Système endocrine

- Homeostasis
- Cell membrane structure
- Cell membrane proteins
- Synthesis and Exocytosis of secreted proteins
- Transcription and Translation
- Transmembrane transport
- Membrane potential

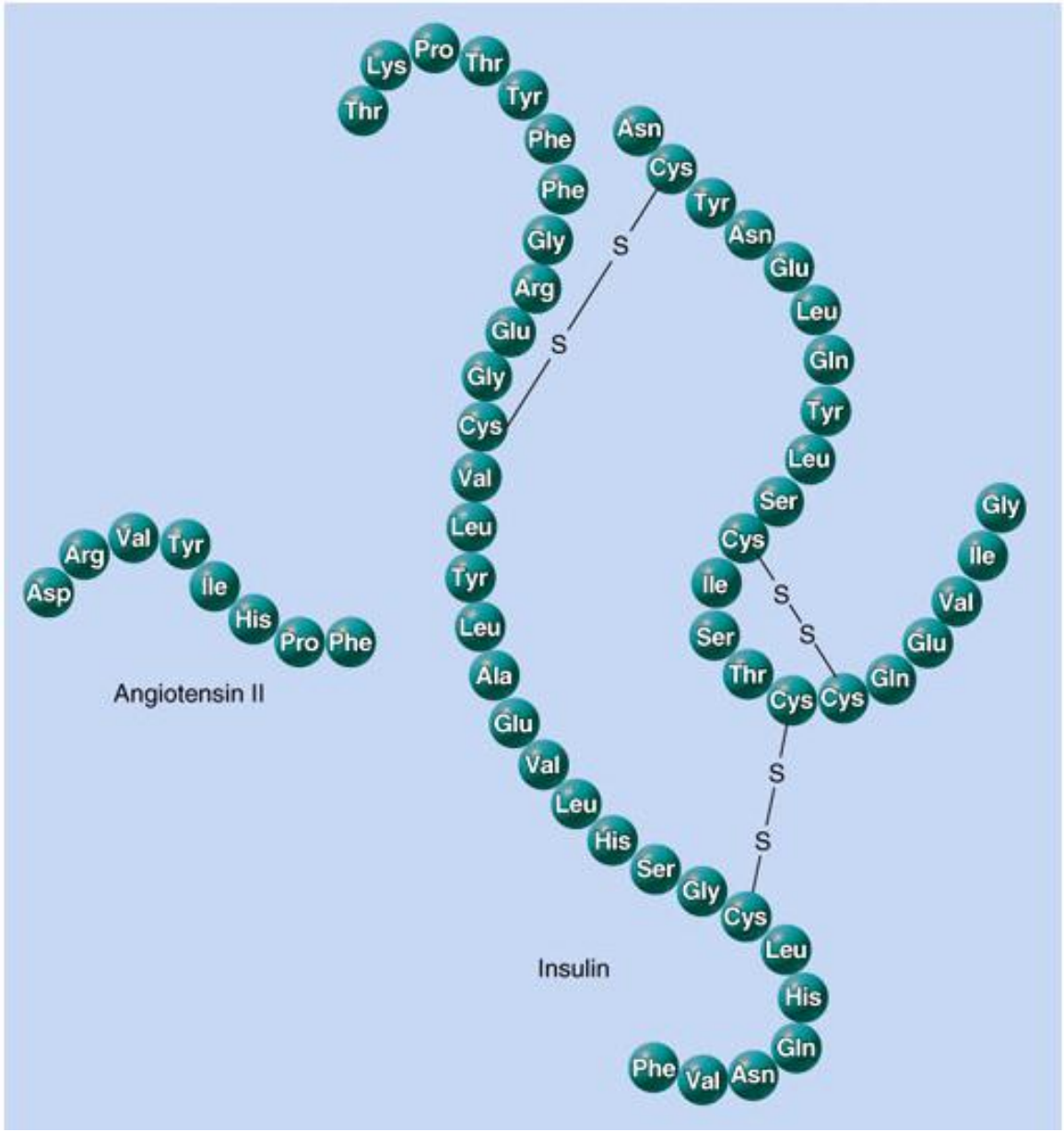
Hormones are secreted from:

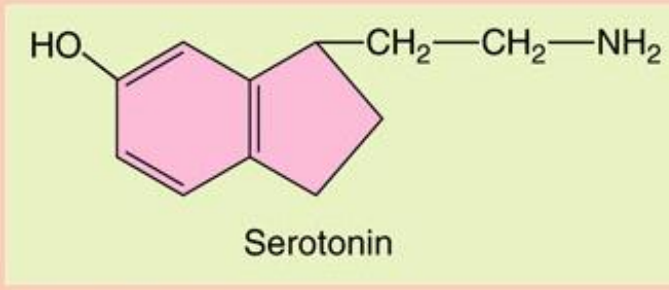
- the glands of the endocrine system
  - see figure
- some organs
  - heart, kidneys, stomach, skin, liver and gonads (ovaries and testes)

Hormones are secreted into the bloodstream and distributed to **all** cells of the body

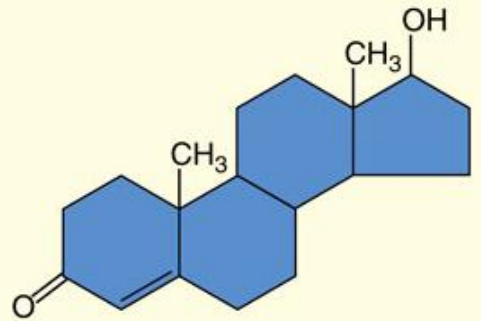
Hormones

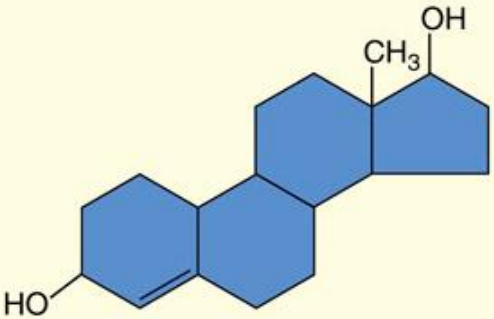
- Hormones that are released by cells are considered to be the first messengers because they are responsible for initiating a series of events that ultimately lead to a response
- 2 distinct groups based on their chemistry and how they behave when they reach their target cells
  - Hydrophobic (non-polar) hormones
    - steroid hormones
      - synthesized from cholesterol
      - names end in the suffix “-one” or “-ol”
  - Hydrophilic (polar) hormones are unable to cross the cell membrane of the target cell and therefore affect the cell from its surface
    - peptide hormones (3 to over 200 amino acids)
    - monoamines (amino acid derivatives)





(b) Monoamines



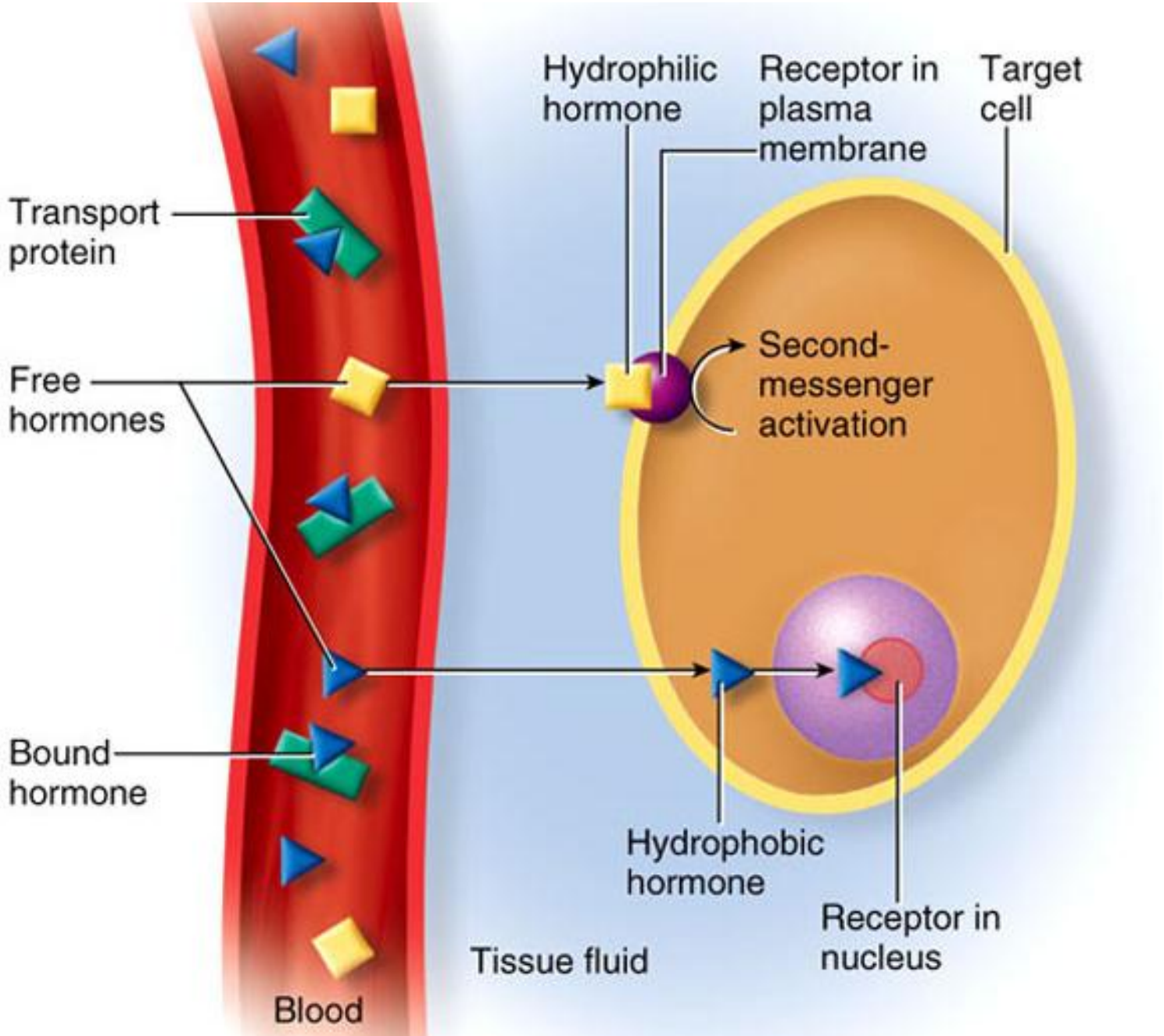


(a) Steroids

Hormone Transport in Blood

- Peptides and monoamines mix easily with blood
- Steroid hormones must bind to hormone binding proteins in the blood
  - the binding of a steroid hormone to the binding protein is reversible
    - **bound** hormones are attached to a binding protein and are moved through the circulatory system
    - once **unbound**, the hormone exits the circulatory system to affect the target cell

Hormone Transport and Action on Target



Receptor Proteins

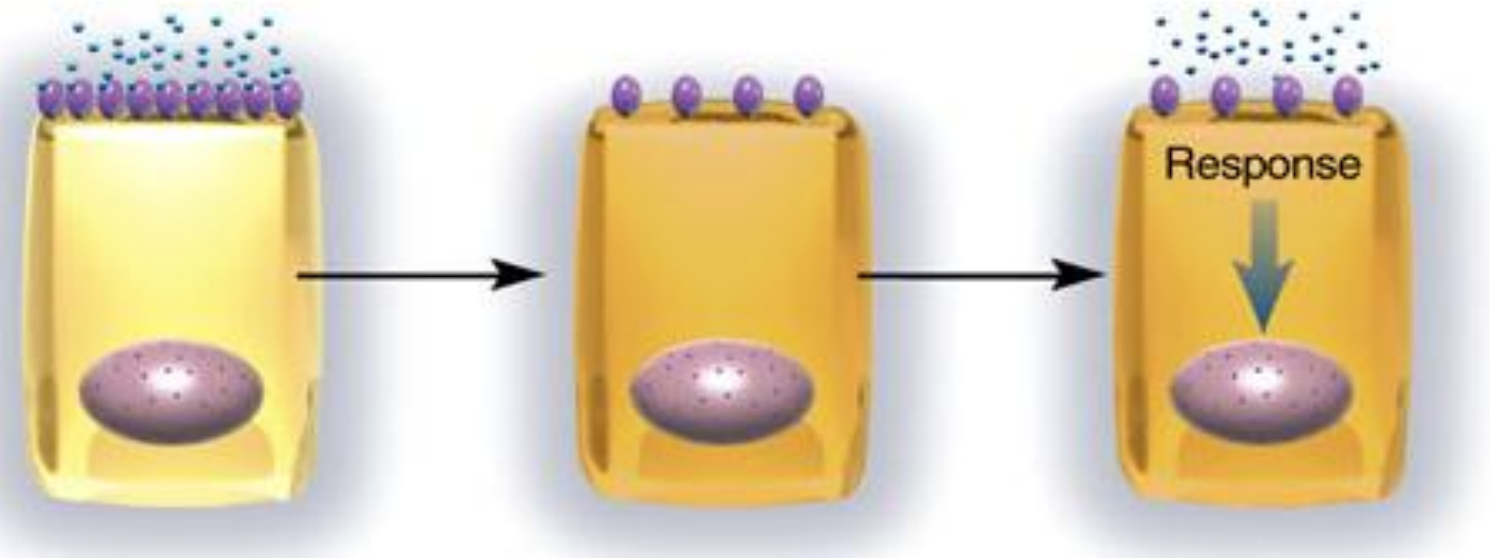
- In order for a hormone to be able to create a response in a target cell, the target cell must possess a receptor protein to which the hormones binds
  - if a cell does not have a receptor protein for a particular hormone, the cell will **not** respond
- Receptor proteins are either located:
  - **on the surface of the cell membrane** for hydrophilic hormones
  - **in the cell** for hydrophobic hormones
- A single cell may have between 500 and 100,000 receptor proteins
- Many cells are targets for multiple hormones because they have receptors to a variety of different hormones

Receptor Proteins and Target Cell Response

- The magnitude of the response of a target cell to a hormone depends largely on the amount of hormone that is delivered to the target cell and the number of receptor proteins that the target cell possesses for a specific hormone
  - ***The greater the amount of hormone at the target cell, the greater the response***
  - ***The greater the number of protein receptors for a specific hormone, the greater the response***
    - the number of receptor proteins for a specific hormone can vary from just a few to hundreds

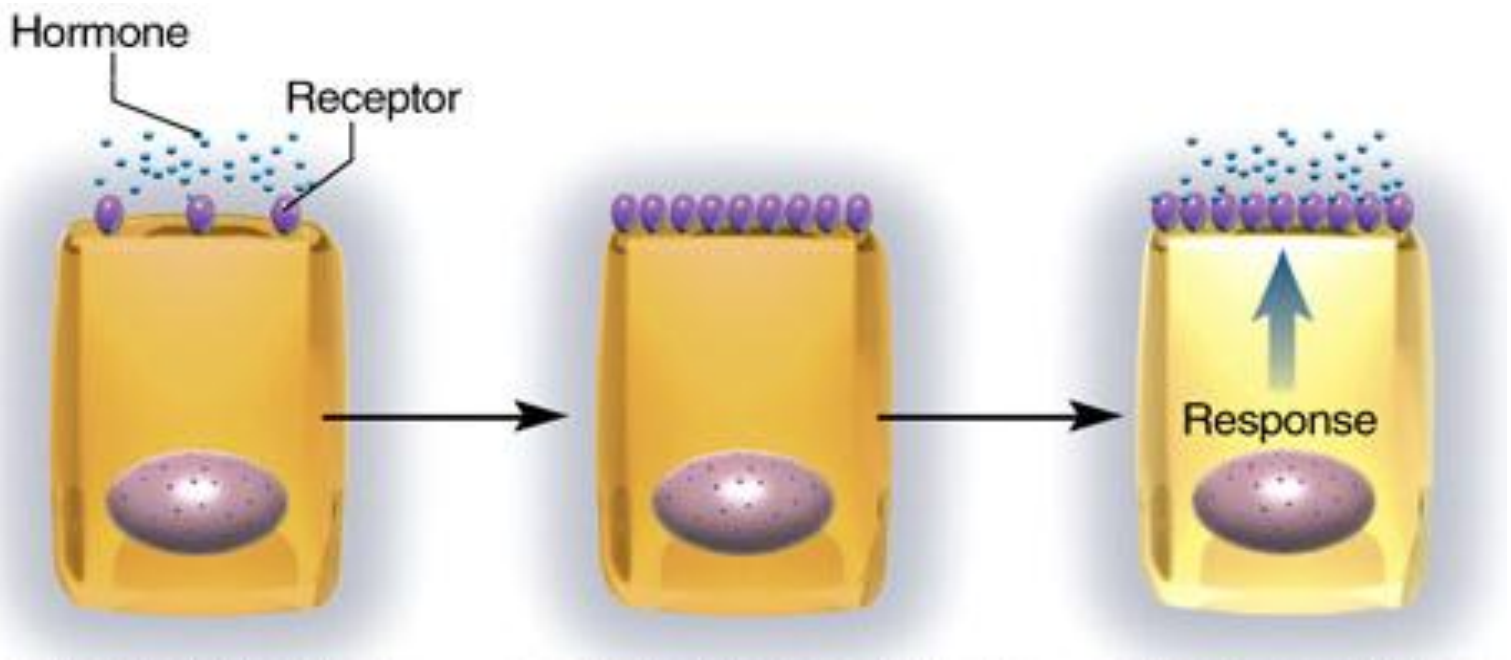
Down-Regulation of Receptor Proteins

- If the signaling chemical concentration is abnormally high for a sustained period of time creating too large of a response, the target cell can bring the response back to normal by a reduction of the receptors
- Down-regulation is partially responsible for drug tolerance, where the response of a given dose decreases despite constant exposure
  - increasing doses are therefore required to elicit a constant response



Up-Regulation of Receptor Proteins

- Up-regulation of protein receptors is the opposite whereby a decrease in the concentration of signaling chemical causes the target cell to increase the number of protein receptors to normalize the response

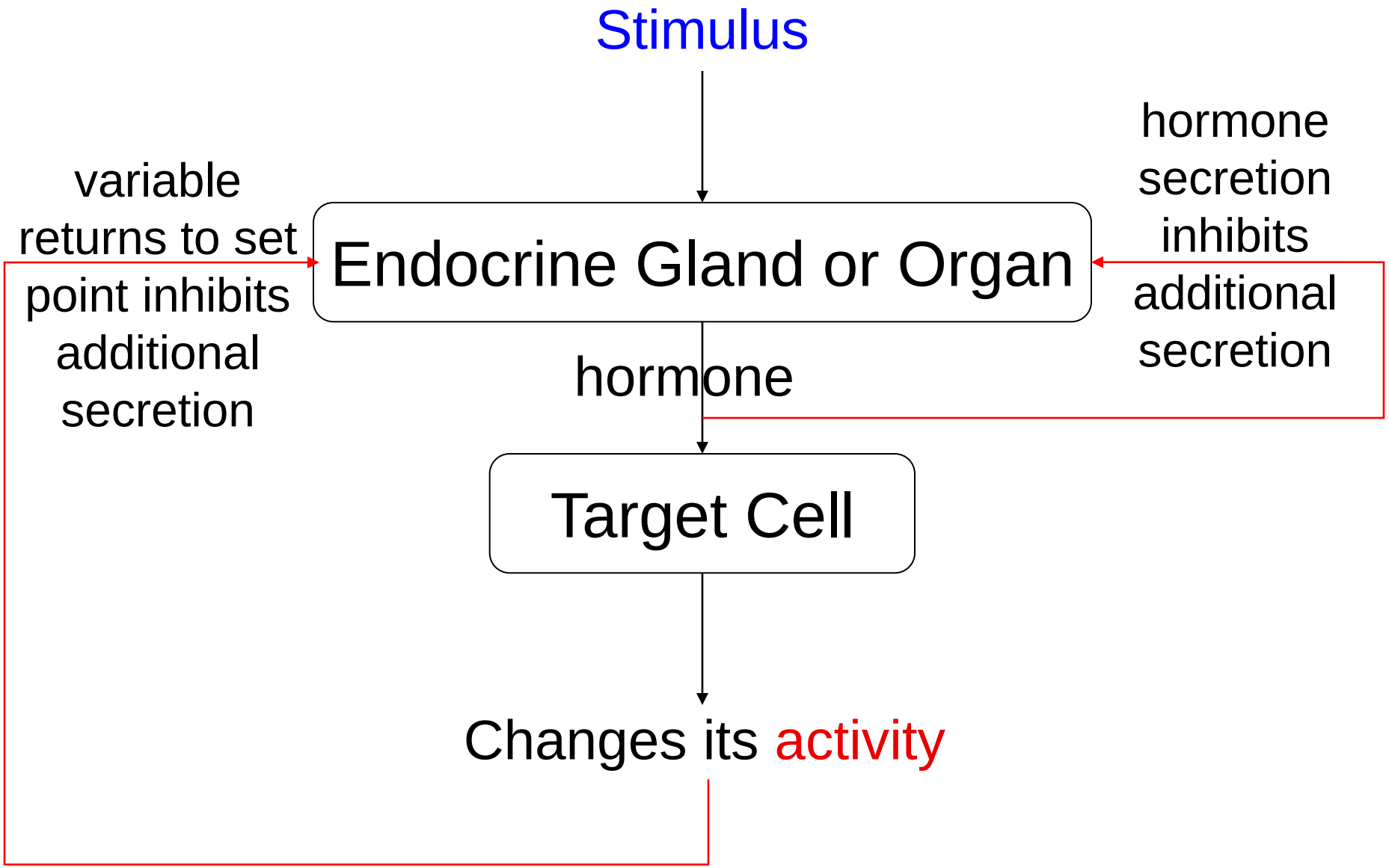


Hormone Secretion

- The amount hormone that is released from endocrine cells reflects the amount of response required to maintain homeostasis
  - ***The amount of hormone released is directly proportional to the extent of a homeostatic imbalance***
- The hypersecretion or hyposecretion of a hormone from a gland leads to too high or inadequate levels of circulating hormone leading to pathological conditions

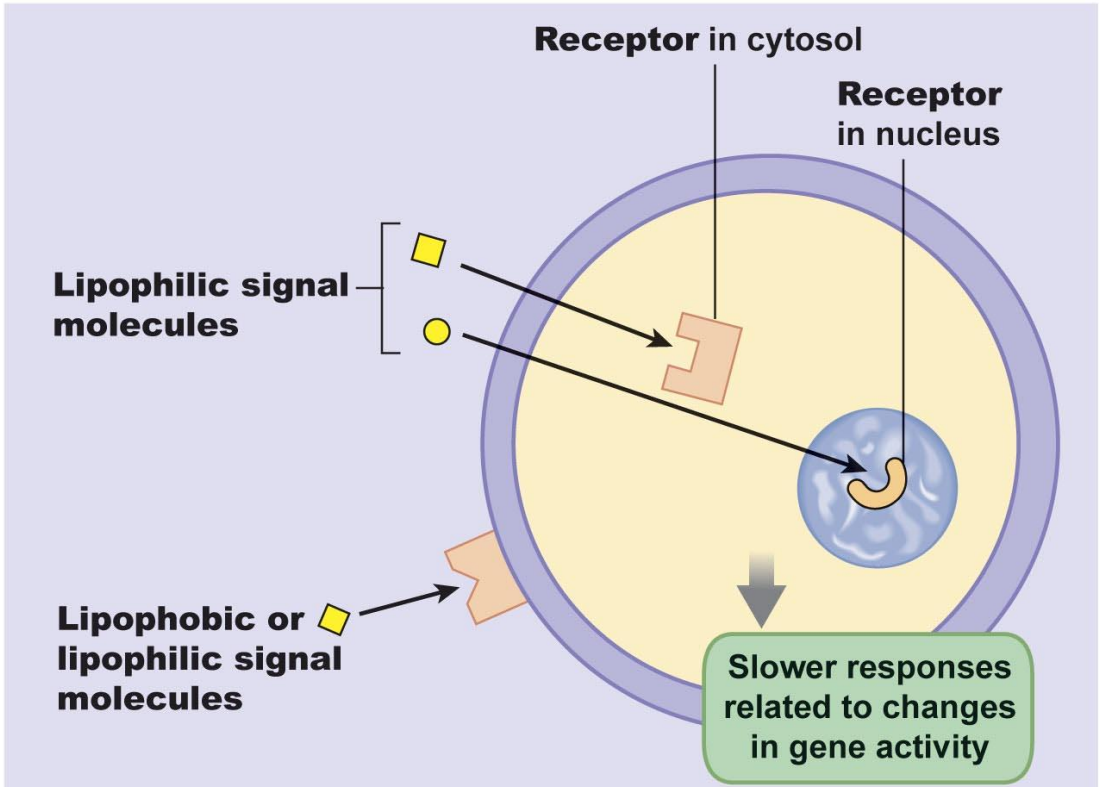
Control of Hormone Secretion (Release)

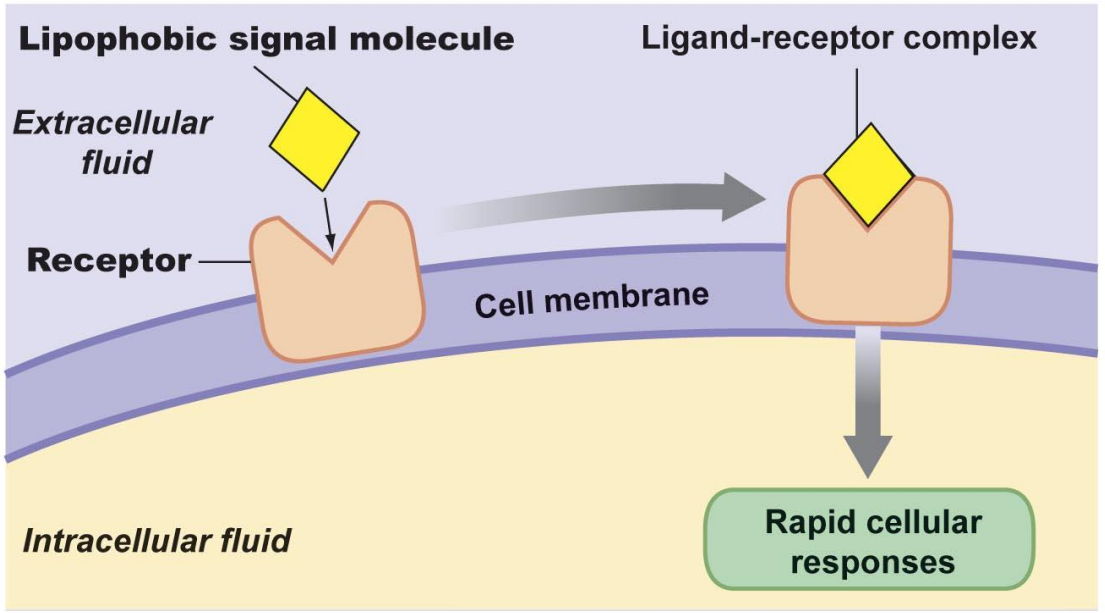
- Following a particular stimulus, the gland can **increase** *or* **decrease** the rate of secretion
- Circulating (blood) levels of hormones are not permitted to get too high because they are controlled by 2 separate negative feedback loops
  - activity of the target returns variable to the set point
  - circulating hormones decrease further secretion from the gland of origin
    - endocrine cells have protein receptors to the hormones that they secrete and hormone secretion from the cells is decreased when these receptors are bound by a hormone (autocrine)


Stimulus
Endocrine Gland or Organ
hormone
Target Cell
Changes its activity
variable returns to set point inhibits additional secretion
hormone secretion inhibits additional secretion

Hormone Action at Target Cells

- **Both** classes of hormones will change the activity of a target cell by changing the **activity of proteins** in a cell (recall proteins perform **EVERY** cellular function)
  - some proteins will be activated, some will be inactivated and some will be unaffected
    - the response of a target cell is **very specific**
- **Hydrophobic hormones** **alter gene transcription to increase or decrease the number of proteins in a target cell** (slow response)
- **Hydrophilic hormones** **activate or deactivate the proteins in a target cell** (fast response)
  - "flipping" a molecular switch ON or OFF

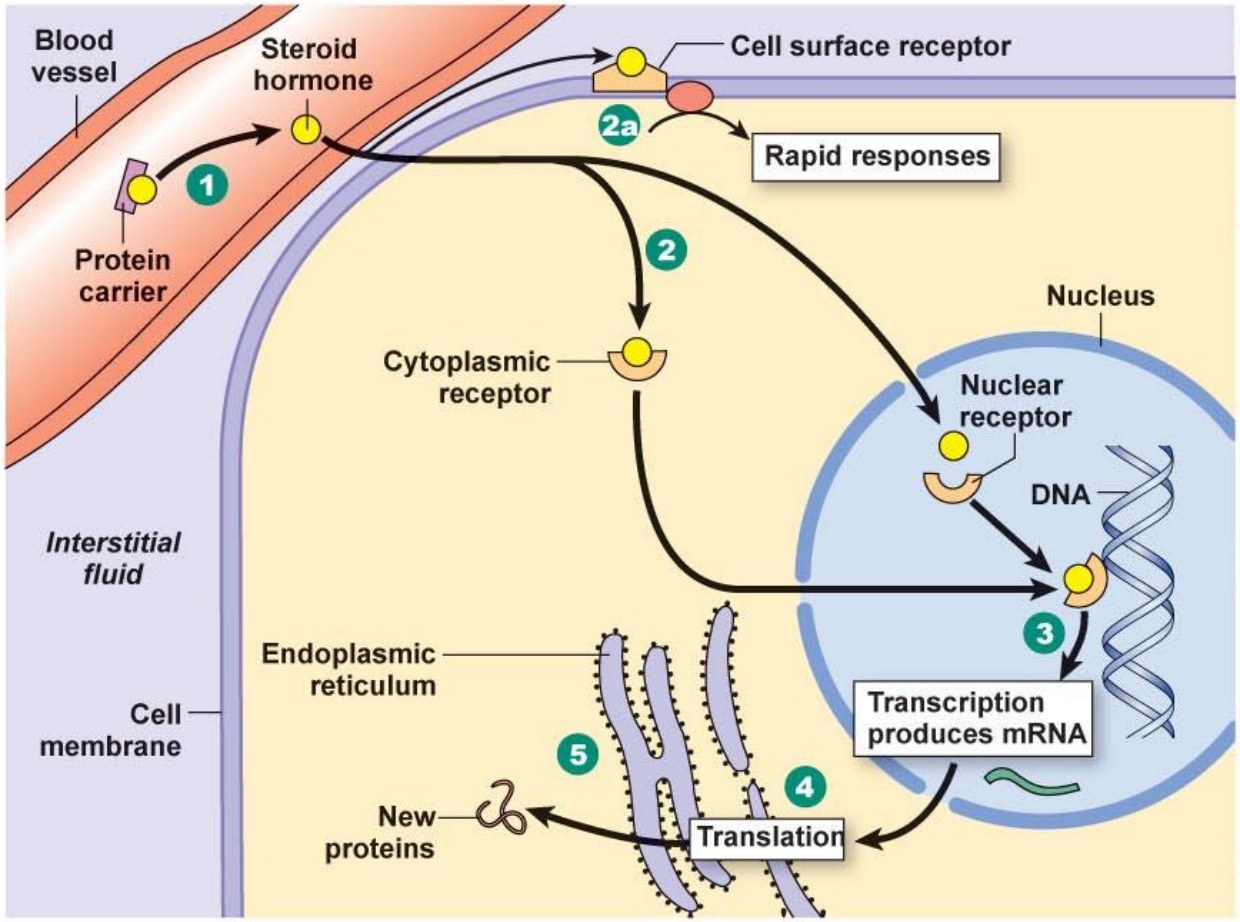

Receptor in cytosol
Receptor in nucleus
Lipophilic signal molecules
Lipophobic or lipophilic signal molecules
Slower responses related to changes in gene activity


Lipophobic signal molecule
Ligand-receptor complex
Extracellular fluid
Receptor
Cell membrane
Intracellular fluid
Rapid cellular responses

Hydrophobic Hormones

- Following the diffusion of these chemicals into the cytoplasm of a target cell they bind to a receptor protein located either in the cytoplasm or in the nucleus
- The binding of the hormone to the protein receptor initiates changes in the rate of transcription of genes in the target cell
- This ultimately changes the number of proteins in the target cell thus altering its activity

Mechanism of Steroid Hormone Action

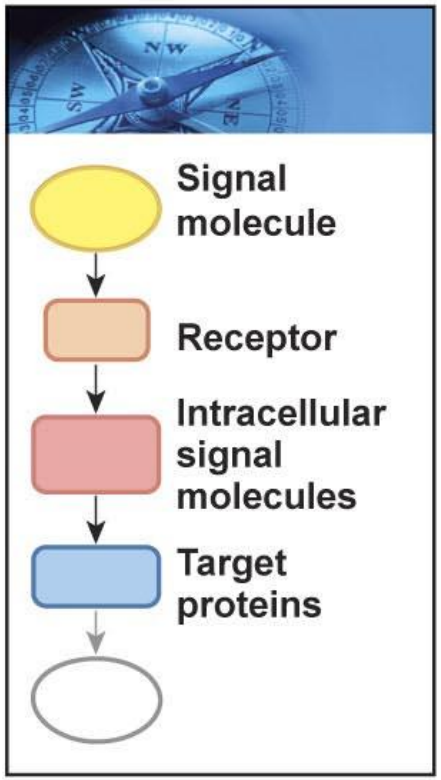


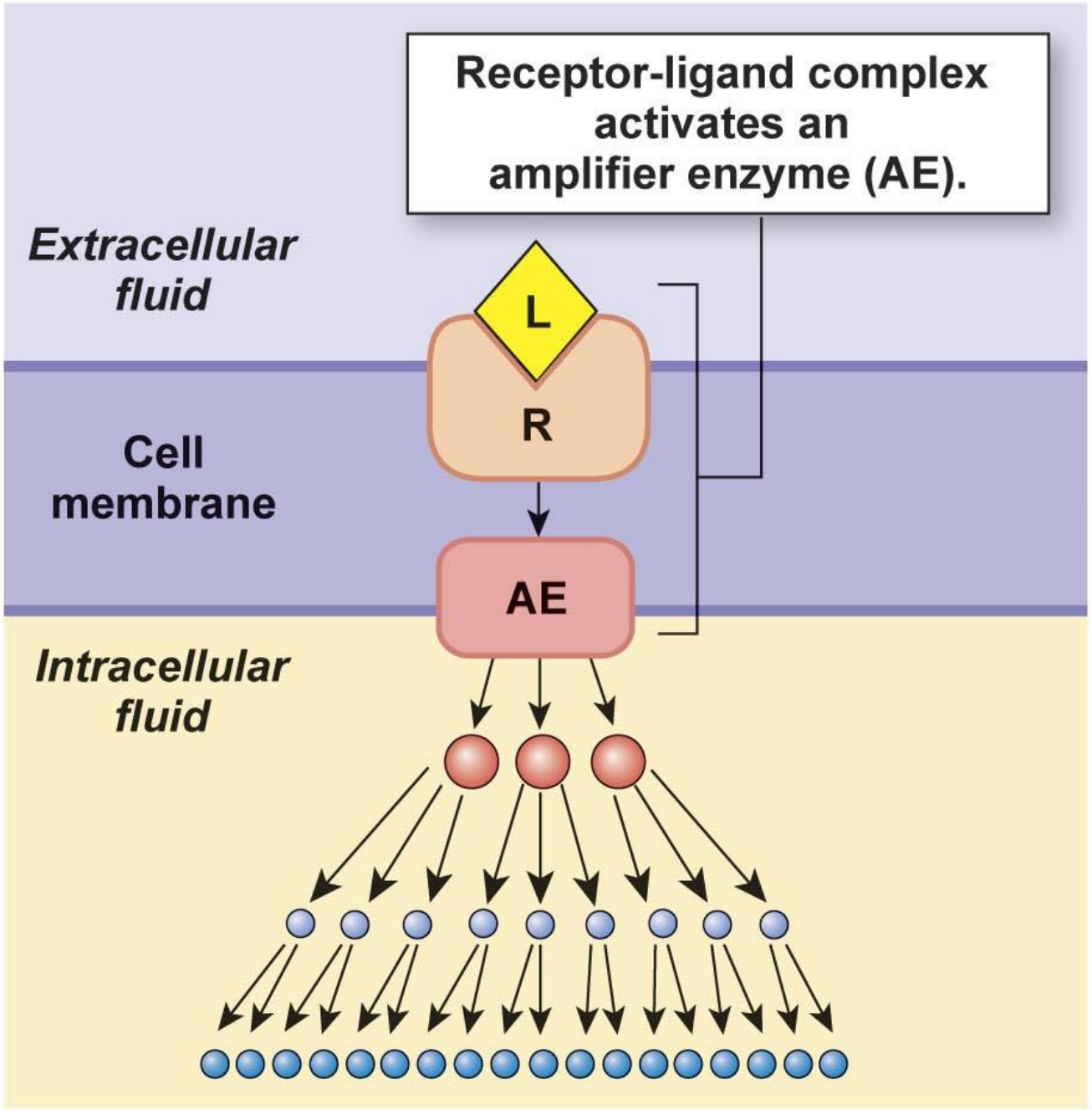
1. Most hydrophobic steroids are bound to plasma protein carriers. Only unbound hormones can diffuse into the target cell.
2. Steroid hormone receptors are in the cytoplasm or nucleus.
2a. Some steroid hormones also bind to membrane receptors that use second messenger systems to create rapid cellular responses.
3. The receptor-hormone complex binds to DNA and activates or represses one or more genes.
4. Activated genes create new mRNA that moves back to the cytoplasm.
5. Translation produces new proteins for cell processes.

Hydrophilic Hormones

- Following the binding of the signaling chemical to the protein receptor, information is transferred through the cell membrane of the target cell and initiates an intracellular signaling cascade (pathway) which generates an intracellular response
  - this process is referred to as signal transduction
- In biological systems the signal is not only converted, but it is also amplified (made larger)

NAVIGATOR


Signal molecule
Receptor
Intracellular signal molecules
Target proteins


Receptor-ligand complex activates an amplifier enzyme (AE).
Extracellular fluid
L
R
Cell membrane
AE
Intracellular fluid

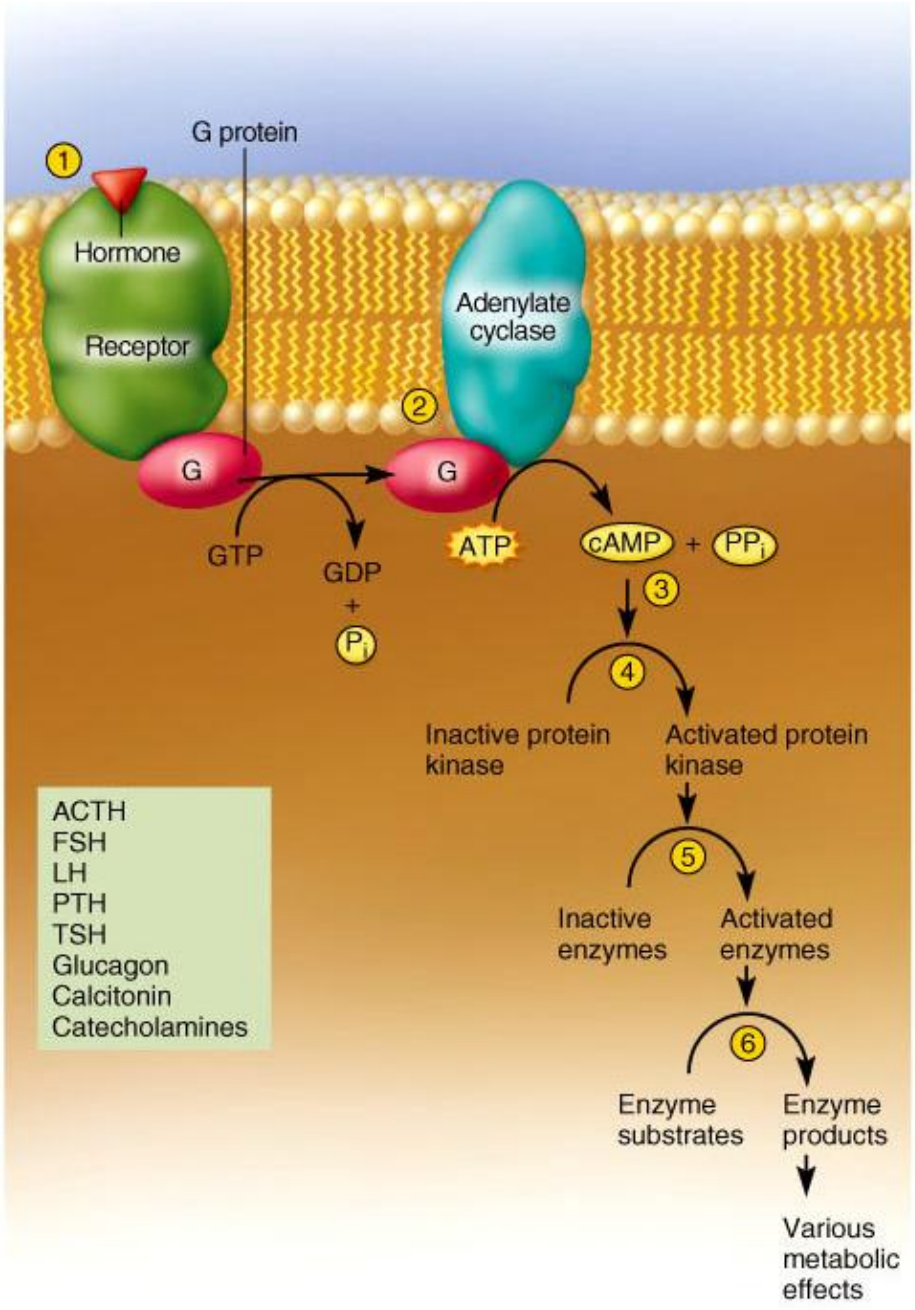
Signal Amplification

- Each hormone molecule binds to a receptor protein and activates an amplifier enzyme
- Each amplifier enzyme synthesizes **many** intracellular second messenger molecules which influence the internal functioning of a cell
- Each second messenger molecule activates **many** protein kinases (an enzyme)
- Each protein kinase enzyme alters the activity of cellular proteins (some are ACTIVATED some are INACTIVATED) resulting in an altered function of that cell

Amplifier Enzymes, Second Messengers and Protein Kinases

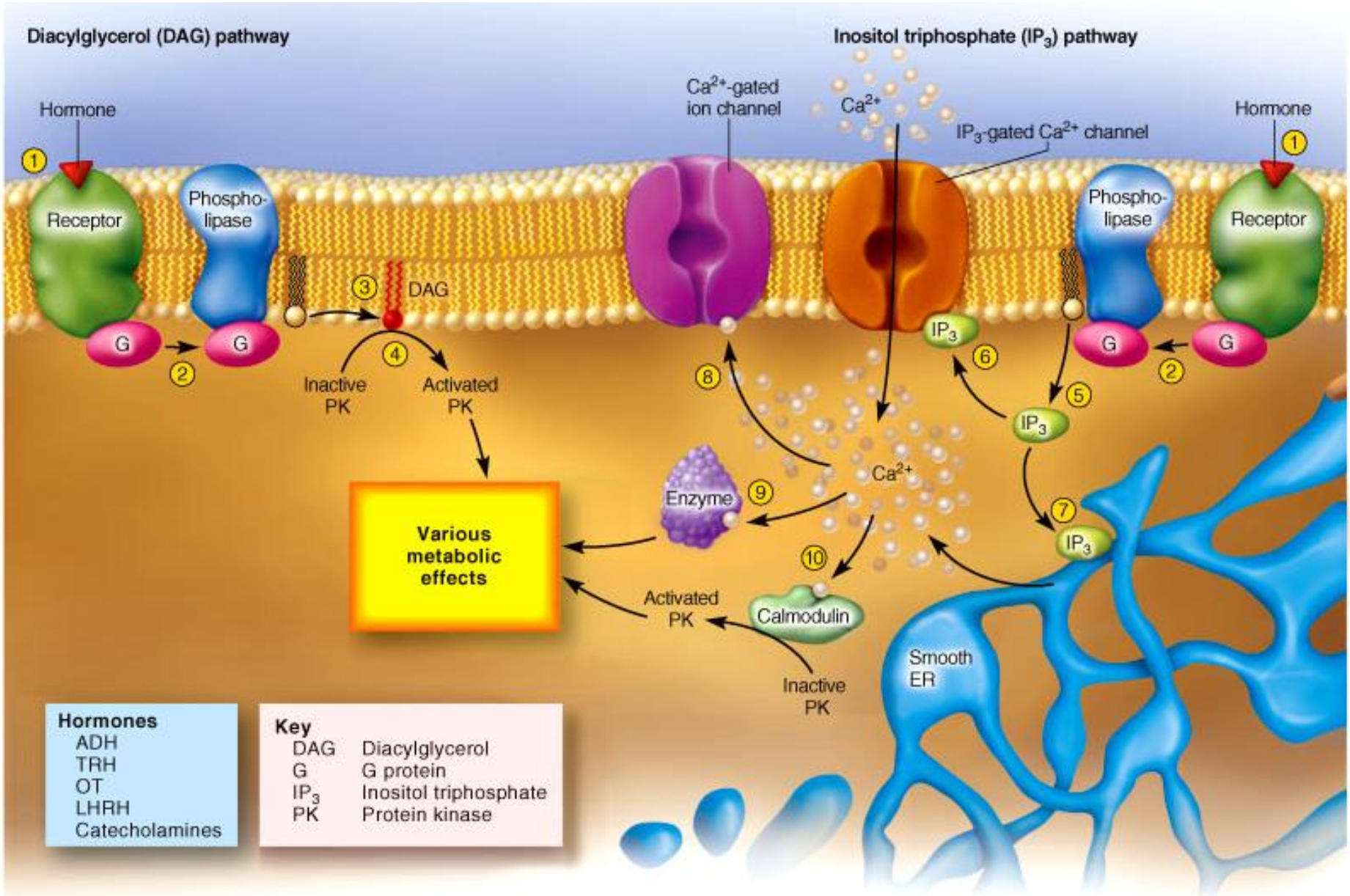
- 2 key enzymes that synthesize 2nd messengers
  - adenylyl cyclase catalyzes the conversion of ATP into the second messenger cyclic AMP (cAMP)
  - phospholipase C catalyzes the conversion of a membrane phospholipid into 2 different 2nd messengers
    - Diacylglycerol (DAG)
    - Inositol triphosphate (IP_3)
      - in some signal cascades IP_3 stimulates the release of calcium ions from the smooth ER into the cytoplasm acting as a third messenger
- Each unique second messenger molecule activates a different type of protein kinase to create a unique/specific response by the cell

Adenylyl cyclase and cyclic AMP (cAMP)

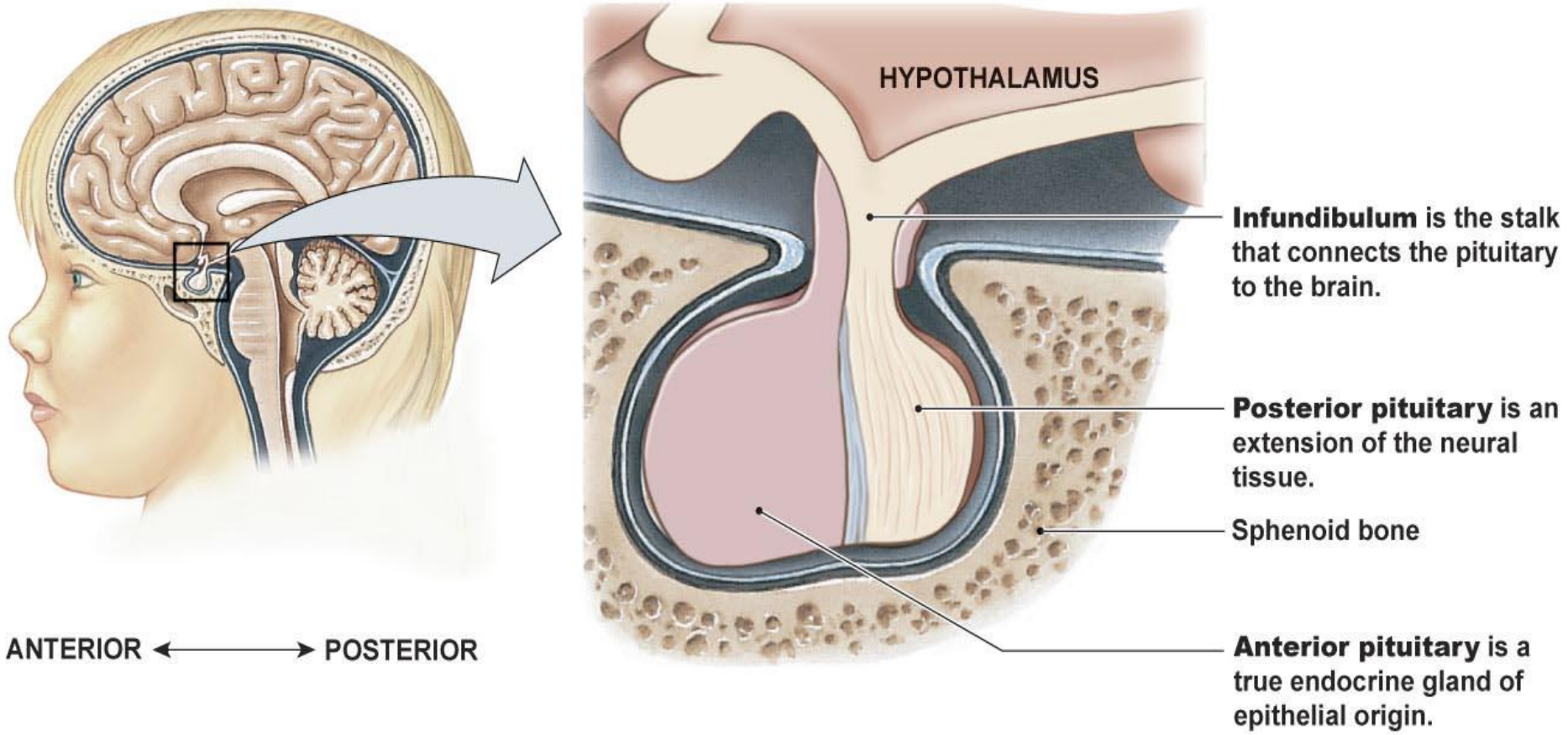


1. Hormone–receptor binding activates a G protein.
2. G protein activates adenylate cyclase.
3. Adenylate cyclase produces cAMP.
4. cAMP activates protein kinases.
5. Protein kinases phosphorylate enzymes. This activates some enzymes and deactivates others.
6. Activated enzymes catalyze metabolic reactions with a wide range of possible effects on the cell.

Phospholipase C and IP_3 and DAG and Ca^{2+}



Hypothalamus and Pituitary (Hypophysis)

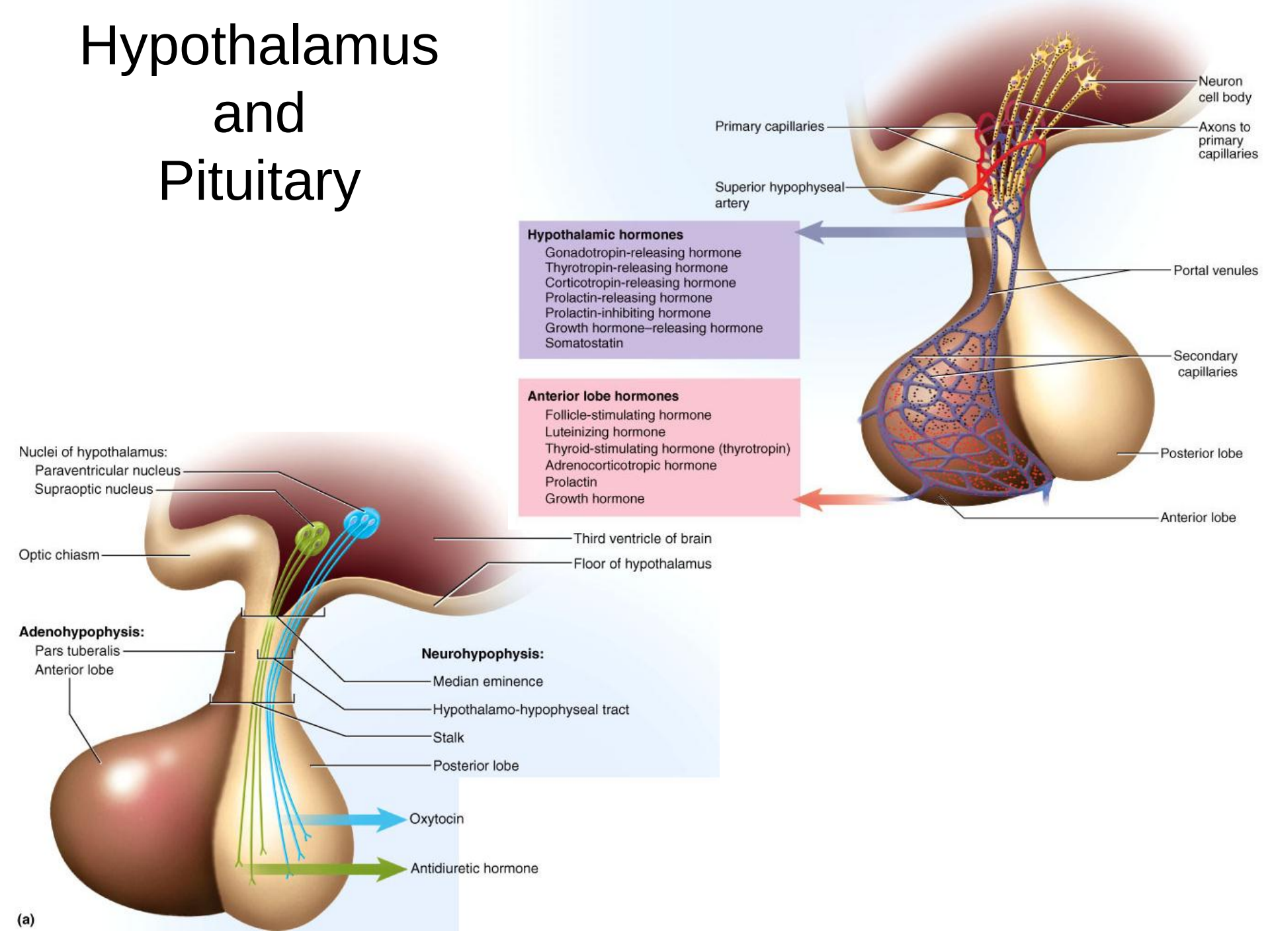


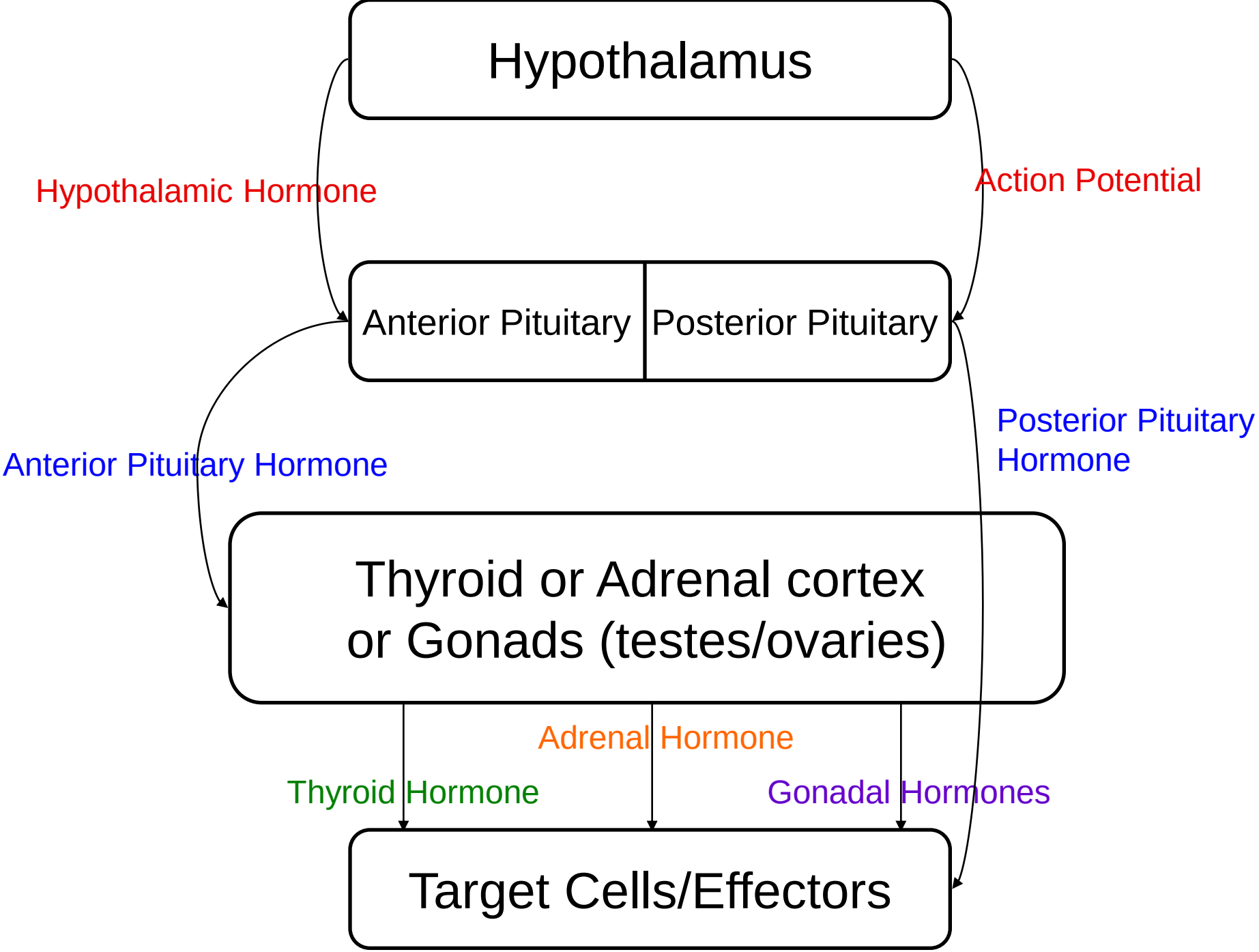
- Located in the brain, the **hypothalamus** and **pituitary** work together to regulate some of the fundamentally controlled parameters of the body
  - blood pressure, body temp., metabolite balance, growth, reproduction, water and ion balance…

Hypothalamus and Pituitary (Hypophysis)

- The hypothalamus, which is composed of neurons, controls the secretion of the pituitary gland
  - secretes hormones into the bloodstream which are carried directly to the anterior pituitary
  - sends action potentials along axons that extend to the posterior pituitary
- The pituitary gland is divided into two halves
  - Anterior (**adenohypophysis**) is composed of glandular (epithelial) tissue
    - secretes hormones which stimulates the secretion of hormones from other glands such as the thyroid, adrenals and gonads (testes/ovaries)
  - Posterior (**neurohypophysis**) is composed of collection of axons and axon termini whose somas and dendrites **<u>are located in the hypothalamus</u>**

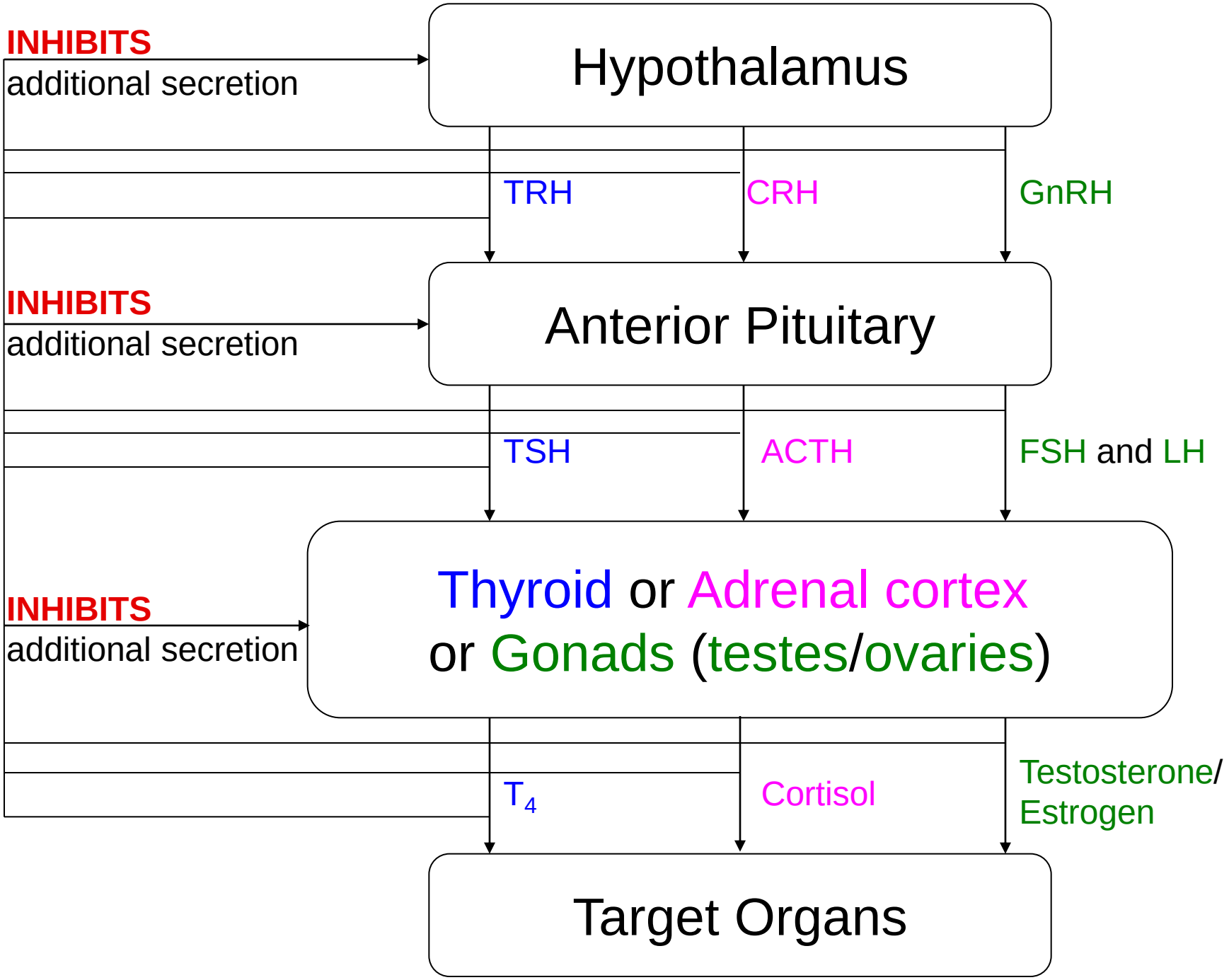
Hypothalamus and Pituitary




Hypothalamus
Hypothalamic Hormone
Action Potential
Anterior Pituitary
Posterior Pituitary
Posterior Pituitary Hormone
Anterior Pituitary Hormone
Thyroid or Adrenal cortex or Gonads (testes/ovaries)
Adrenal Hormone
Thyroid Hormone
Gonadal Hormones
Target Cells/Effectors

Hypothalamic Hormone Secretion

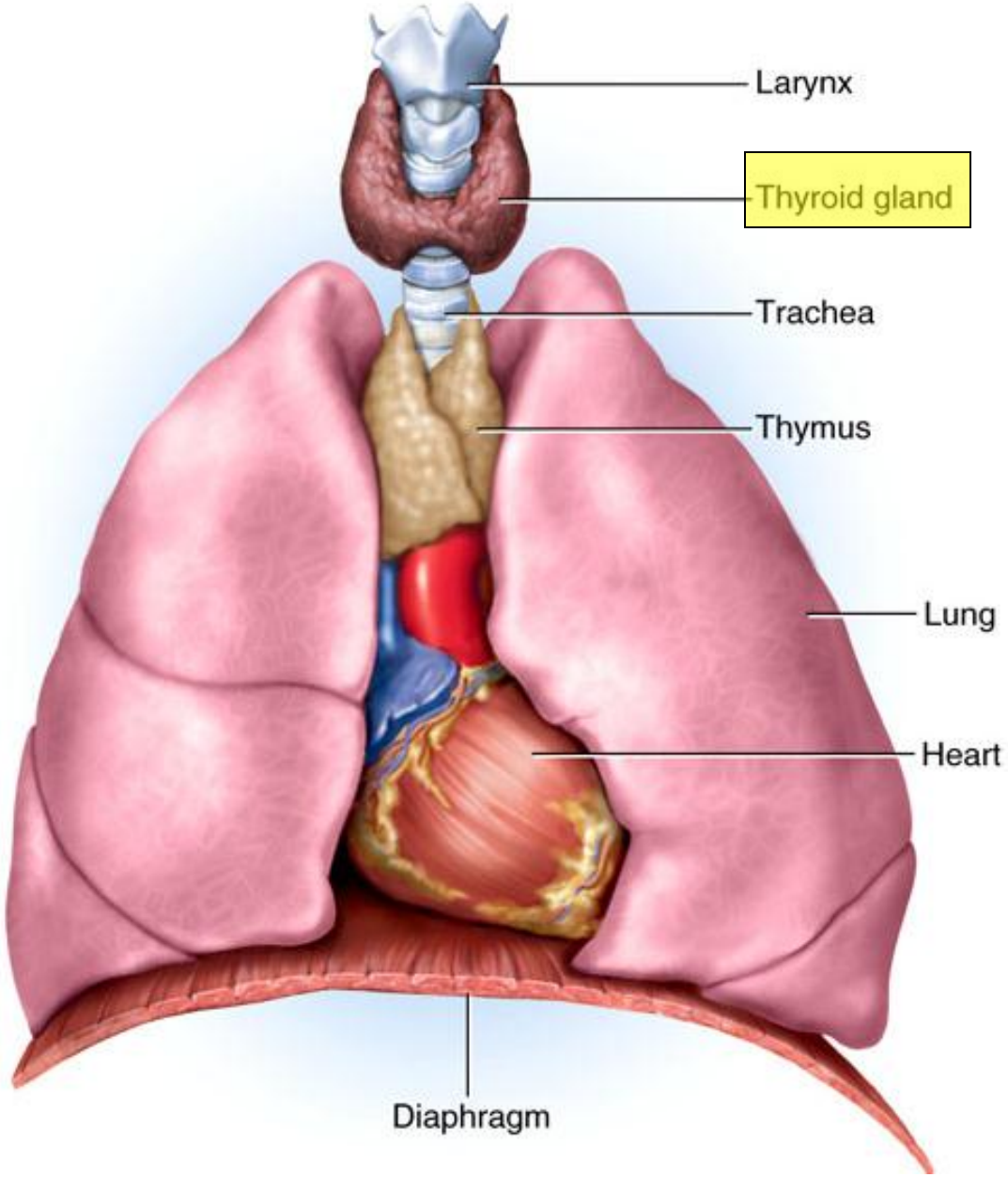
- The hypothalamus secretes **releasing hormones** in response to a variety of stimuli which travel through a **portal circulation** and stimulate the secretion of **stimulating hormones** from the anterior pituitary which target other endocrine glands including the thyroid gland, adrenal gland and the gonads (testes and ovaries) to cause the secretion of their respective hormones
- The hormones from the thyroid, adrenal and gonads target various tissues and organs creating desired effects
- The releasing, stimulating and thyroid, adrenal and gonadal hormones are also involved in negative feedback loops to control the circulating levels of these hormones


INHIBITS
additional secretion
Hypothalamus
TRH
CRH
GnRH
INHIBITS
additional secretion
Anterior Pituitary
TSH
ACTH
FSH and LH
INHIBITS
additional secretion
Thyroid or Adrenal cortex
or Gonads (testes/ovaries)
T4
Cortisol
Testosterone/
Estrogen
Target Organs

Hypothalamic Control of the Thyroid Gland

- Thyrotropic Releasing Hormone (**TRH**) is secreted when **body temperature is too low**
  - stimulates the secretion of Thyroid stimulating hormone (**TSH**) from the anterior pituitary
    - stimulates the secretion of thyroid hormones from the thyroid gland
- Thyroid hormone increases the metabolic rate by accelerating the rate of *cell respiration* which produces a significant amount of heat energy
- ↓BT → TRH → TSH → thyroid hormone → ↑BT

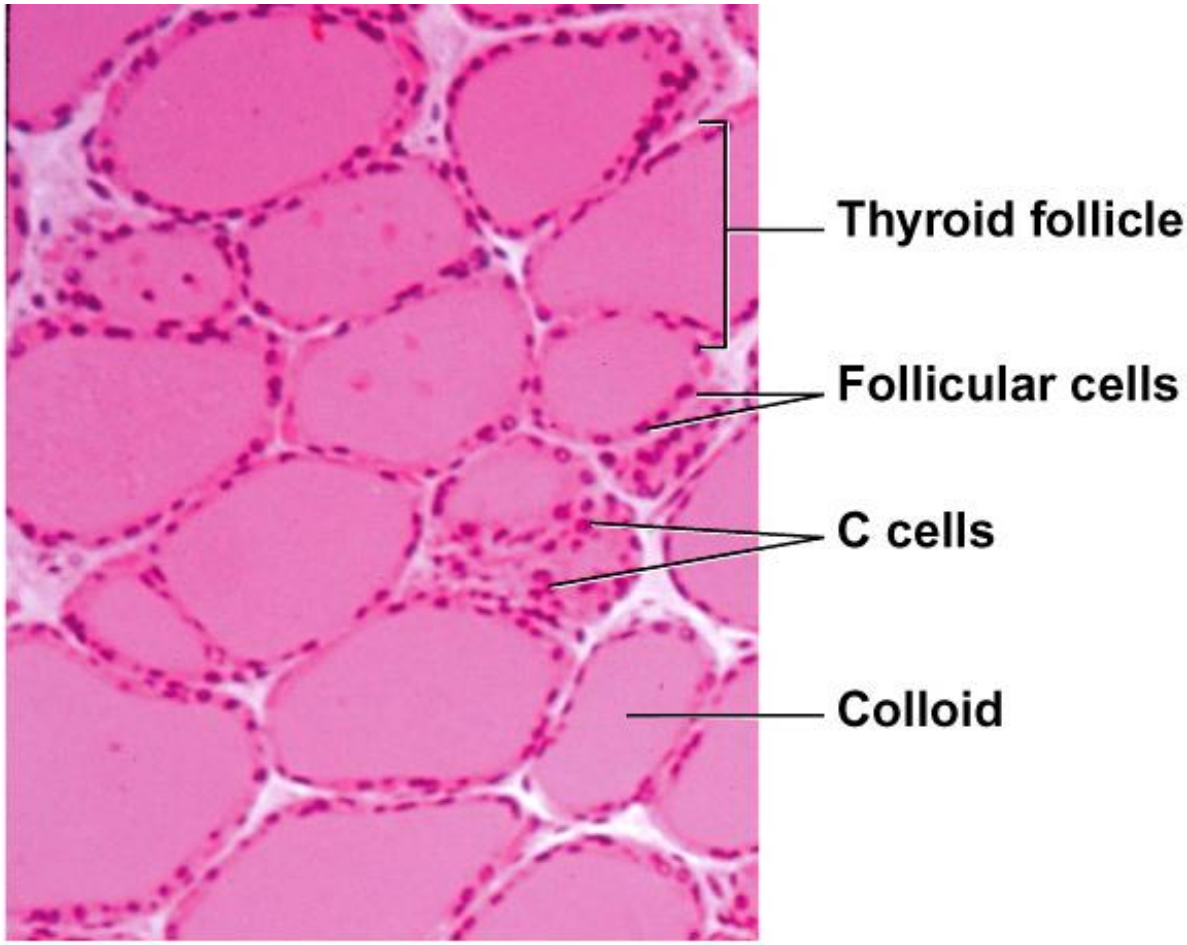
Thyroid Gland



- Largest pure endocrine gland
- Covers the anterior and lateral sides of trachea

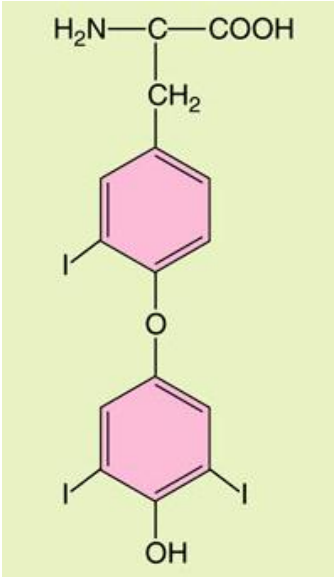
Thyroid Gland

- The thyroid gland consists of thousands of follicles are spheres bordered by follicular cells (simple cuboidal epithelium) filled with **colloid** secrete the thyroid hormones
- Parafollicular (C) cells are found between follicles secrete the hormone calcitonin



Thyroid Hormones

- Thyroid hormone, T_4 (thyroxine) and T_3, are considered to be steroid-like hormones
  - are nonpolar
  - have intracellular receptors that influence gene transcription
- Made from 2 nonpolar **amino acids** of tyrosine bound to each other and complexed with either 4 (T_4) or 3 (T_3) atoms of iodine



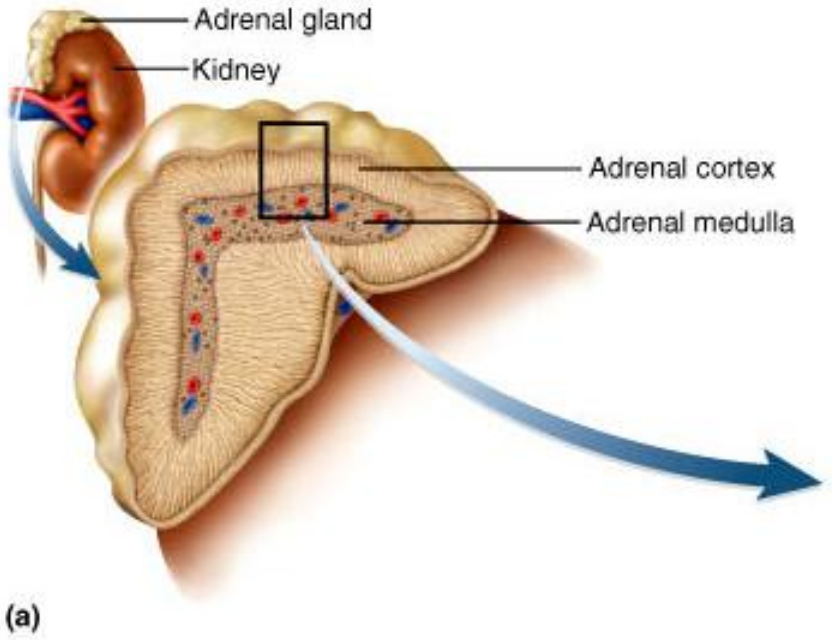
Hypothalamic Control of the Adrenal Gland

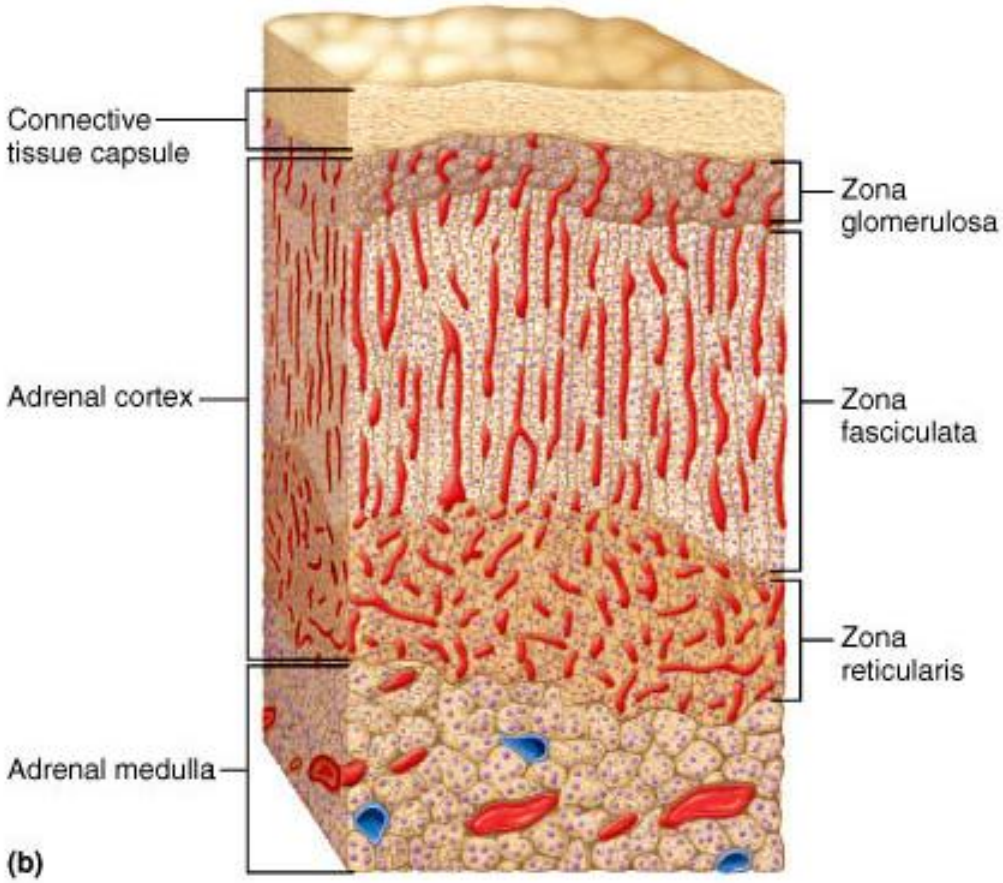
- Corticotropic Releasing Hormone (**CRH**) is secreted in **times of stress** (physical/emotional)
  - stimulates the secretion of Adrenocorticotropic hormone (**ACTH**) from the anterior pituitary
    - stimulates the secretion of aldosterone and cortisol from the adrenal gland
- Aldosterone maintains a balance of Na^+ and K^+ in the body to optimize nervous and muscle tissue function which uses these ions for action potentials
- Cortisol regulates glucose and fatty acid levels in the blood
- Stress → CRH → ACTH → aldosterone/cortisol

Adrenal Glands

- The adrenal glands (toward kidney) are pyramid-shaped glands on top of each kidney are structurally and functionally two glands in one:
  - Adrenal cortex (outside)
    - epithelial tissue organized in 3 layers (zona)
      - Zona glomerulosa (superficial layer)
      - Zona fasciculata (middle layer)
      - Zona reticularis (deep layer)
  - Adrenal medulla (center of gland)
    - nervous tissue that is the hormonal branch of the sympathetic nervous system (fight/flight)

Adrenal Glands





Adrenal Cortex

- Secretes hormones called **corticosteroids**
- Different corticosteroids are produced in each zona
  - Zona glomerulosa
    - mineralocorticoids (mainly **aldosterone**)
      - control body levels of sodium and potassium
  - Zona fasciculata
    - glucocorticoids (mainly **cortisol**)
      - control blood levels of substrates for metabolism (glucose, fatty acids and amino acids)
  - Zona reticularis
    - gonadocorticoids (mainly **androgens** (male sex steroid hormones))
      - secreted at **low** levels in males and females and *may* attribute to the onset of puberty

Aldosterone (mineralocorticoid)

- Is secreted in response to **any** of the following stimuli:
  - an **increase** in blood K^+ levels
  - a **decrease** in blood Na^+ levels
  - a **decrease** in blood pressure
  - secretion of ACTH from the anterior pituitary
- The target of aldosterone is the kidney
  - The kidneys respond to aldosterone by:
    - **increasing** K^+ urination (which **decreases** blood K^+ levels)
    - **decreasing** Na^+ urination (which **increases** blood Na^+ levels)
      - an **increase** in Na^+ levels in the blood causes an increase in vascular water retention which **increases** blood pressure

Cortisol (glucocorticoid)

- Is secreted in response to **long term stress** (hours to months) and helps cope with stress by increasing circulating levels of metabolites used for energy (ATP synthesis)
- LTS → CRH → ACTH → cortisol
- Targets include:
  - Liver causing **gluconeogenesis**
    - the enzymatic synthesis of glucose from non-carbohydrate molecules such as amino acids which is subsequently released of into the blood
  - Adipose causing **lipolysis** of triglycerides
    - the free fatty acids which are subsequently released into the blood

Adrenal Medulla

- A sympathetic condition (fight or flight) stimulates the sympathetic centers of the medulla oblongata which fires APs that propagate along sympathetic nerves that synapse with **chromaffin** cells (modified sympathetic neurons) of the adrenal medulla and secrete 2 **catecholamines** into circulation
  - **epinephrine** (epi) (adrenaline)
  - **norepinephrine** (norepi) (noradrenaline)
- Epinephrine and norepinephrine bind to adrenergic receptors on targets including:
  - Liver stimulating the enzymatic hydrolysis of glycogen (glycogenolysis) into glucose in the liver which is subsequently released into the blood
  - Adipose stimulates lipolysis to ↑ blood fatty acids
  - Cardiovascular system which increases the heart rate, strength of the heart beat and blood pressure to send blood around the body more quickly

Hypothalamic Control of the Gonads

- Gonadotropic Releasing Hormone (**GnRH**) is secreted when **testosterone or estrogen levels are too low**
  - stimulates the secretion of Follicle stimulating hormone (**FSH**) & Luteinizing hormone (**LH**) from the anterior pituitary
    - stimulates the secretion of testosterone from the testes and estrogen from the ovaries
- Testosterone supports spermatogenesis as well as increases bone and muscle density; growth of facial, axillary and genital hair growth and the lengthening of vocal cords
- Estrogen is important in triggering ovulation, maintenance of bone density and the growth of the endometrial lining of the uterus

Posterior Pituitary

- Secretes 2 **neurohormones** into circulation following stimulation of the hypothalamus:
- **Antidiuretic hormone** (**ADH**) or **Vasopressin**
  - secreted in response to:
    - a decrease in body water content
    - decrease in blood pressure
    - an increase in extracellular solute concentration
  - targets the kidneys and causes a reduction in the volume of urine produced
    - retains body H_2O
    - increases in blood pressure
    - decreases extracellular solute concentration
- **Oxytocin**
  - stimulates the contraction of smooth muscle in the uterus and breasts during childbirth and nursing

Hypothalamic Control of the Posterior Pituitary