Chapter 13 Biosynthesis of amino acids, nucleotides, and related molecules

* Most of the nitrogen is bound up in **amino acids and nucleotides.**
* Amino acid 생합성 : 엽산, SAM

1. Overview of nitrogen metabolism

1) The nitrogen cycle maintains a pool of biologically available nitrogen

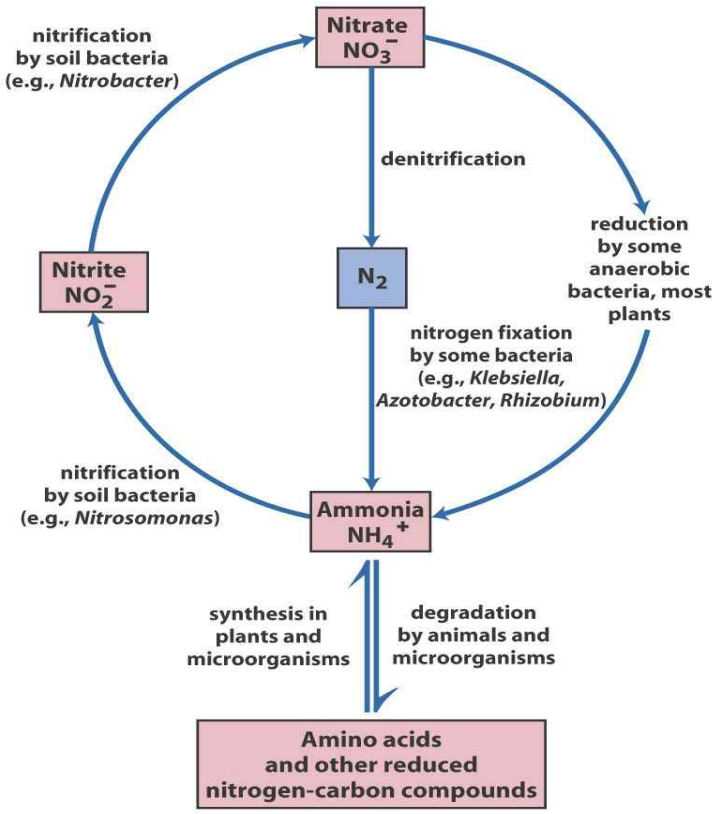

Fig. The nitrogen cycle

Nitrification (질산화), Denitrification (탈질산화)

2) Nitrogen is fixed by enzymes of the nitrogenase complex

* 질소고정균 : *Azotobacter, Cyanobacteria,* symbionts(공생체)
* 질소고정효소 : **Nitrogenase complex**
  - $N_2 + 10H^+ + 8e^- + 16ATP \longrightarrow 2NH_3 + 16ADP + H_2$
* The key two components of nitrogenase complex are **dinitrogenase reductase and dinitrogenase**
* **Leghemoglobin : 산소결합단백질 (nodule)**
  - deliver oxygen to electron transfer system of the bacteria

3) **Ammonia incorporated into biomolecules through glutamate and glutamine (암모니아는 글루탐산과 글루타민을 경유하여 생체분자로 편입된다.)**

* 대부분의 아미노산은 **아미노기전달반응**(transamination reaction)을 통하여 **글루탐산**으로부터 아미노기를 도입한다.

① The biosynthetic pathways to glutamate and glutamine

* **Glutamine synthetase (모든 organism에서 발견)**

- Glutamate + NH_4^+ + ATP ⟶ Glutamine + ADP + Pi + H^+

* **Glutamate synthase (세균, 식물에 존재)**

- α-ketoglutarate + Glutamine + NADPH + H^+ ⟶ 2 Glutamate + $NADP^+$

* **Net reaction : 세균에서**

α-ketoglutarate + NH_4^+ + NADPH + ATP ⟶
L-Glutamate + $NADP^+$ + ADP + Pi

◎ Glutamate dehydrogenase

- α-ketoglutarate + NH_4^+ + **NADPH** ⟶ Glutamate + $NADP^+$ + H_2O
- 진핵세포 사립체의 바탕질(matrix)에 존재한다.

4) Glutamine synthetase is a primary regulatory point in nitrogen metabolism

(Glutamine synthetase는 질소대사의 중요한 조절점이다)

① **Glutamine synthetase regulation :**

◎ Allosteric regulation (입체다른자리조절) : 생성물에 의한 저해

- Glutamine의 농도가 높을 때 감소, α-ketoglutarate, ATP있으면 증가

◎ Covalent modification (공유결합변형) : 아데닐화(AMP의 부가반응)

- adenylyltransferase가 촉매, Tyr 잔기의 AMP 부가

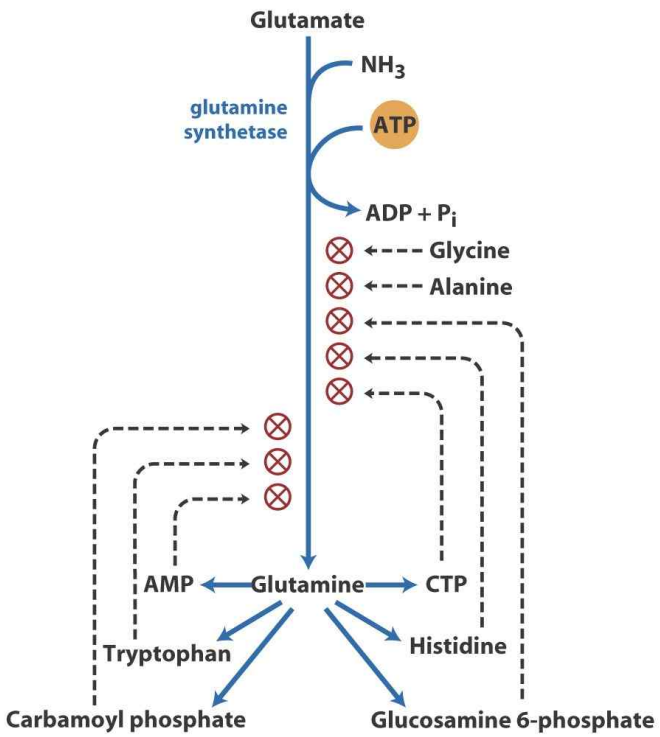

Fig. Allosteric regulation of glutamine synthetase

2. 아미노산 생합성(Biosynthesis of amino acids)

1) All amino acids are derived from intermediates in **glycolysis, the citric acid cycle, or the pentose phosphate pathways.**

TABLE 22–1 Amino Acid Biosynthetic Families, Grouped by Metabolic Precursor

α-Ketoglutarate	**Pyruvate**
Glutamate	Alanine
Glutamine	Valine*
Proline	Leucine*
Arginine	Isoleucine*
3-Phosphoglycerate	**Phosphoenolpyruvate and erythrose 4-phosphate**
Serine	Tryptophan*
Glycine	Phenylalanine*
Cysteine	Tyrosine†
Oxaloacetate	**Ribose 5-phosphate**
Aspartate	Histidine*
Asparagine	
Methionine*	
Threonine*	
Lysine*	

*Essential amino acids.
†Derived from phenylalanine in mammals.

2) Nitrogen enters these pathways by way of **glutamate and glutamine**

3) **Chorismate** is a key intermediate in the synthesis of **Trp, Phe, Tyr**

4) Histidine biosynthesis uses precursors of **purine biosynthesis**

◎ **효소의 다중도 (enzyme multiplicity) :**
동종효소에 의하여 촉매되는 반응은 같은 경로의 다른 생성물이 필요할 때 최종산물이 그 전체 경로의 핵심단계를 폐지하지 않도록 방지하고 있다.
ex) 아스파르트산 → 아스파틸-β-인산 **(3가지 동종효소작용)**

5) 아미노산과 뉴클레오타이드 합성에 필수적인 보조효소

① **Biotin** : 다양한 **카르복실화 반응**에서 **이동성카르복실기 운반체**로 작용

② **Tetrahydrofolate(THF)** : **활성화된 1-탄소단위를 운반**

- 운반되는 1-탄소 단위체는 **N-5 나 N-10 또는 동시에 N^5, N^{10}**의 질소원자와 결합하여 이동한다.
- **테트라하이드로폴산(엽산)은 임신초기의 신경계발달에 중요한 역할**

③ **S-Adenosylmethionine (SAM) : 메틸기의 공여체 작용**

- Methionine + ATP $\xrightarrow[\text{Methionine adenosyltransferase}]{}$ S-Adenosylmethionine + PPi + Pi

3. Molecules derived from amino acids

* **Amino acids are precursors of many specialized biomolecules,** including hormones, coenzymes, nucleotides, alkaloids, cell-wall polymer, porphyrins, antibiotics, pigments, and neurotransmitters

1) Glycine is a precursor of porphyrins

* Porphyrin is heme protein (hemoglobin, cytochromes, chlorophyll)

2) Heme is the source of bile pigments

* Bilirubin binds to serum albumin and is transported to the liver

* Bilirubin glucuronide (water soluble) : bile pigment

3) Amino acids are precursors of creatine and glutathione

① **Phosphocreatine : an important energy reservoir in skeletal muscle**

- Precursor : glycine, arginine, and methionine

② **Glutathione (GSH, 환원형) : serves as reducing agent**

- a tripeptide derived from **glycine, glutamate, and cysteine**

- GSSG(산화형) : disulfide bond에 의하여 연결된 두 개의 글루타티온 분자

③ D-amino acids are found primarily in bacteria

④ Aromatic amino acids are precursors of many plant substances

- Tryptophan ⟶ indole acetic acid (auxin)

- Phe + Tyr ⟶ lignin

⑤ Biological amines are products of amino acid decarboxylation

(생체아민은 아미노산의 탈카르복실화의 산물이다)

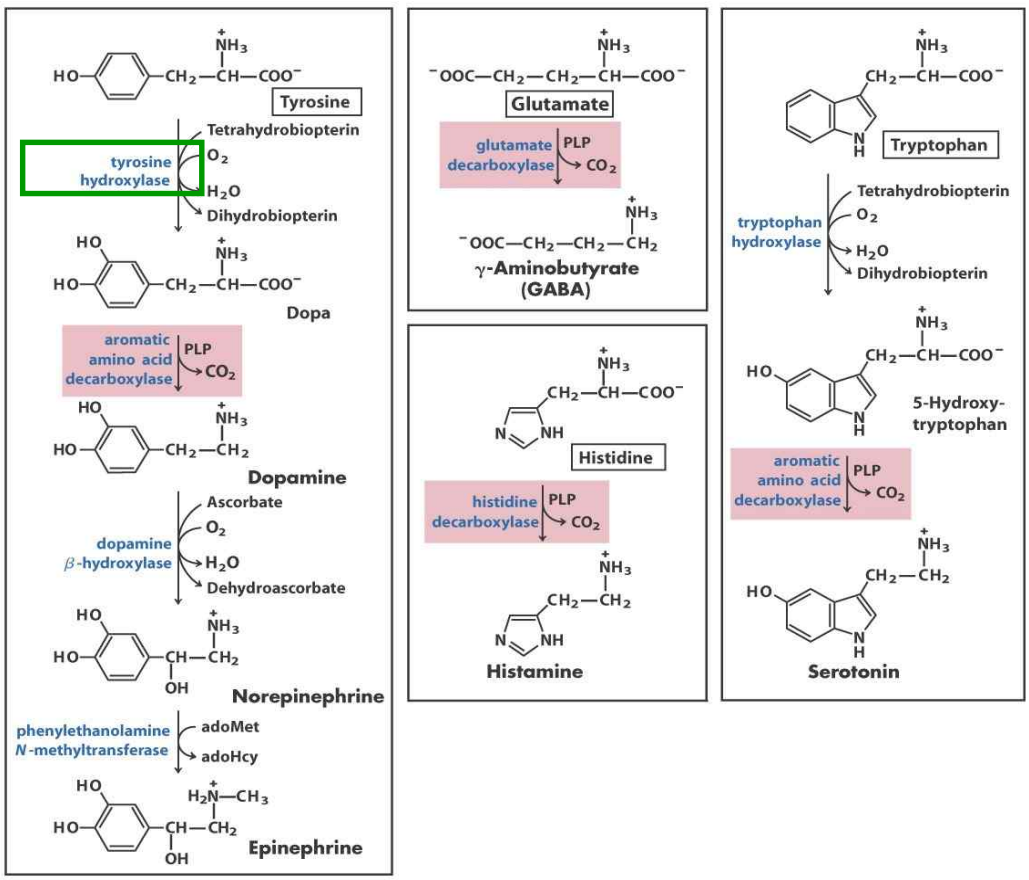

Fig. Biosynthesis of some neurotransmitters from amino acids

⑥ Nitric oxide (NO) 합성

- Arginine is the precursors for biological synthesis of nitric oxide
- 일산화질소(NO)는 포유동물의 생체 내에서 합성되는 것으로 밝혀졌다
- 합성효소(NO synthase) : NADPH , Ca^{++}-calmodulin의존

◎ **생리적 기능 :**

- **생물학적 신호 전달자**, 혈액응고, 혈압조절, 혈관의 평창, 혈소판 응집 저해 등의 생리과정을 조절작용
- cGMP 생성 촉진, 심장근육의 이완작용, 신경전달물질