Synthesis and Degradation of Hormones

Chemistry of Hormones

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

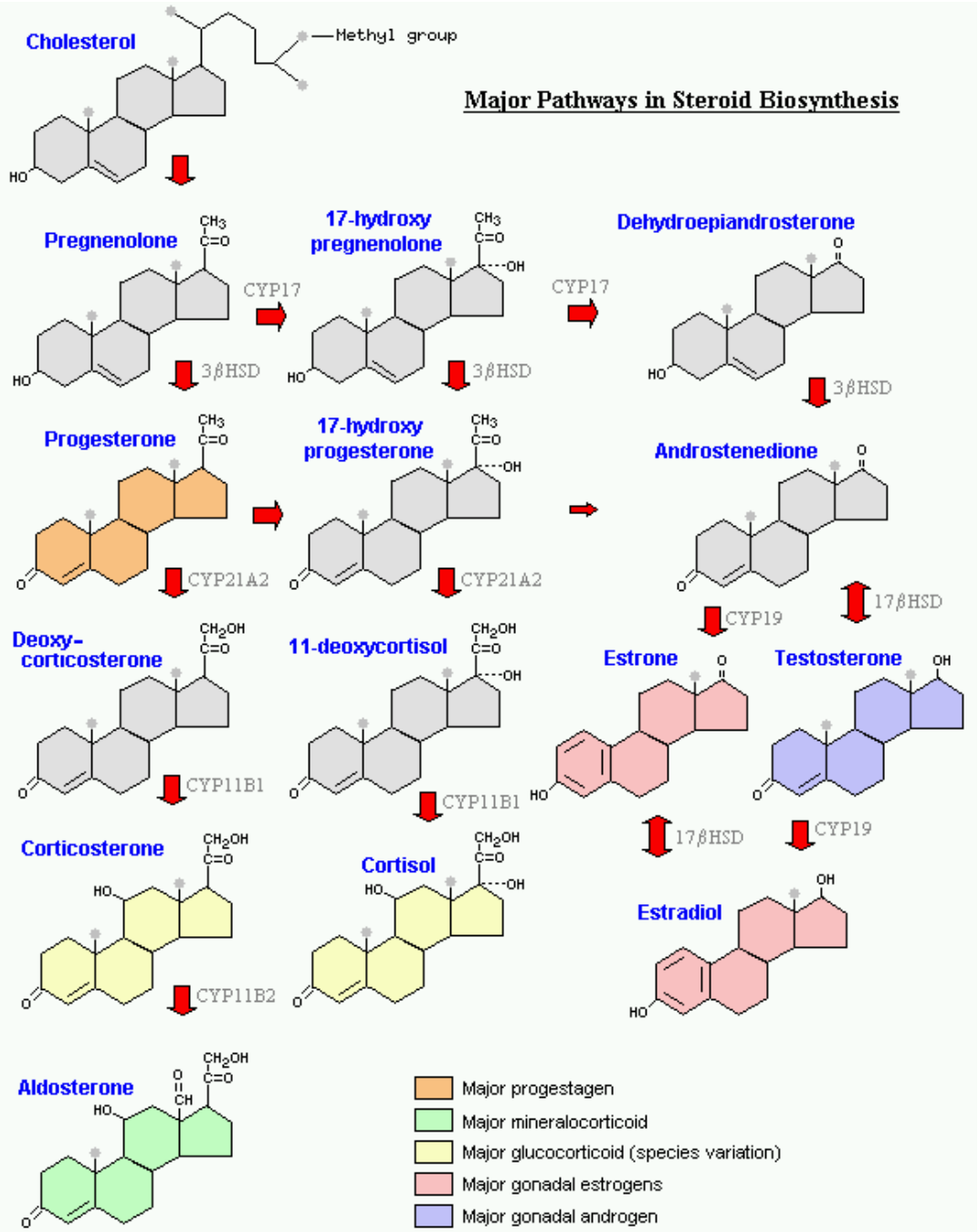
  - Catecholamines
- Proteins and peptides
- FA derivates - eicosanoids

Receptor inside the cell

Surface receptor

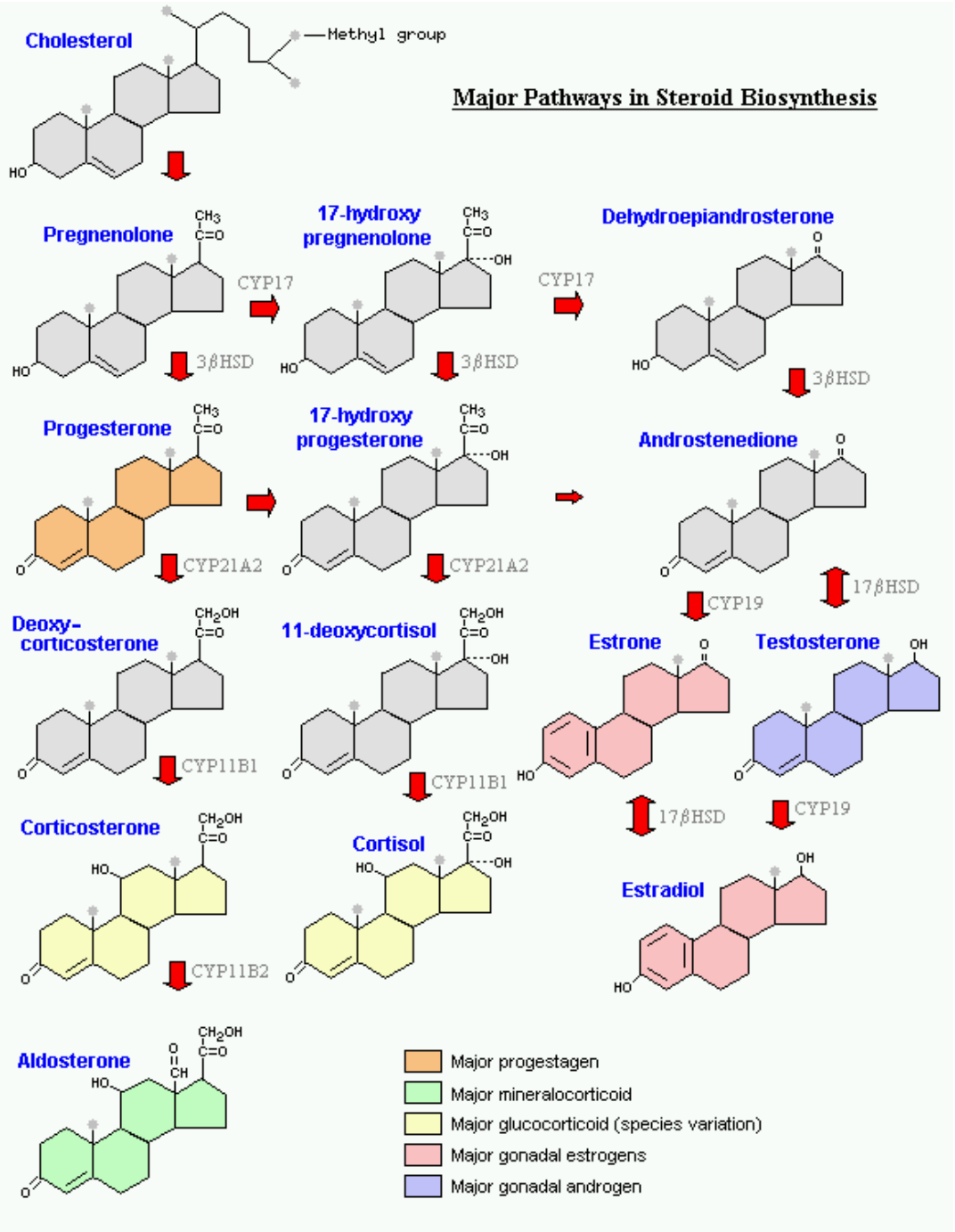
Steroid hormone synthesis

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



Steroid hormone synthesis

- 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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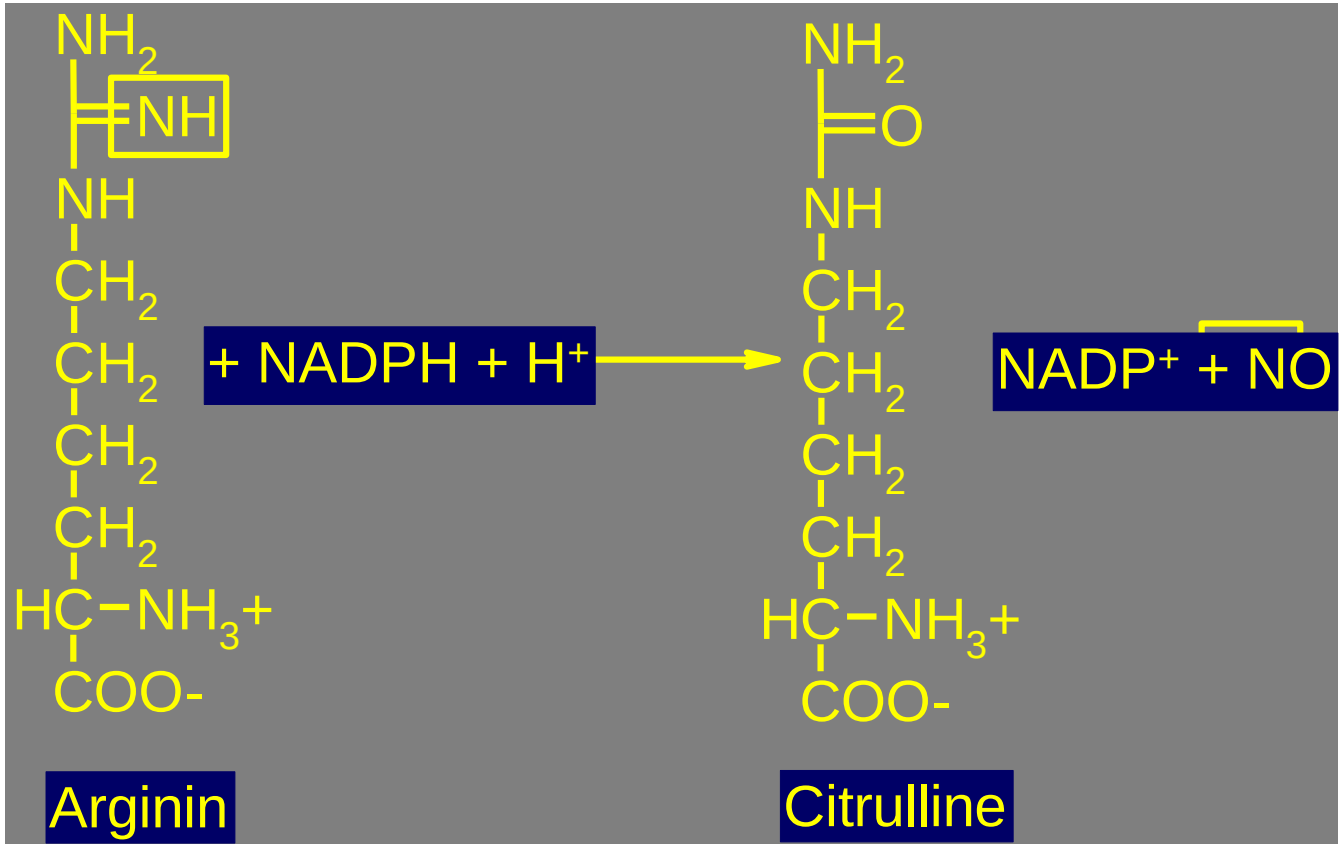
Receptor inside the cell

Surface receptor

Nitric oxide (NO)

- NO: synthetized by NO-synthase



Nitric oxide synthase iszymes

- NO-synthase (NOS)
  - In neurons (NOS-I): neurotransmission
  - In macrophages (NOS-II): kills bacteria
  - Endothelial (NOS-III): smooth muscle $\rightarrow$ cGMP$\rightarrow$ vasodilation

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

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Receptor inside the cell

Catecholamines –

- Proteins and peptides
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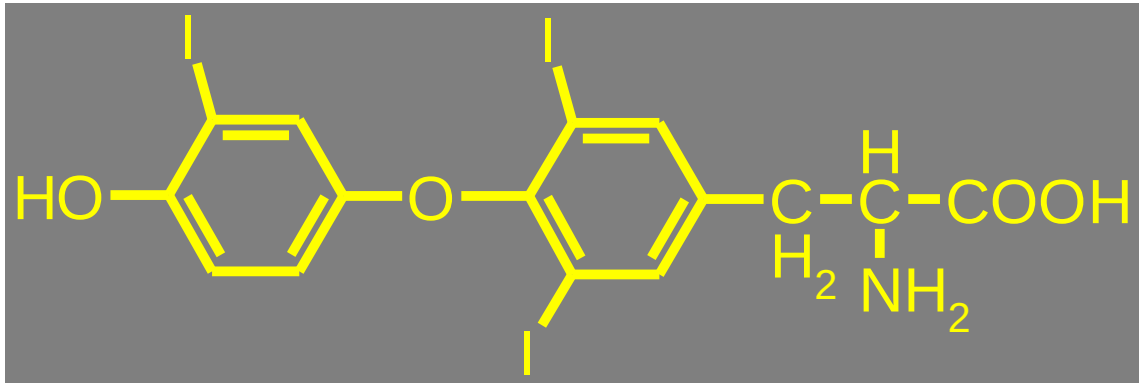
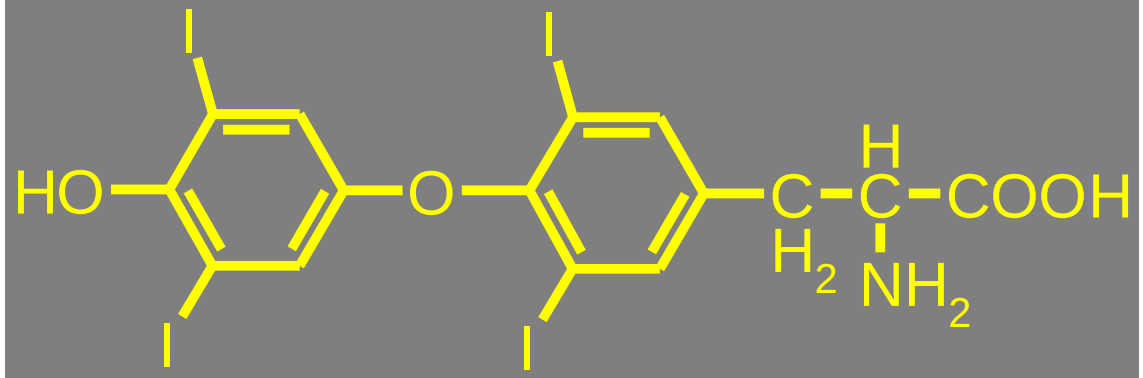
Surface receptor

Thyroid hormones



Triiodthyronine (T3)



Thyroxine (T4)

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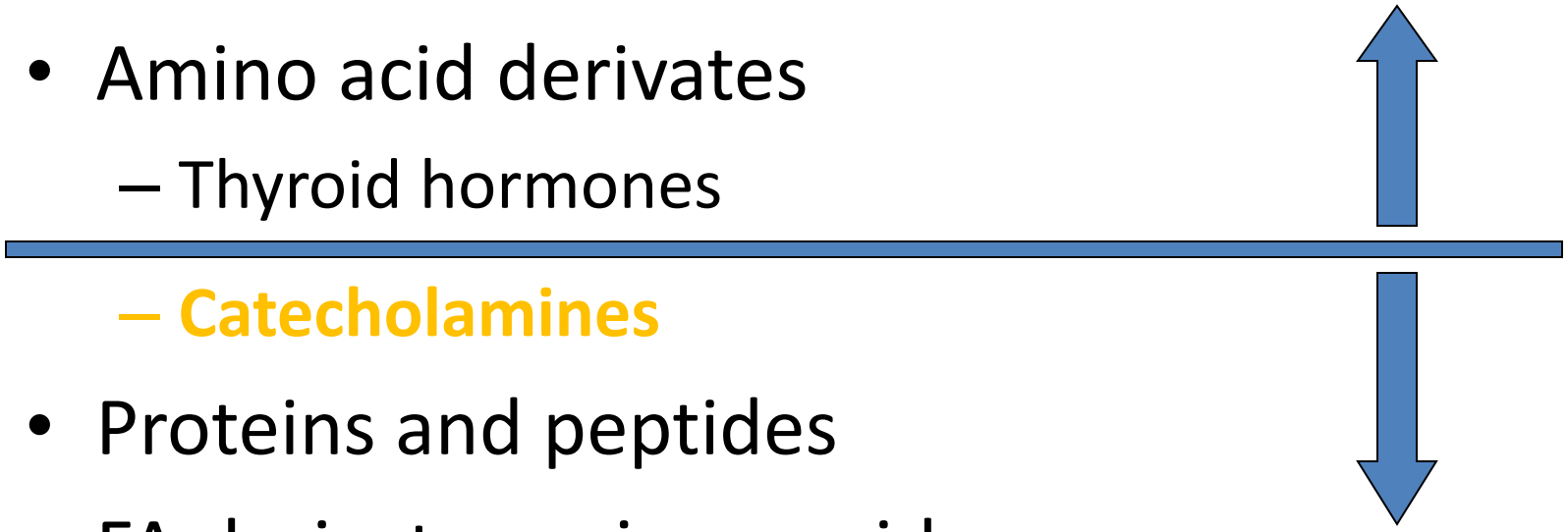
Receptor inside the cell



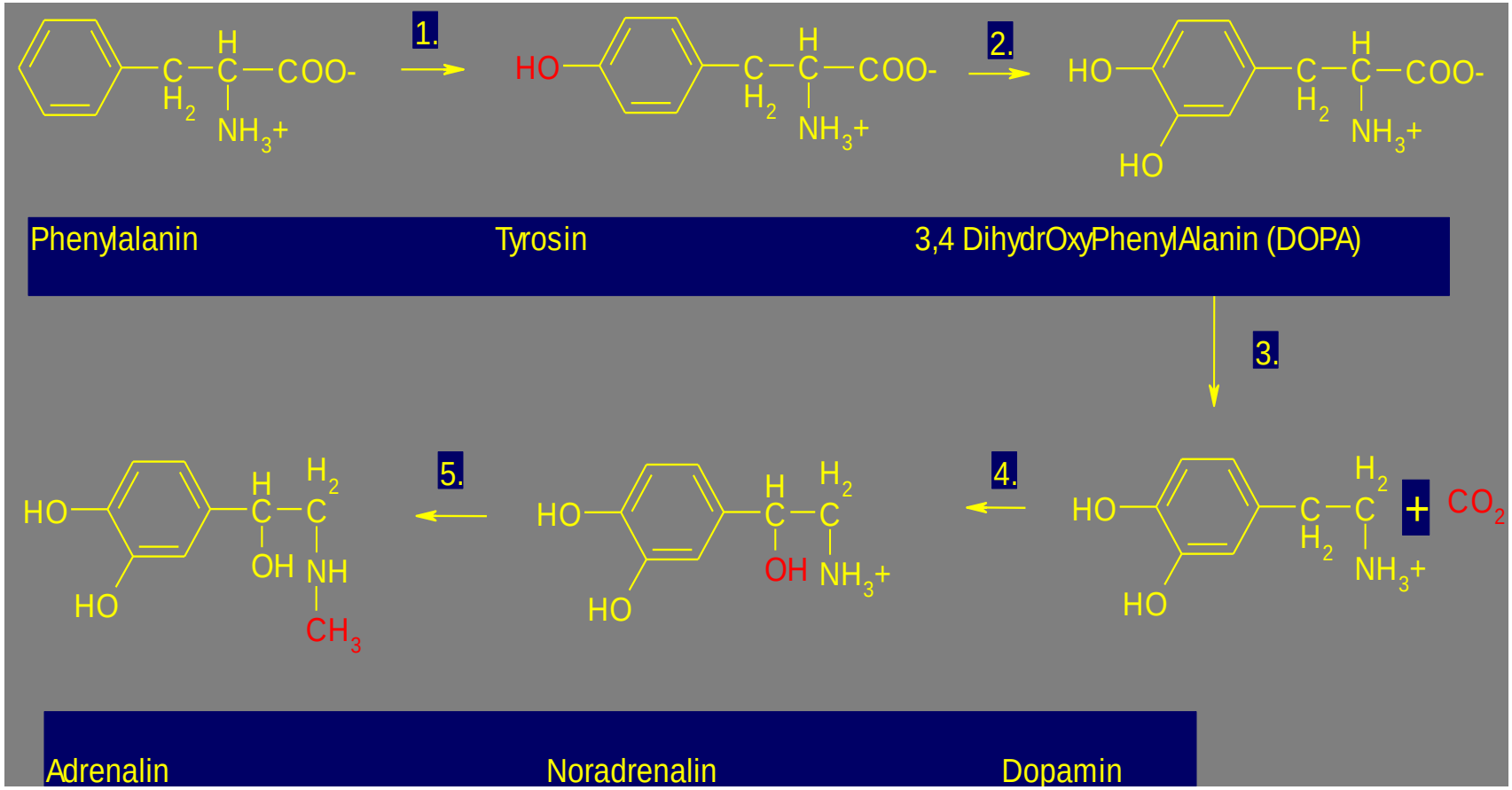
  - **Catecholamines**
- Proteins and peptides
- FA derivates - eicosanoids

Surface receptor

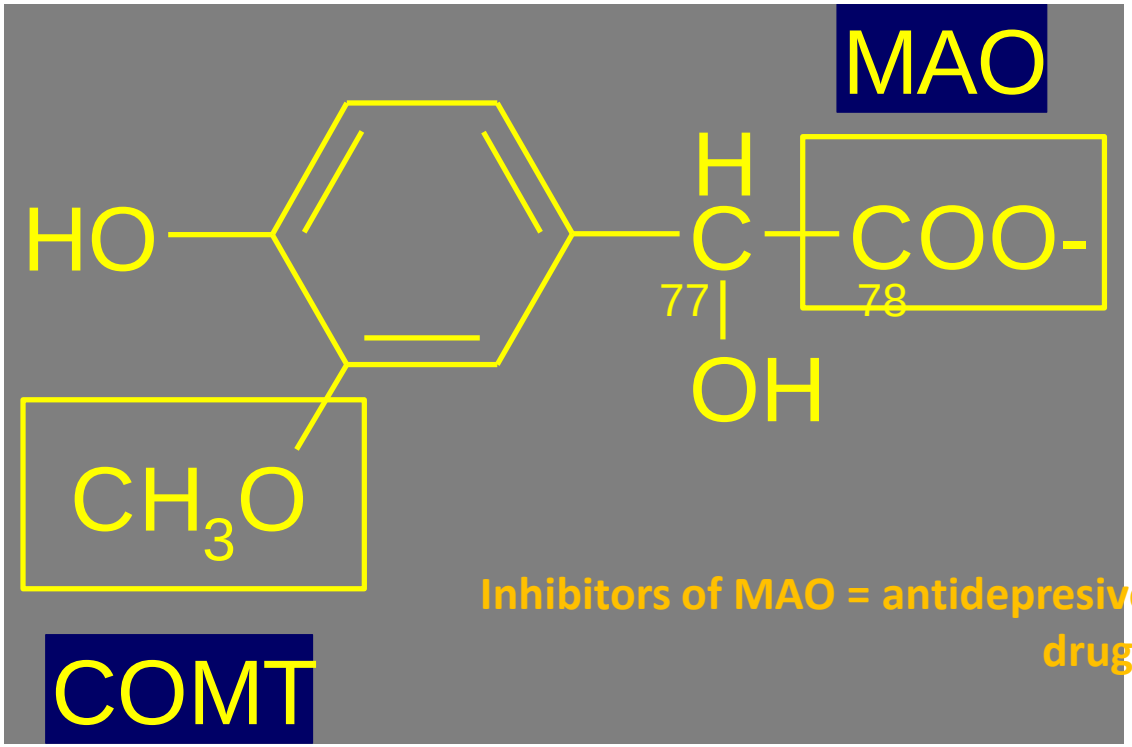
Catecholamine synthesis

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

Catecholamine synthesis



Catecholamine breakdown



Inhibitors of MAO = antidepresive drugs

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Receptor inside the cell

Surface receptor

Protein and peptide hormones

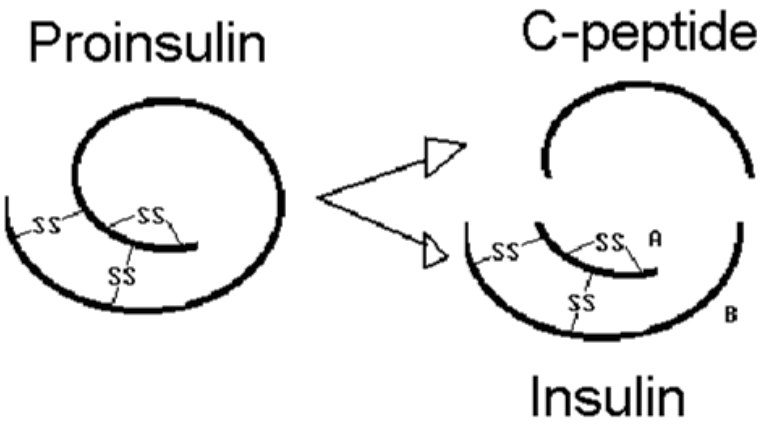
- CNS mediators: neuropeptides, opioids
- Hypothalamic releasing hormones and pituitary peptides
- Insulin and glucagone
- Growth factors: IGF, CSF, EPO

…and many others

General steps of peptide synthesis

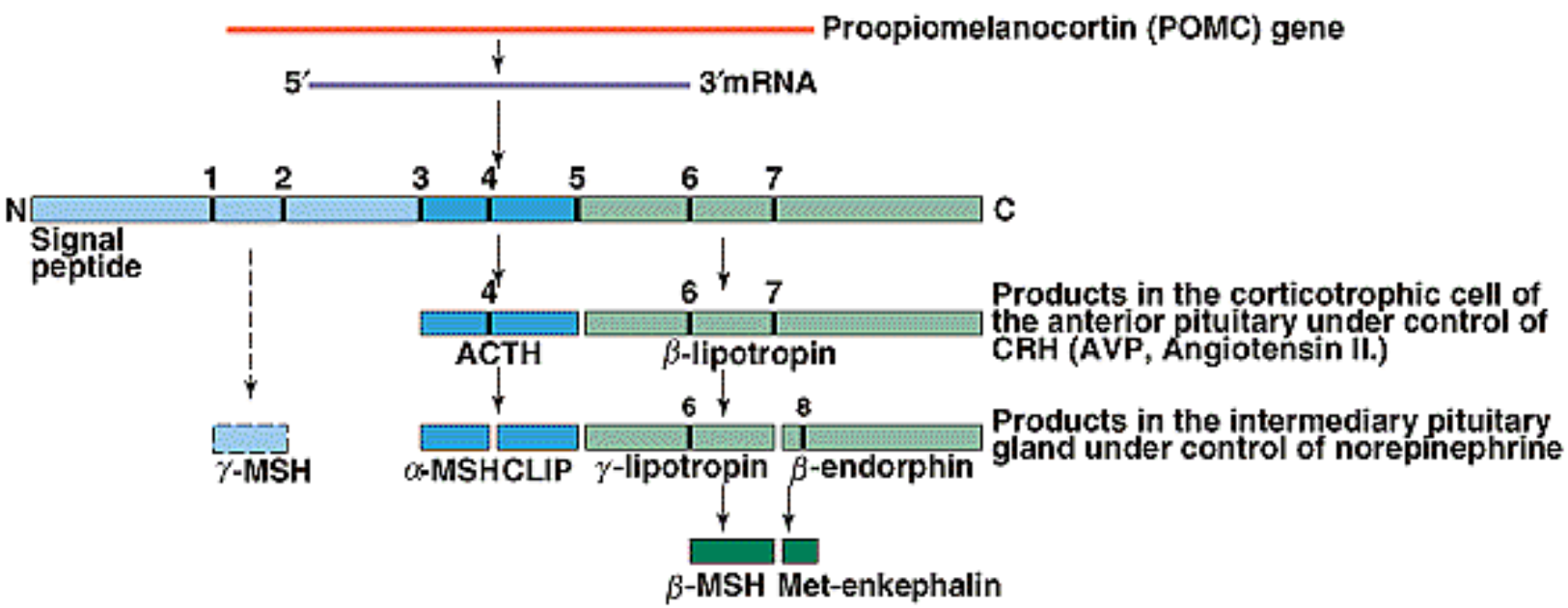
"Precursor Polypeptides"

- 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



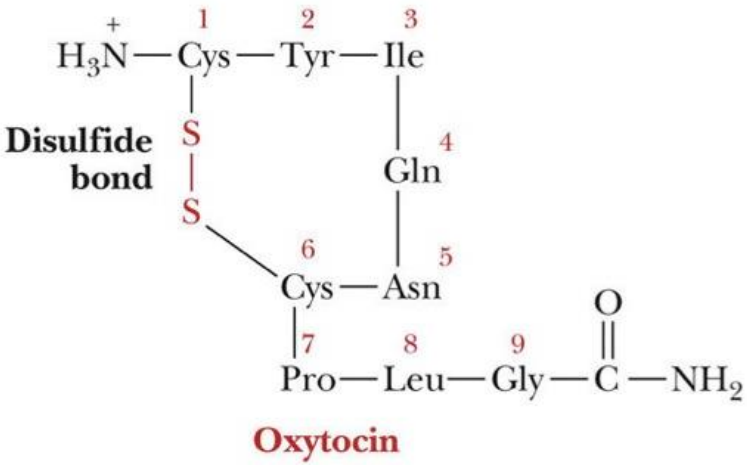
General steps of peptide synthesis

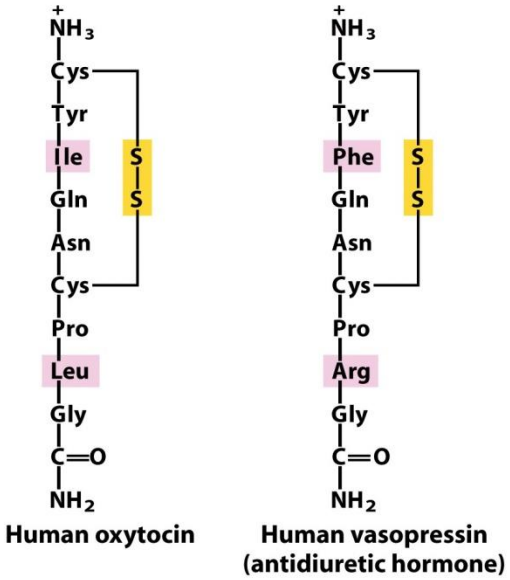
- From precursor polypeptides
  - One gene may code more than one hormone
    - **Proopiomelanocortin** (**POMC**)
  - The cleavage depends on specific enzymes

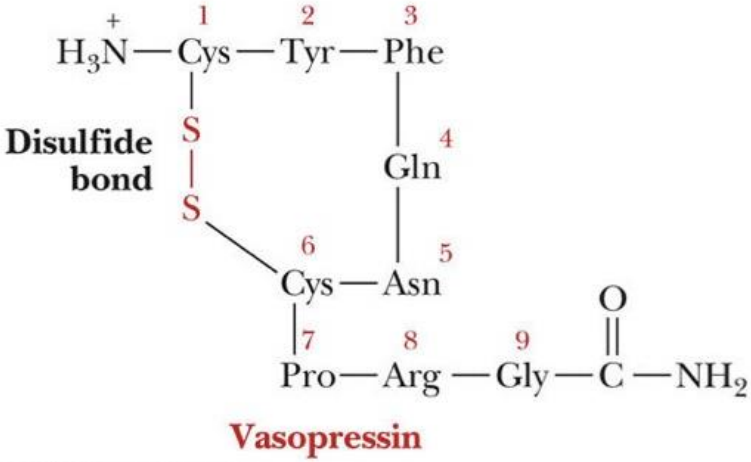


General steps of peptide synthesis

- From precursor polypeptides
  - Vasopressin and oxytocin
  - Synthesis in separate cell bodies of hypothalamic neurons







Degradation of peptide hormones

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

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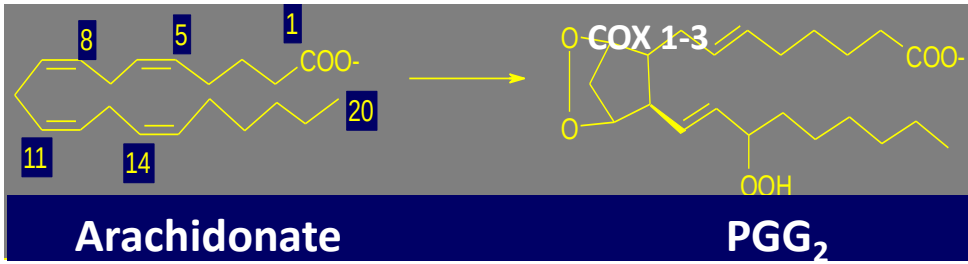
Eicosanoids general synthesis

- **Derivates of arachidonic acid (20C:$\Delta^{5,8,11,14}$).**
  - **Release of arachidonic acid from membrane PL (PLA_2)**
  - **Cyclooxygenase (COX) synthetizes prostaglandines and thromboxanes**
  - **Lipooxygenase synthetizes leucotrienes**



Cyclooxygenase inhibitors