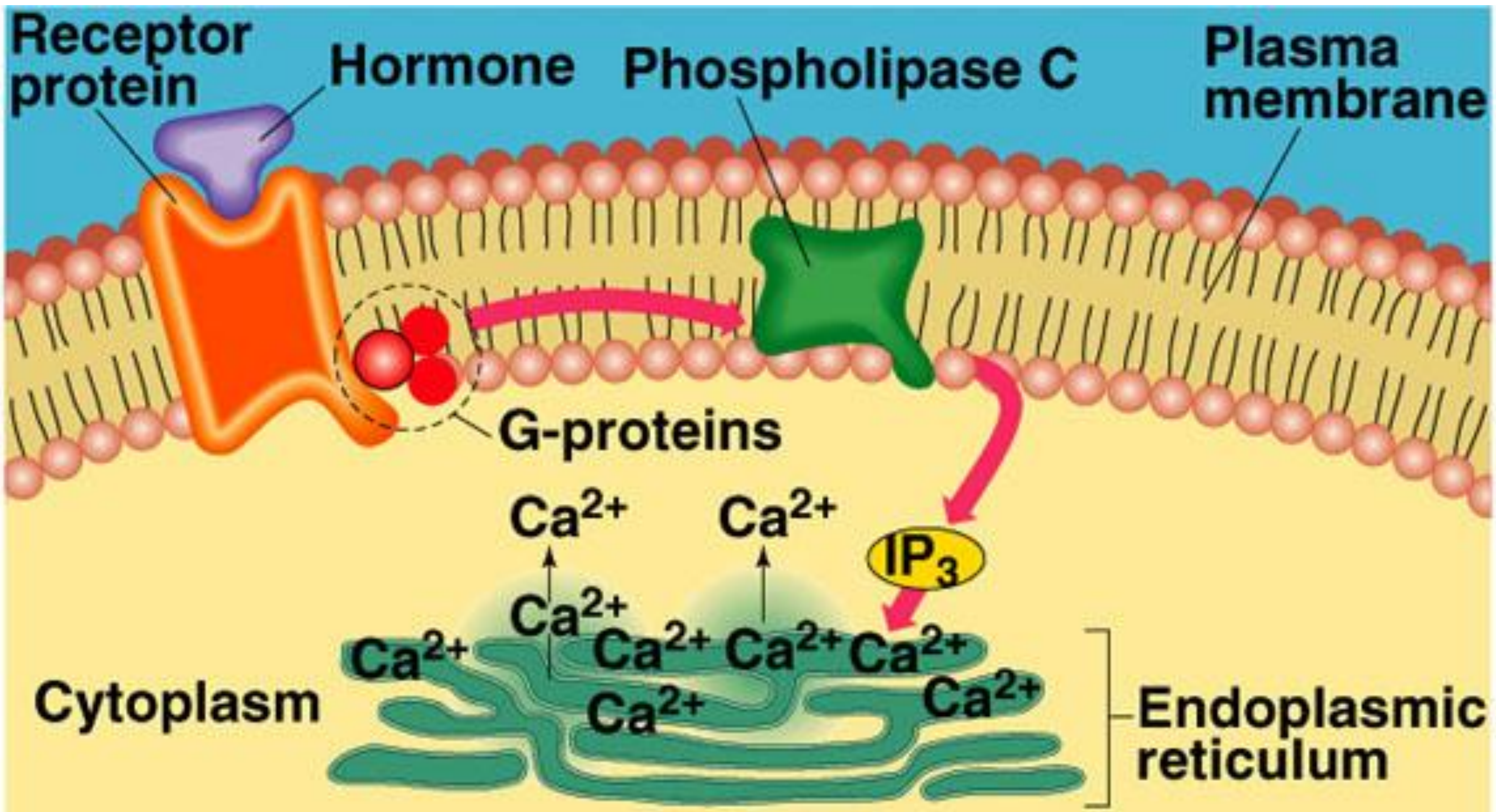


Second Messenger (Adynylate cyclase-cAMP)

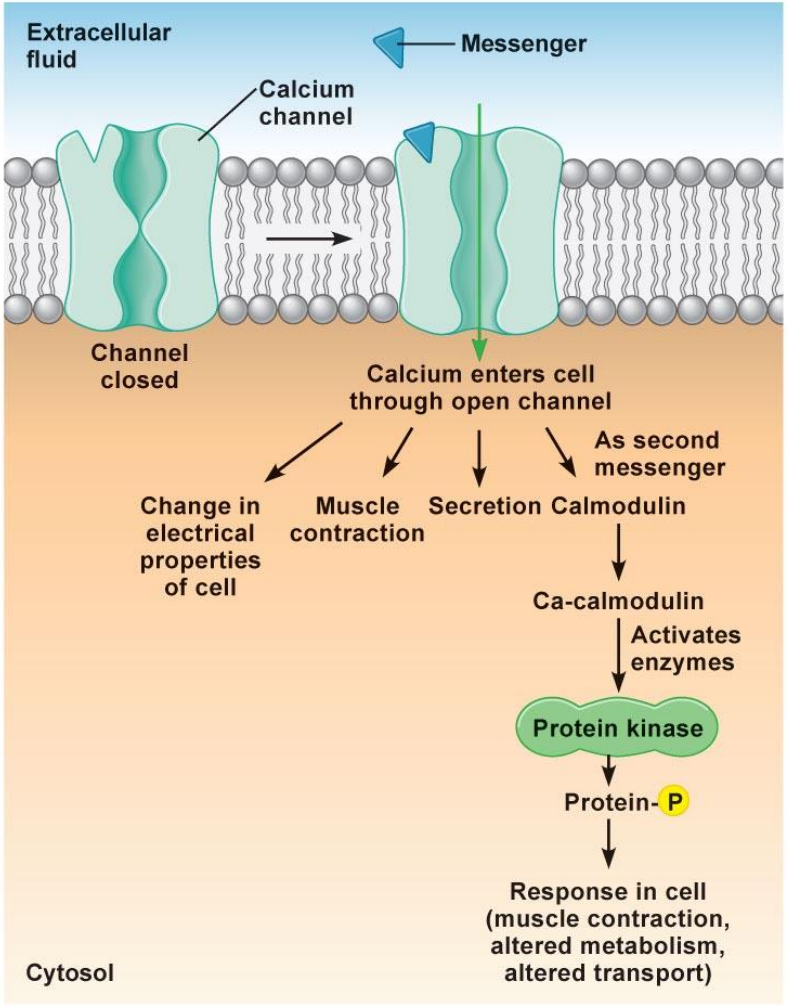




SECOND MESSENGER (PHOSPHOLIPASE C-IP_3)

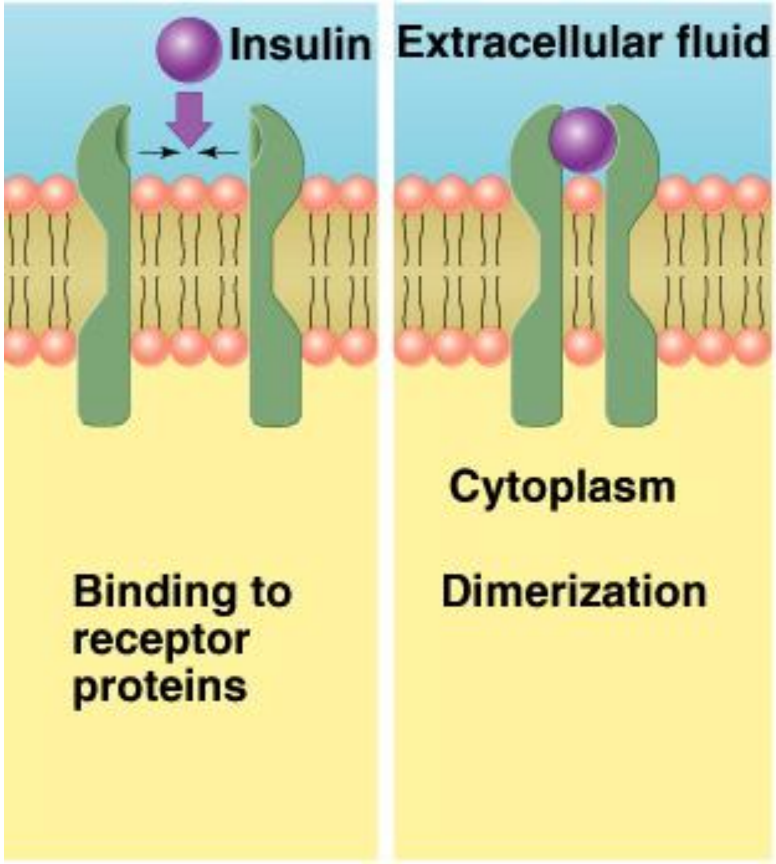


SECOND MESSENGER (CALCIUM-CALMODULIN COMPLEX)



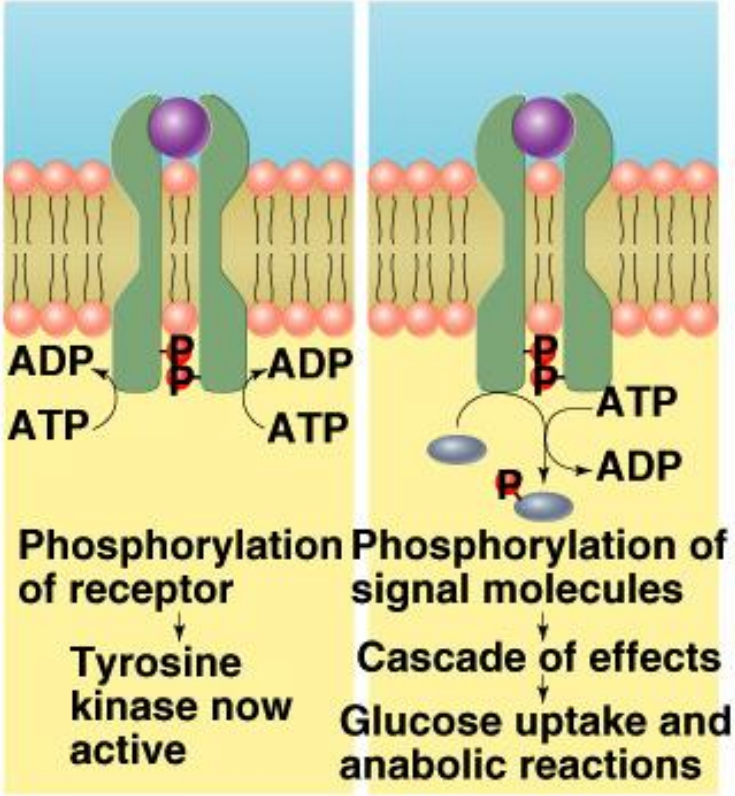
SECOND MESSENGER (TYROSINE KINASE SYSTEM)

- Is used by insulin & many growth factors to cause cellular effects
- Surface receptor is tyrosine kinase
  - Consists of 2 units that form active dimer when insulin binds

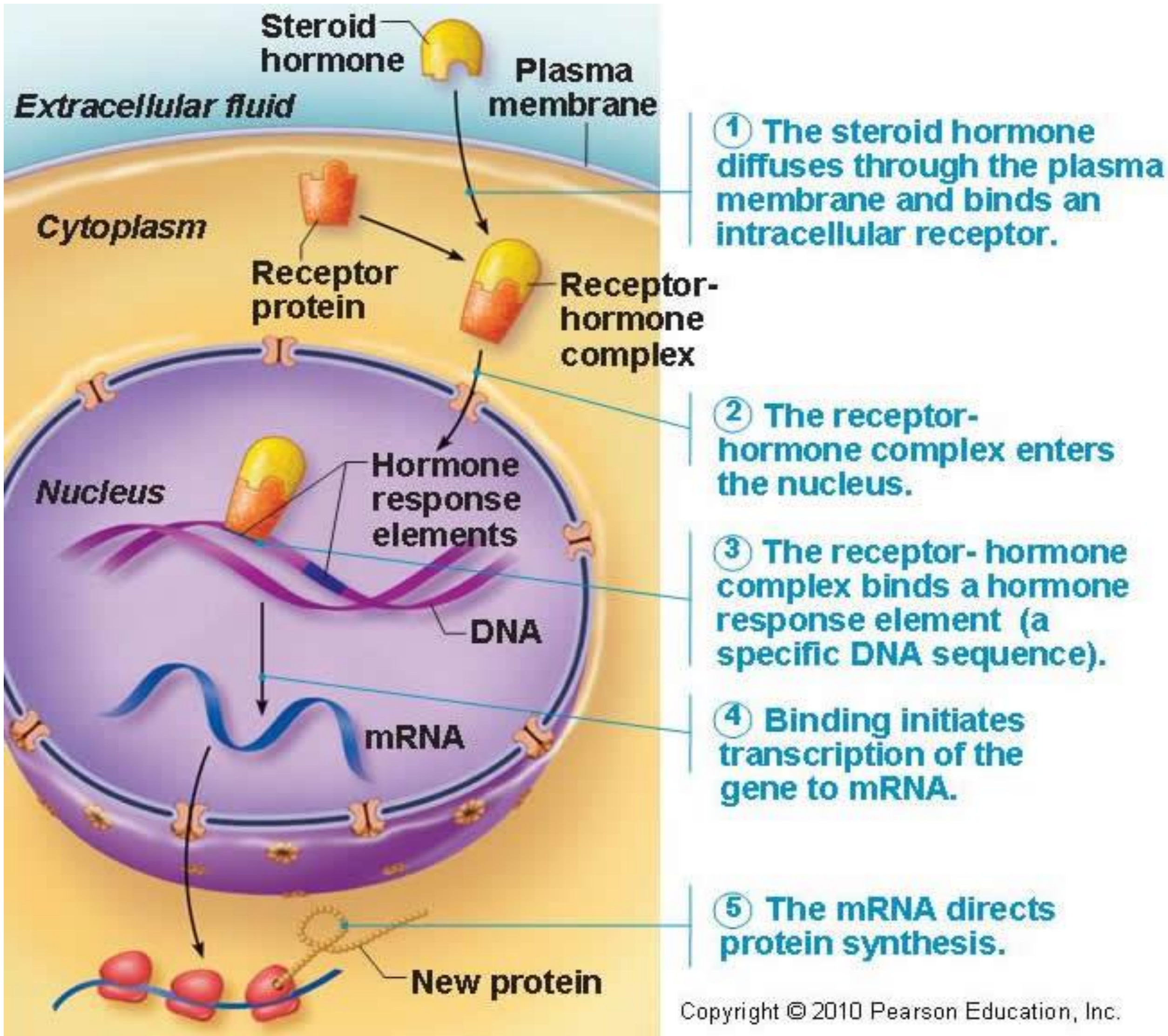


SECOND MESSENGER (TYROSINE KINASE SYSTEM)

- Activated tyrosine kinase phosphorylates signaling molecules
- Inducton of hormone/growth factor effects



MECHANISM OF ACTION (STEROID HORMONES)



REGULATION OF HORMONAL RECEPTORS

- Receptors does not remain constant
  - Inactivated or destroyed
  - Reactivated or manufactured
- Downregulation
  - Increase hormone concentration leads to decrease in the number of active receptors
  - Most peptide hormones have pulsatile secretion which prevents downregulation
- Upregulation
  - The hormone induces greater than normal formation of a receptor or intracellular signaling proteins

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

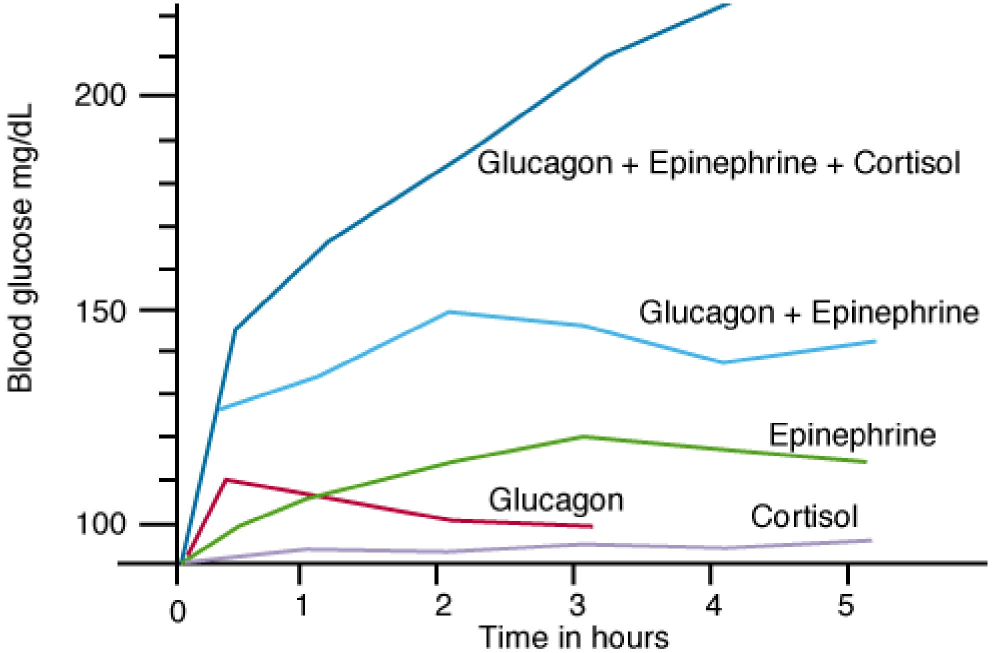
HORMONE INTERACTIONS

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

What is Synergism?
What is permissiveness?
What is antagonism?

SYNERGISM

- Combined action of hormones is more than just additive!
- Example: Blood glucose levels & synergistic effects of glucagon, cortisol and epinephrine



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 –
  - Hormone B diminishes the effect of hormone A
- Example
  - Glucagon antagonizes the action of insulin
  - **Can you mention another example?**