Hormones II

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DIVERSITY OF THE ENDOCRINE SYSTEM

Hormones are synthesized in discrete organs designed solely for this specific purpose, such as the thyroid (triiodothyronine), adrenal (glucocorticoids and mineralocorticoids), and the pituitary (TSH, FSH, LH, growth hormone, prolactin, ACTH). Some organs are designed to perform two distinct but closely related functions. For example, the ovaries produce mature oocytes and the reproductive hormones estradiol and progesterone. The testes produce mature spermatozoa and testosterone. Hormones are also produced in specialized cells within other organs such as the small intestine (glucagon-like peptide), thyroid (calcitonin), and kidney (angiotensin II). Finally, the synthesis of some hormones requires the parenchymal cells of more than one organ—eg, the skin, liver, and kidney are required for the production of 1,25(OH)2-D3(calcitriol). Examples of this diversity in the approach to hormone synthesis, each of which has evolved to fulfill a specific purpose.

Hormones Are Chemically Diverse

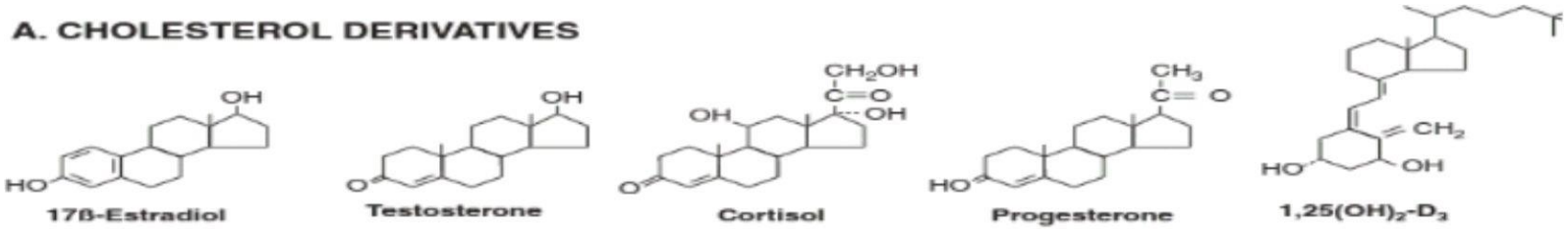
Hormones are synthesized from a wide variety of chemical building blocks. A large series is derived from cholesterol. These include the glucocorticoids, mineralocorticoids, estrogens, progestins, and 1,25(OH)2-D3. In some cases, a steroid hormone is the precursor molecule for another hormone. For example, progesterone is a hormone in its own right but is also a precursor in the formation of glucocorticoids, mineralocorticoids, testosterone, and estrogens. Testosterone is an obligatory intermediate in the biosynthesis of estradiol and in the formation of dihydrotestosterone (DHT). In these examples, described in detail below, the final product is determined by the cell type and the associated set of enzymes in which the precursor exists.

The amino acid tyrosine is the starting point in the synthesis of the catecholamines and of the thyroid hormones tetraiodothyronine (thyroxine; T4) and triiodothyronine (T3). T3 and T4 are unique in that they require the addition of iodine (as I−) for bioactivity Becausese dietary iodine is very scarce in many parts of the world, an intricate mechanism for accumulating and retaining (I) has evolved.

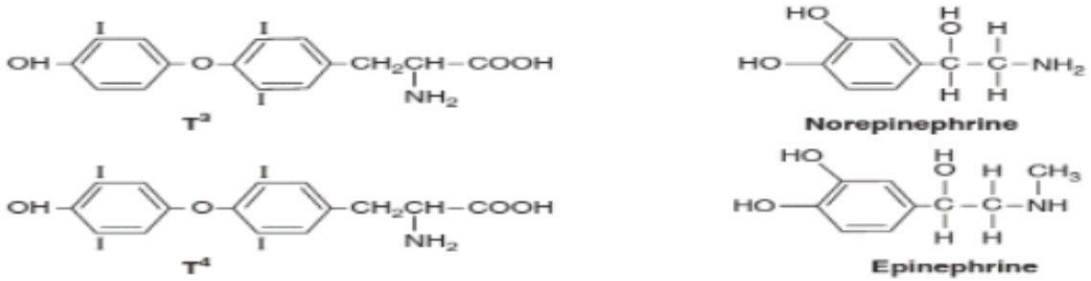
Many hormones are polypeptides or glycoproteins. These range in size from thyrotropin-releasing hormone (TRH), a tripeptide, to single-chain polypeptides like adrenocorticotropic hormone (ACTH; 39 amino acids), parathyroid hormone (PTH; 84 amino acids), and growth hormone (GH; 191 amino acids). Insulin is an AB chain heterodimer of 21 and 30 amino acids, respectively. Follicle-stimulating hormone (FSH), luteinizing hormone (LH), thyroid-stimulating hormone (TSH), and chorionic gonadotropin (CG) are

glycoprotein hormones of αβ heterodimeric structure. The αchain is identical in all of these hormones, and distinct β chains impart hormone uniqueness. These hormones have a molecular mass in the range of 25–30 kDa depending on the degree of glycosylation and the length of the β chain.

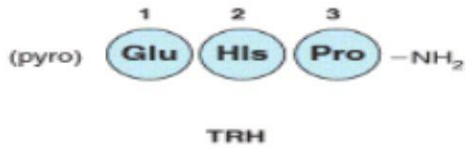
A. CHOLESTEROL DERIVATIVES

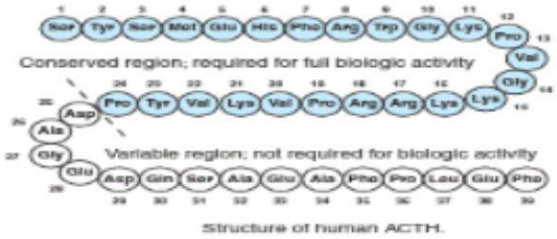


B. TYROSINE DERIVATIVES



C. PEPTIDES OF VARIOUS SIZES

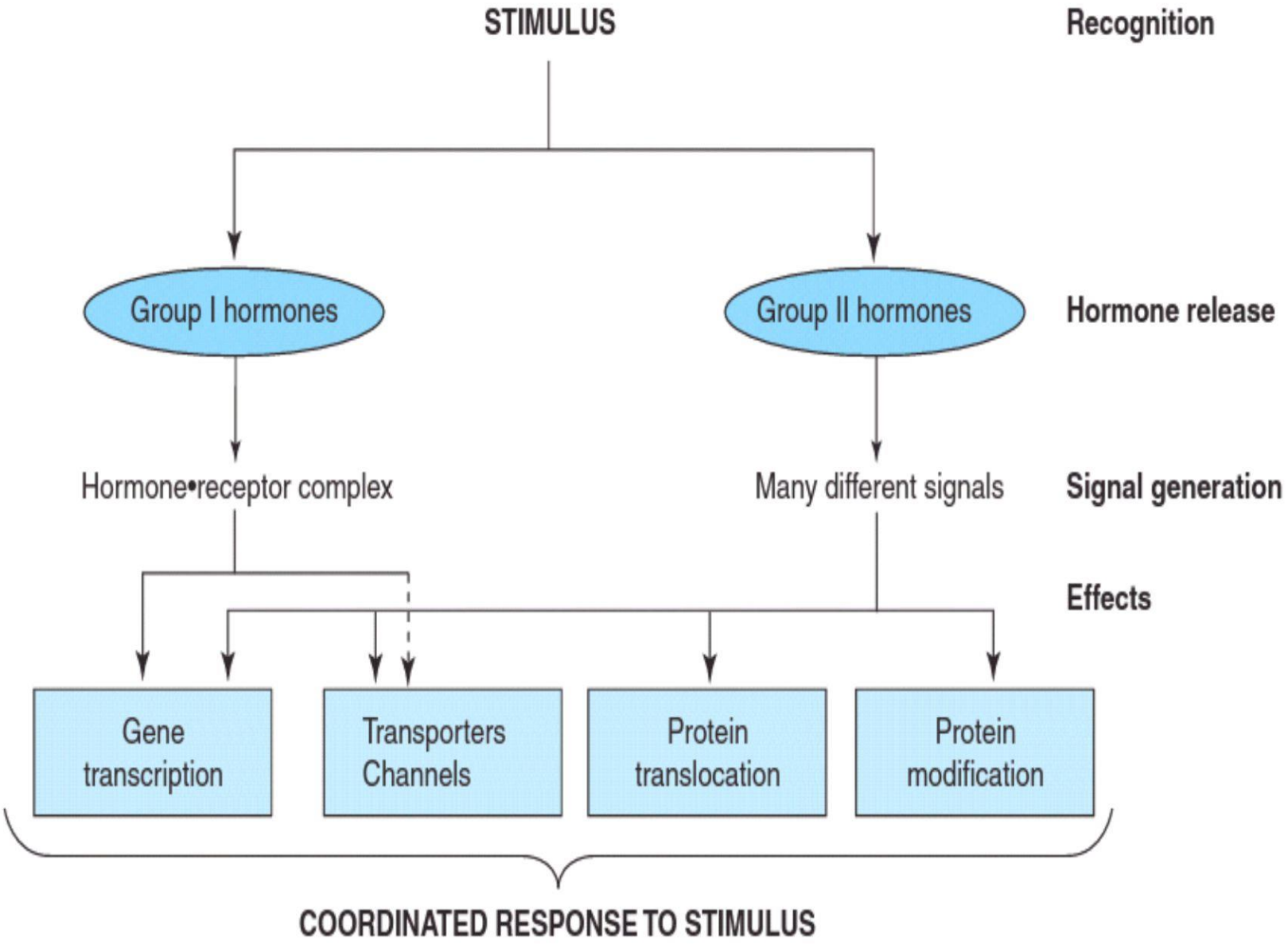


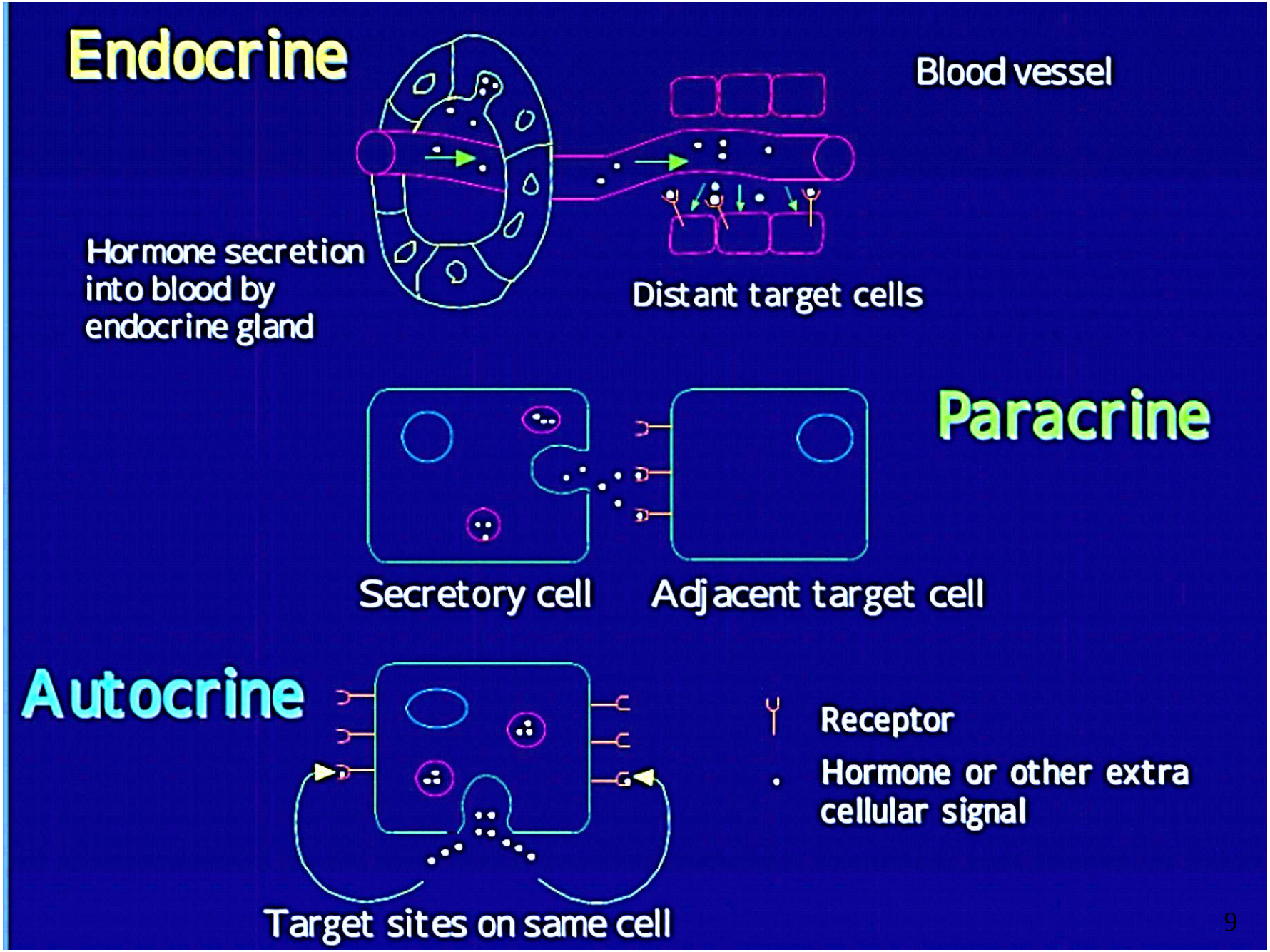


D. GLYCOPROTEINS (TSH, FSH, LH)

common α subunits
unique β subunits

Figure 42–2. Chemical diversity of hormones. **A.** Cholesterol derivatives. **B.** Tyrosine derivatives. **C.** Peptides of various sizes **D.** Glycoproteins (TSH, FSH, LH) with common α subunits and unique β subunits.


STIMULUS
Recognition
Group I hormones
Group II hormones
Hormone release
Hormone•receptor complex
Many different signals
Signal generation
Effects
Gene transcription
Transporters Channels
Protein translocation
Protein modification
COORDINATED RESPONSE TO STIMULUS


Endocrine
Blood vessel
Hormone secretion into blood by endocrine gland
Distant target cells
Paracrine
Secretory cell
Adjacent target cell
Autocrine
Target sites on same cell
Receptor
Hormone or other extra cellular signal

Selected hormones & their functions

Hormone	Source	Principal functions
Insulin	Pancreas	Controls blood-sugar level and storage of glycogen.
Glucagon	Pancreas	Stimulates conversion of glycogen to glucose; raises blood sugar level.
Oxytocin	Pituitary gland	Stimulates contraction of the uterine muscles and secretion of milk by the mammary glands.
Vasopressin	Pituitary gland	Controls water excretion by the kidneys; stimulates contraction of the blood vessels.
Growth hormone	Pituitary gland	Stimulates growth.
Adrenocorticotrophic hormone (ACTH)	Pituitary gland	Stimulates the adrenal cortex, which, in turn, releases several steroid hormones.
Prolactin	Pituitary gland	Stimulates milk production by the mammary glands after birth of baby.
Epinephrine	Adrenal glands	Stimulates rise in blood pressure, acceleration of heartbeat, decreased secretion of insulin, and increased blood sugar.

Selected hormones & their functions cont...

Hormone	Source	Principal functions
Cortisone	Adrenal glands	Helps control carbohydrate metabolism, salt and water balance, formation and storage of glycogen.
Thyroxine & Triiodothyronine	Thyroid gland	Increases the metabolic rate of carbohydrates and proteins.
Calcitonin	Thyroid gland	Prevents the rise of calcium and phosphate in the body.
Parathyroid	Parathyroid gland	Regulates the metabolism of calcium and phosphate in hormone in the body.
Gastrin	Stomach	Stimulates secretion of gastric juice.
Secretin	Duodenum	Stimulates secretion of pancreatic juice.
Estrogen	Ovaries	Stimulates development and maintenance of female sexual characteristics.
Progesterone	Ovaries	Stimulates female sexual characteristics and maintains pregnancy.
Testosterone	Testes	Stimulates development and maintenance of male sexual characteristics.

Examples of hormone antagonists used in therapy

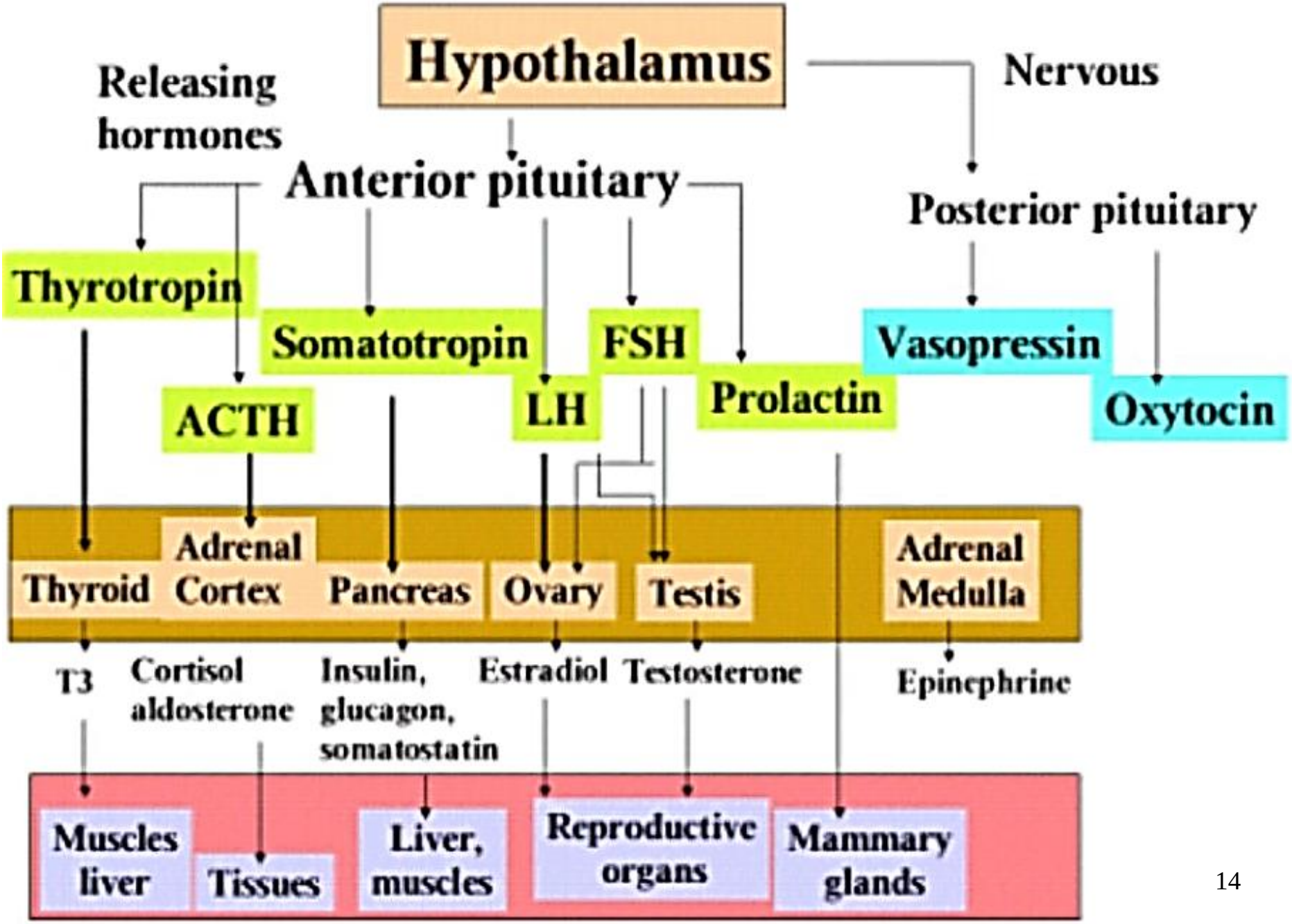
Antagonist to	Use	
Growth Hormone	Acromegaly, Diabetes	
Progesterone	Contraceptive, abortion	
Glucocorticoid Syndrome	Spontaneous Cushing's	
Mineralo-corticoid	Primary and secondary mineralocorticoid excess	
Androgen	Prostate cancer	
Estrogen	Breast cancer	← Tamoxifin
GnRH	Prostate cancer	
Adrenrgic	Hypertension, hyperthyroidism	
Prostaglandin	Acute and chronic inflammatory disease	

Hormone Receptors

Nuclear receptors
estrogens

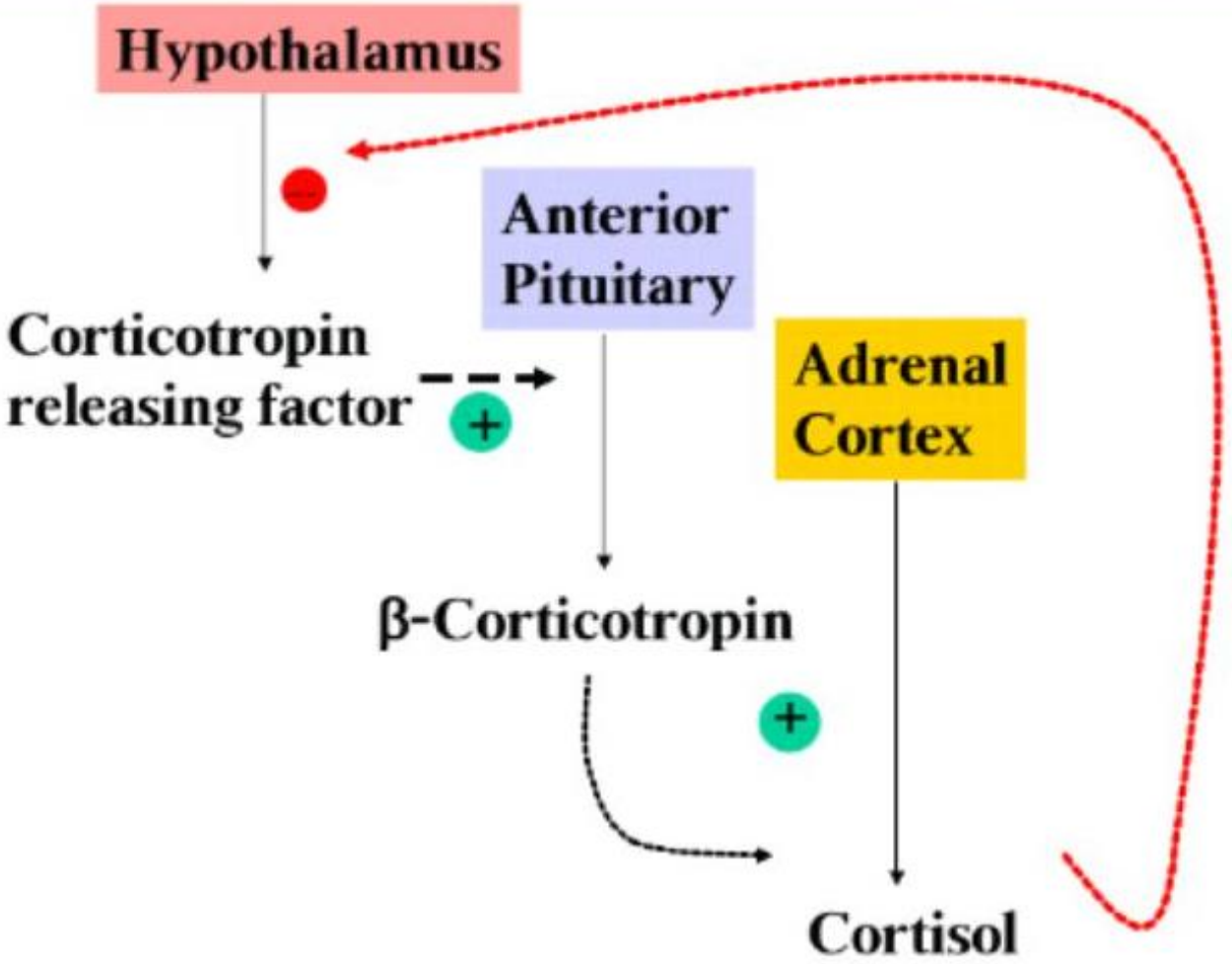
Cytoplasmic receptors
Most steroid and thyroid hormones

Cell surface **membrane** receptors
Polypeptide hormones and catecholamines

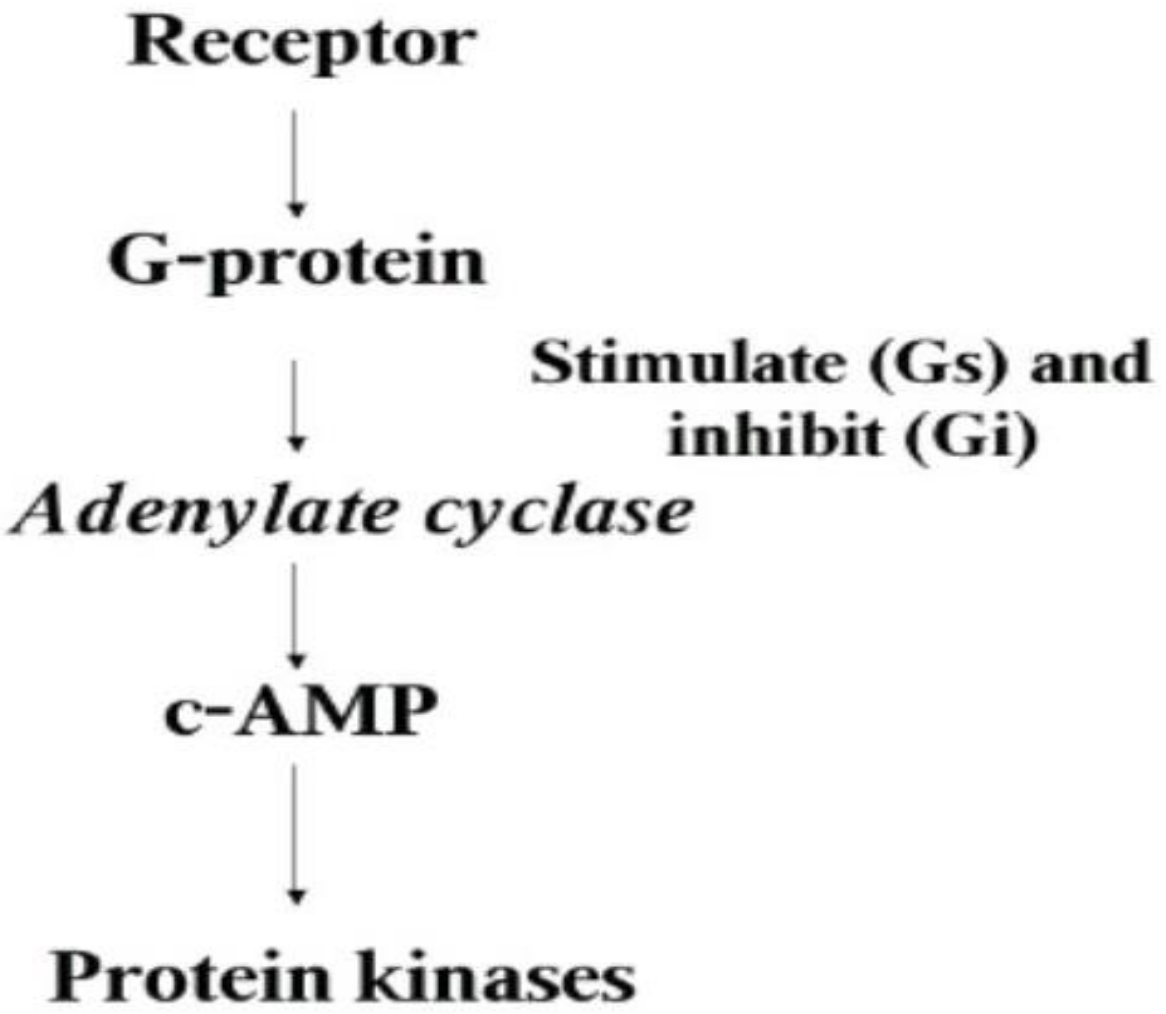

Hypothalamus
Releasing hormones
Nervous
Anterior pituitary
Posterior pituitary
Thyrotropin
Somatotropin
FSH
Vasopressin
ACTH
LH
Prolactin
Oxytocin
Adrenal Cortex
Thyroid
Pancreas
Ovary
Testis
Adrenal Medulla
T3
Cortisol aldosterone
Insulin, glucagon, somatostatin
Estradiol
Testosterone
Epinephrine
Muscles liver
Tissues
Liver, muscles
Reproductive organs
Mammary glands

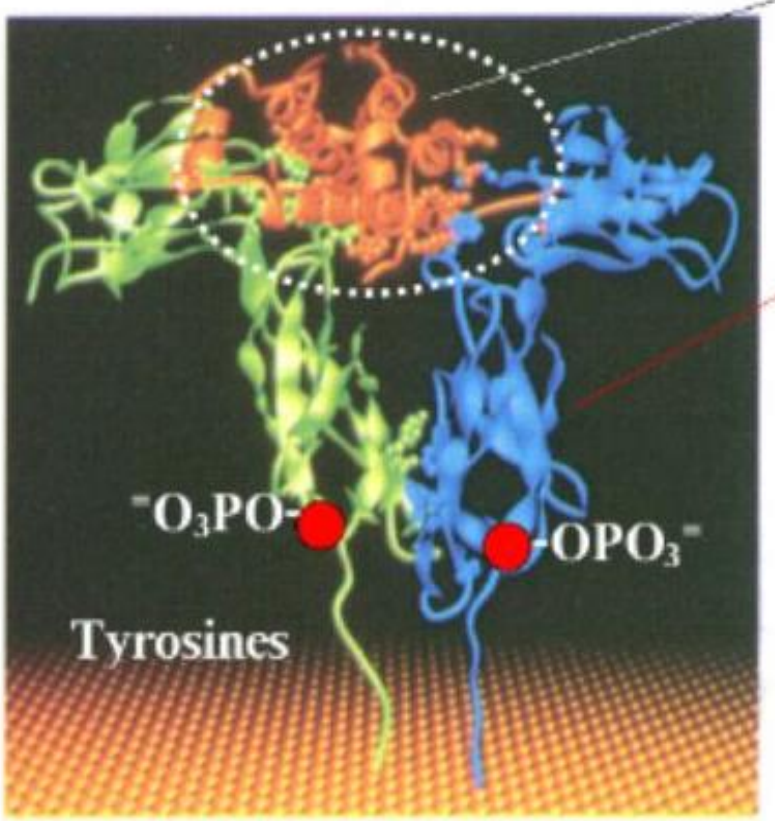
Feedback Loops

Rule: Hormones elicit their own shut off mechanism

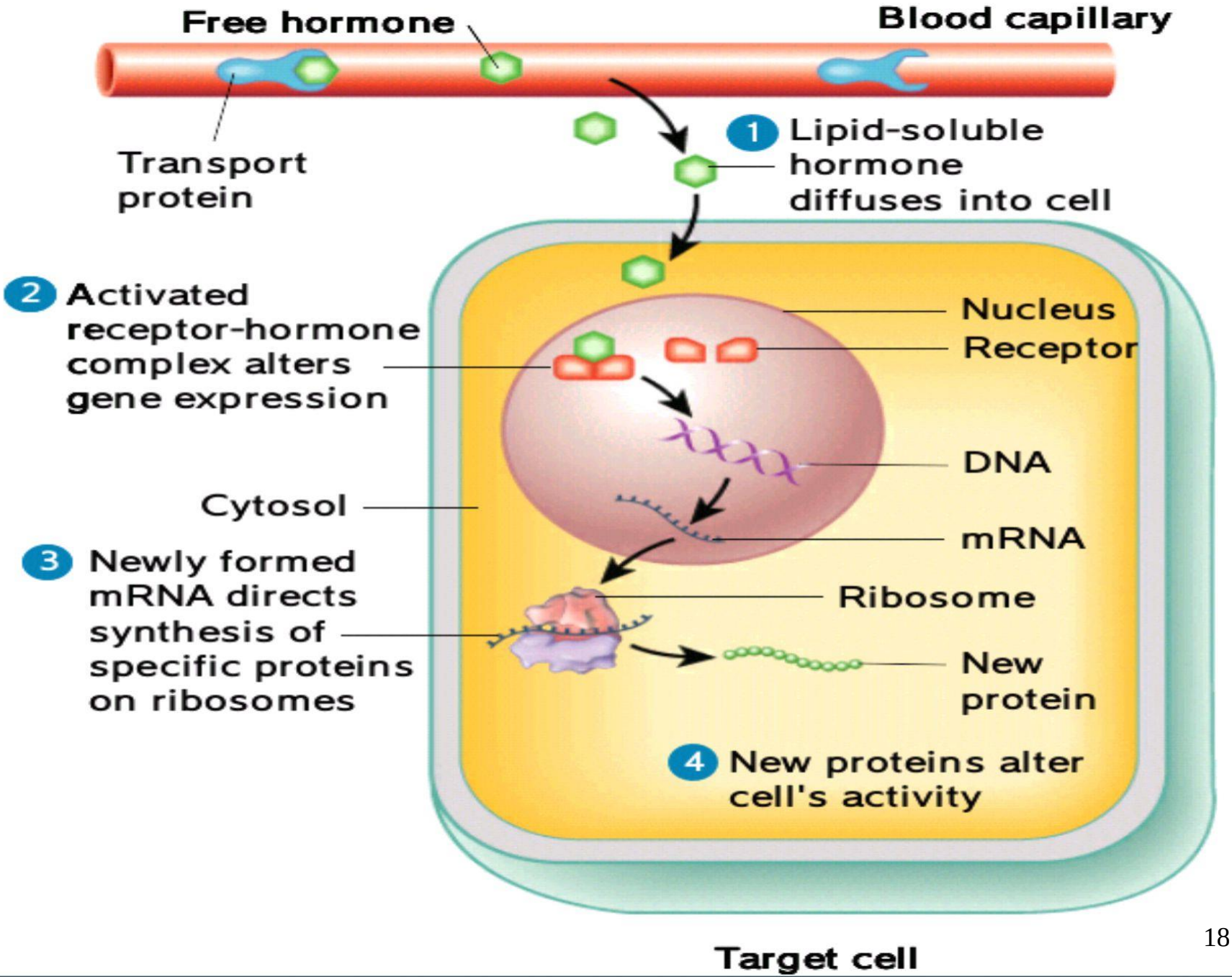


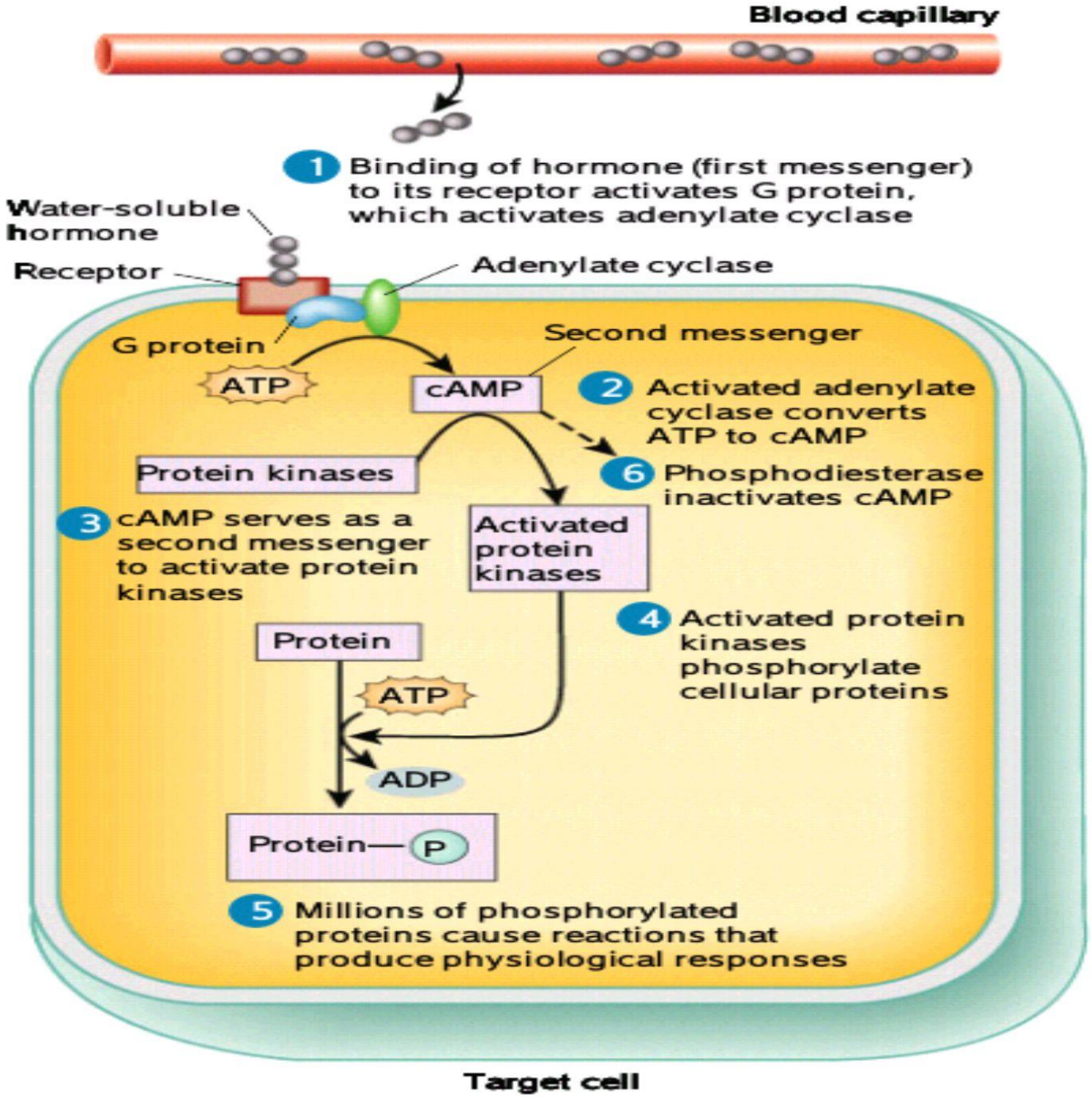
Cyclic AMP System





Growth Hormone Receptor


Free hormone
Blood capillary
Transport protein
1 Lipid-soluble hormone diffuses into cell
2 Activated receptor-hormone complex alters gene expression
Nucleus
Receptor
DNA
Cytosol
mRNA
3 Newly formed mRNA directs synthesis of specific proteins on ribosomes
Ribosome
New protein
4 New proteins alter cell's activity
Target cell


Blood capillary
1 Binding of hormone (first messenger) to its receptor activates G protein, which activates adenylate cyclase
Water-soluble hormone
Receptor
Adenylate cyclase
G protein
ATP
Second messenger
cAMP
2 Activated adenylate cyclase converts ATP to cAMP
Protein kinases
6 Phosphodiesterase inactivates cAMP
3 cAMP serves as a second messenger to activate protein kinases
Activated protein kinases
4 Activated protein kinases phosphorylate cellular proteins
Protein
ATP
ADP
Protein—P
5 Millions of phosphorylated proteins cause reactions that produce physiological responses
Target cell

Any questions ??