

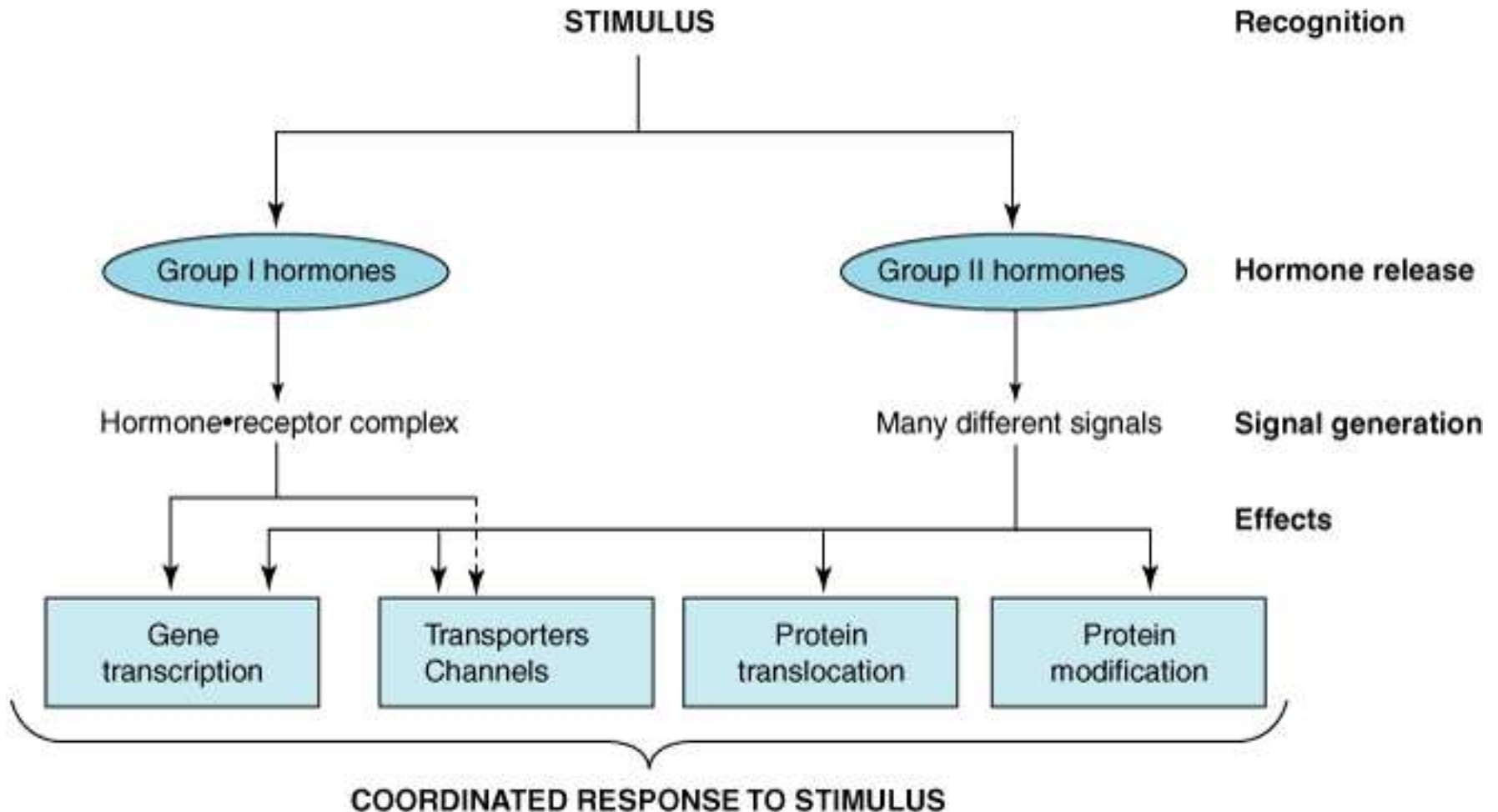
Biochemistry of hormones-2.

Individual endocrinology

Lecture #27

Lecturer A. N. Koval

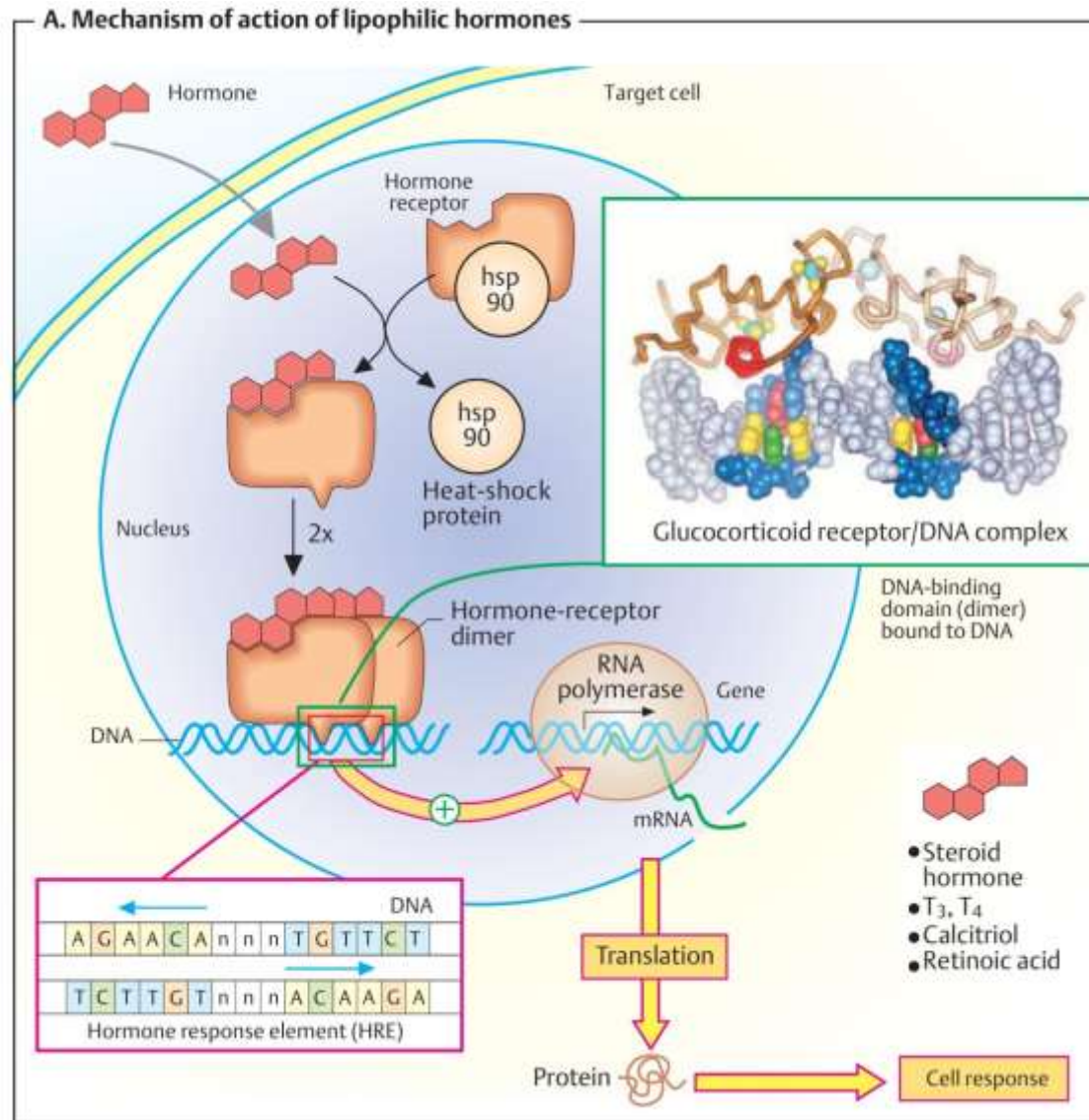
Hormones Transduce Signals to Affect Homeostatic Mechanisms



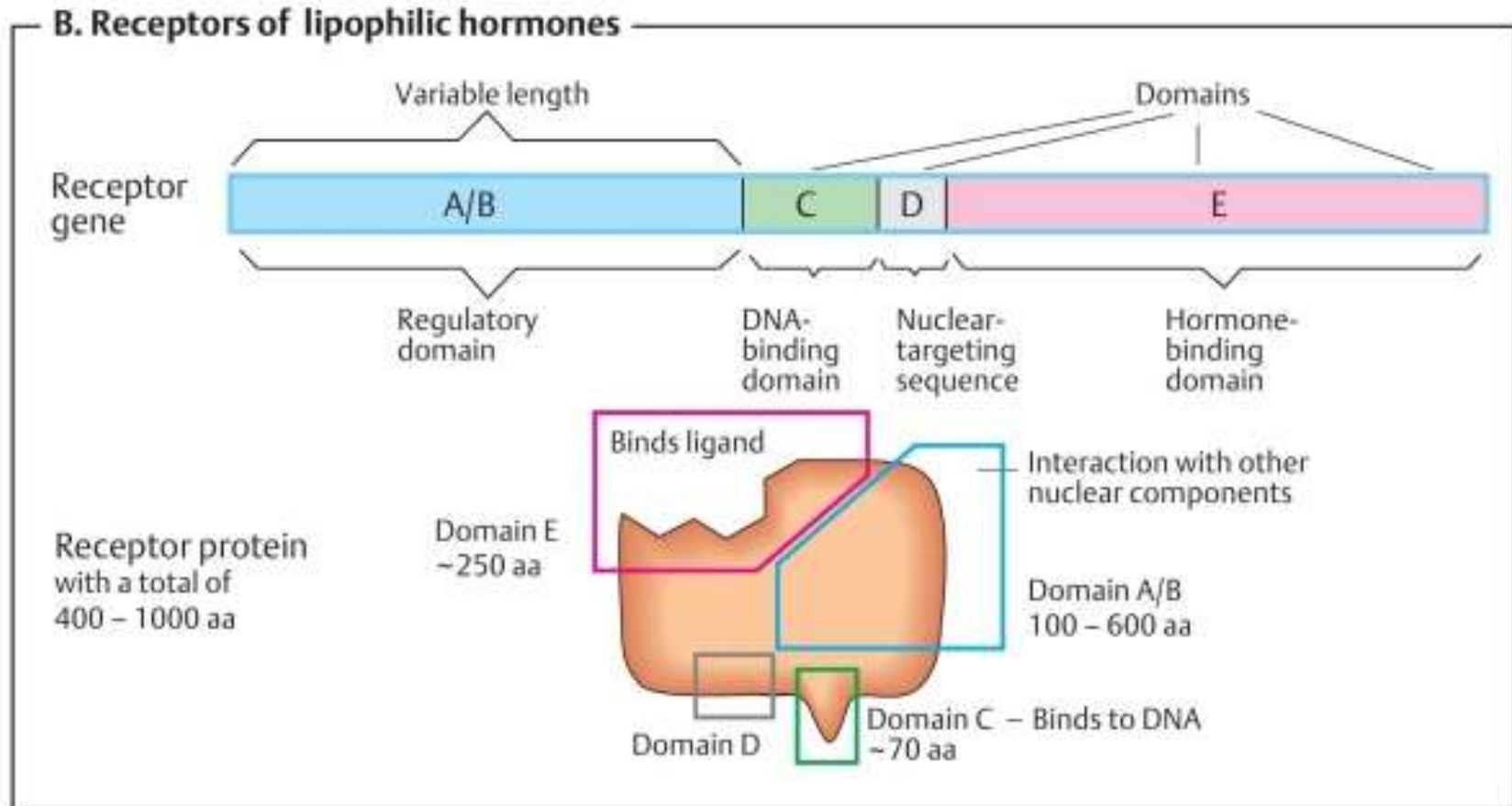
Lipophilic hormones

- Classifying hormones into hydrophilic and lipophilic molecules indicates the chemical properties of the two groups of hormones and also reflects differences in their mode of action.

Mechanism of Action of Lipophilic Hormones

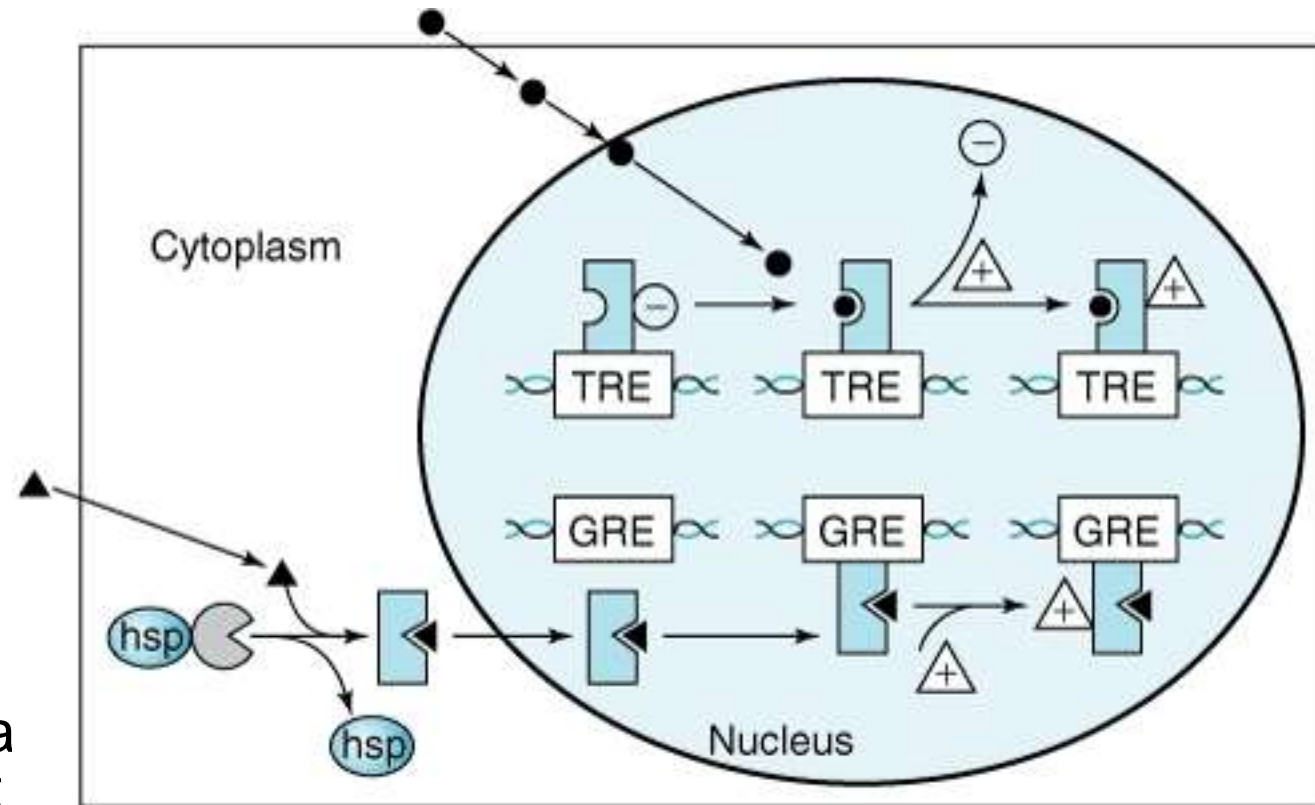


Receptors of Lipophilic Hormones

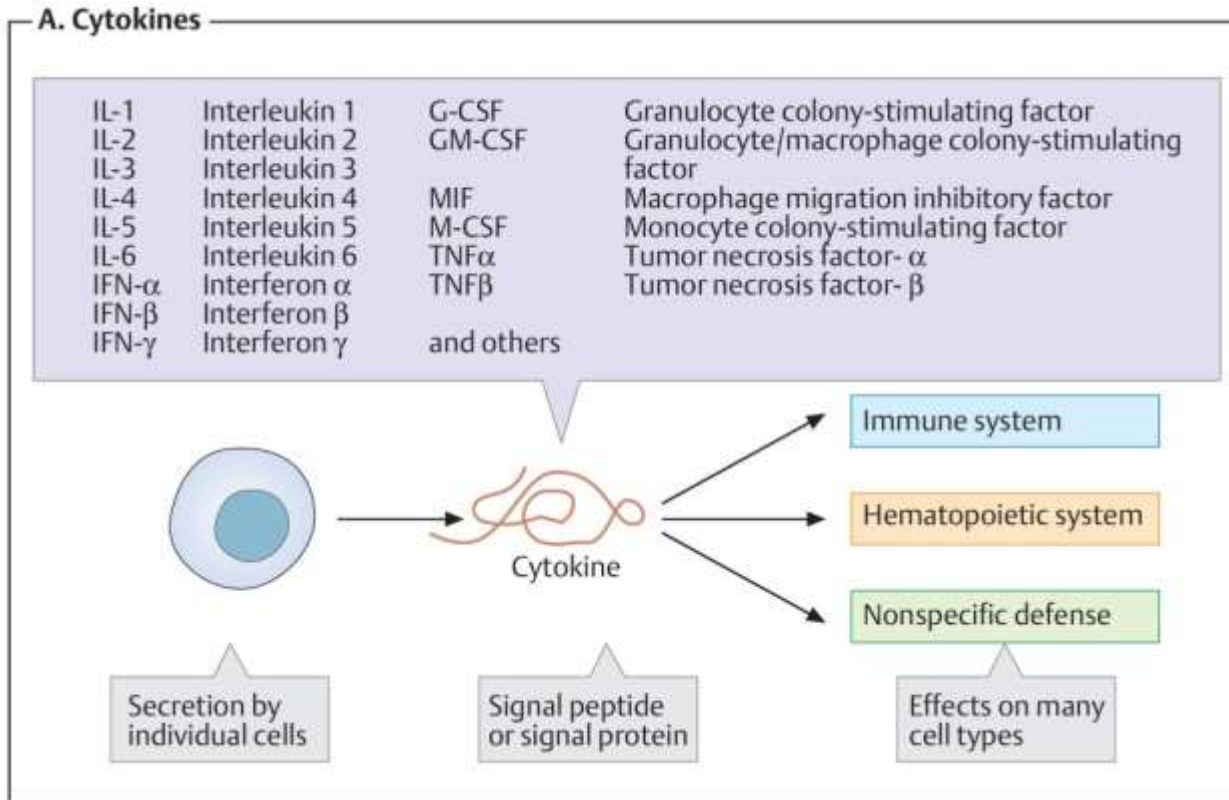


Regulation of gene expression by class I hormones

- Steroid hormones readily gain access to the cytoplasmic compartment of target cells.
- Glucocorticoid hormones (solid triangles) encounter their cognate receptor in the cytoplasm, where it exists in a complex with heat shock protein 90 (hsp).



Cytokines



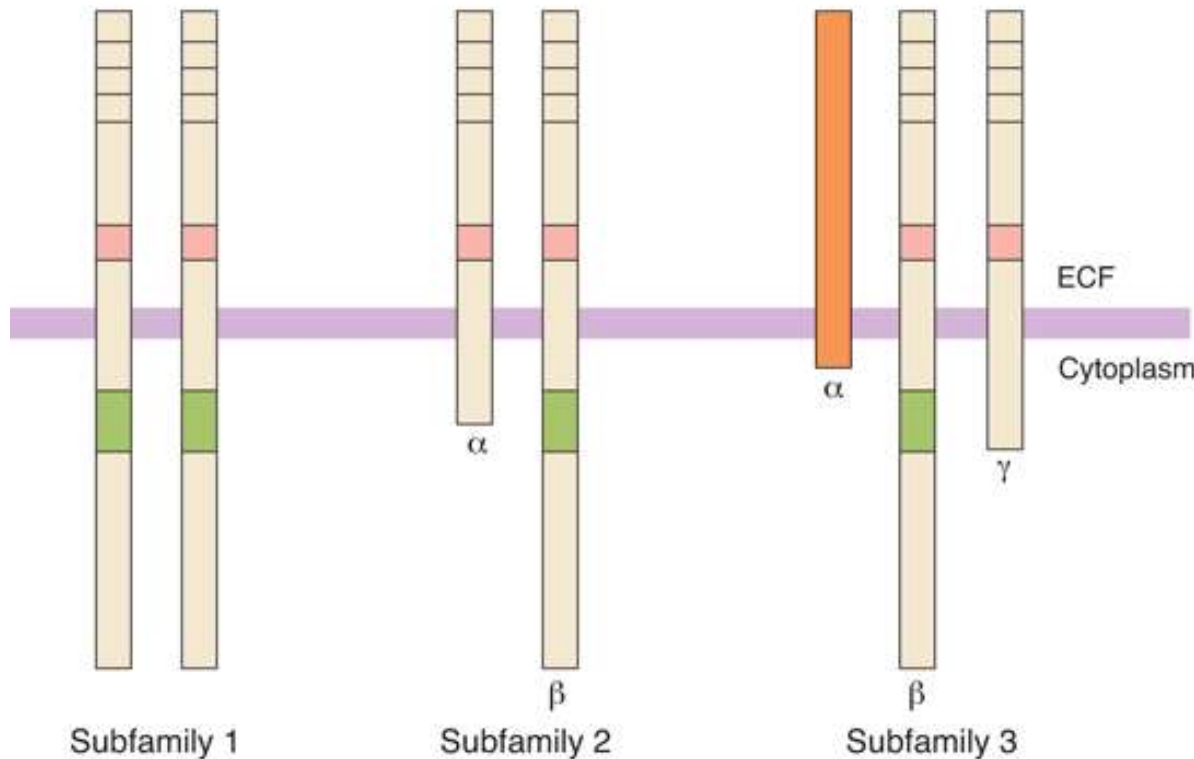
Cytokines are growth factors that specifically act to orchestrate the development of hemopoietic cells and the immune response

Erythropoietin
G-CSF
IL-4
IL-7
Growth hormone
PRL

IL-3
GM-CSF } Shared β
subunit
IL-5
IL-6 } Shared gp130
subunit
IL-11
LIF
OSM
CNTF

IL-2
IL-4
IL-7
IL-9
IL-15

Members of one of the cytokine receptor superfamilies, showing shared structural elements



All the subunits except the subunit in subfamily 3 have four conserved cysteine residues (open boxes at top) and a Trp-Ser-X-Trp-Ser motif (pink).

Many subunits also contain a critical regulatory domain in their cytoplasmic portions (green).

CNTF, ciliary neurotrophic factor;

LIF, leukemia inhibitory factor;

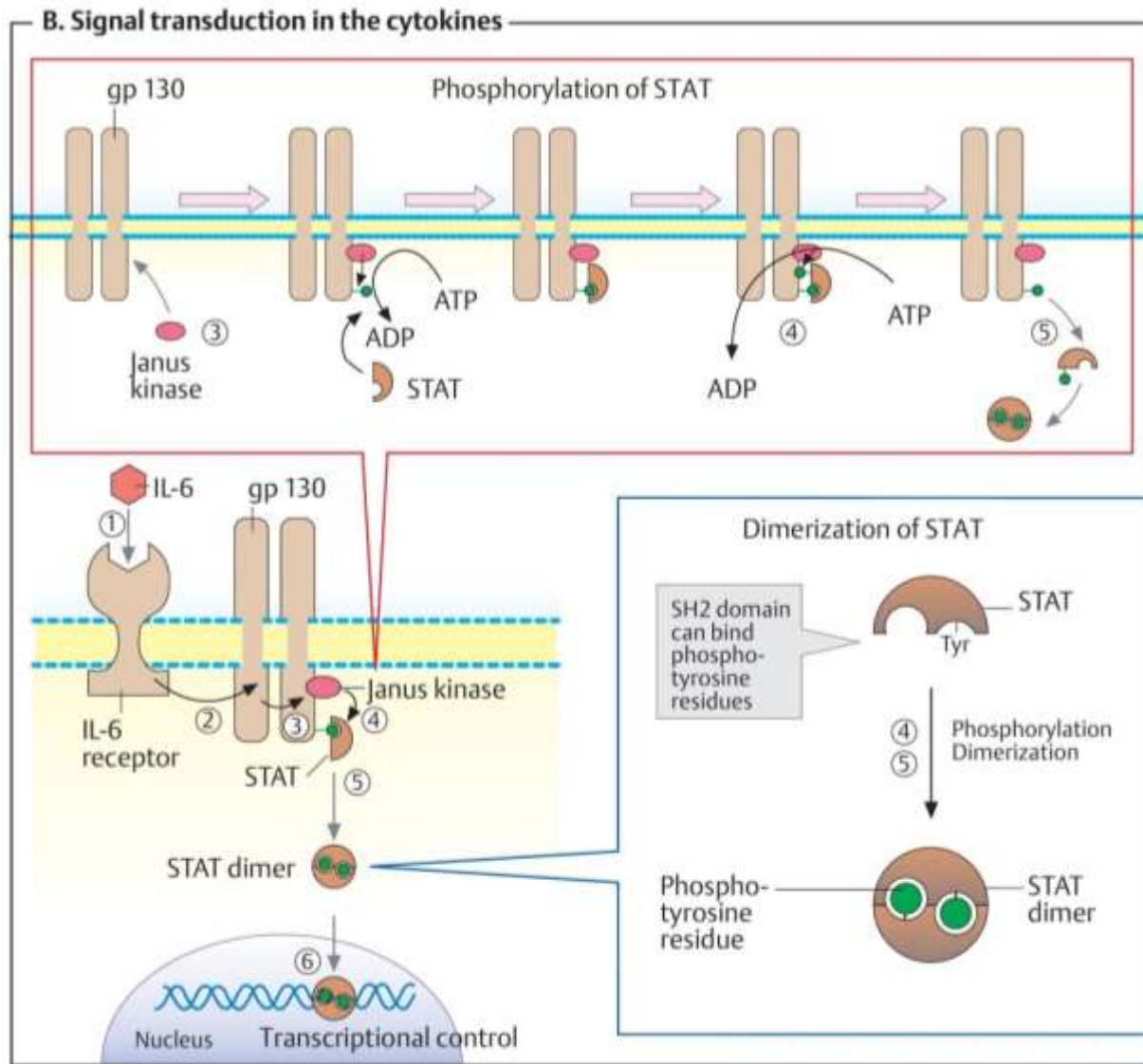
OSM, oncostatin M;

PRL, prolactin.

Source: Barrett KE, Barman SM, Boitano S, Brooks H: *Ganong's Review of Medical Physiology, 23rd Edition*: <http://www.accessmedicine.com>

Copyright © The McGraw-Hill Companies, Inc. All rights reserved.

Signal Transduction in the Cytokines



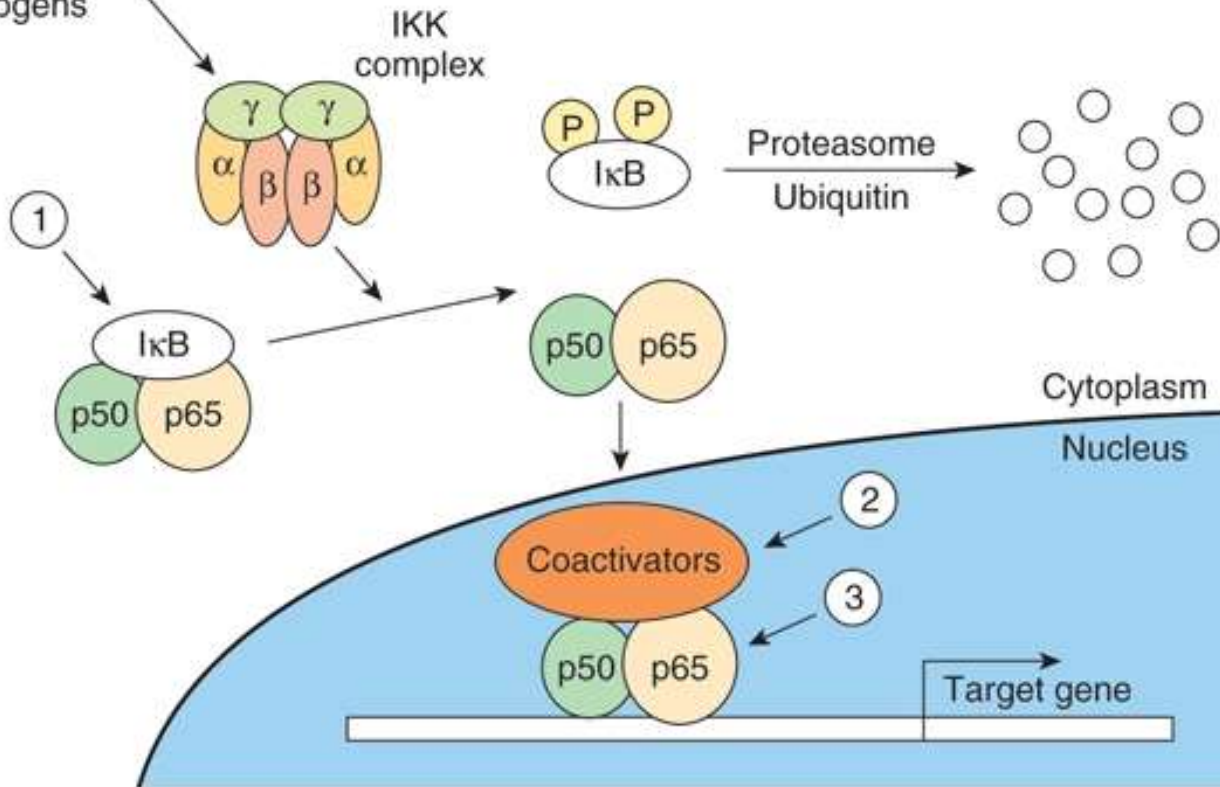
As peptides or proteins, the cytokines are hydrophilic signaling substances that act by binding to receptors on the cell surface.

Binding of a cytokine to its receptor leads via several intermediate steps to the activation of transcription of specific genes.

Regulation of the NF- κ B pathway

NF- κ B activators

Proinflammatory cytokines
Bacterial and viral infection
Reactive oxygen species
Mitogens



NF- κ B consists of two subunits, p50 and p65. important for the inflammatory response. NF- κ B is restricted from entering the nucleus by I κ B, an inhibitor of NF- κ B.

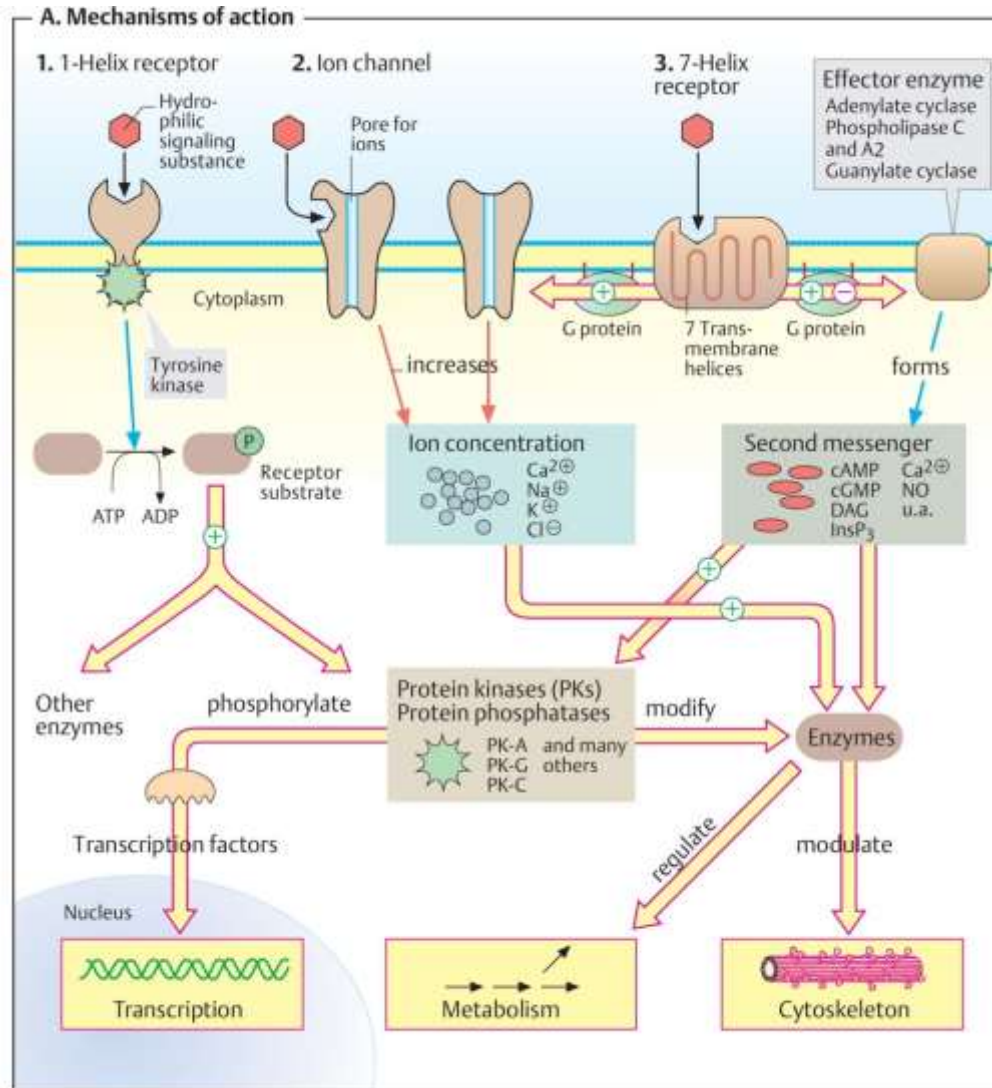
This cytoplasmic protein is phosphorylated by an IKK complex which is **activated** by cytokines, reactive oxygen species, and mitogens.

I κ B can be degraded, thus releasing its hold on NF- κ B.

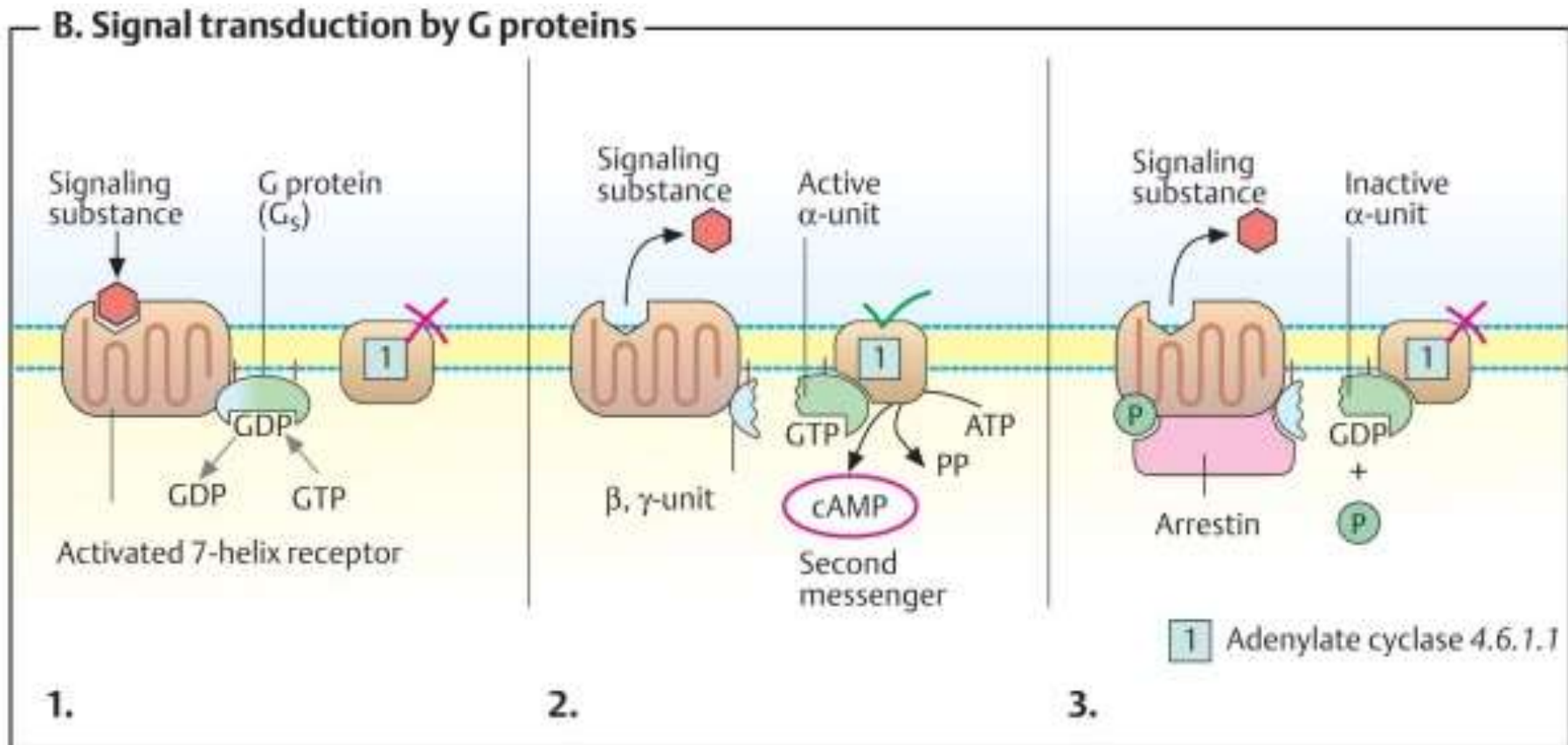
Glucocorticoids, potent antiinflammatory agents, can affect this process.

Source: Murray RK, Bender DA, Botham KM, Kennelly PJ, Rodwell VW, Weil PA: *Harper's*

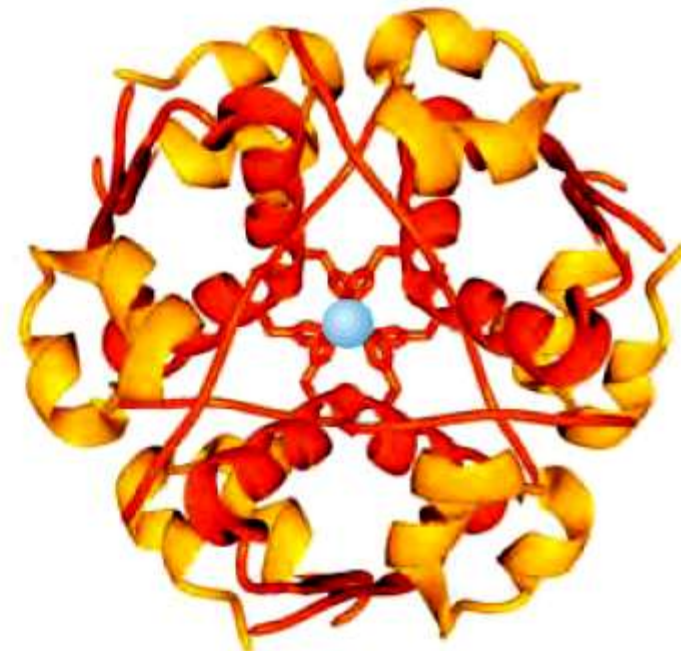
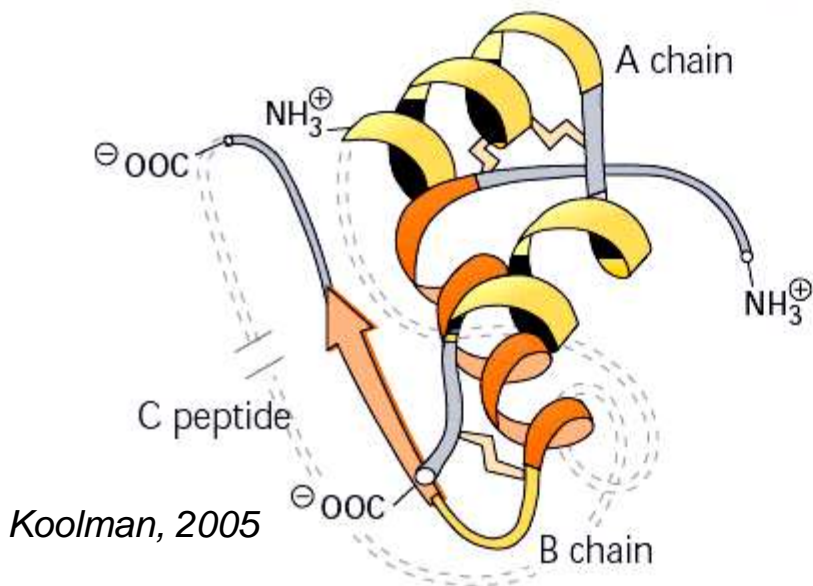
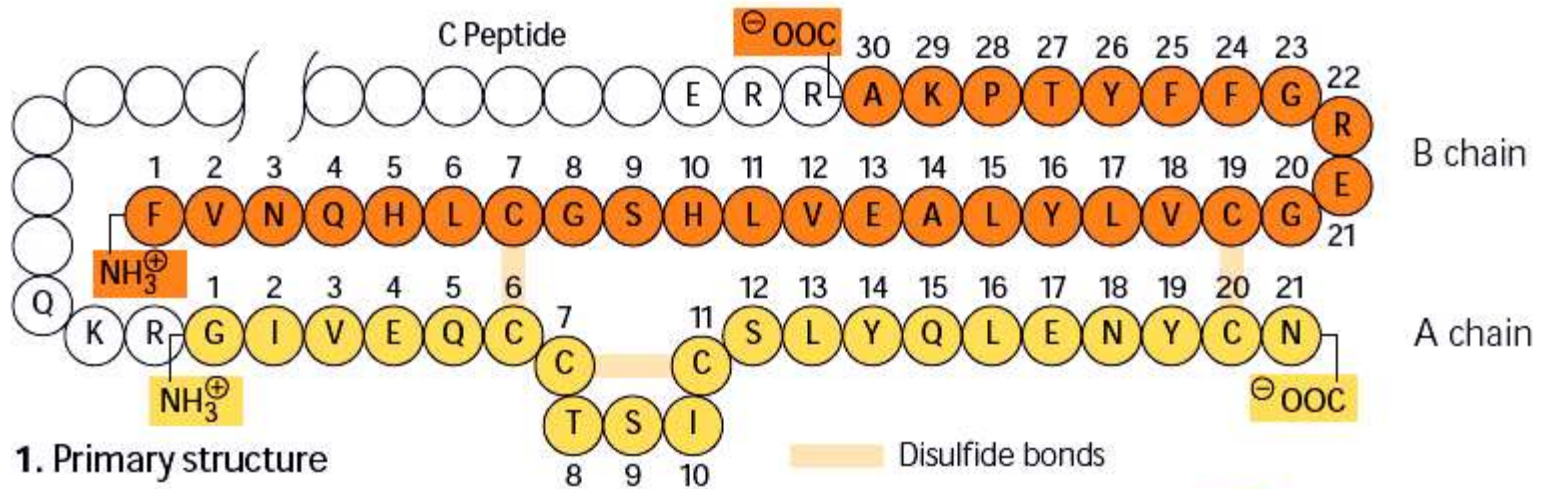
Mechanism of Action of Hormones



Signal Transduction by G-proteins



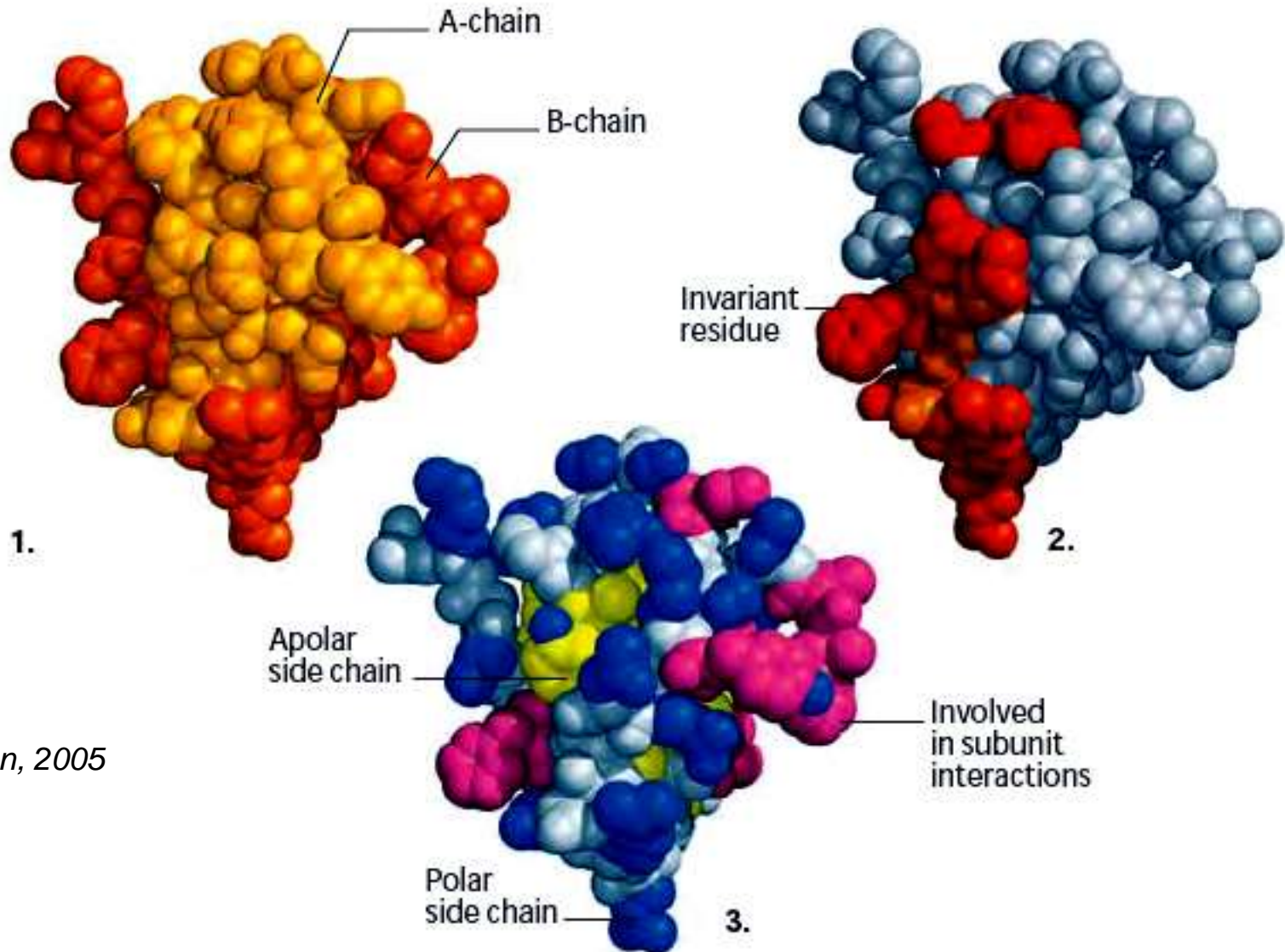
Insulin Structure



10. **2. Secondary and tertiary structure**

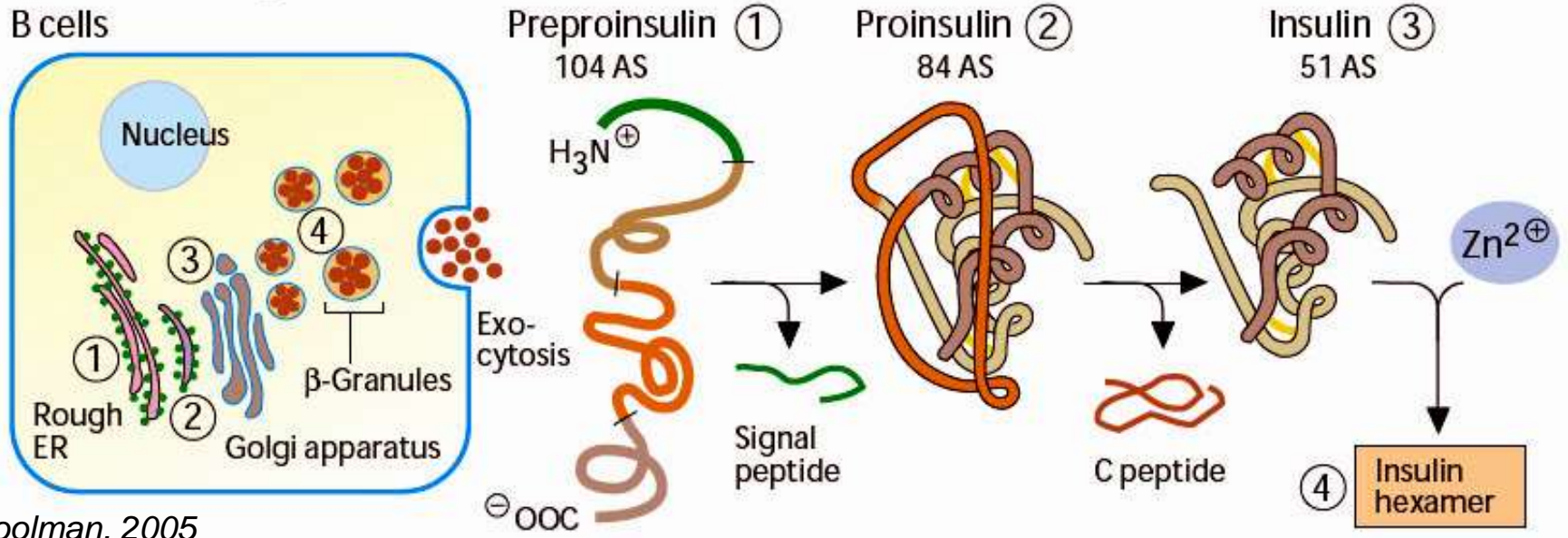
3. Quaternary structure

Insulin (Monomer)



Koolman, 2005

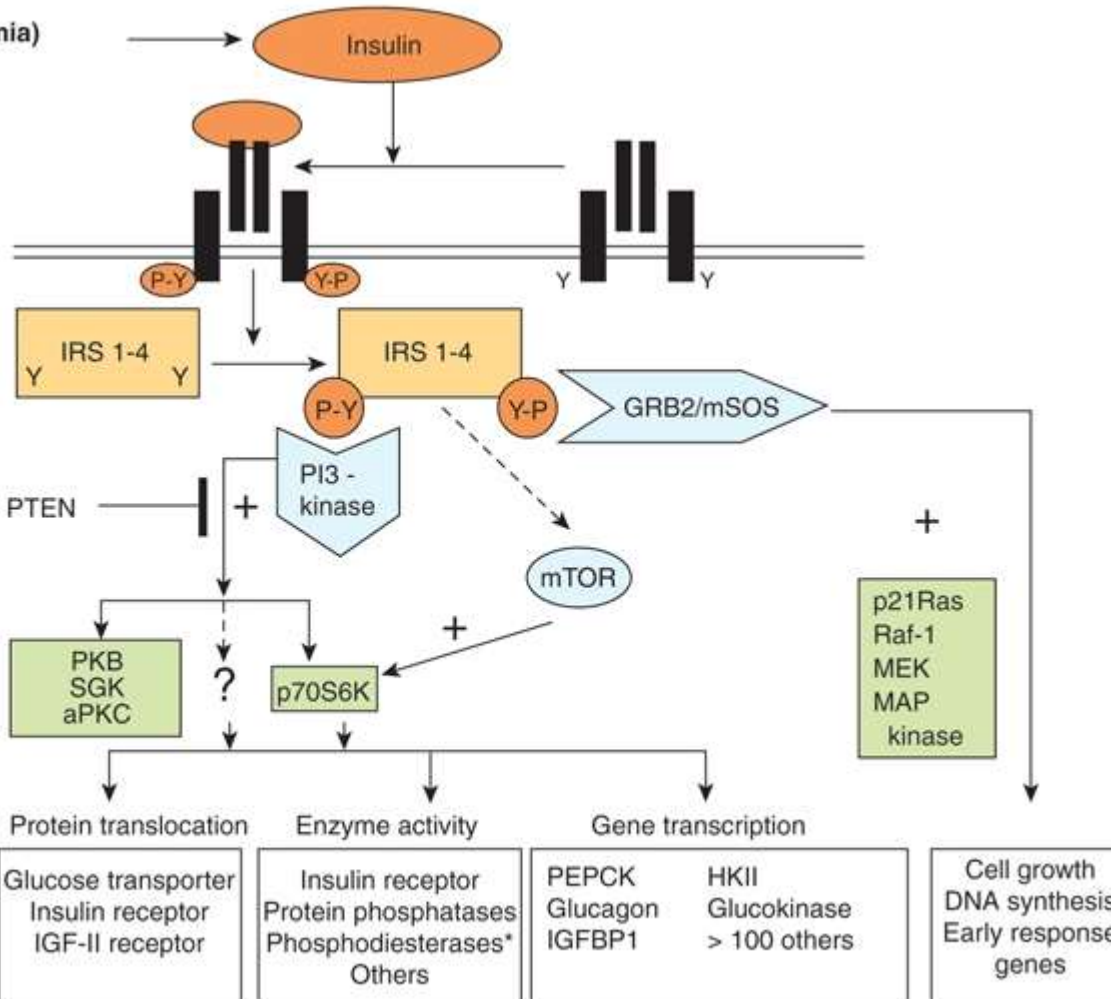
Insulin biosynthesis



Koolman, 2005

Insulin signaling pathways

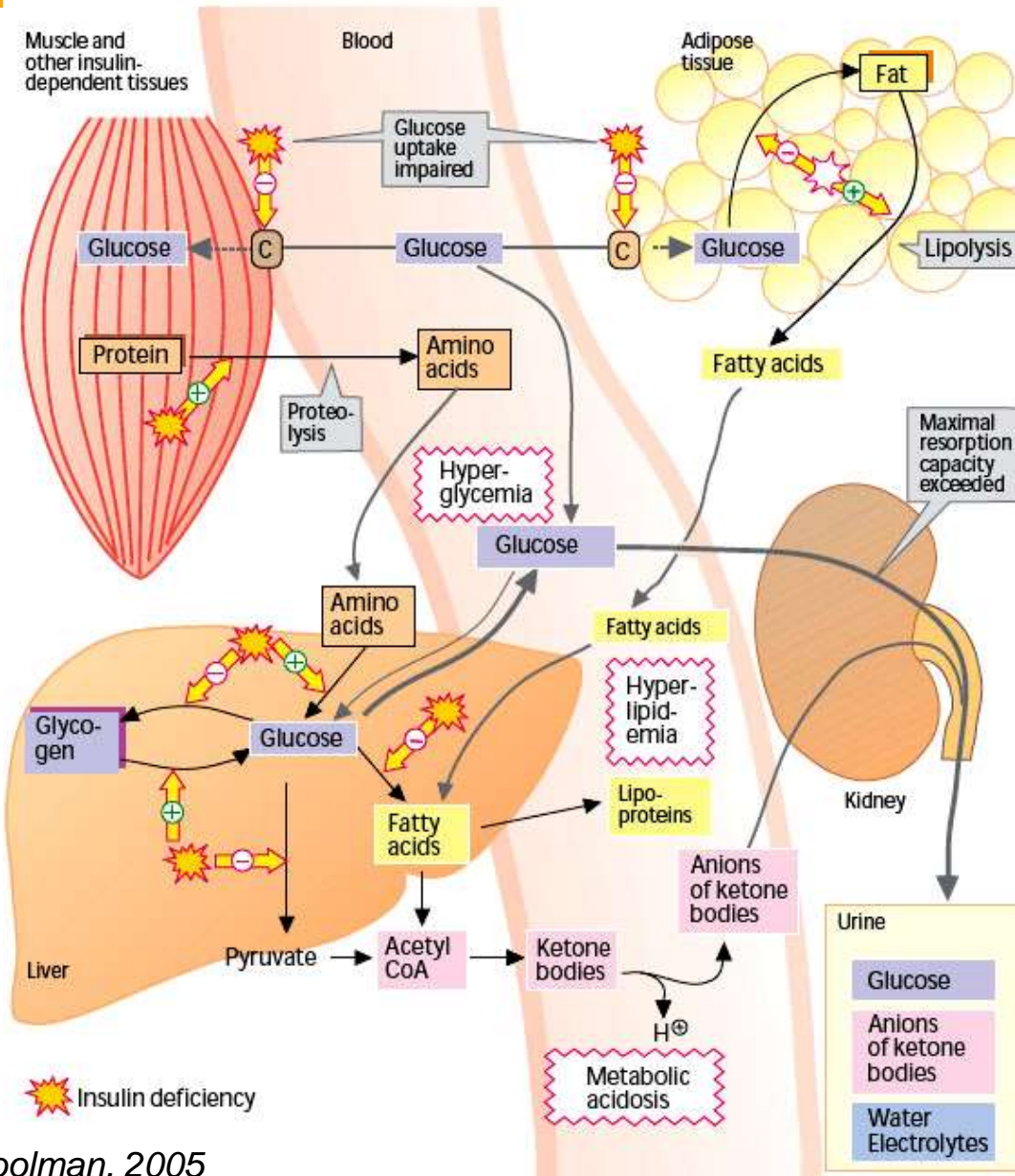
Recognition
(hyperglycemia)



IGFBP, insulin-like growth factor binding protein;
IRS 1-4, insulin receptor substrate isoforms 1-4;
PI-3 kinase, phosphatidylinositol 3-kinase;
PTEN, phosphatase and tensin homolog deleted on chromosome 10;
PKB, protein kinase B;
SGK, serum and glucocorticoid-regulated kinase;
aPKC, atypical protein kinase C;
p70S6K, p70 ribosomal protein S6 kinase;
mTOR, mammalian target of rapamycin;
GRB2, growth factor receptor binding protein 2;
mSOS, mammalian son of sevenless;
MEK, *MAP kinase* kinase and ERK kinase;
MAP kinase, mitogen-activated protein kinase

Source: Murray RK, Bender DA, Botham KM, Kennelly PJ, Rodwell VW, Weil PA: *Harper's*

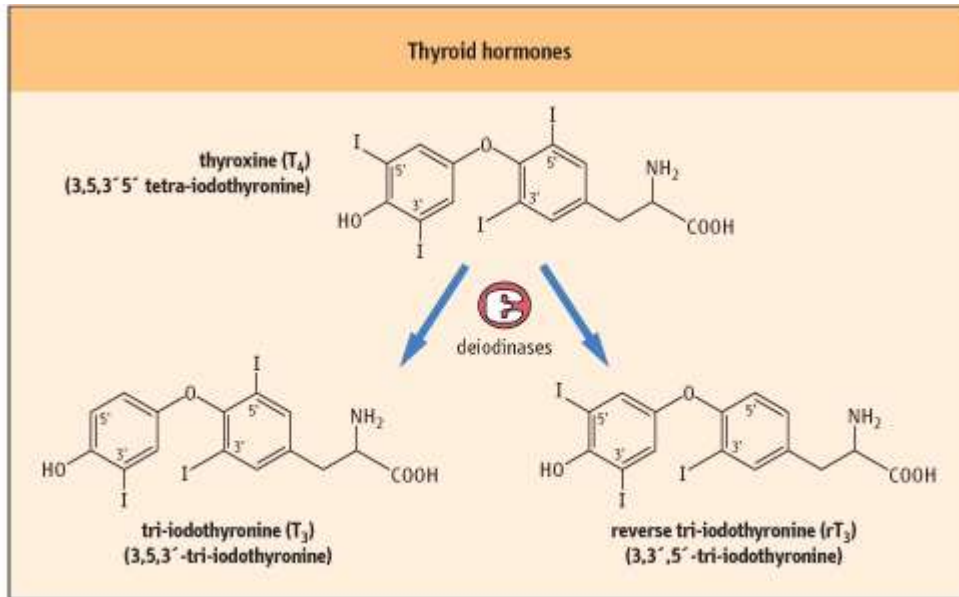
Effects of Insulin Deficiency



Koolman, 2005

- Hyperglycemia
 - glucosuria
- Hyperlipidemia
 - atherosclerosis
- Metabolic acidosis
 - Ketosis
 - Diabetic coma
- Hyperosmolarity of blood

Thyroid Hormone Biochemistry



© Elsevier Ltd. Baynes & Dominiczak: Medical Biochemistry 2E www.studentconsult.com

T₃ and T₄ increase the metabolic rate of tissues and affect the basal metabolic rate.

- Altered transcription after the binding of T₃ to its nuclear receptor.
- ↑ thermogenesis, mitochondrial oxidative metabolism,
- ATP utilization, Na⁺/K⁺-ATPase.
- Lipolysis is stimulated by cAMP-dependent activation of hormone sensitive lipase => fatty acids oxidized => ATP used for thermogenesis.

- The thyroid hormones may be considered the accelerator pedal of metabolism.

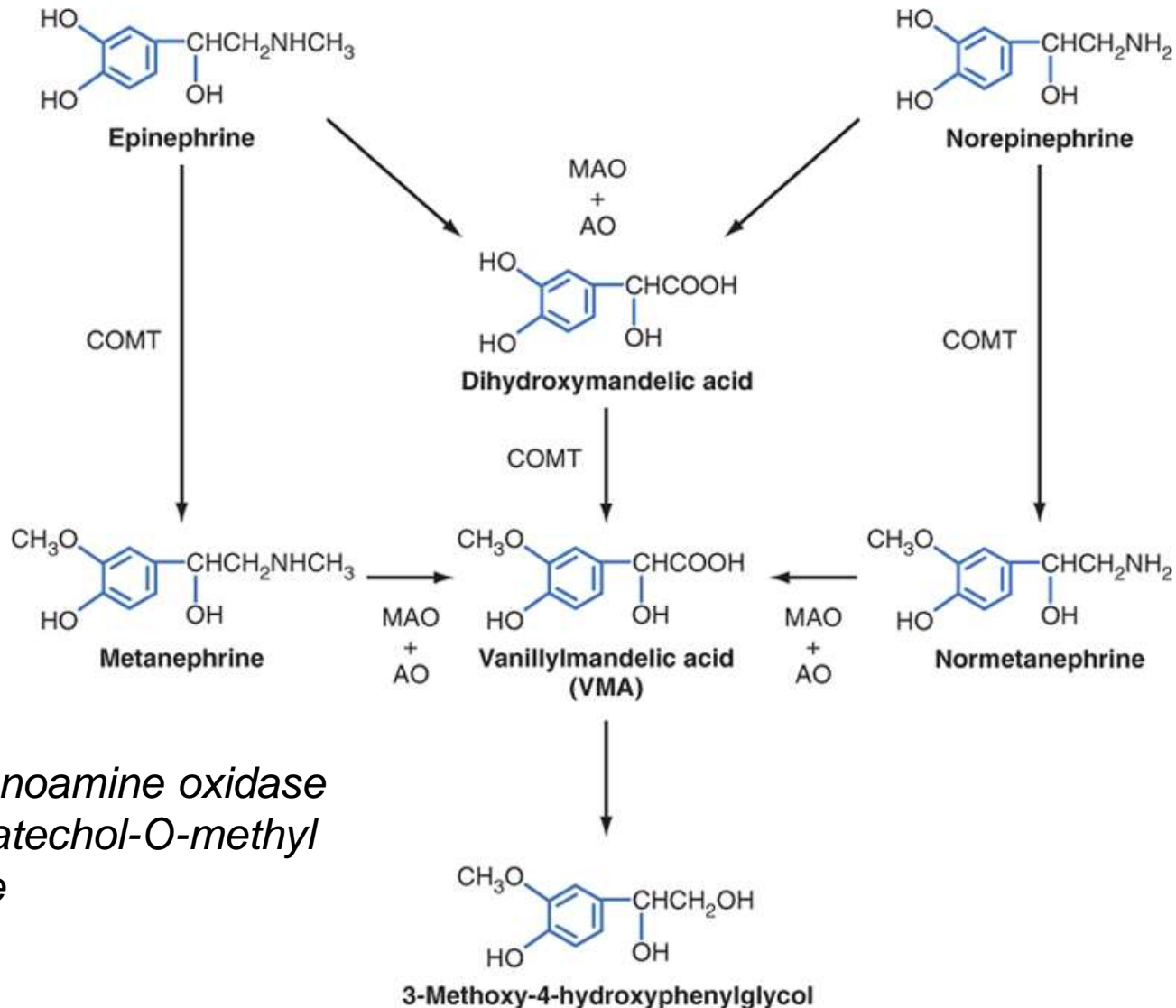
Effects of Thyroid Hormones

- There are 3 groups of the effects:
 1. **Anabolic action** - influence on growth and differentiation of tissues.
 2. **Metabolic effects** – increase of catabolic processes intensity (oxidation, lipolysis).
 3. **Sensibilizing effects** – increase of cell sensitivity to action of other hormones, in particular *estrogens* and *catecholamines*.

Sensibilizing and Permissive Effect of Hormones

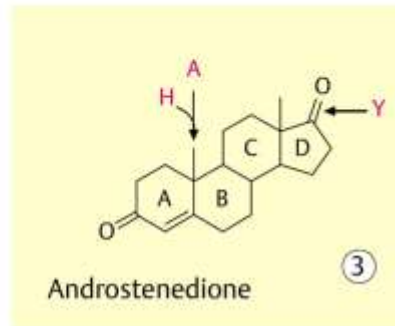
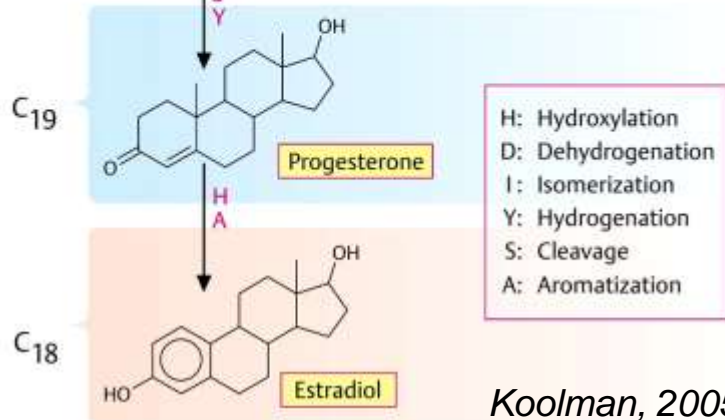
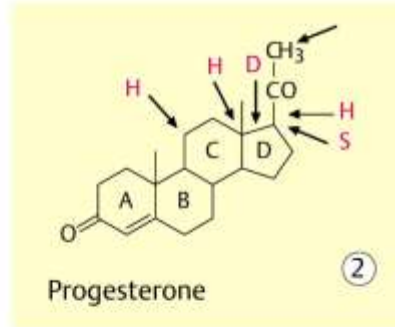
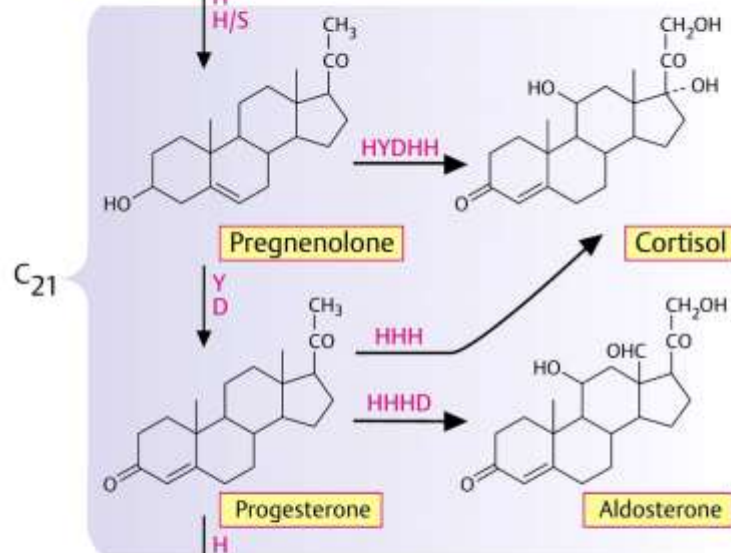
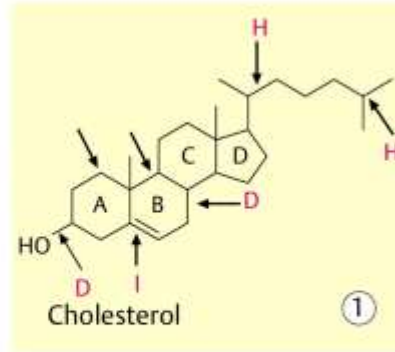
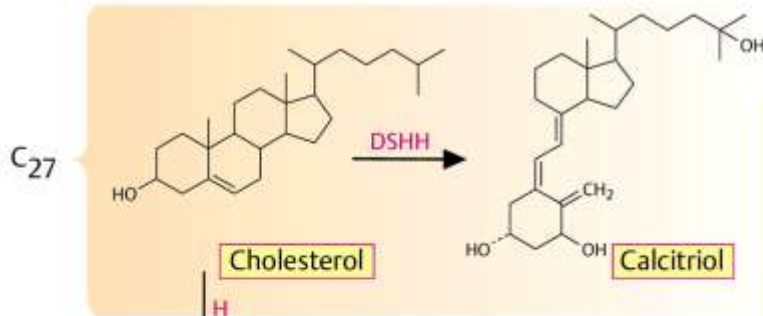
- Sensibilizing effect – when one hormone increases the effect of the others.
- Permissive effect – when there is no effect of other hormones in the absence of one hormone.

Catabolism of Catecholamines



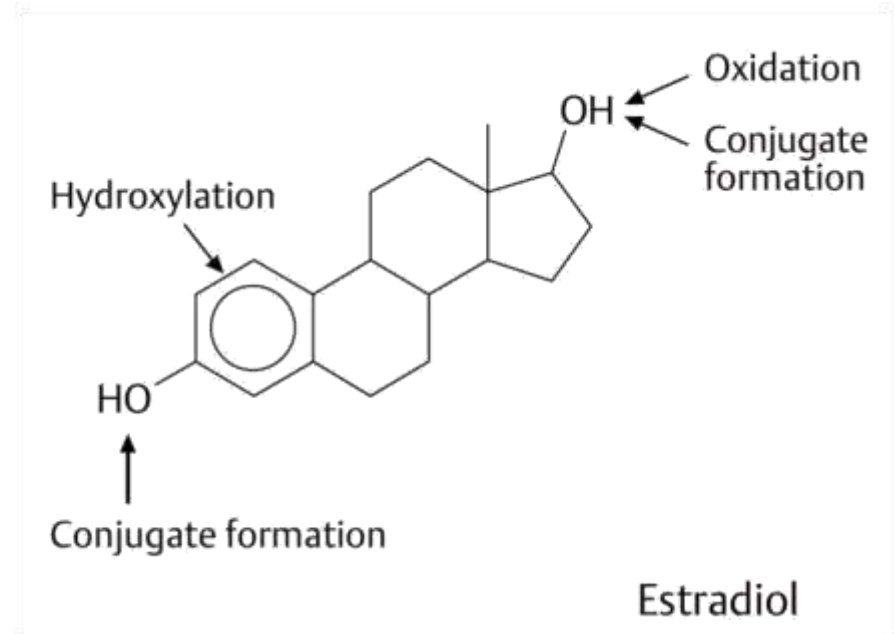
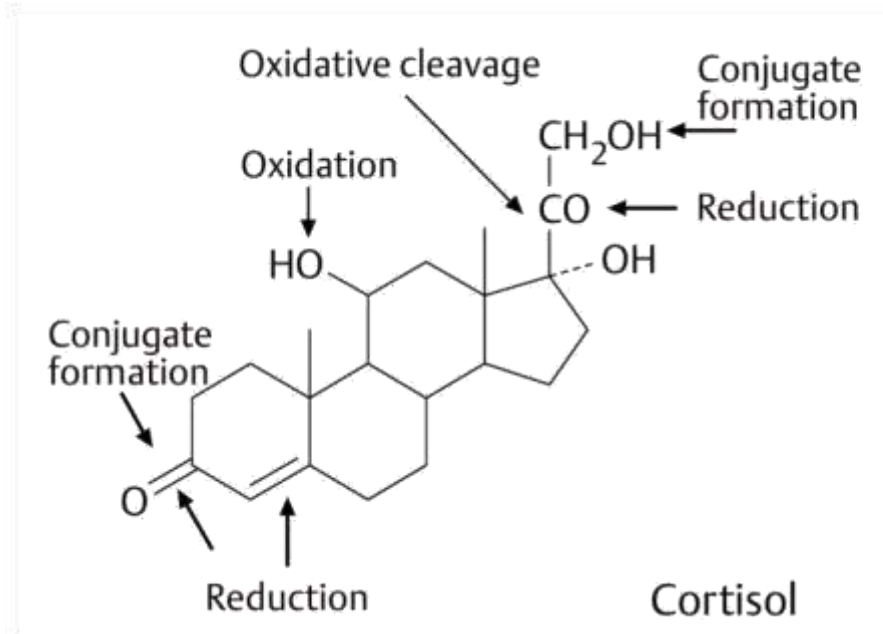
MAO – monoamine oxidase
COMT – catechol-O-methyl transferase

Biosynthesis of Steroid Hormones



- All **steroid hormones** derived from cholesterol.
- Hydroxylase reactions are catalyzed by *monooxygenases* ("hydroxylases"), *cytochrome P450* family.
- Estrogens possess specific **aromatic A ring** as a result of *aromatase* action.
- **Pregnenolone** as important intermediate. Also **progesterone**.

Inactivation of Steroid Hormones





Thank you
for your attention