



Synthesis and Degradation of hormones



Chemistry of Hormones

- **Steroids**
- Small molecules - NO
- Amino acid derivatives
 - Thyroid hormones

- Catecholamines
- Proteins and peptides
- FA derivatives - eicosanoids

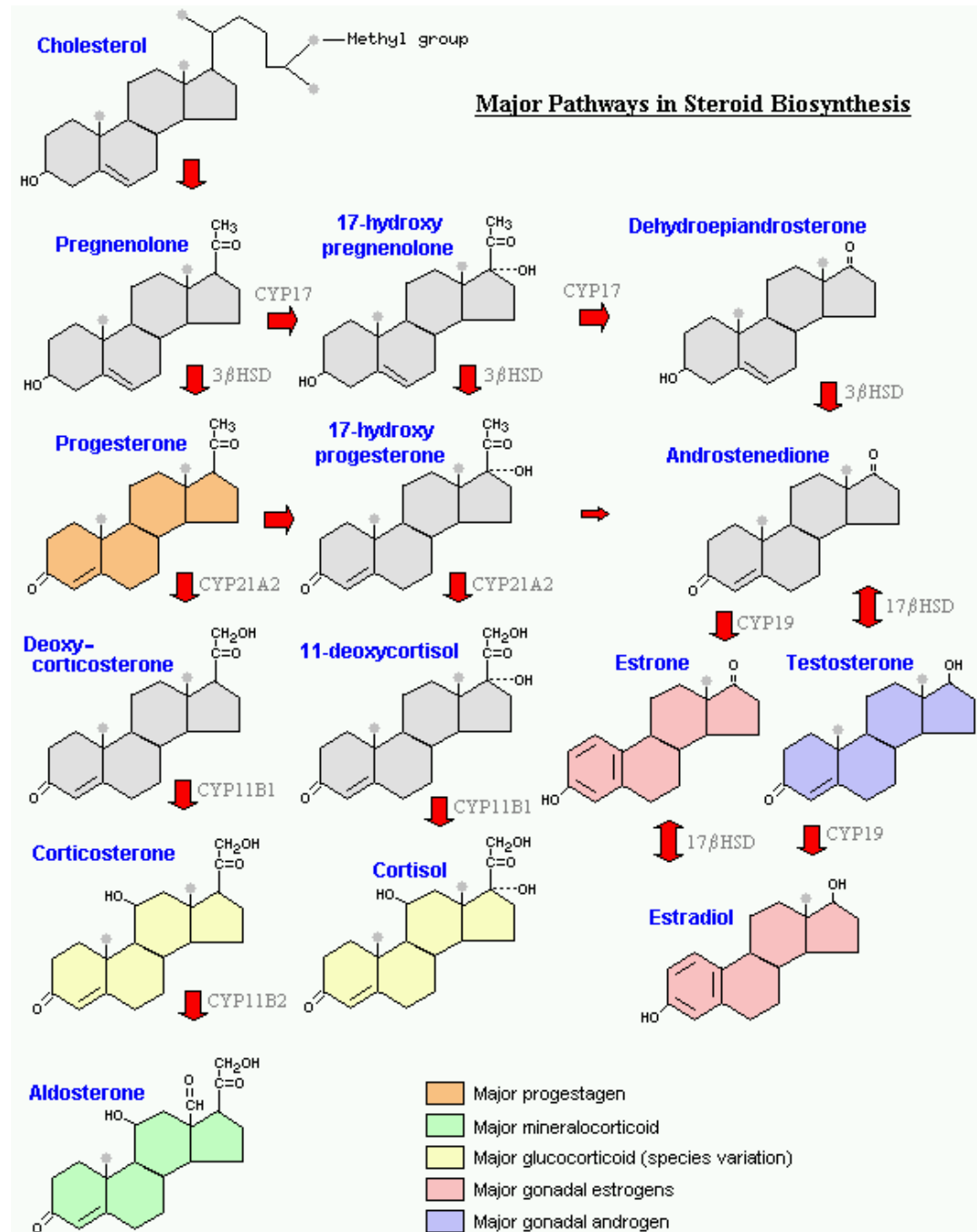
Receptor inside the cell



Surface receptor

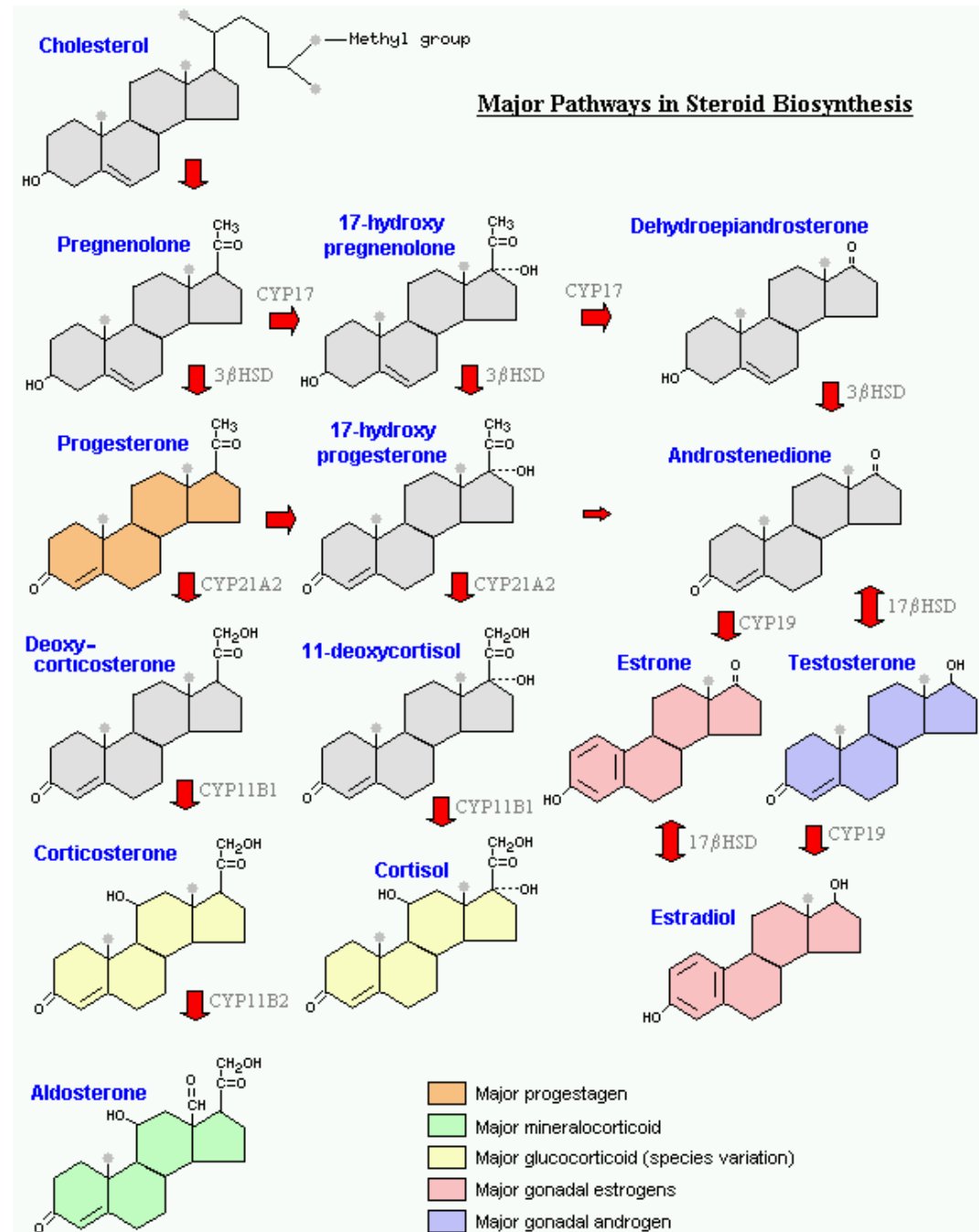


- C21:
 - Progesterone: directly from pregnenolone
 - Cortisol & Aldosterone: from progesterone





- C19
 - Testosterone
 - from progesterone or pregnenolone
 - 2c shortage
- C18 (estrogen):
 - Aromatase
 - Cleaves C18
 - Reduction





Steroid hormone breakdown

- Steran core cannot be cleaved
- In the liver: hydroxylation and conjugation with glucuronides or sulphates
- Urinary excretion:
 - ✓ Of metabolites
 - ✓ Of unchanged hormones



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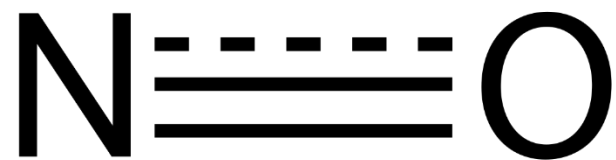
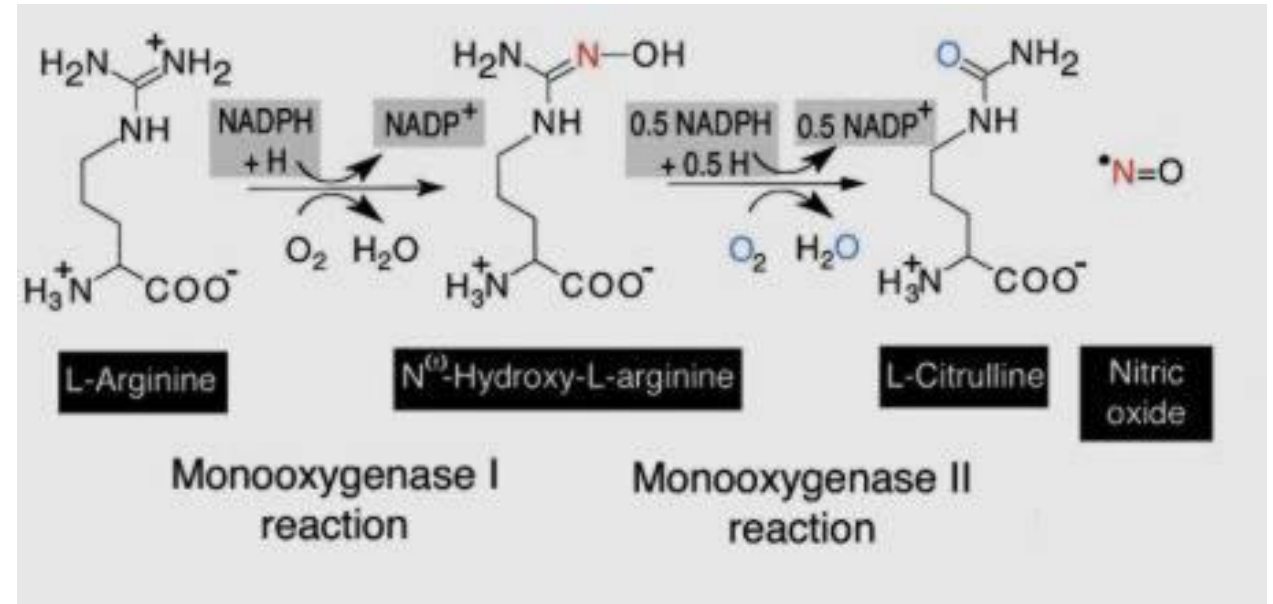
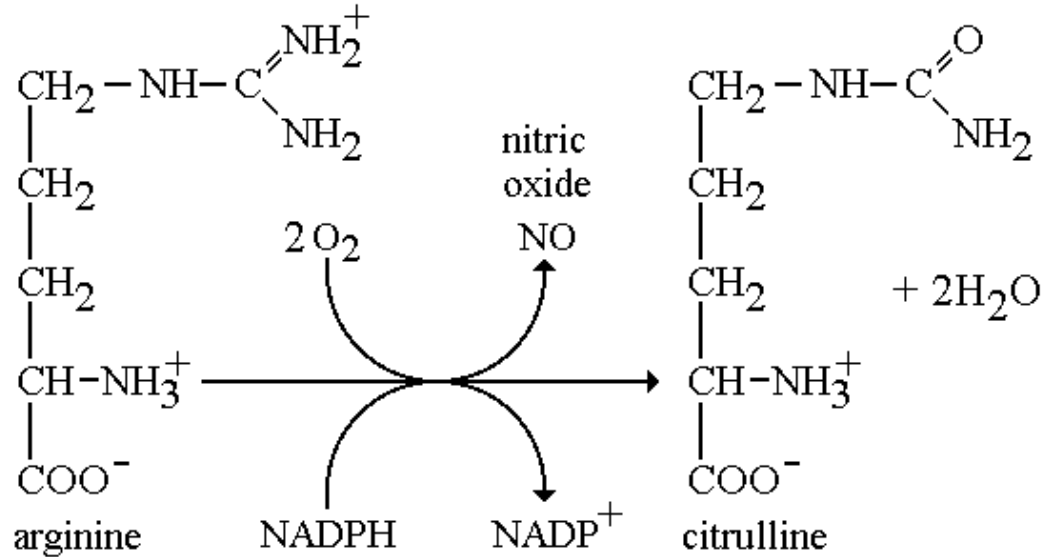


Surface receptor



Nitric oxide (NO)

➤ NO: synthesized by NO-synthase





Nitric oxide synthase isozymes

- NO-synthase (NOS)
 - ✓ In neurons (NOS-I): neurotransmission
 - ✓ In macrophages (NOS-II): kills bacteria
 - ✓ Endothelial (NOS-III): smooth muscle → **cGMP** → vasodilation

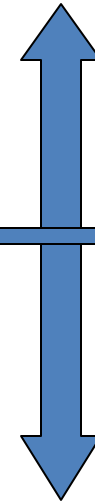
- Clinical correlation:
 - ✓ Nitrates in the treatment of angina
 - ✓ Refractory hypotension during septic shock



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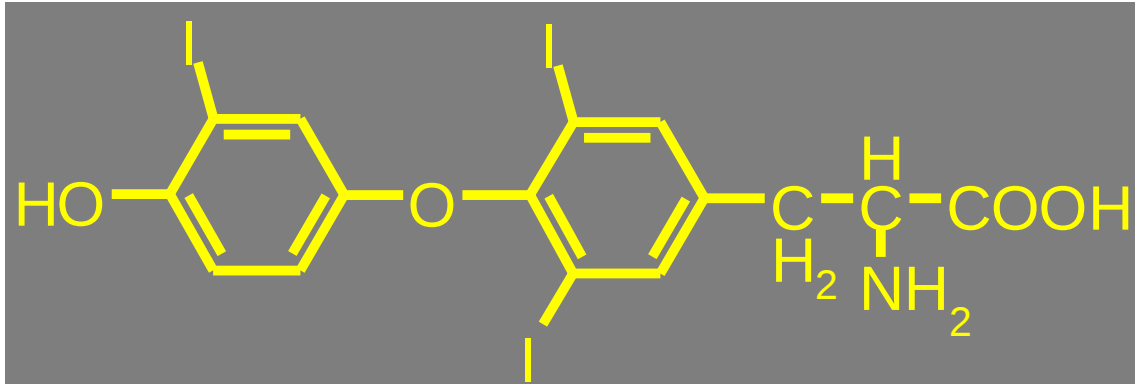
Receptor inside the cell



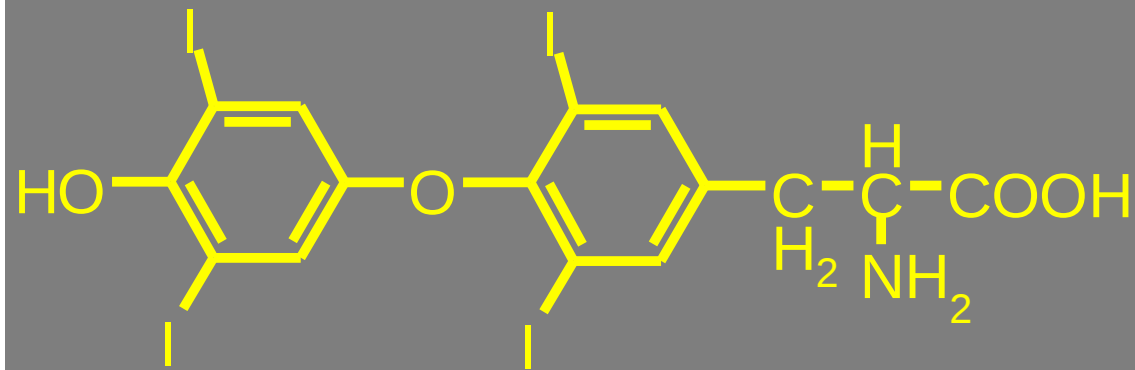
Surface receptor



Thyroid hormones



Triiodothyronine (T3)

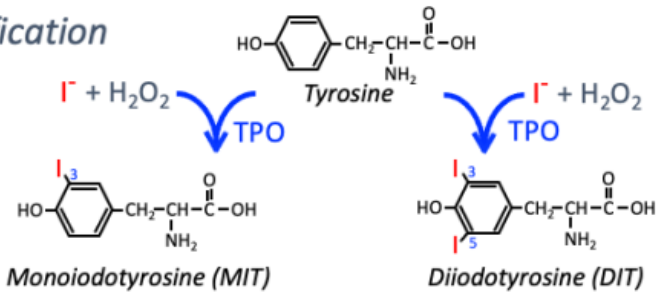


Thyroxine (T4)

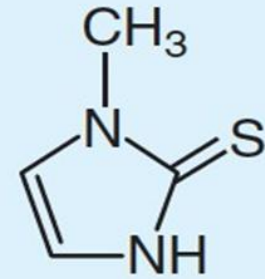


Thyroid hormones

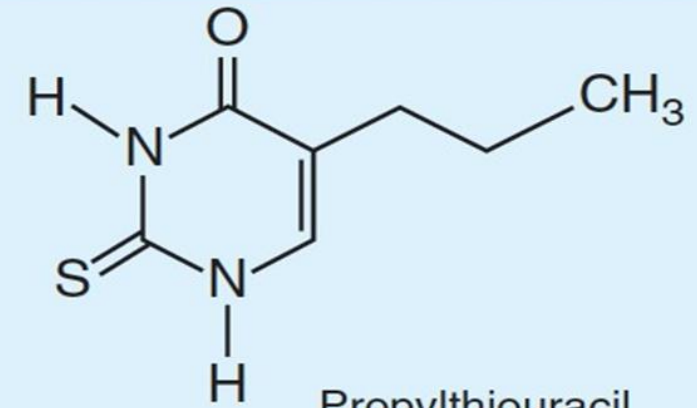
Organification



Inhibitors of TPO
Methimazole
PTU



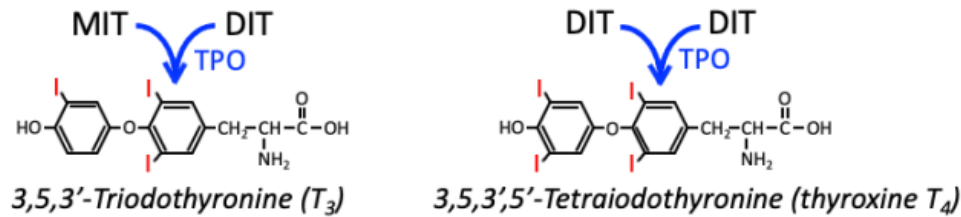
Methimazole



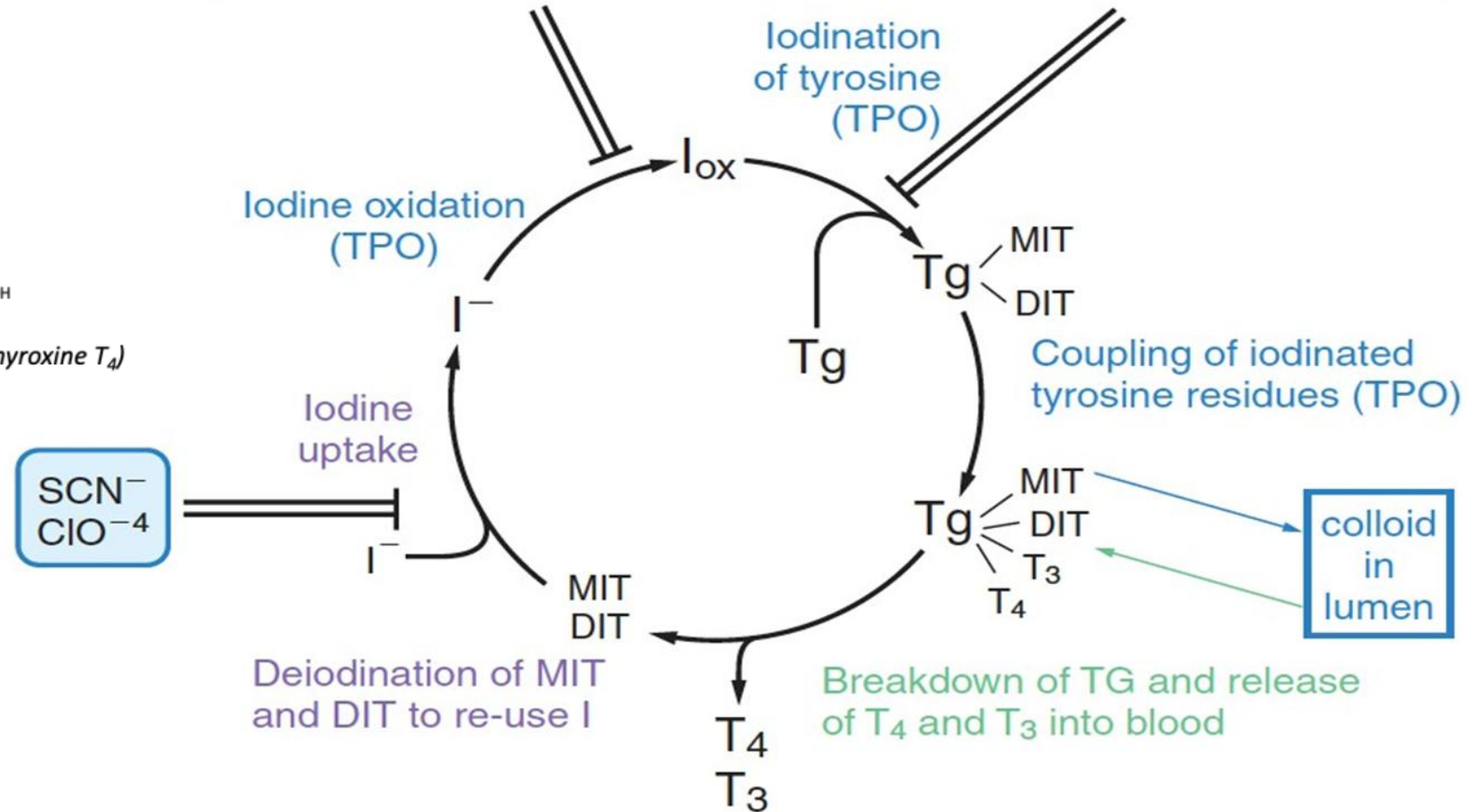
Propylthiouracil

Coupling

(phenolic coupling)

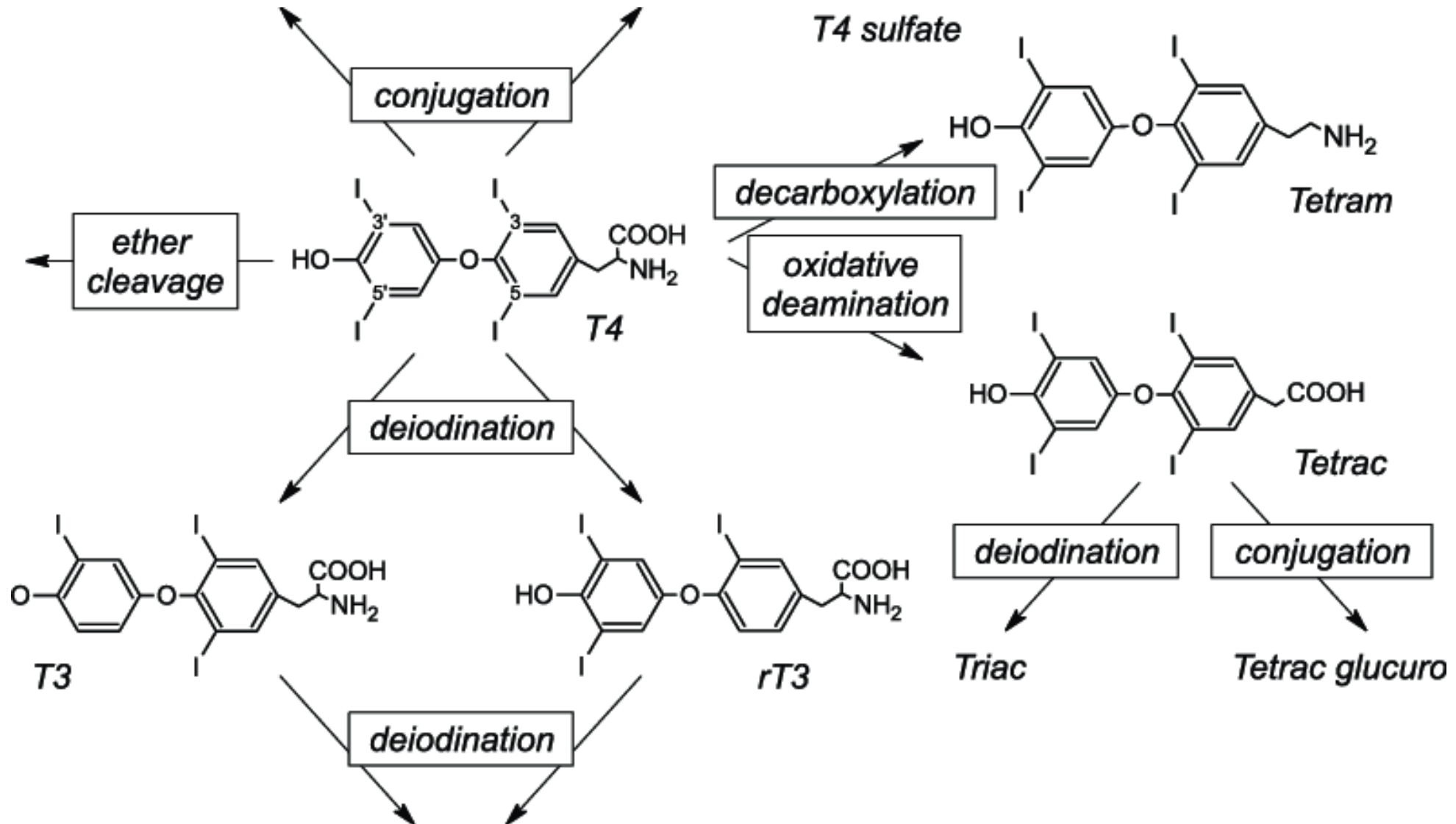


- ✓ TPO, thyroid peroxidase;
- ✓ Tg, thyroglobulin;
- ✓ MIT, monoiodotyrosine;
- ✓ DIT, diiodotyrosine;
- ✓ SCN^- , thiocyanate;
- ✓ ClO_4^- , perchlorate.





Thyroid hormones degradation





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Receptor inside the cell



Surface receptor

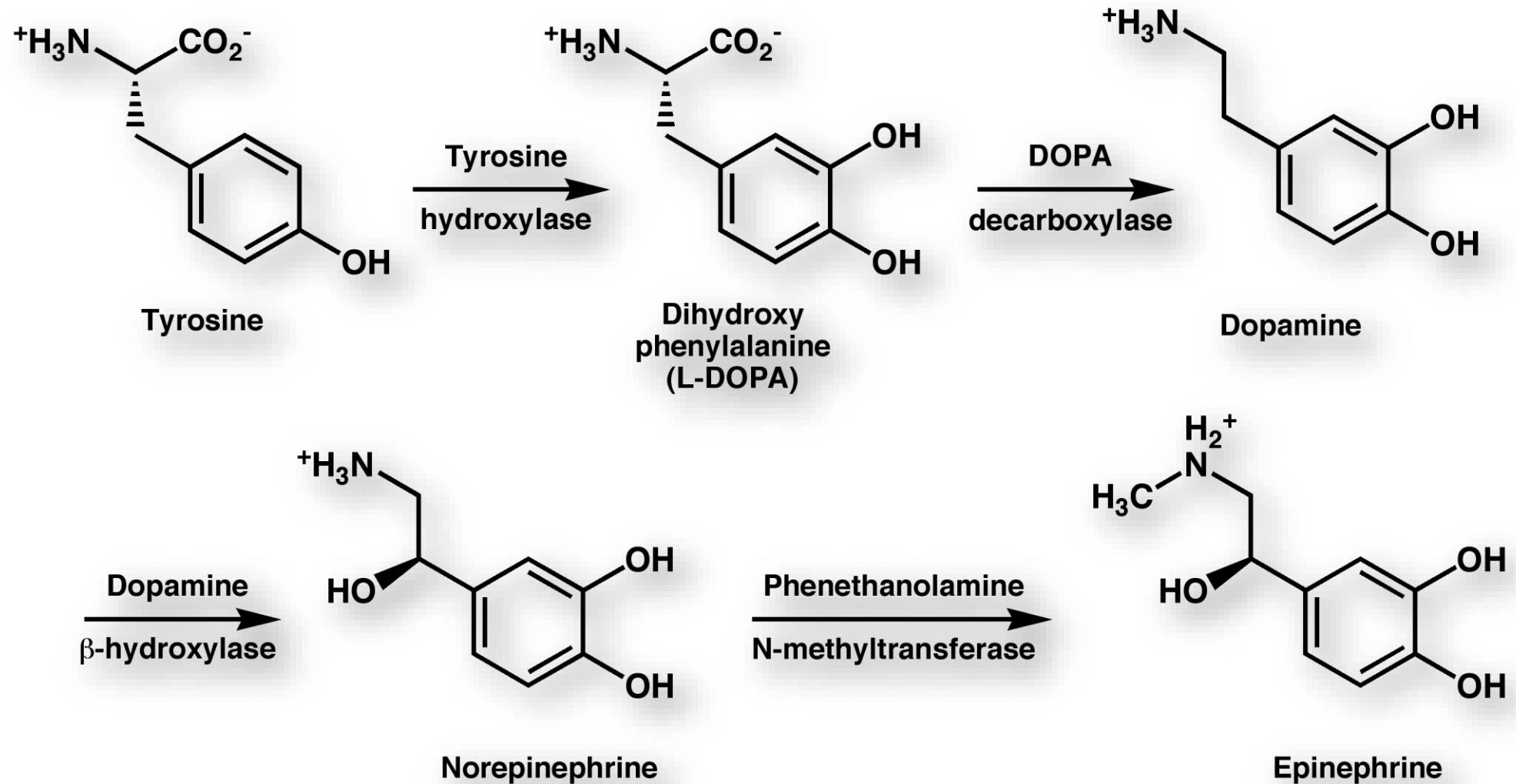


Catecholamine synthesis

- Substrate = Phe or Tyr
- Synthesis located in: adrenal medulla, nerve tissue
- Products:
 - Dopamine, adrenaline (hormones)
 - Noradrenaline (neurotransmitter)

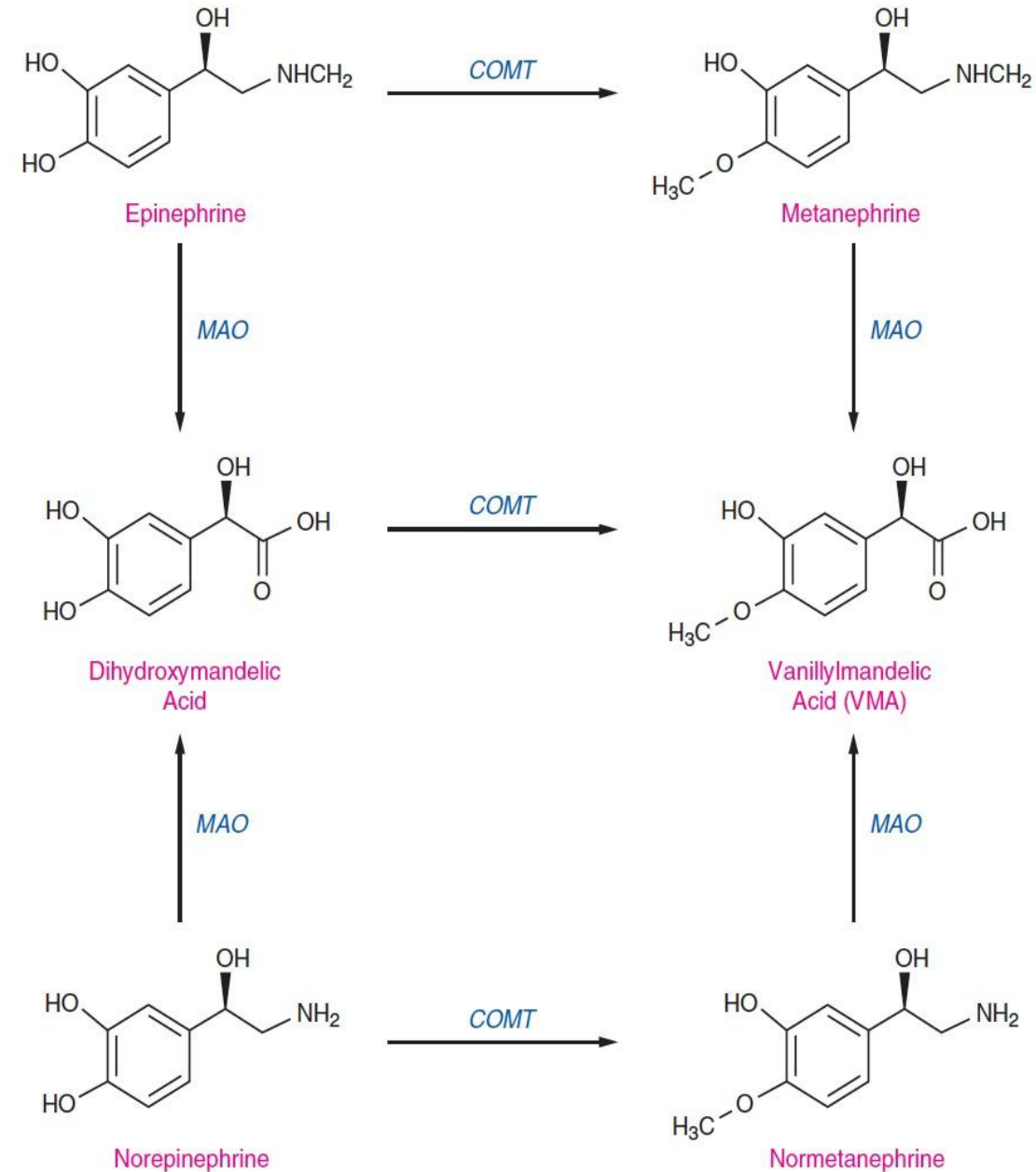
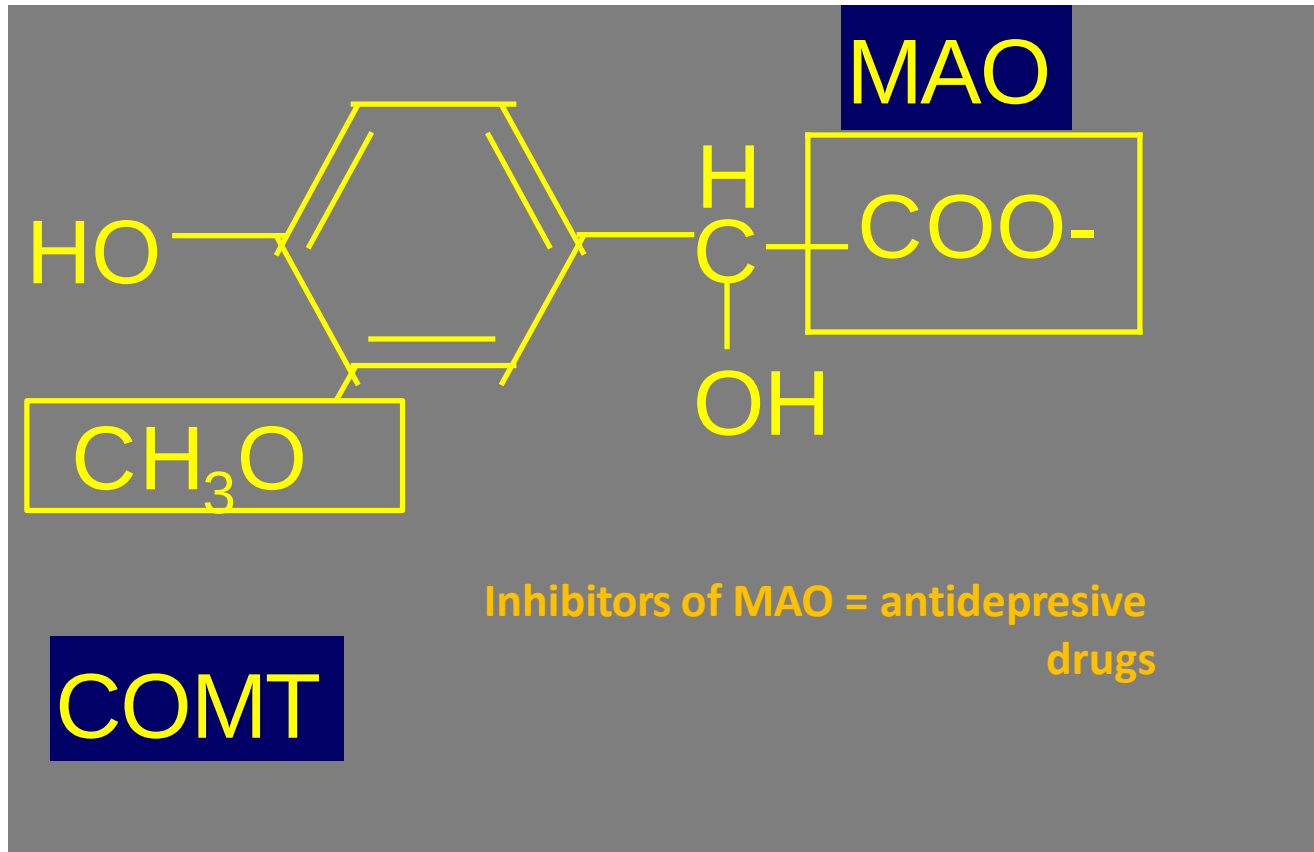


Catecholamine synthesis

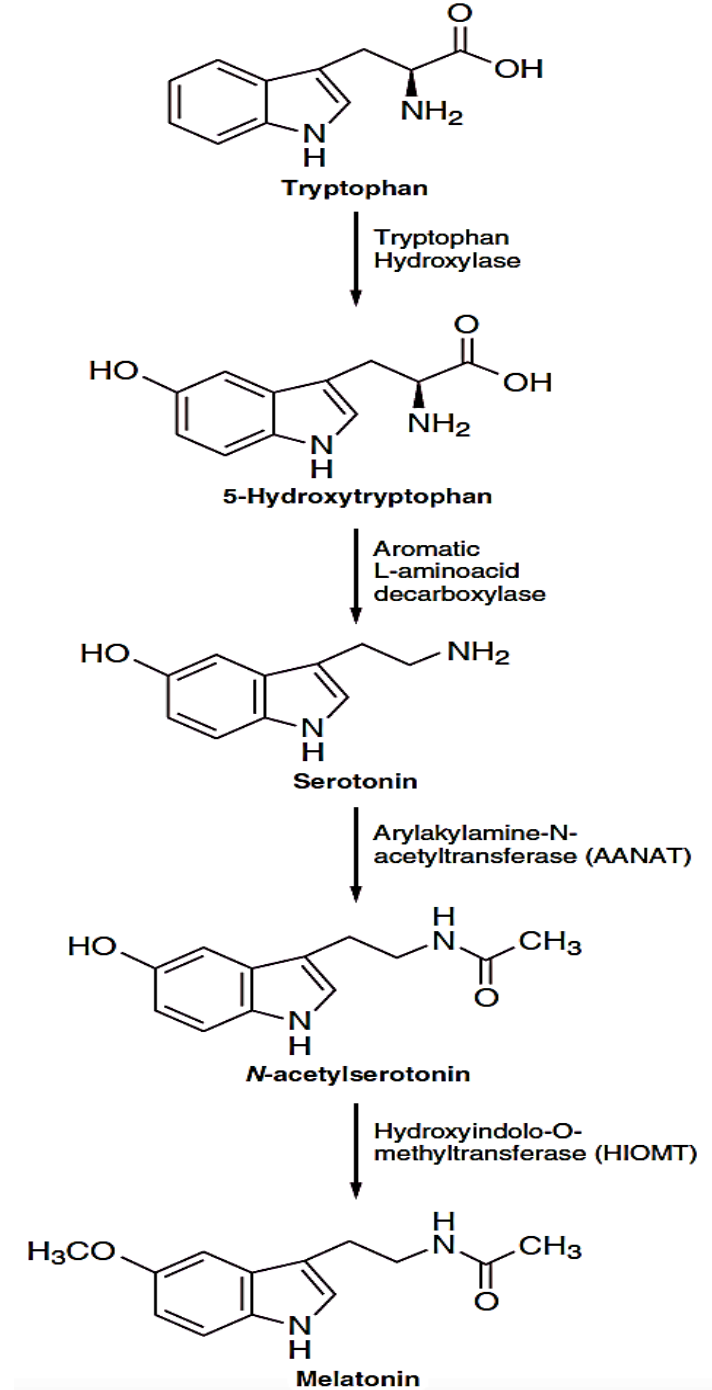
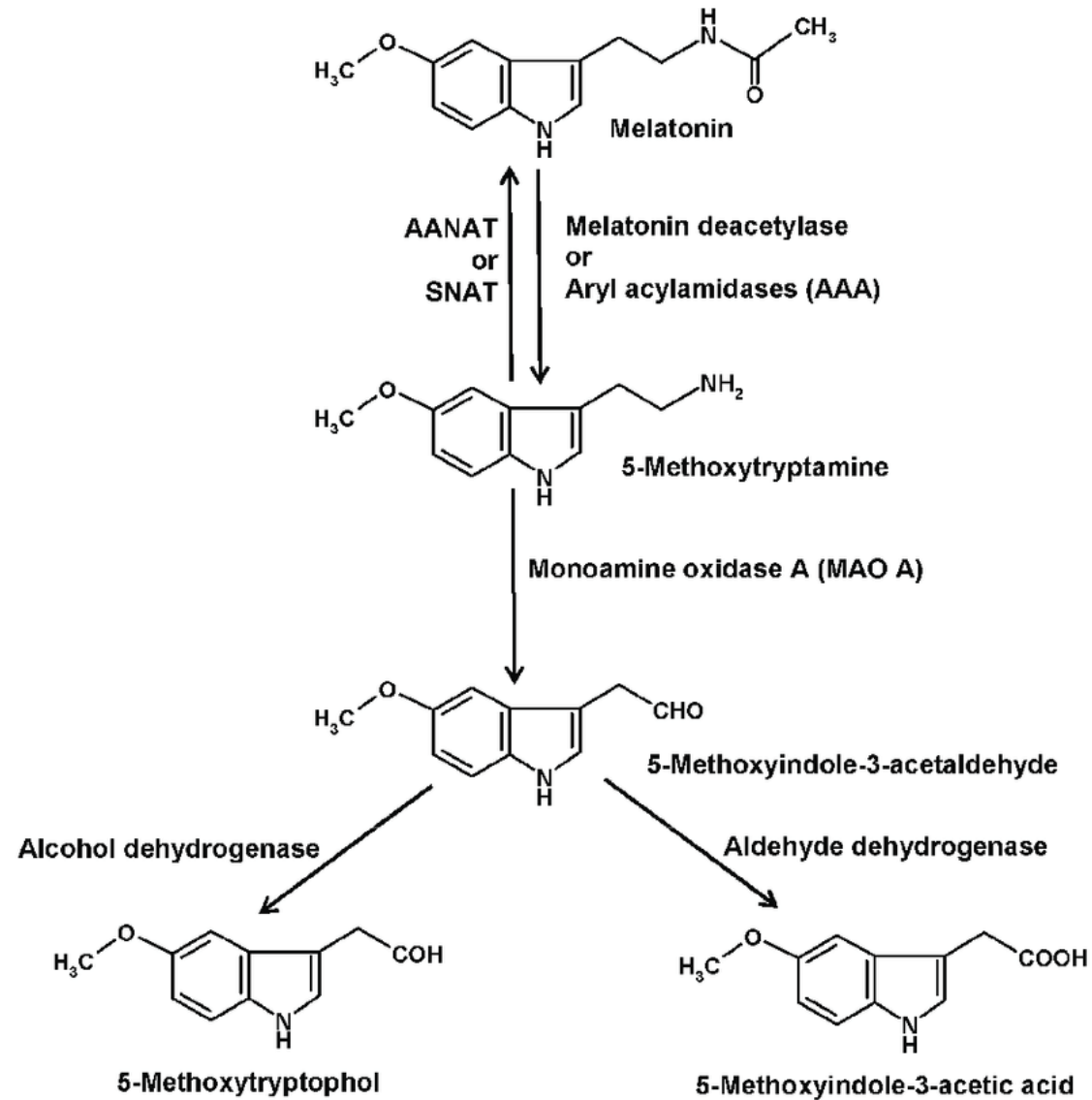




Catecholamine breakdown



Melatonin





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Surface receptor



Protein and peptide hormones

- CNS mediators: neuropeptides, opioids
- Hypothalamic releasing hormones and pituitary peptides
- Insulin and glucagone
- Growth factors: IGF, CSF, EPO

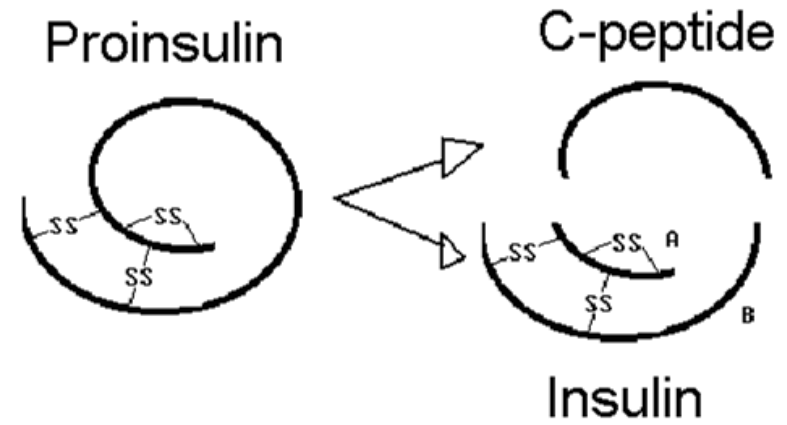
...and many others



General steps of peptide synthesis

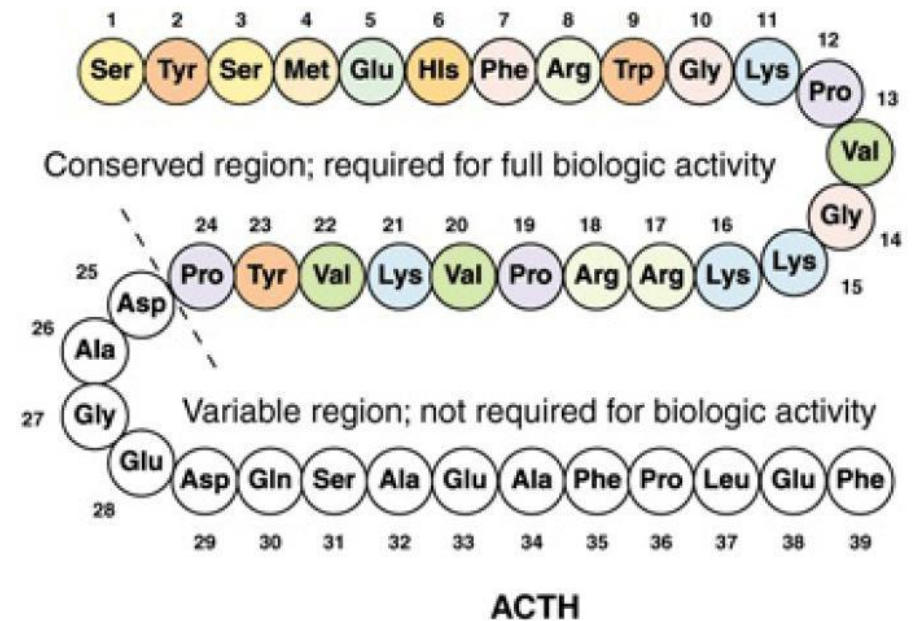
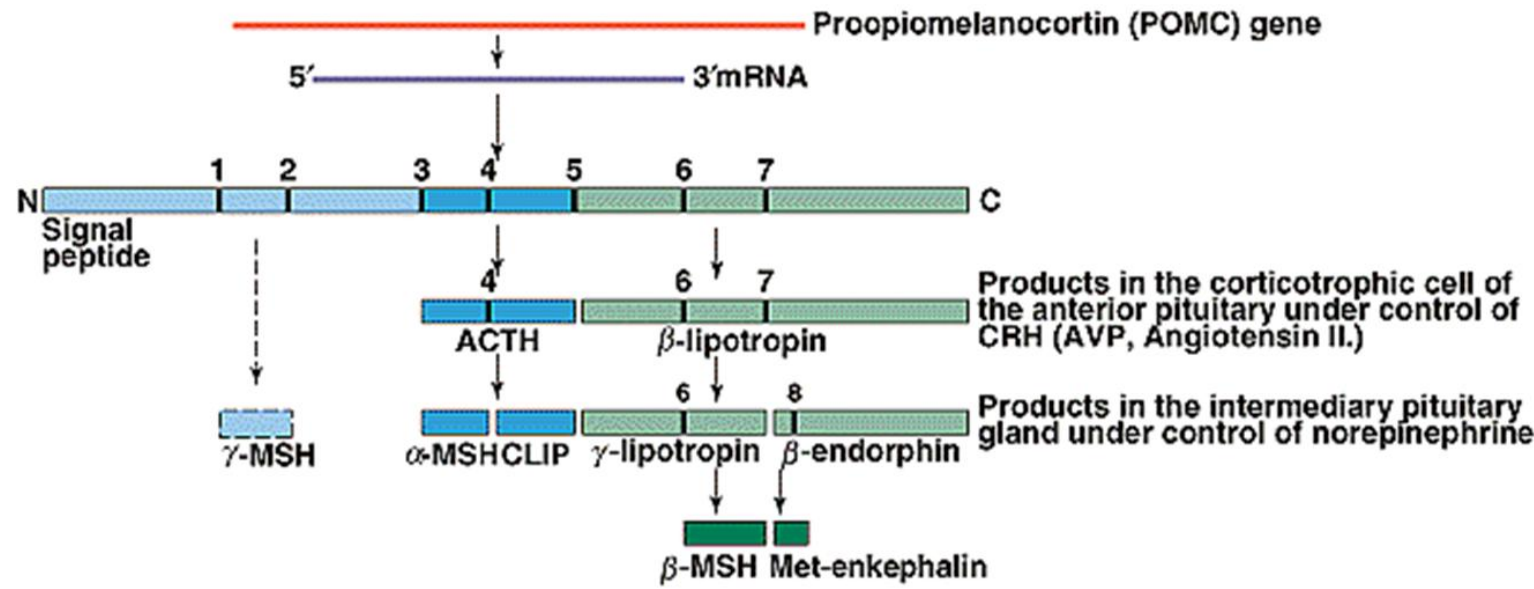
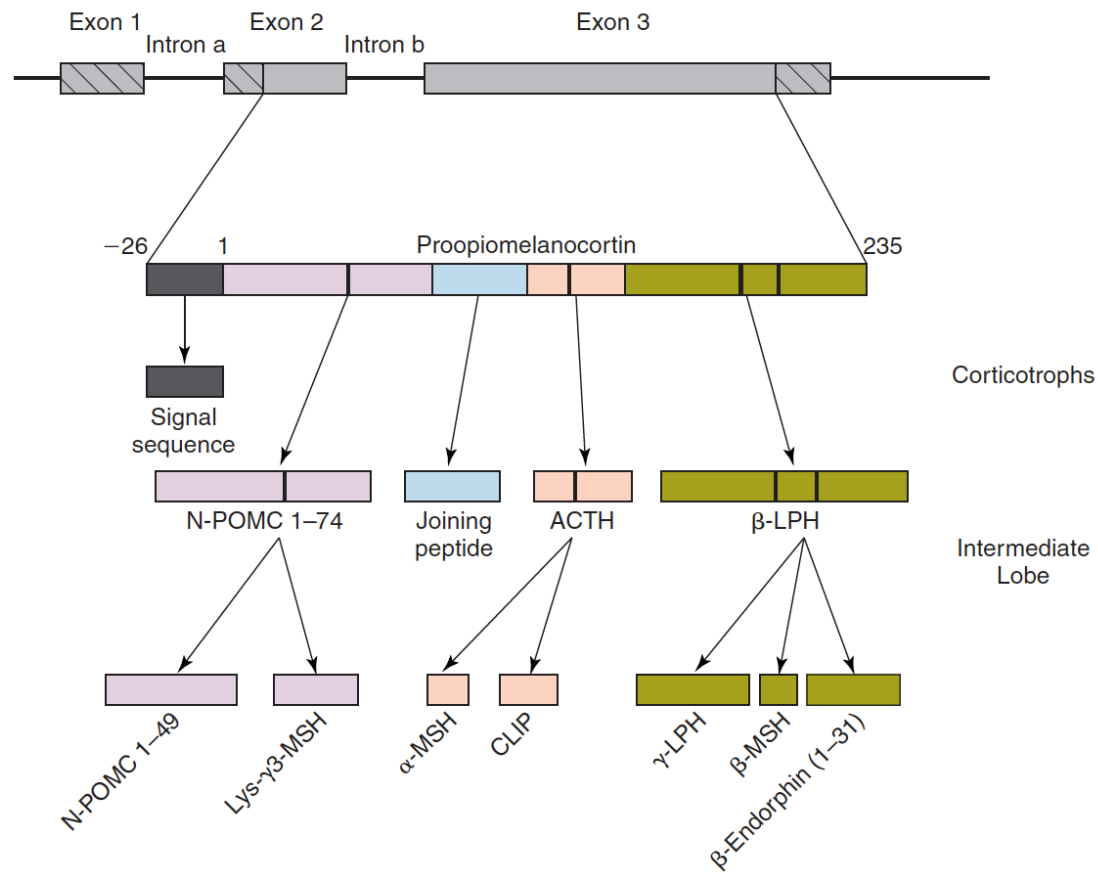
“Precursor Polypeptides”

- Expression of “pre-pro” protein
- Transport to ER
- Splitting the signaling sequence
- Cleavage to definite peptide(s) and final modification in Golgi
 - Proinsulin to insulin
 - Proopiomelanocortine (POMC) to MSH and ACTH





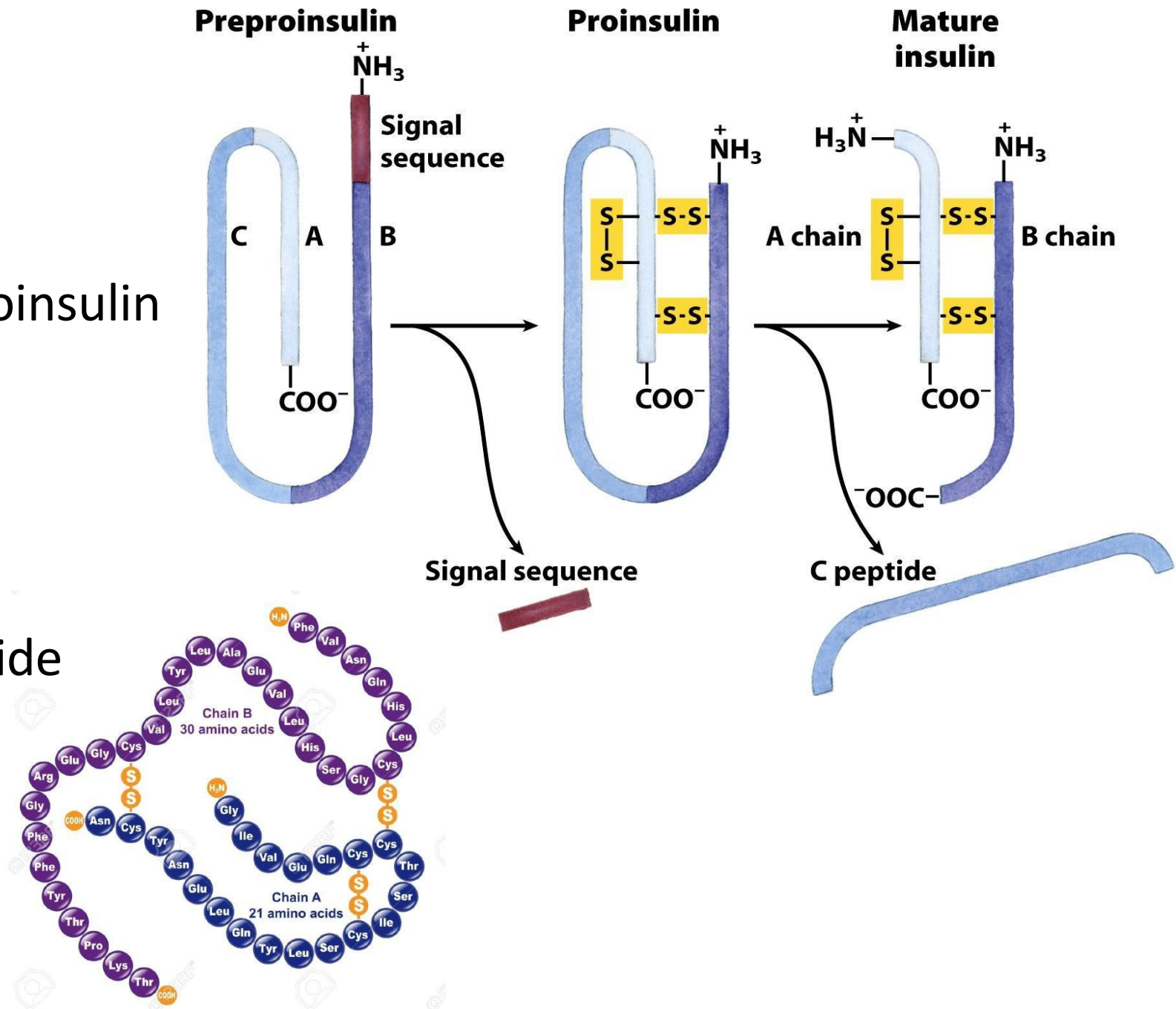
Proopiomelanocortin (POMC)





Insulin

- A larger precursor preproinsulin
 - ✓ 23 aa signal sequence
 - ✓ 3 disulfide bonds
- Proinsulin
 - ✓ Removal of the C peptide
- Mature insulin
 - ✓ A and B chains





Degradation of peptide hormones

- Lysosomal after endocytosis of complex hormone-receptor
- Chemical modification (liver): rearrangement of S-S bridges, cleavage
- Renal excretion of small peptides



Target cell interactive effects

- **Permissive effects** – one hormone enhances the effect of a later hormone
 - ✓ **Estrogen up-regulates progesterone receptors** in uterus
 - ✓ **Thyroid hormone increases the effect of epinephrine** on breakdown of triglycerides in adipocytes

- **Integrative effects** – hormones produce complementary effects on different tissues
 - ✓ **PTH and calcitriol increase ECF calcium**



Target cell interactive effects

- **Synergistic effects:**
 - ✓ Both **FSH** and **estrogen** necessary for **normal oocyte development**
 - ✓ **FSH** and **testosterone** together increase **spermatogenesis**

- **Antagonistic effects:**
 - ✓ **Insulin** and **glucagon**