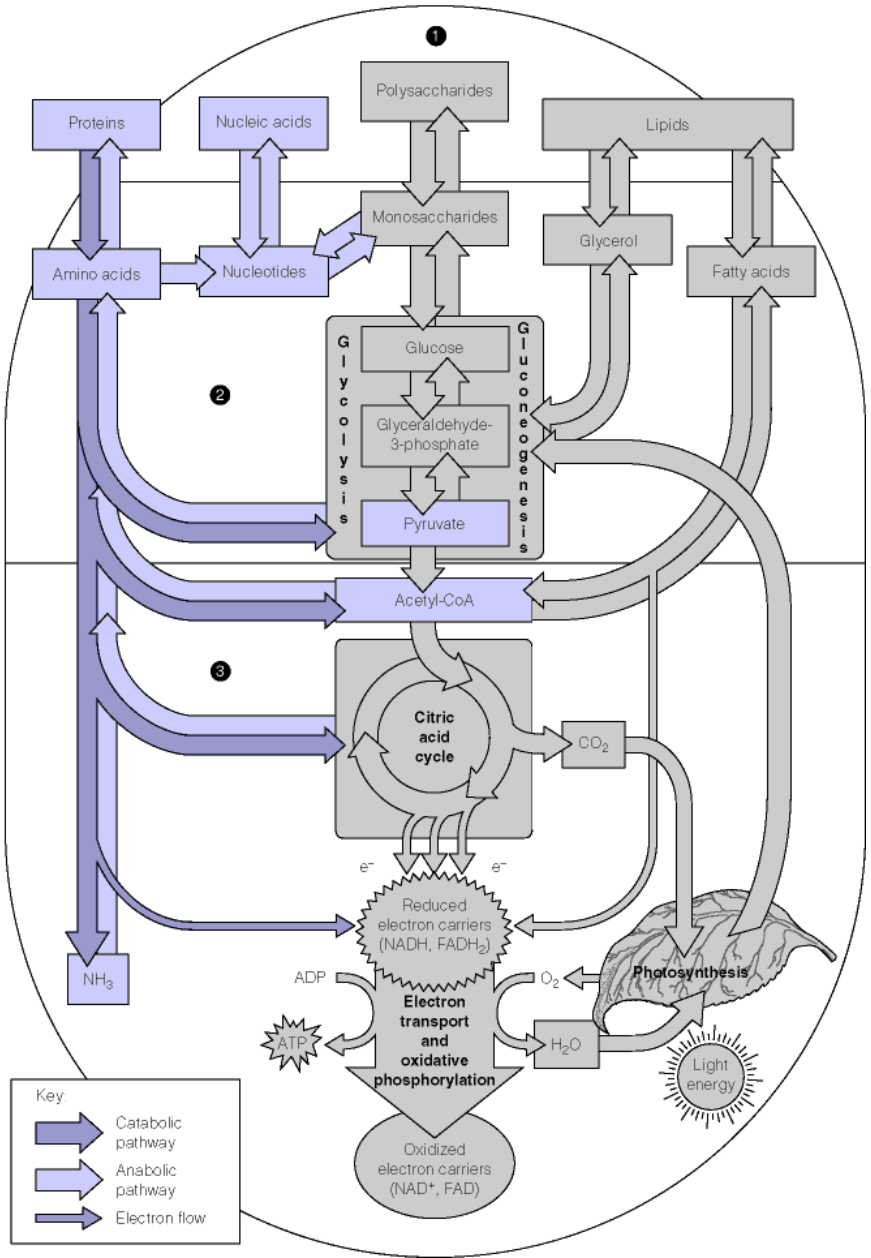
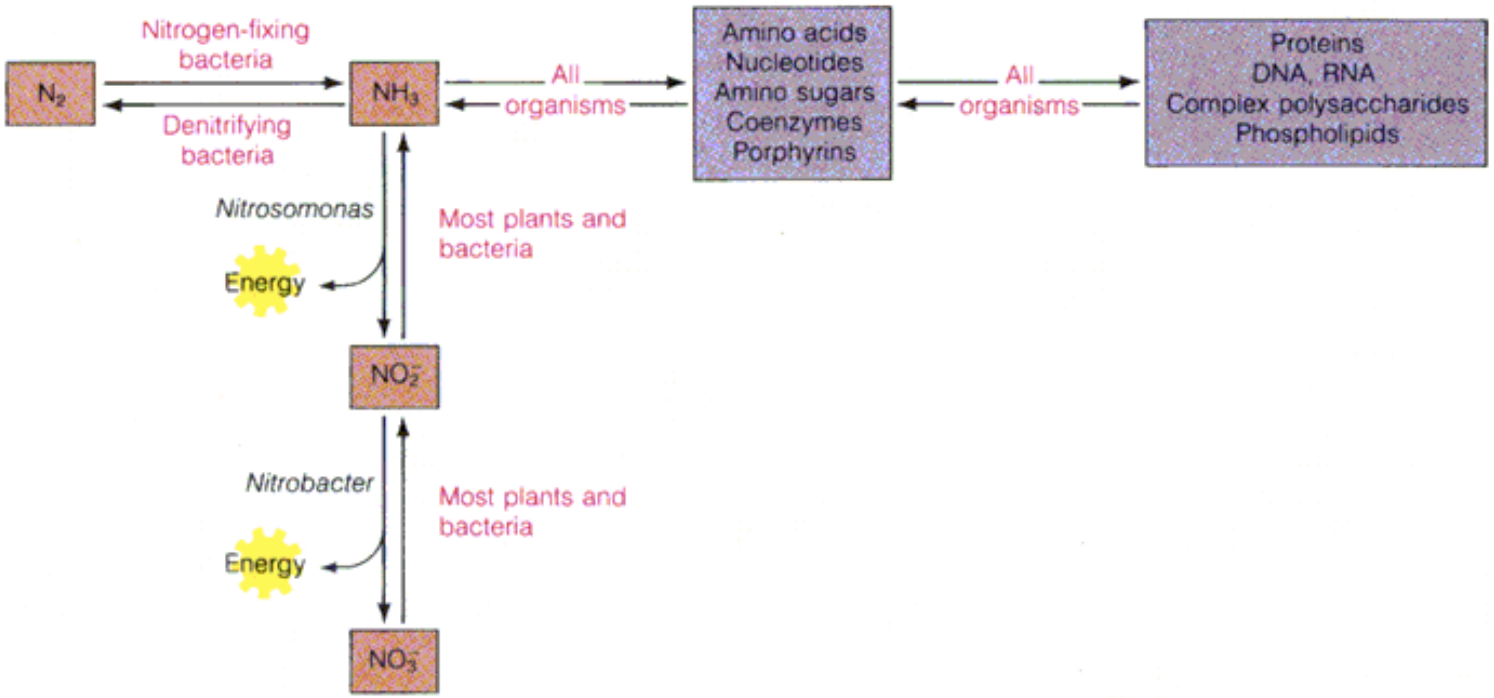
# 3. BIOSYNTHESIS OF AMINO ACIDS AND RELATED COMPOUNDS

# THE NITROGEN ECONOMY

- **Nitrogen** is an essential element of biological molecules, such as amino acids, nucleotides, proteins, and DNA.
- Most organisms have no polymeric nitrogen compounds whose function is to be stored and released on demand.
- All organisms can convert ammonia ($NH_3$) to organic **nitrogen** compounds (substances containing C-N bonds).
- The reduction of $N_2$ to $NH_3$, on the other hand, which is called biological nitrogen fixation, can only be carried out by certain microorganisms, sometimes in symbiotic relationship with plants.
- The reduction of $NO_3^-$ to $NH_3$, however, is widespread among both plants and microorganisms.



# THE NITROGEN ECONOMY




- Within the biosphere a balance is maintained between total inorganic and total organic forms of **nitrogen**.
- The conversion of inorganic **nitrogen** to organic **nitrogen**, which starts with **nitrogen** fixation and nitrate reduction, is counterbalanced by catabolism, denitrification, and decay.
- *Nitrosomonas* oxidizes ammonia to nitrite and *Nitrobacter* oxidizes nitrite to nitrate. Other bacteria, the denitrifying bacteria, convert ammonia to $N_2$ just the opposite of the **nitrogen**-fixing bacteria.

# THE NITROGEN CYCLE

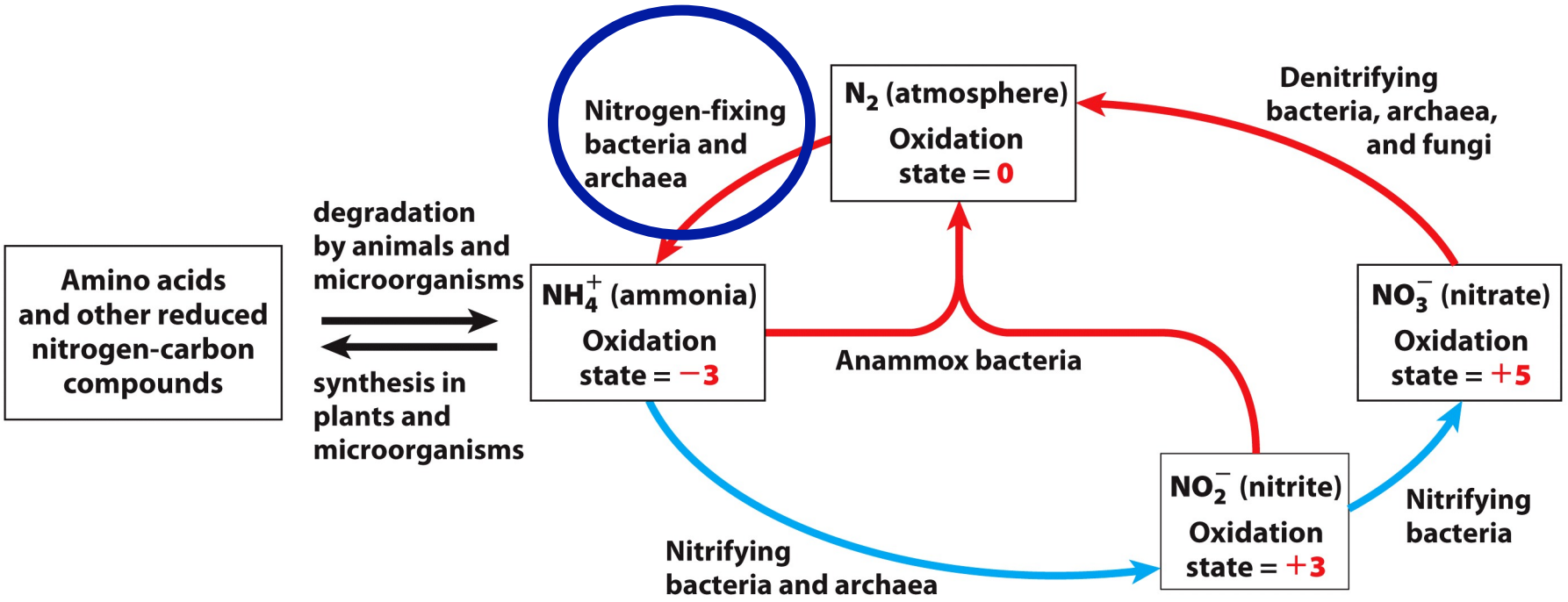



**Figure 22-1**
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# THE NITROGEN FIXATION: NITROGENASE

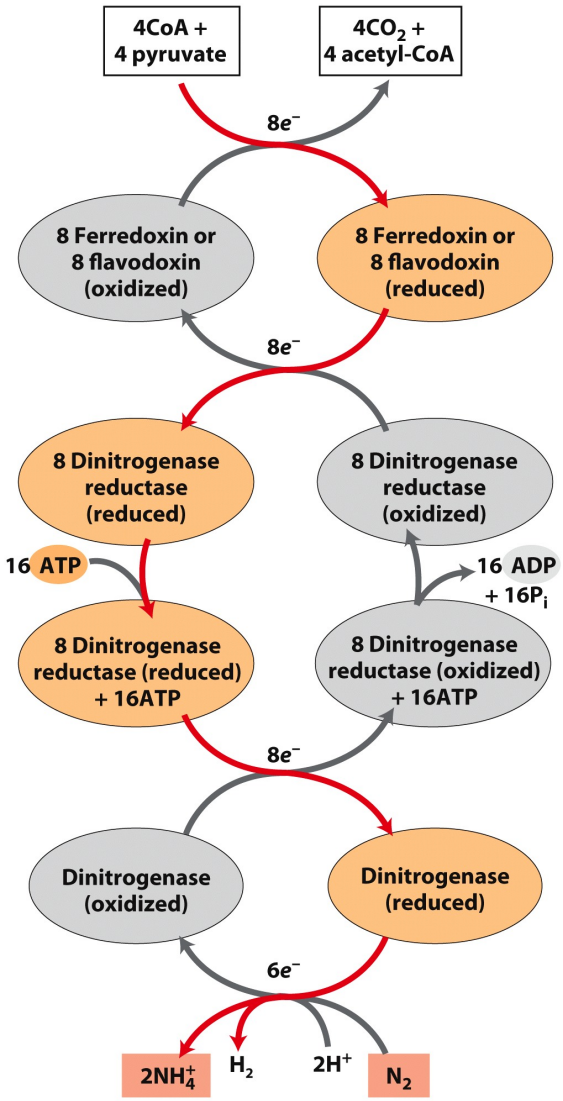


**Figure 22-4**
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- The reduction of atmospheric nitrogen ($N_2$) to ammonia ($NH_3$) is called biological **nitrogen fixation** and it occurs in relatively few living systems.
- These include some free-living soil bacteria, such as *Klebsiella* and *Azotobacter*, cyanobacteria, and *Rhizobium*, which is a symbiont on the roots of leguminous plants.
- The infecting bacterium assumes a modified form, called a bacteroid, inside the cells of infected plants.
- The enzymes involved are very sensitive to oxygen and must be studied only under anaerobic conditions.
- In root nodules of plants, the anaerobic environment is provided by the protein leghemoglobin, which binds any $O_2$ that makes its way into the nodules.

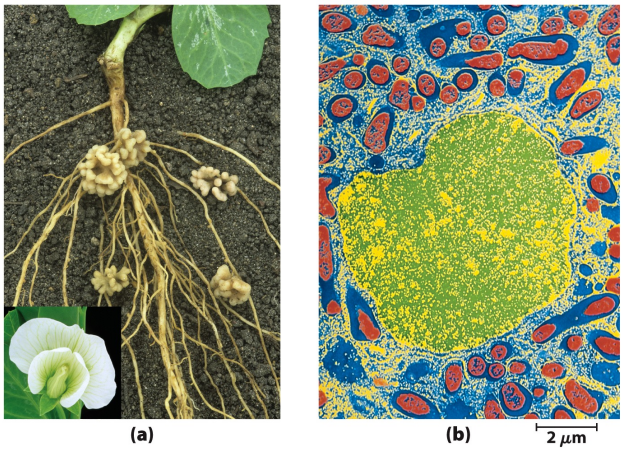


Figure 22-6
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# THE NITROGEN FIXATION: NITROGENASE

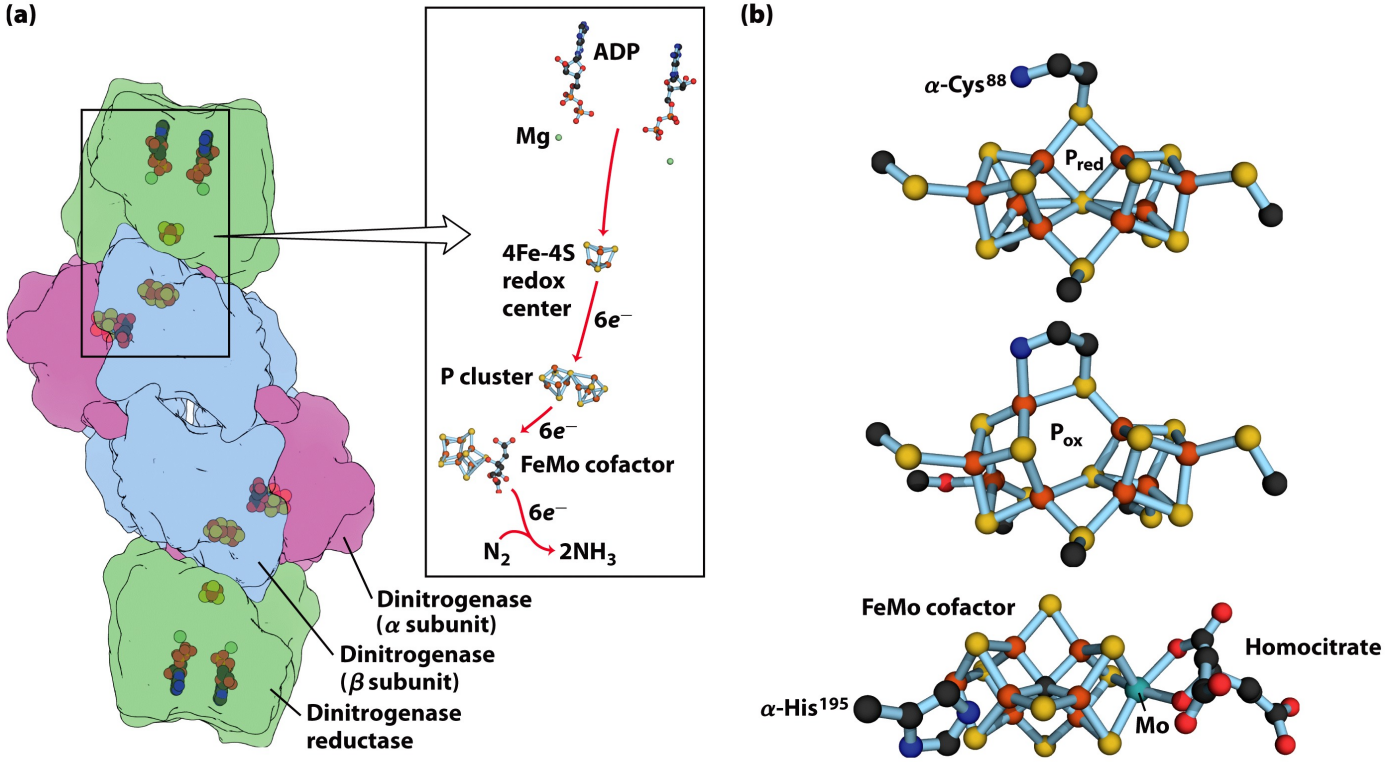


**Figure 22-3**
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- The enzyme system responsible for $N_2$ reduction, called the nitrogenase complex, consists of two separate proteins.
- One protein-called **component I**, nitrogenase, or molybdenum iron protein-catalyzes the reduction of $N_2$
- The other-called **component II, nitrogenase reductase**, or **iron protein**-transfers electrons from ferredoxin or flavodoxin to component I.
- Both component I and component II contain $Fe_4S_4$ iron-sulfur clusters, and component I also contains molybdenum, in the form of a tightly bound iron-molybdenum cofactor (FeMoCo).

# NITRATE UTILIZATION

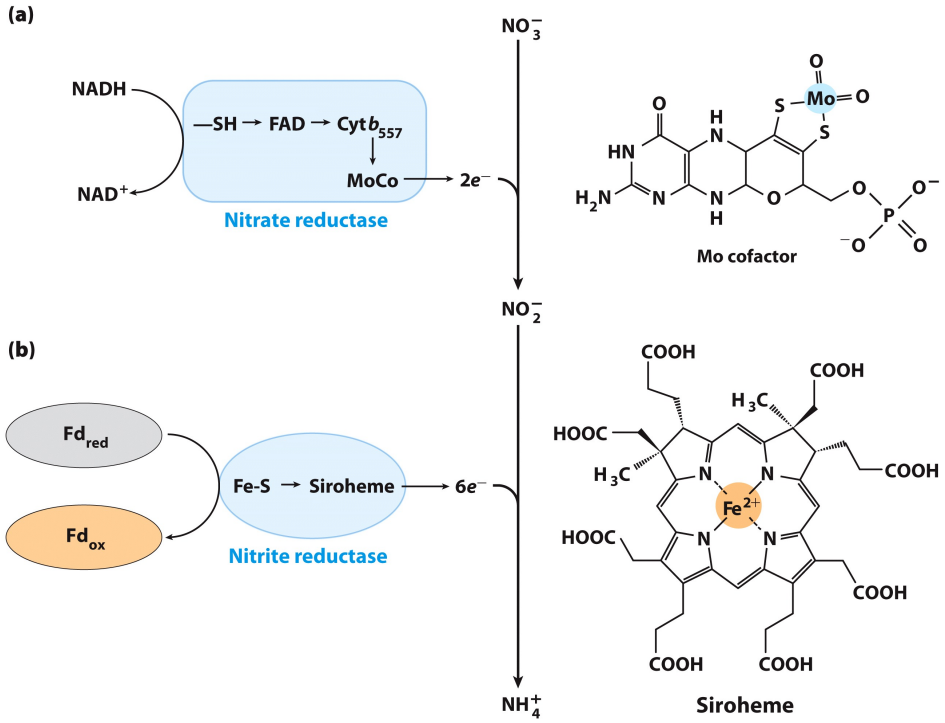


**Figure 22-2**
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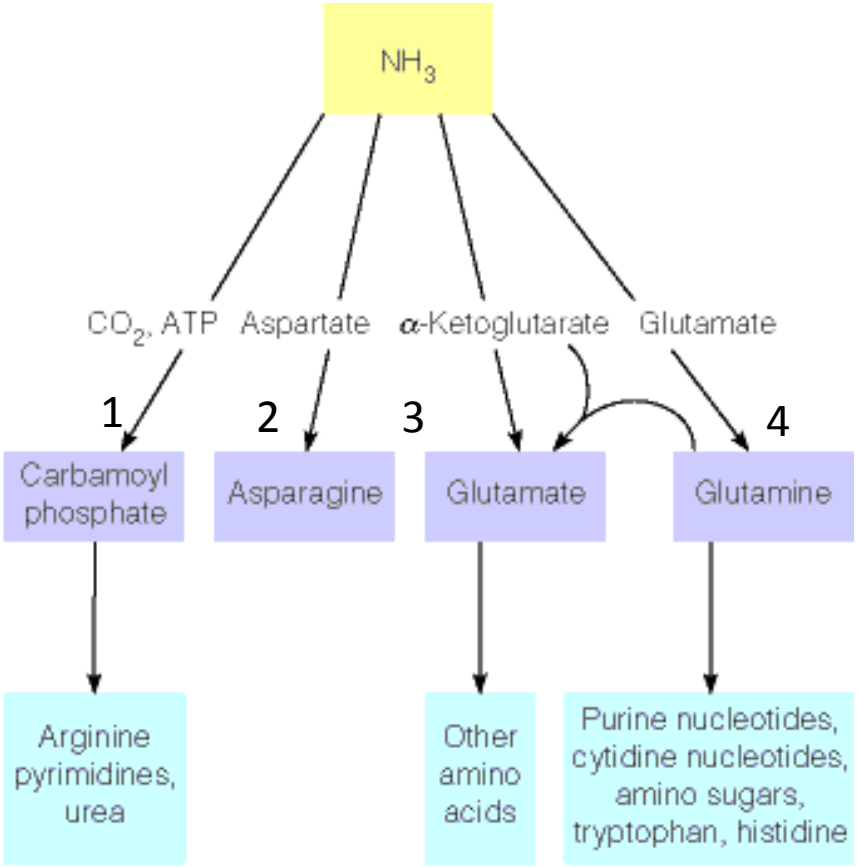
- The ability to reduce nitrate ($NO_3^-$) to ammonia ($NH_3$) is common to virtually all plants, fungi, and bacteria. It occurs in the following four steps:
- $NO_3^-$ -> $NO_2^-$ -> $NO^-$ -> $NH_2OH$ -> $NH_3$
- The first step, conversion of $NO_3^-$ to $NO_2^-$, is catalyzed by a large and complex enzyme called **nitrate reductase**.
- Nitrate reductase is a multi-subunit enzyme with MW of about 800 kDa.
- It contains bound FAD, molybdenum, and a cytochrome called cytochrome 557 (which contains an $Fe_4S_4$ complex).
- Nitrate reductase carries out the following reaction:

$NO_3^-$ + NAD(P)H + H+ -> $NO_2^-$ + $NADP^+$ + $H_2O$

# UTILIZATION OF AMMONIA



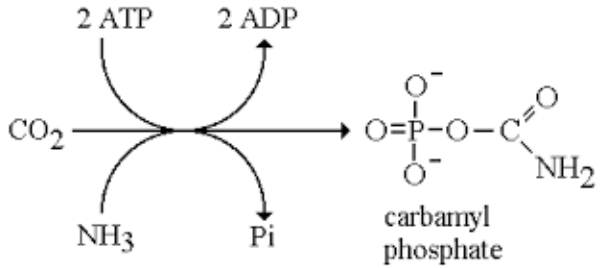

- Virtually all organisms share a few common routes for the utilization of inorganic nitrogen in the form of ammonia.
- At low levels, ammonia is a central metabolite, but at high levels it is quite toxic.
- Ammonia is a substrate for enzymes that convert it to various organic nitrogen compounds:

1) CARBAMOYL PHOSPHATE SYNTHETASE,

2) ASPARAGINE SYNTHETASE,

3) GLUTAMATE DEHYDROGENASE,

4) **GLUTAMINE SYNTHETASE**.




- Carbamoyl phosphate synthetase I (mitochondria, urea cycle)
- Carbamoyl phosphate synthetase II (cytosol, pyrimidine metabolism).

# UTILIZATION OF AMMONIA: GLUTAMINE SYNTHETASE

**Glutamate** + $NH_3$ + ATP -> **Glutamine** + ADP + Pi

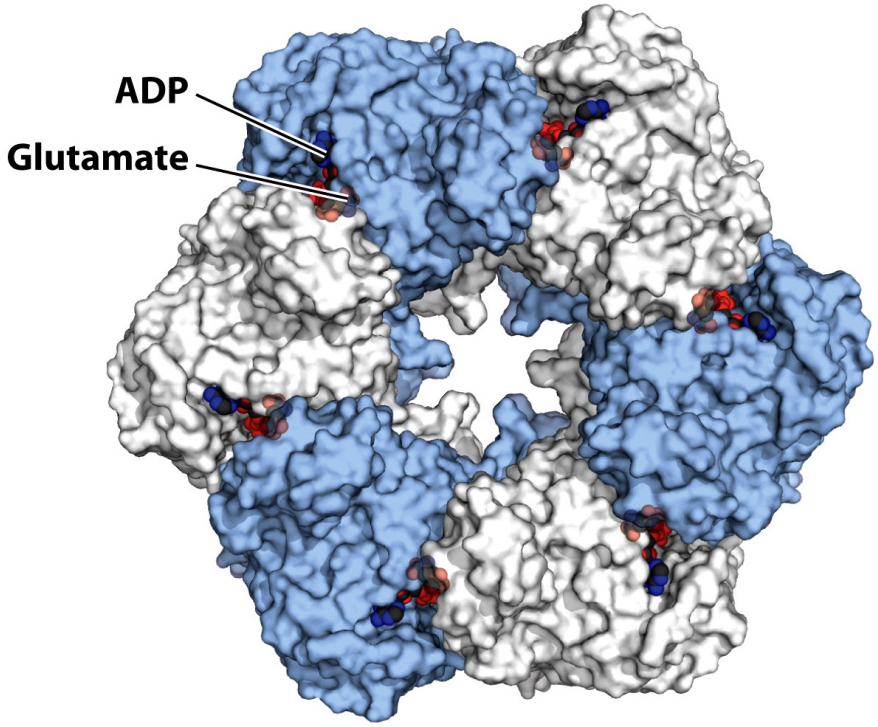



**Figure 22-7**
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- The *E. coli* **glutamine synthetase** is a dodecamer, with 12 identical subunits and the complex has a molecular weight of about 600,000 Daltons.
- The amide nitrogen of glutamate is used for the synthesis of several amino acids, purine and pyrimidine nucleotides, and amino sugars, so **glutamine synthetase** plays a central role in nitrogen metabolism.
- In animals, the enzyme is a key participant in detoxifying ammonia, particularly in the brain, and in ammonia excretion in the kidney.
- Accumulation of glutamate and glutamine depletes α-ketoglutarate, which would interfere with the citric acid cycle

# UTILIZATION OF AMMONIA: GLUTAMINE SYNTHETASE

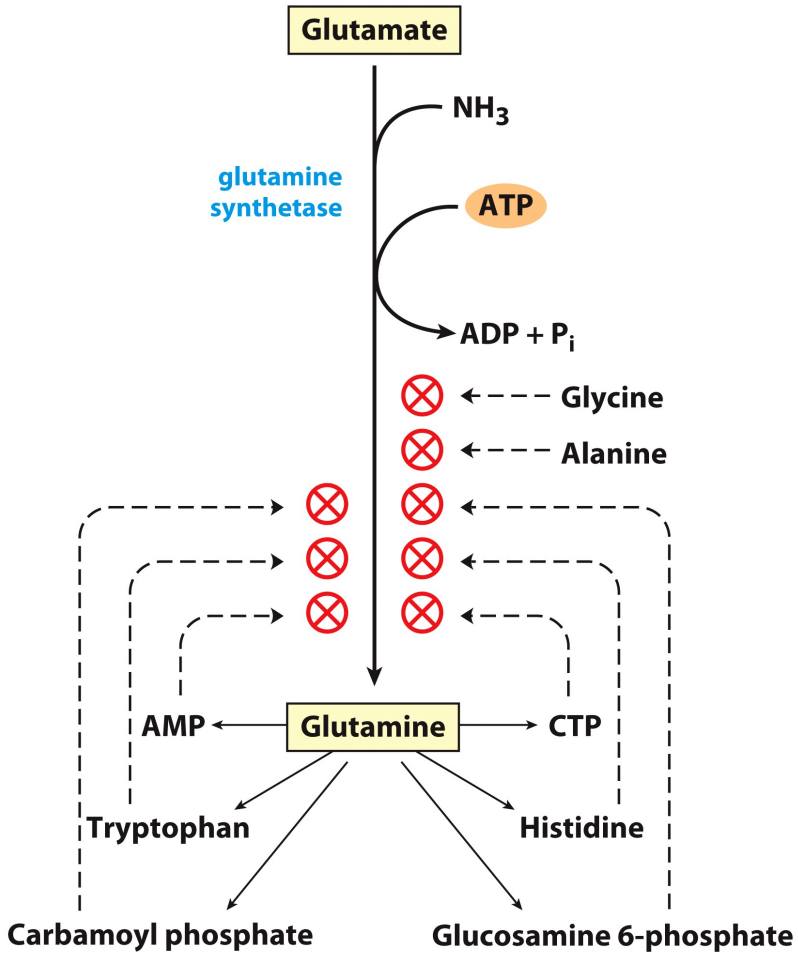


**Figure 22-8**
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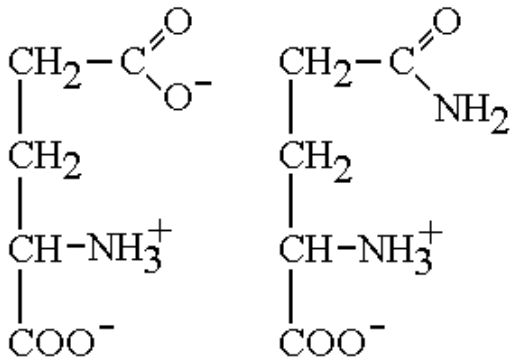
**Glutamine synthetase** is tightly regulated. Mechanisms controlling the activity of **glutamine synthetase** include the following:

1. **Cumulative feedback Inhibition** - Eight specific feedback inhibitors, which are either metabolic end products of glutamine (tryptophan, histidine, glucosamine-6-phosphate, carbamoyl phosphate, CTP, or AMP) or indicators of the general status of amino acid metabolism (alanine or glycine), can bind to any of the subunits of the enzyme and at least partially inhibit it. The more inhibitors that bind, the greater the inhibition.



# UTILIZATION OF AMMONIA: GLUTAMINE SYNTHETASE

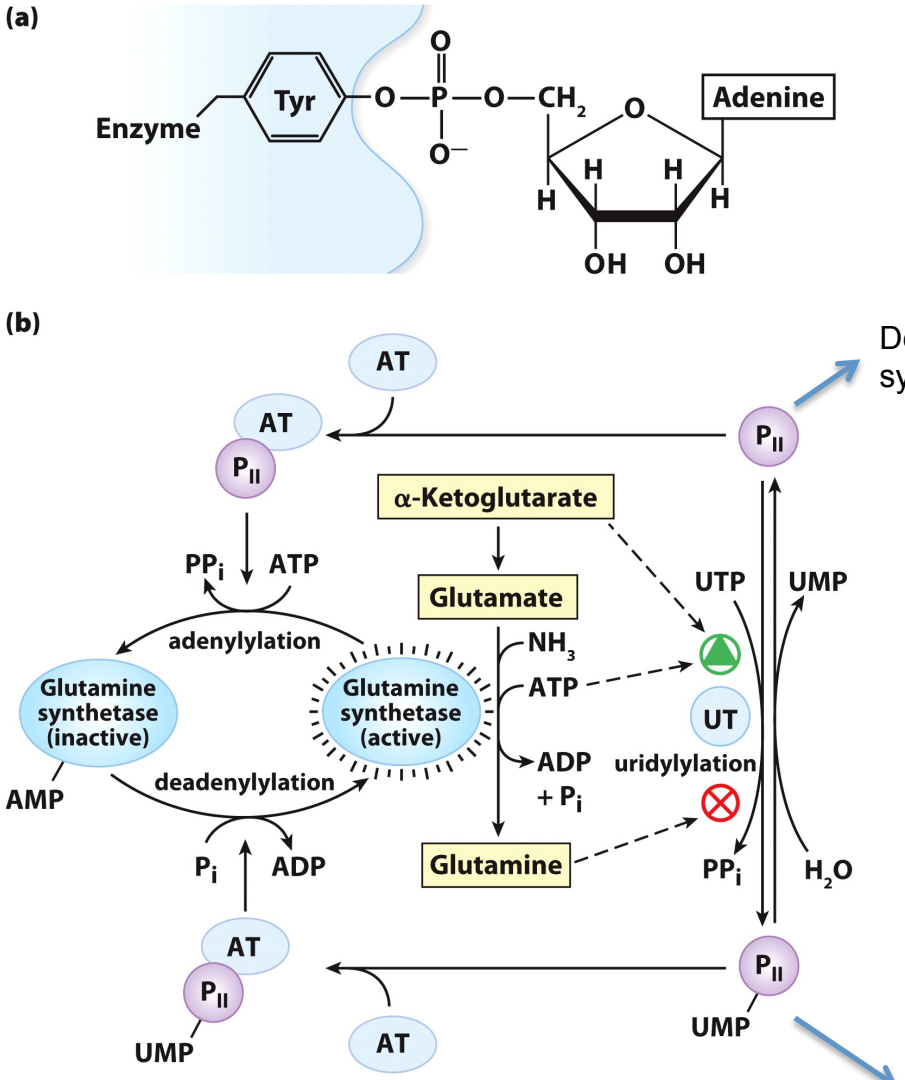



**Figure 22-9**
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**Glutamine synthetase** is tightly regulated. Mechanisms controlling the activity of **glutamine synthetase** include the following:

**2. Covalent modification (adenylylation)** - A specific tyrosine residue in glutamine synthetase can react with ATP to form a phosphate ester with AMP. Adenylylation renders the catalytic site of the enzyme inactive. Adenylylation and deadenylylation involve a complex series of regulatory cascades.
Adenylation can occur on the different subunits and can also partially incativate the enzyme.

AT = adenylyltransferase
UT = uridylyltransferase
$P_{II}$ is a regulatory protein

# GLUTAMINE AMIDOTRANSFERASE

- Glutamine is the main physiological source of ammonia in more than 10 known biosynthetic reactions

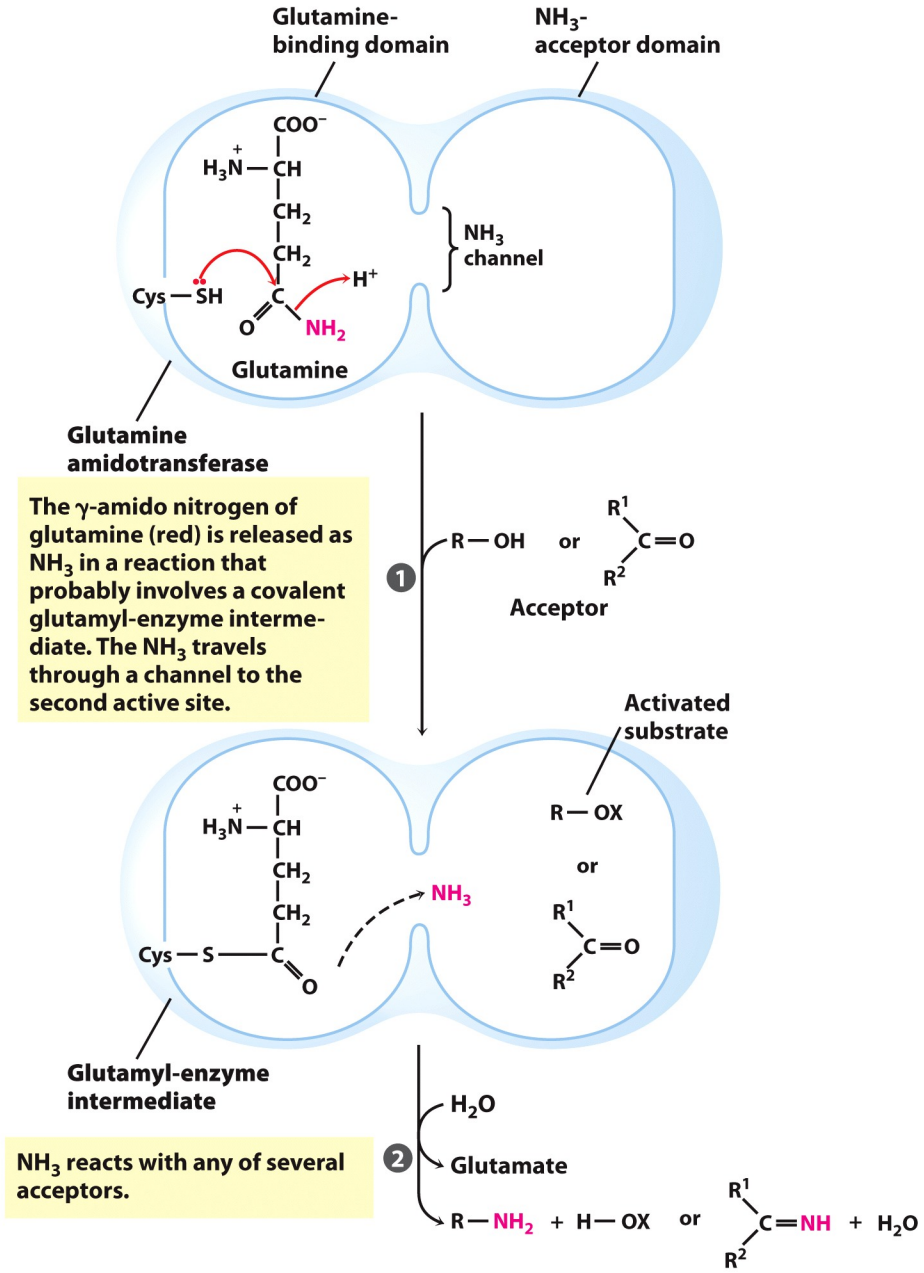


**Figure 22-10**
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# BIOSYNTHETIC CAPACITIES OF ORGANISMS

- Organisms vary widely in their ability to synthesize amino acids.
- Many bacteria and most plants can synthesize all of their nitrogenous metabolites starting from a single nitrogen source, such as ammonia or nitrate.
- Many microorganisms will use a preformed amino acid, when available (extreme case is *Lactobacillus*).
- Mammals are intermediate, being able to biosynthesize about half of the amino acids in quantities needed for growth and for maintenance of normal nitrogen balance → EVOLUTION

- Essential amino acids: they must be provided by diet
- Nonessential amino acids: they can be biosynthesized in adequate amounts

**Table 1. Dietary Requirements for Amino Acids in Humans**

| Essential | Nonessential |
|---|---|
| Histidine | Alanine |
| Isoleucine | Arginine |
| Leucine | Asparagine |
| Lysine | Aspartate |
| Methionine | Cysteine |
| Phenylalanine | Glutamate |
| Threonine | Glutamine |
| Tryptophan | Glycine |
| Valine | Proline |
| | Serine |
| | Tyrosine |

# BIOSYNTHETIS OF AMINO ACIDS

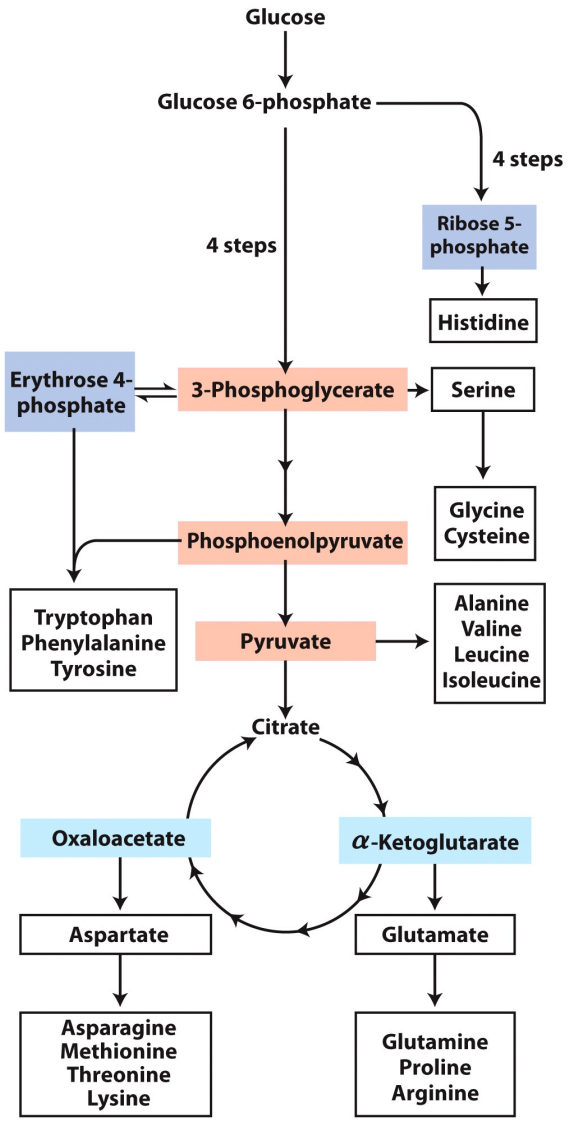


**Figure 22-11**
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**TABLE 22–1** **Amino Acid Biosynthetic Families, Grouped by Metabolic Precursor**

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

***Essential amino acids in mammals.**

**†Derived from phenylalanine in mammals.**

**Table 22-1**
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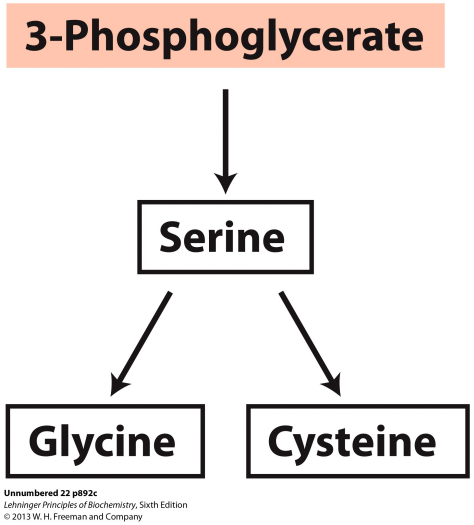
# AMINO ACIDS FROM INTERMEDIATES OF GLYCOLYSIS

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- Serine is involved in glycine, phospholipid and cysteine synthesis.
- Glycine is also a precursor for gluthatione, purine nucleotides and porphyrines.
- Serine and glycine are both major contributors to the pool of activated one-carbon groups, as 5,10-methylentethrahydrofolate,

For further reading:
https://biocyc.org/HUMAN/new-image?type=PATHWAY&object=SER-GLYSYN-PWY-1

Biosynthesis of serine and glycine

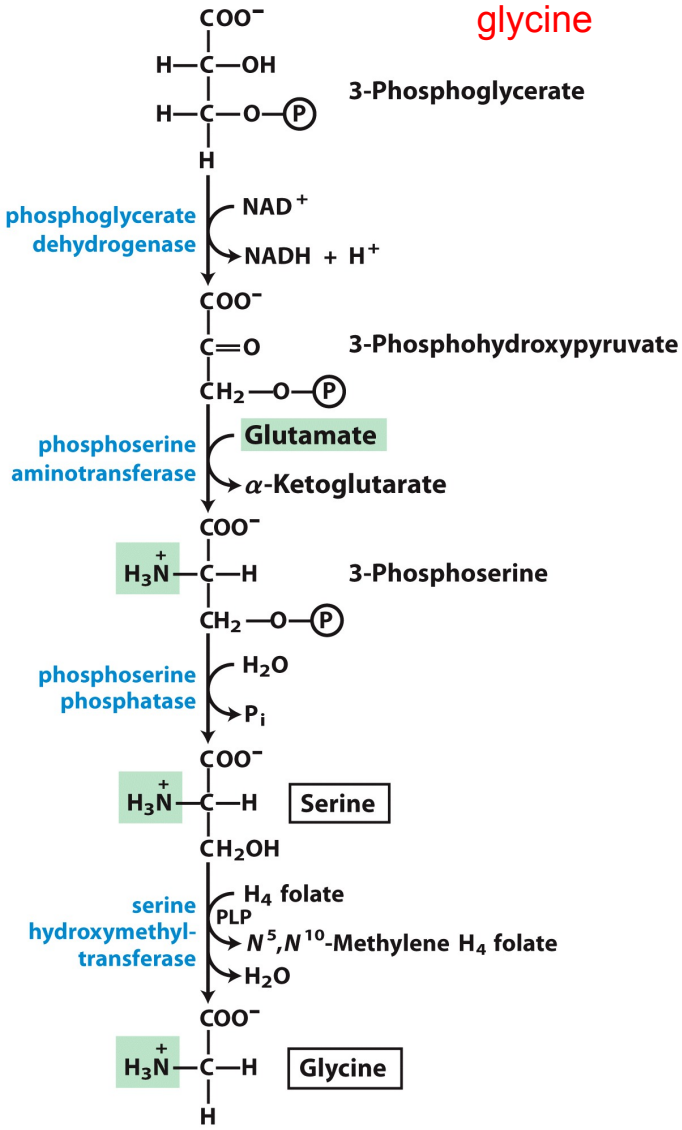


**Figure 22-14**
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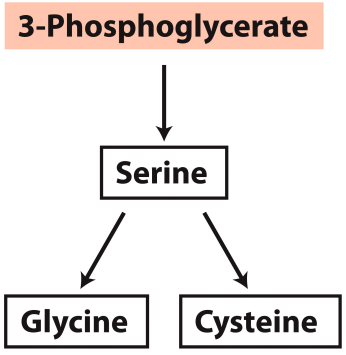
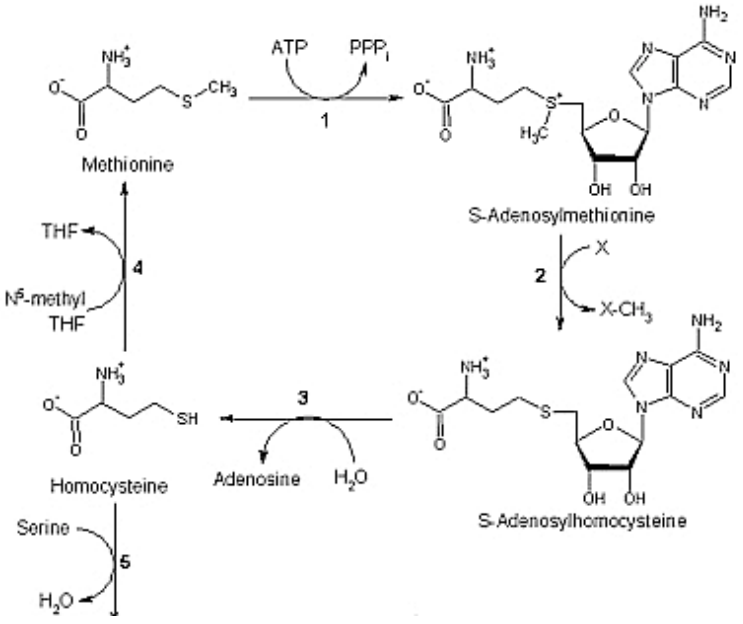
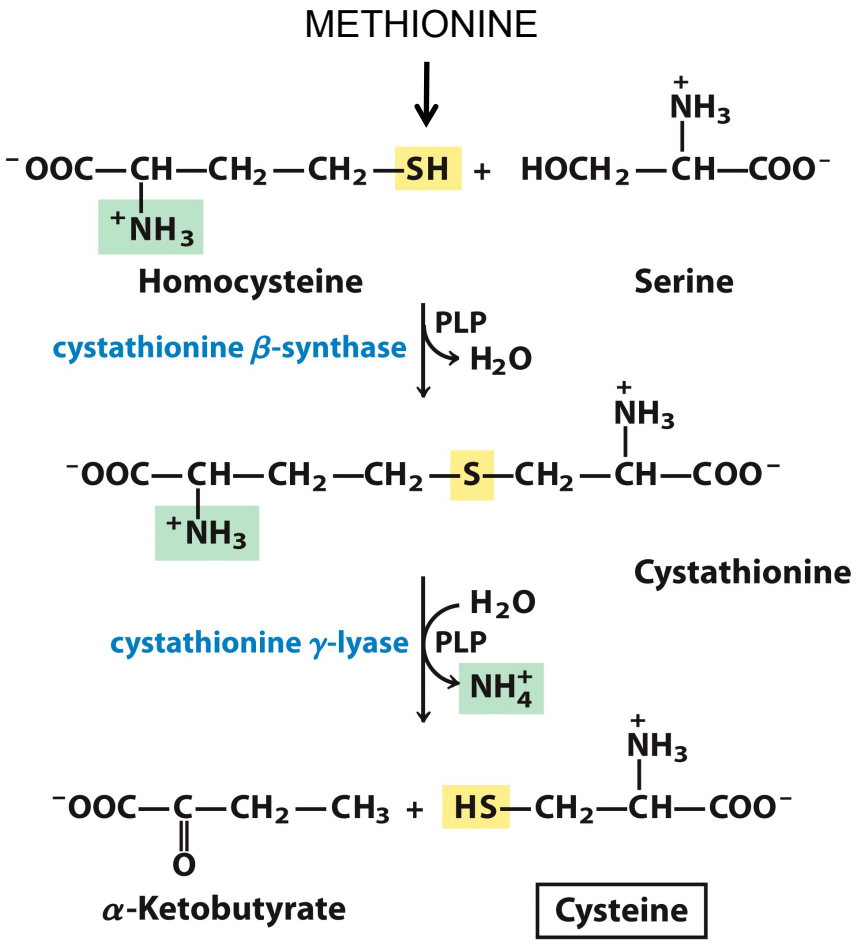
# AMINO ACIDS FROM INTERMEDIATES OF GLYCOLYSIS

- Plants and bacteria synthesize cysteine from inorganic sulfur and synthetize methionine from cysteine.
- Animals synthesize cysteine from dietary methionine




Biosynthesis of cysteine in animals

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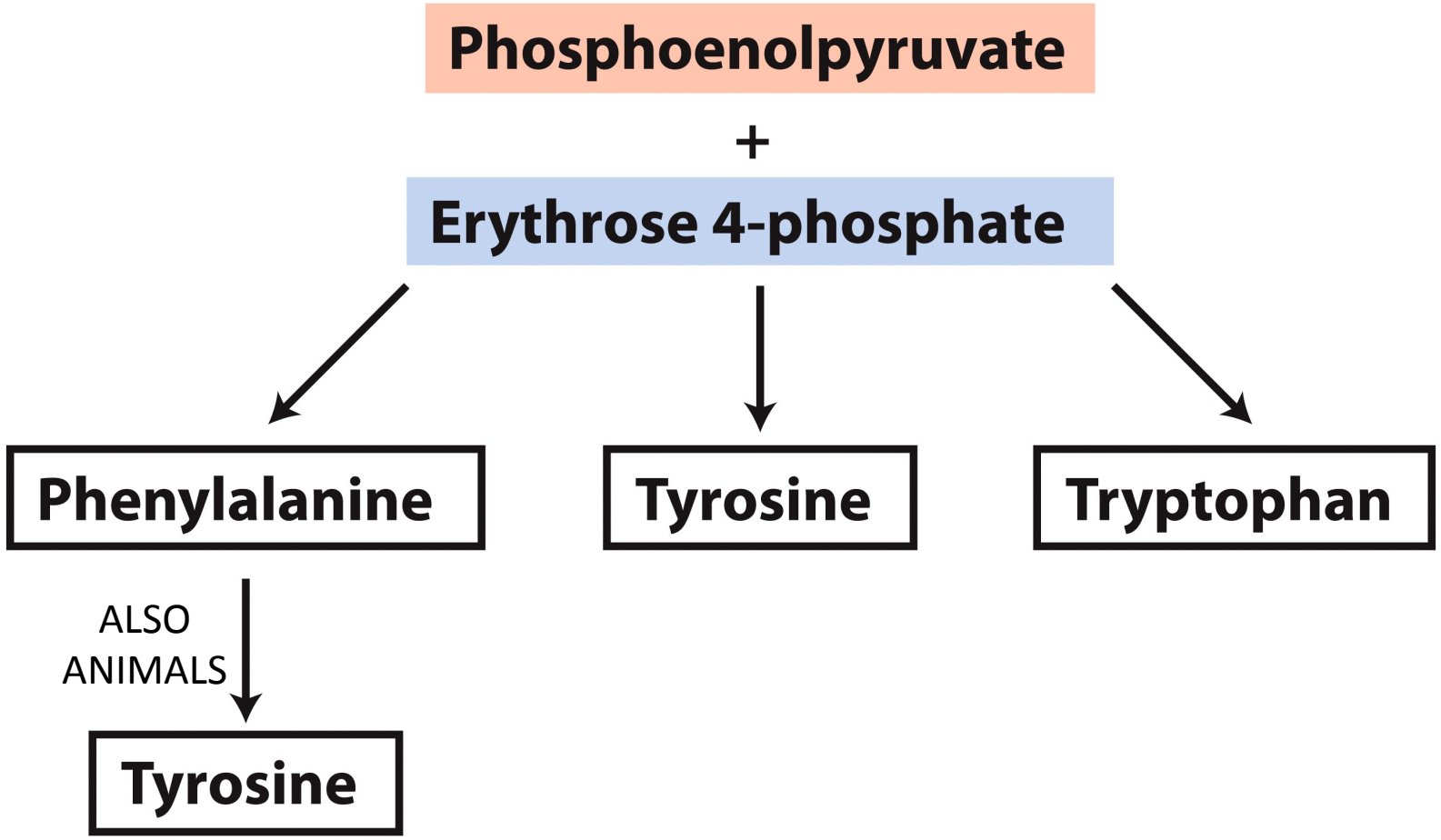
# AMINO ACIDS FROM INTERMEDIATES OF GLYCOLYSIS (PLANTS AND BACTERIA)

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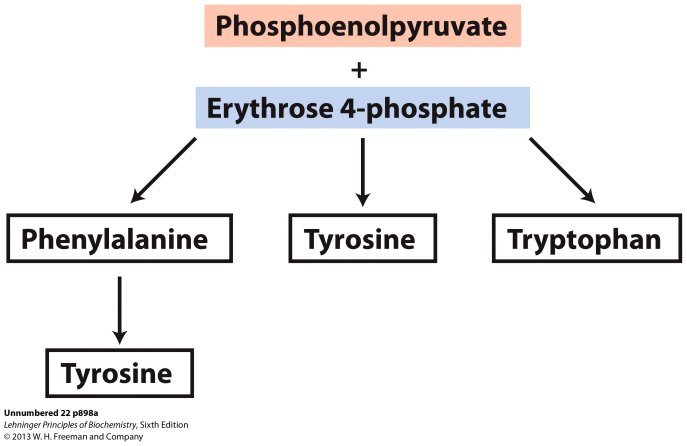
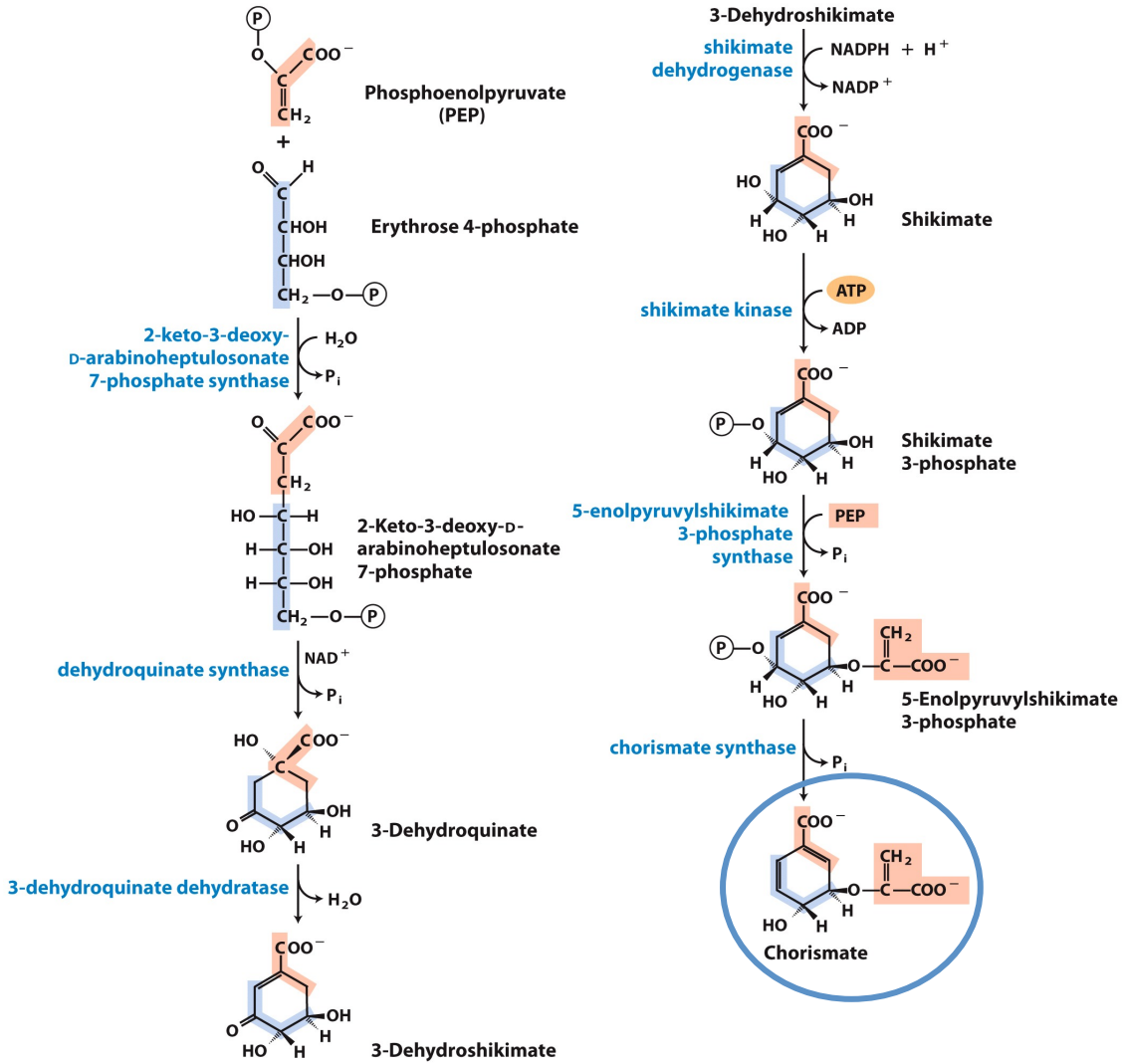
# AMINO ACIDS FROM INTERMEDIATES OF GLYCOLYSIS (PLANTS AND BACTERIA)




- The shikimic acid pathway leads to synthesis of nearly all aromatic compounds, including lignin.
- It is one of the most productive pathway in biology.

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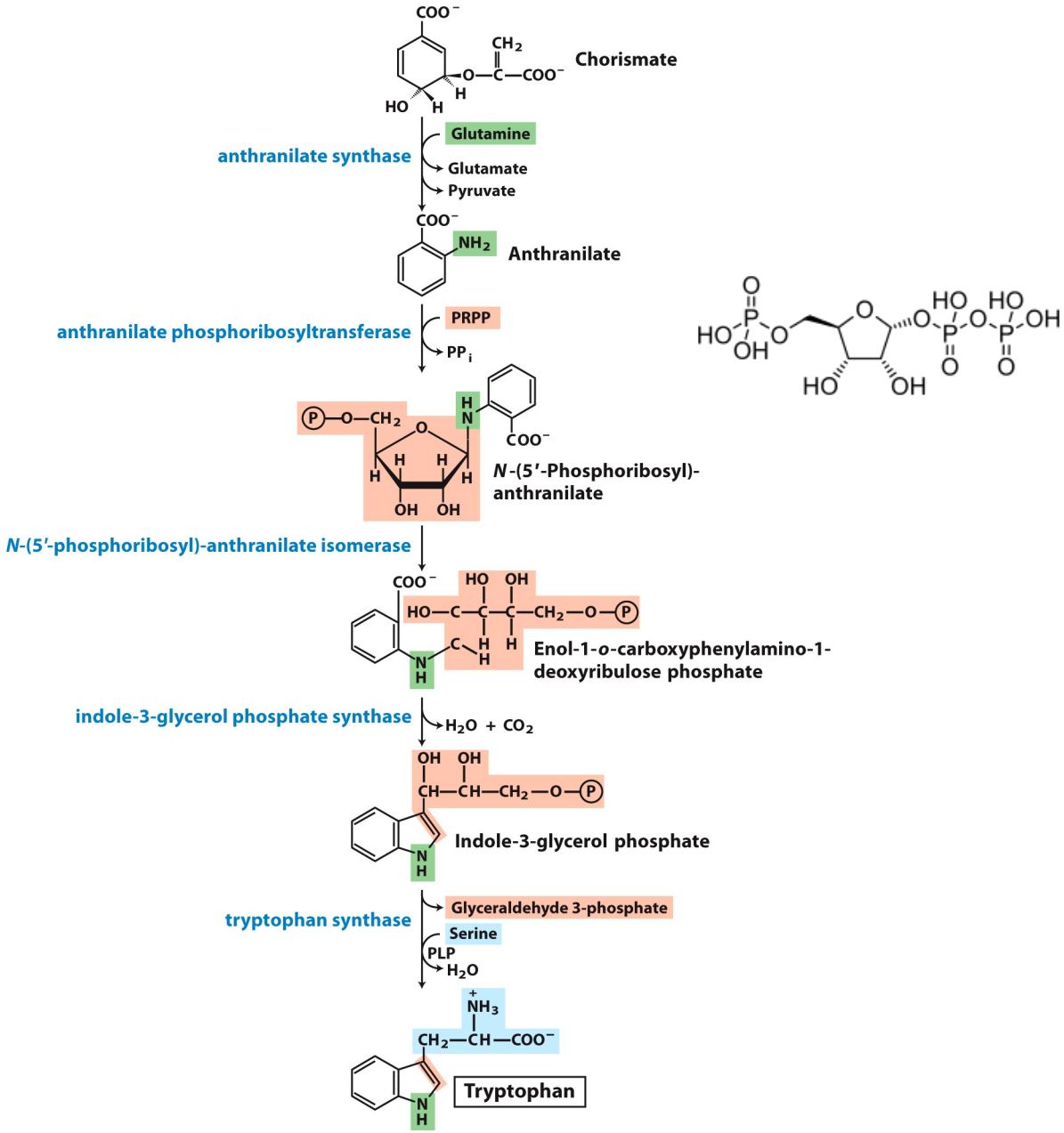


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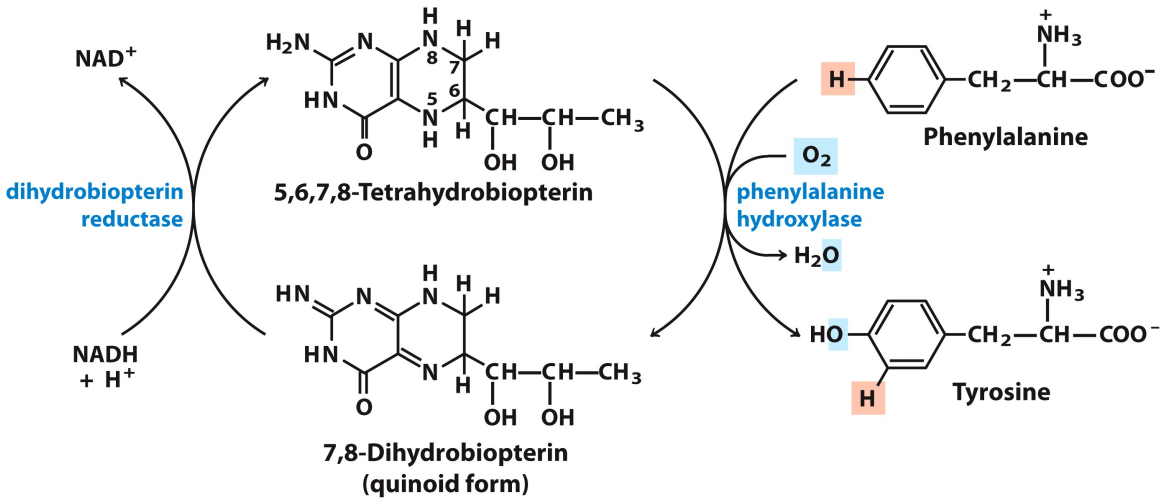
# AROMATIC AMINO ACIDS IN ANIMALS

- Animal cells do not synthesize aromatic rings.
- Instead, animal cells extensively modify amino acids with aromatic rings.
- Examples include the synthesis of tyrosine from phenylalanine, the synthesis of pigments and hormones from tyrosine, and the use of tyrosine, tryptophan, and histidine in synthesis of biogenic amines - compounds that serve as hormones and neurotransmitters.

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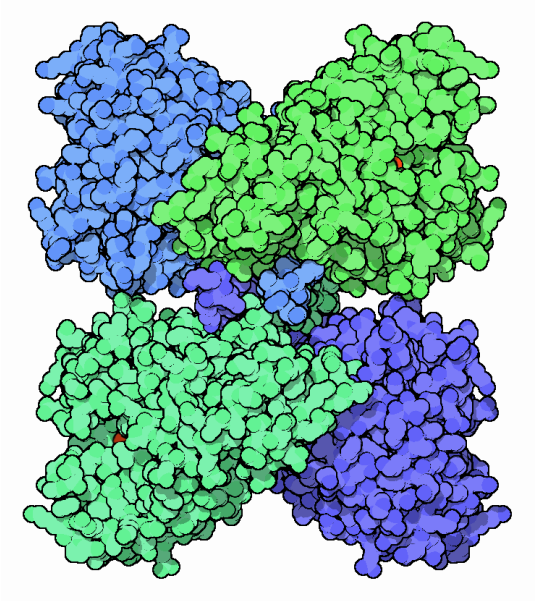
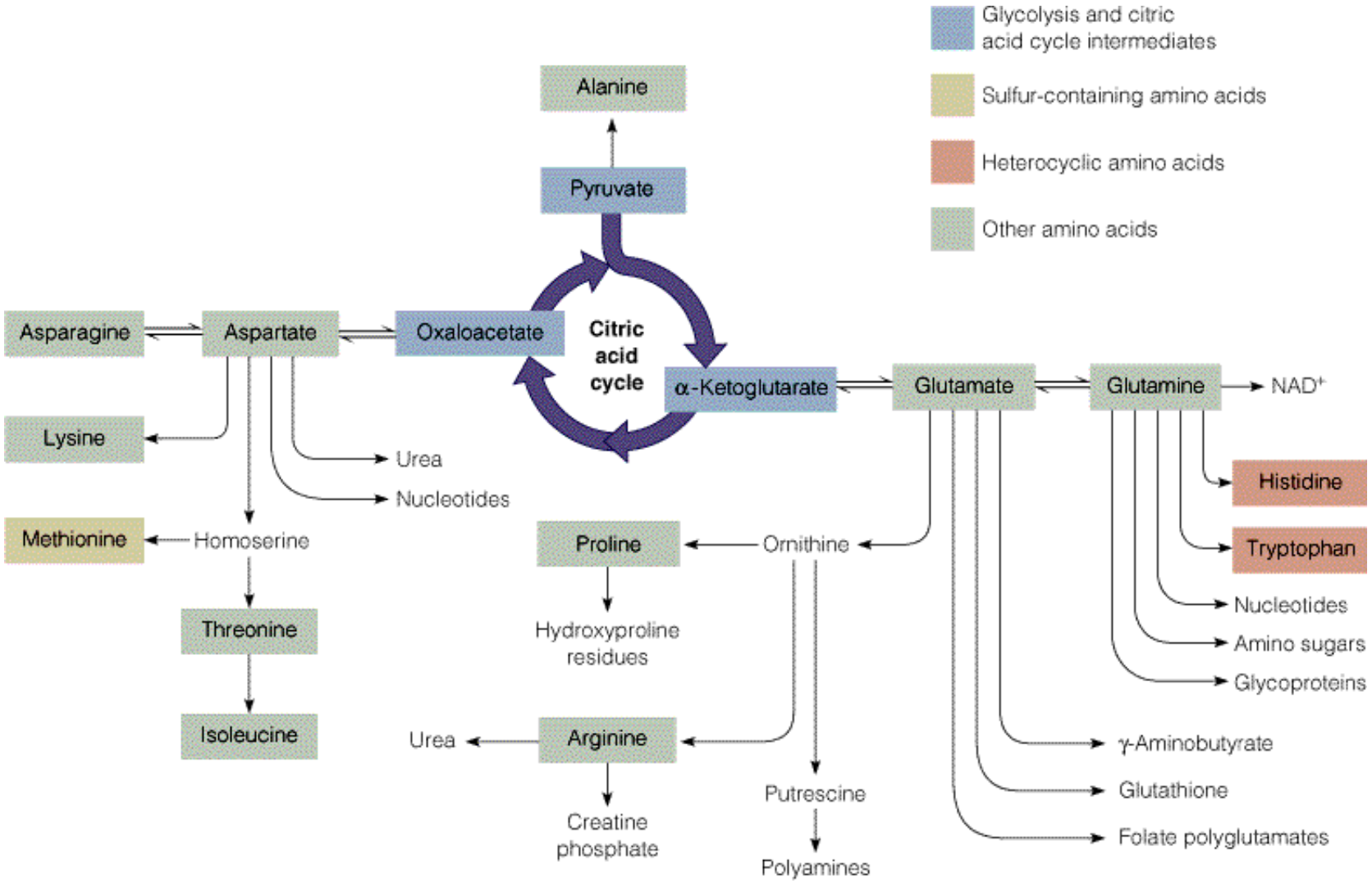


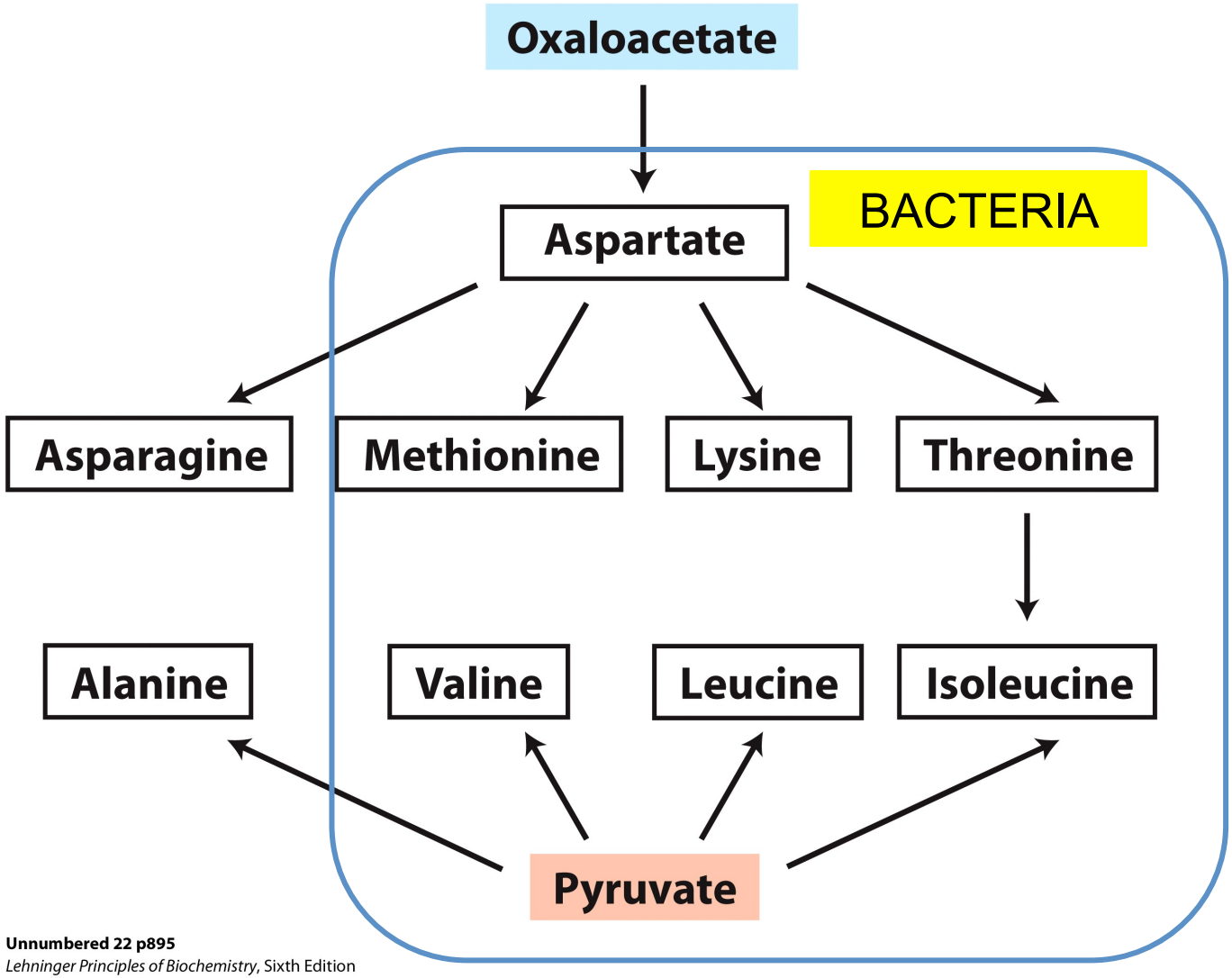
- Phenylalanine hydroxylase regulates the clearance of about 75% of the excess phenylalanine from our body by converting it to tyrosine.
- But in 1934, a Norwegian doctor, Asbjorn Folling, showed that the urine of two of his young mentally handicapped patients had a high level of phenylalanine. These were the first diagnosed cases of **phenylketonuria**.
- Within the next few years it was shown that the absence or malfunction of phenylalanine hydroxylase or lack of the tetrahydrobiopterin leads to this serious genetic disorder.

# AMINO ACIDS RELATED TO CITRIC ACID CYCLE INTERMEDIATES




Half oh the 20 amino acids are biosynthesised more or less directly from the intermediates of the citrc acid cycle or from pyruvate

# AMINO ACIDS RELATED TO CITRIC ACID CYCLE INTERMEDIATES

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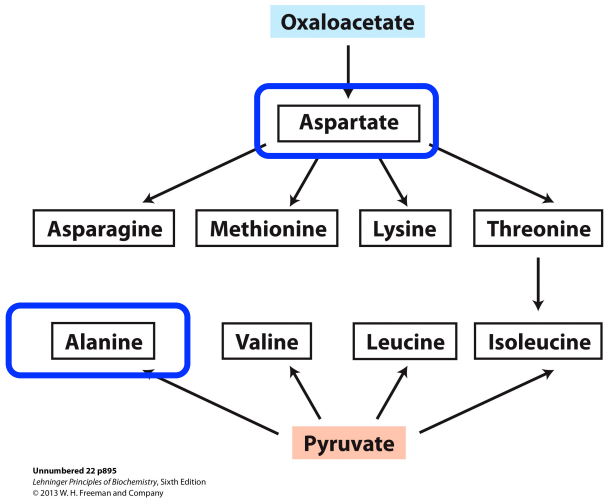
# AMINO ACIDS RELATED TO CITRIC ACID CYCLE INTERMEDIATES

- Transamination is the process by which an amino group, usually from glutamate, is transferred to an α-keto acid, with formation of the corresponding amino acid plus α-ketoglutarate.

- Thus, transamination provides a route for redistribution of amino acid nitrogen. Transamination reactions are catalyzed by transaminases (aminotransferases).

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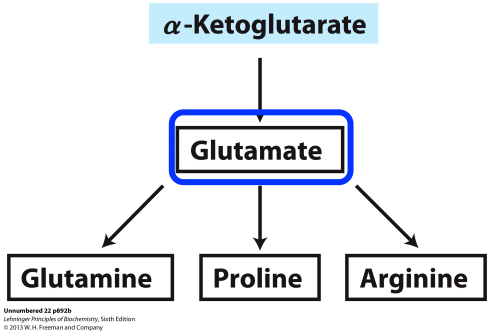


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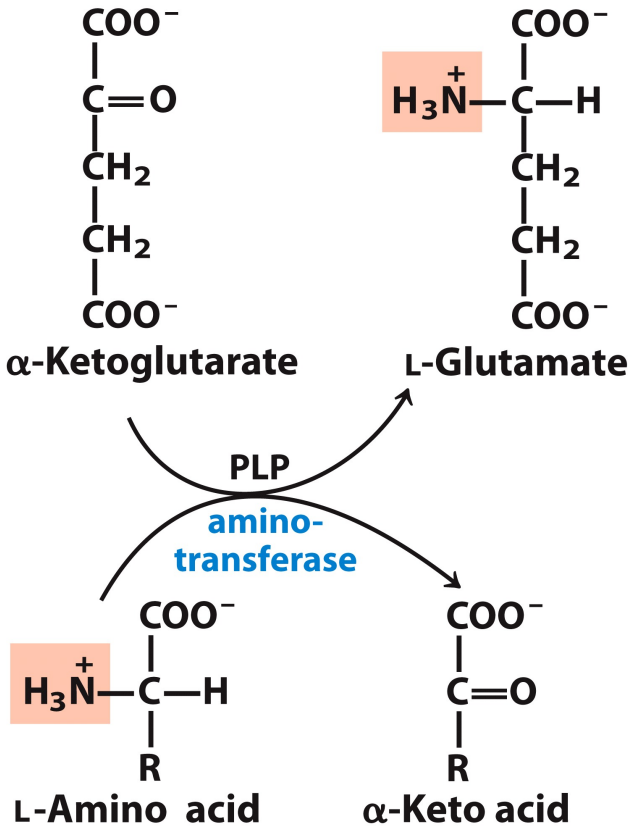


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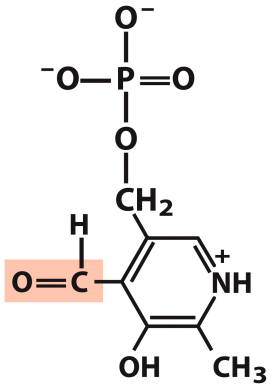
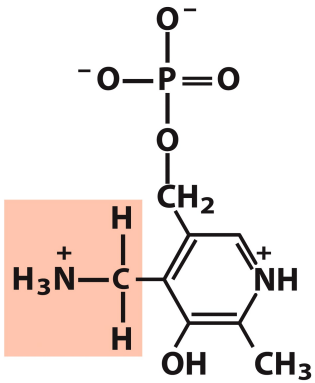
# AMINO ACIDS RELATED TO CITRIC ACID CYCLE INTERMEDIATES



Pyridoxal phosphate (PLP)



Pyridoxamine phosphate

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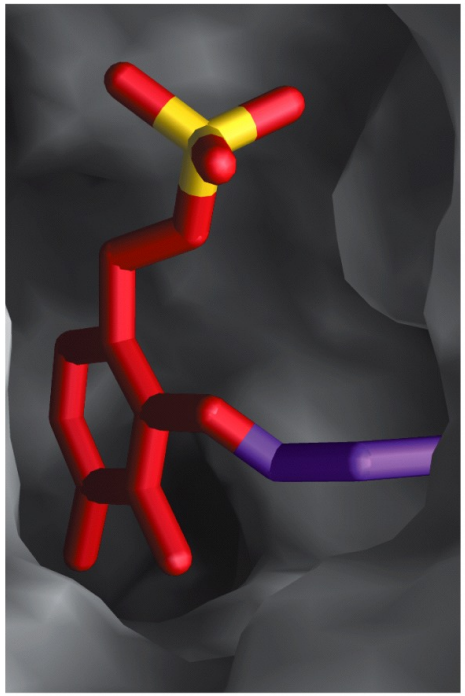

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Figure 18-5de
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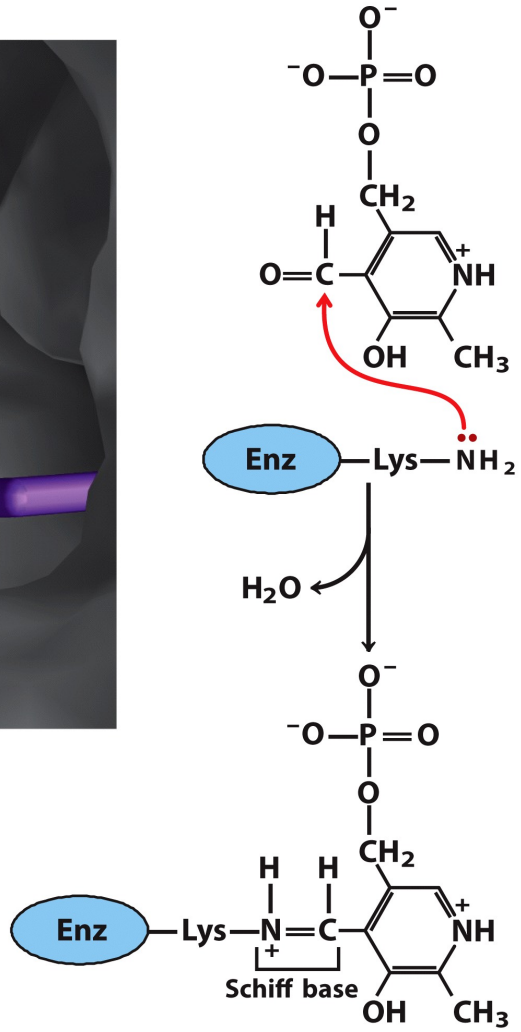


Figure 18-5b
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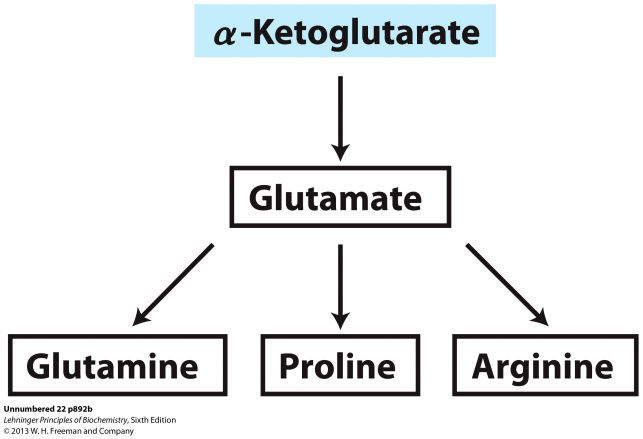
# AMINO ACIDS RELATED TO CITRIC ACID CYCLE INTERMEDIATES

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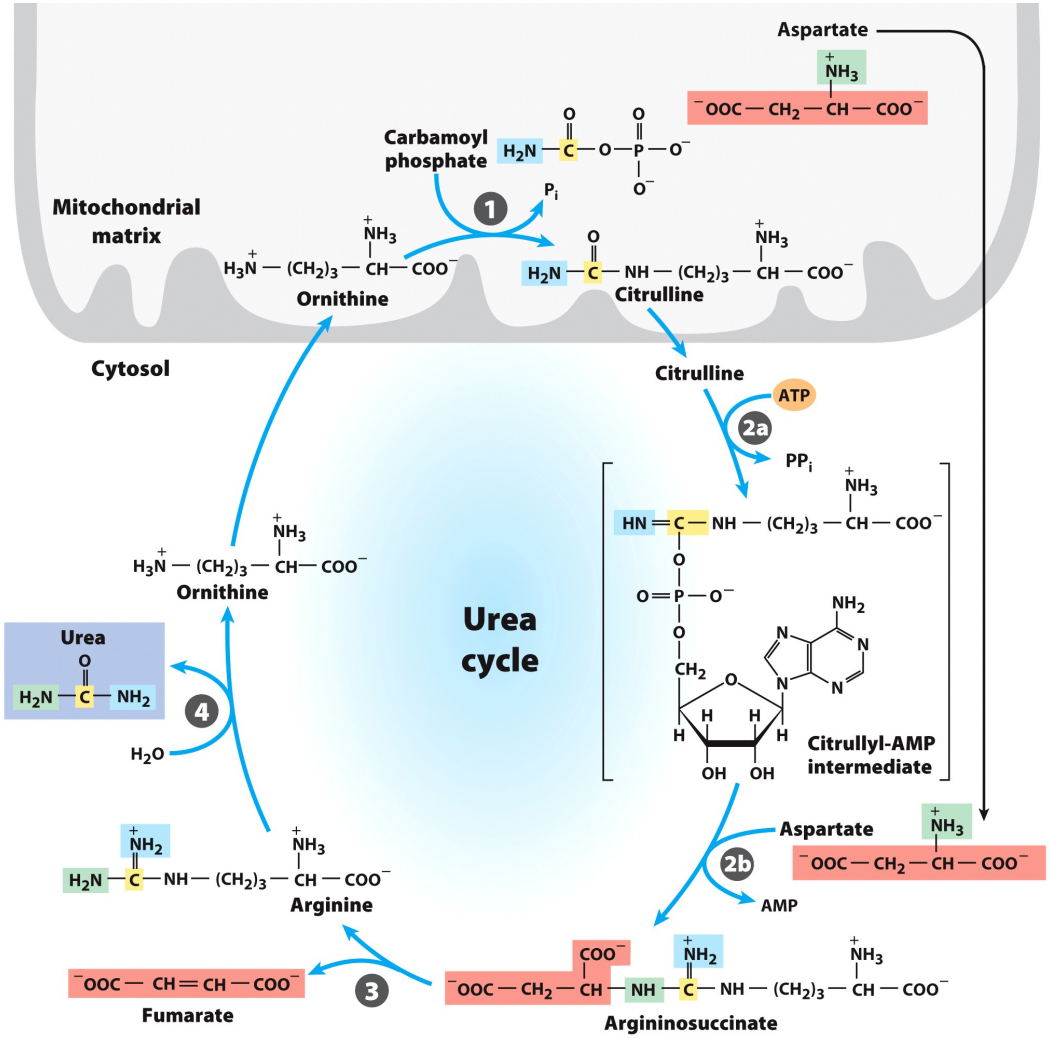


**Figure 18-10 part 2**
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# BIOSYNTHESIS OF AMINO ACIDS: SUMMARY

- Plants and bacteria synthesize all 20 amino acids
- Mammals can synthesize half of them, whereas the others must be provided by diet

## Among non-essential amino acids

- glutamate derives from α-ketoglutarate and it is the precursor of glutamine, proline and arginine
- alanine and aspartate derives from pyruvate and ossalacetate, respectively, through transamination.
- 3-phosphoglycerate is the precursor for serine and glycine
- Cysteine is produced from methionine and serine

## Among essential amino acids

- Aromatics derive from corismate
- Histidine biosyhtetic pathways is interconnected with purine biosynthesis
- Tyrosine can derive from phenilalanine hydroxylation (also in animals)

# BIOSYNTHESIS OF AMINO ACIDS: REGULATION

- Allosteric inhibition by end products is the main regulatory mechanism of amino acid biosynthetic pathways
- In general, the first enzyme of the metabolic pathways is regulated
- The regulation of the different pathways is coordinated and can be at genic level (protein expression)

## EXAMPLES OF REGULATION

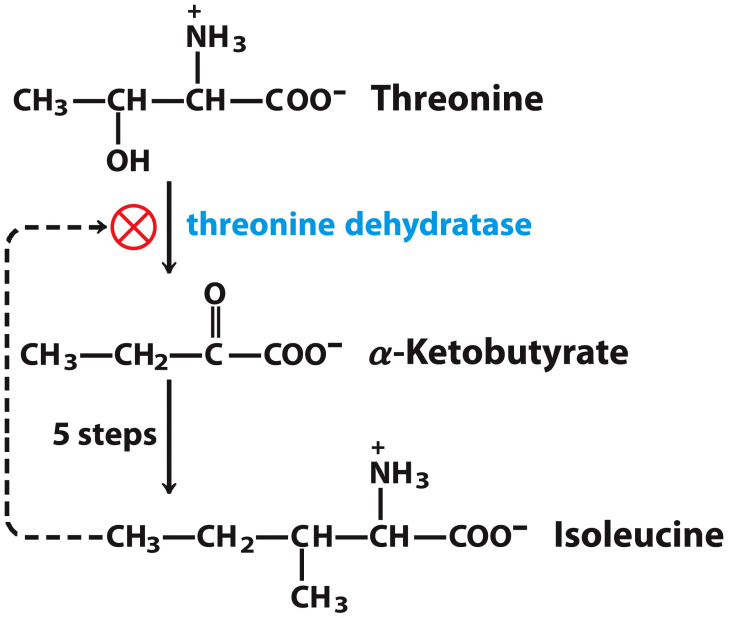


Figure 22-23
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- Isoleucine biosynthesis in bacteria from threonine.
- The first reaction is inhibited by the end product.

# BIOSYNTHESIS OF AMINO ACIDS: REGULATION

## EXAMPLES OF REGULATION

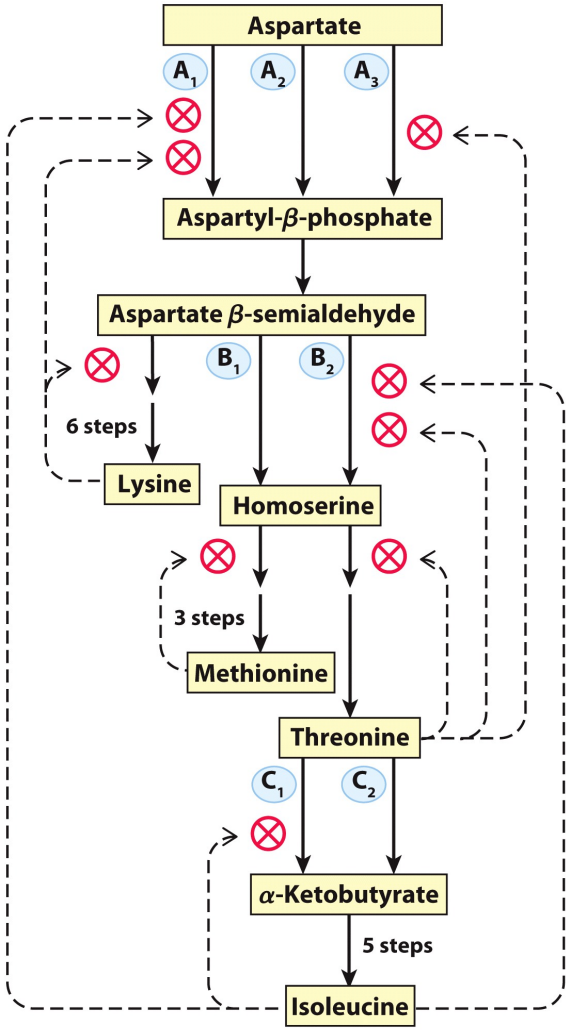


**Figure 22-24**
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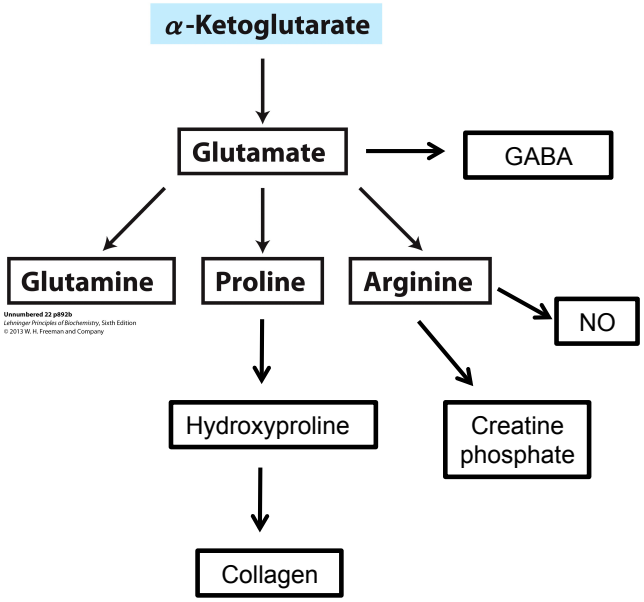
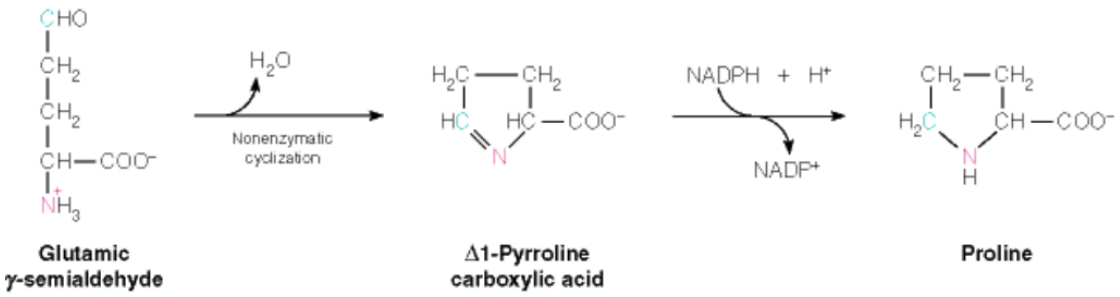
- Inter-dependent mechanisms of regulation for the biosynthesis of some amino acids deriving from aspartate in *Escherichia coli*.
- Enzymes A, B and C are present in 2 or three isoforms.
- They are not controlled by allosteric regulation
- Their synthesis rate is controlled and **enzyme multiplicity** avoids that the end product inhibit foundamental steps when other products from the same pathway are required.

# BIOSYNTHESIS OF MOLECULES DERIVED FROM AMINO ACIDS

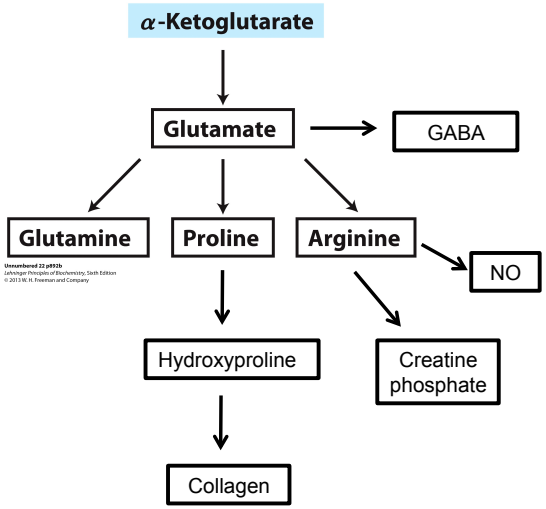
Glutamate is the most active of all the amino acids in terms of its number of metabolic roles.



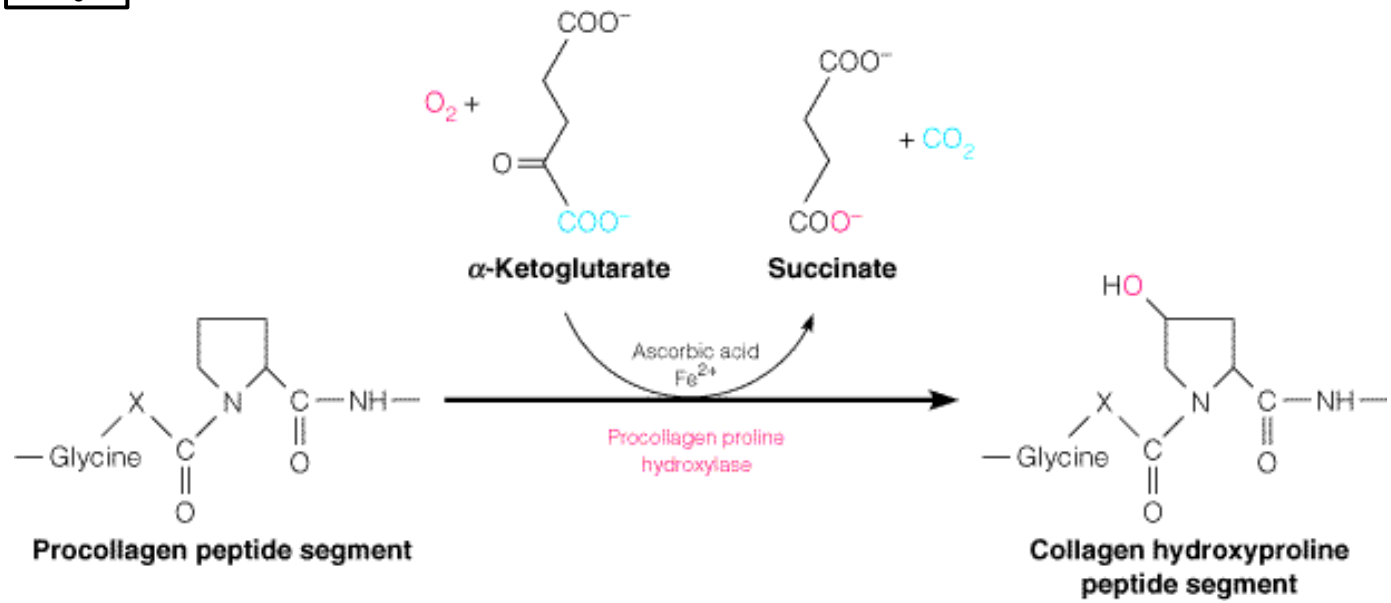

Biosynthesis of serine and proline



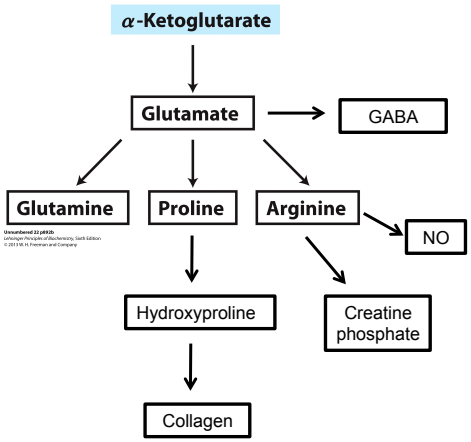
# PROLINE, HYDROXYPROLINE AND COLLAGEN



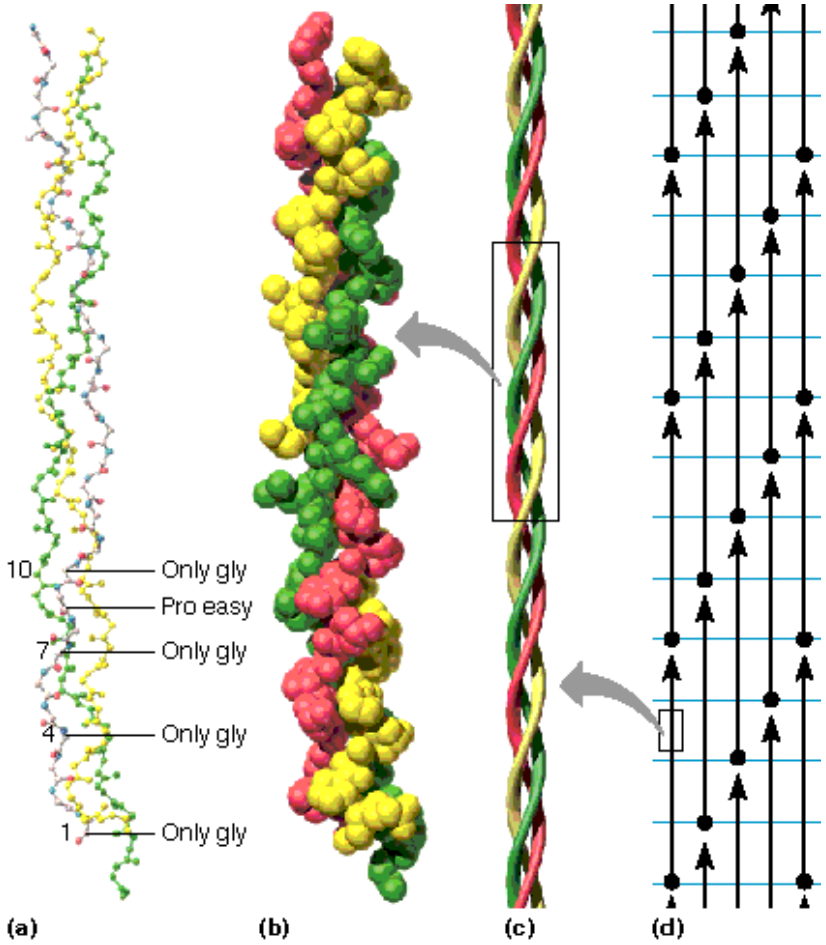

- The protein collagen is unusual in its widespread modification of **<u>proline</u>** to **4-hydroxyproline** (also called **hydroxyproline**).
- The OH groups of **hydroxyproline** participate in stabilizing the structure.
- Hydroxylation of **<u>lysine</u>** residues in collagen also occurs but is much less frequent.
- It plays a different role, serving to form attachment sites for **<u>polysaccharides</u>**.



# PROLINE, HYDROXYPROLINE AND COLLAGEN




- **Collagen** is the most abundant single protein in most vertebrates.
- In large animals, it may make up a third of the total protein mass.
- **Collagen** fibers form the matrix, or cement, material in bone, on which the mineral constituents precipitate. These fibers constitute the major portion of tendons.
- A network of **collagen** fibers is an important constituent of skin. Basically, **collagen** holds most animals together.



# CREATINE AND PHOSPHOCREATINE

## Biosynthesis of phosphocreatine

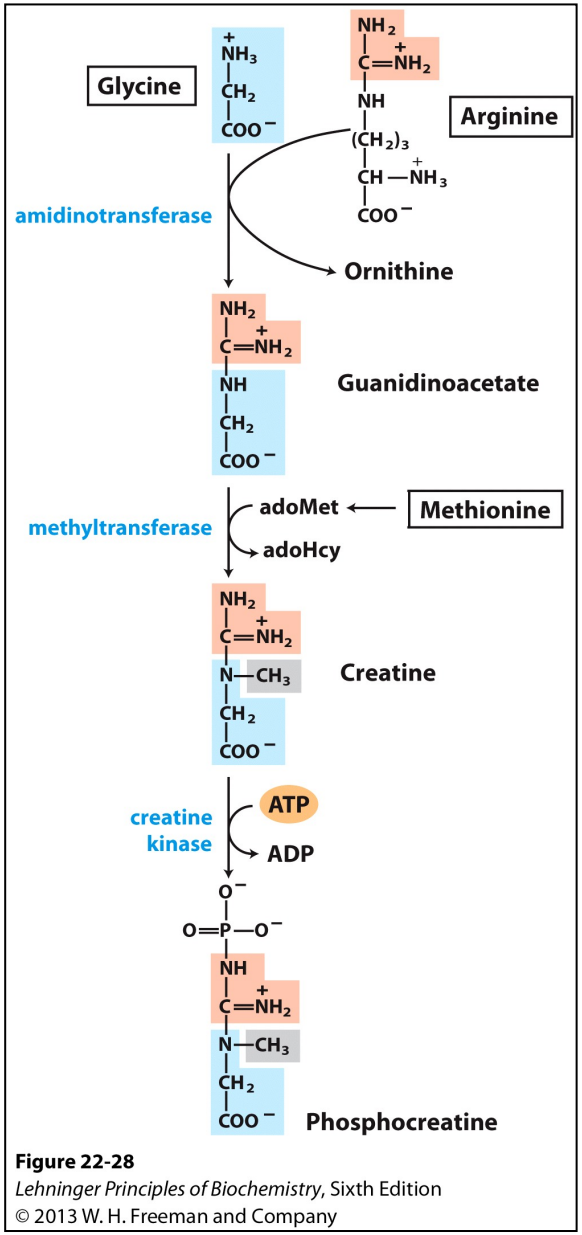



**Figure 22-28**
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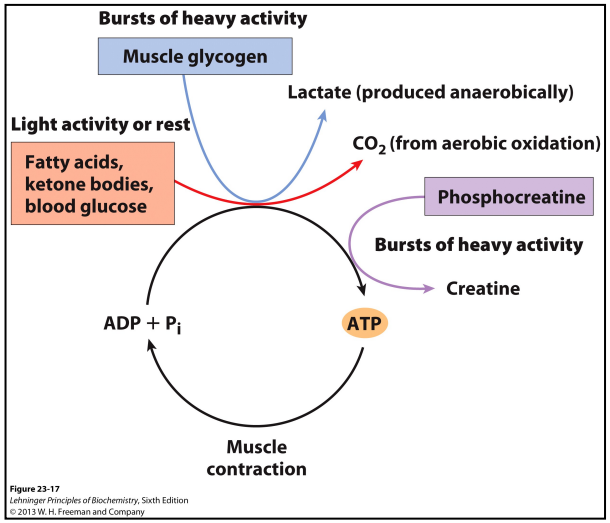
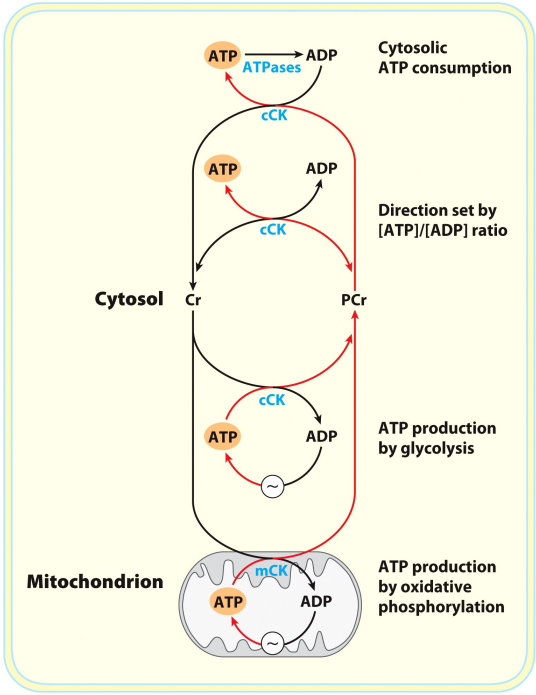
- **Creatine phosphate** shuttles high-energy phosphate from mitochondria to sites of muscle contraction.
- An energy-rich muscle has lots of **creatine phosphate**, whereas a fatigued muscle has little **creatine phosphate**, and also has decreased ATP and increased ADP and AMP levels.
- The reaction is catalyzed by the enzyme creatine kinase as follows:

  Creatine + ATP <=> Creatine Phosphate + ADP

- The reaction is strongly endergonic as written.
- However, the level of ATP is very high in mitochondria, so the reaction proceeds to the right.
- Creatine phosphate then diffuses from mitochondria to the myofibrils, where it provides the energy for muscle contraction.




**Box 23-2 Figure 1**
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# GLUTHATIONE (GSH)

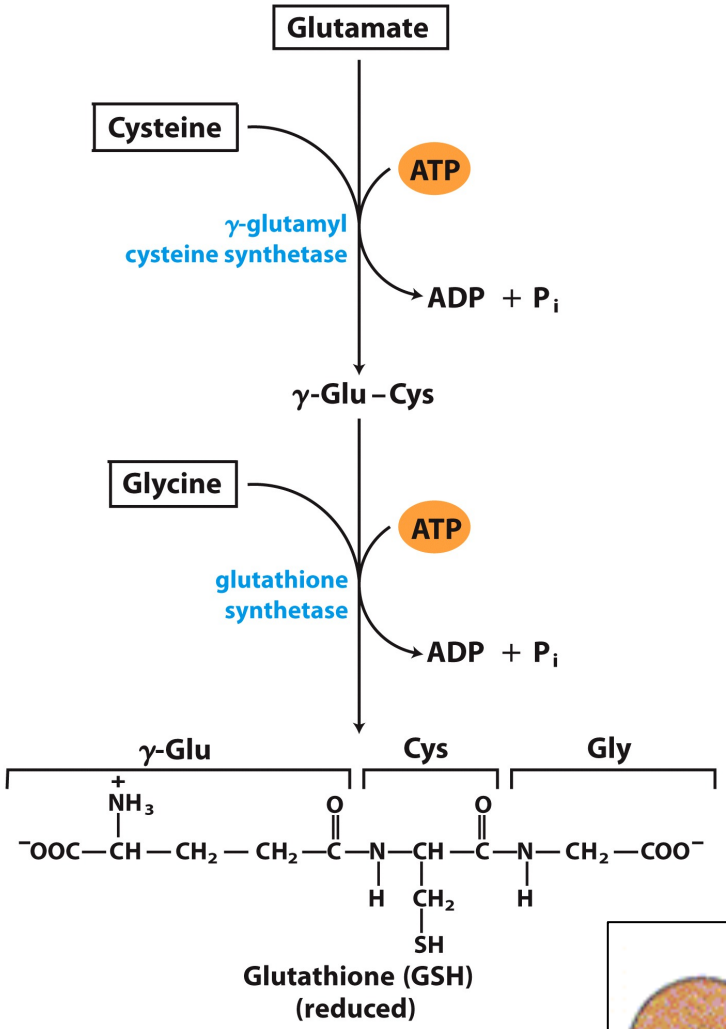


**Figure 22-29a**
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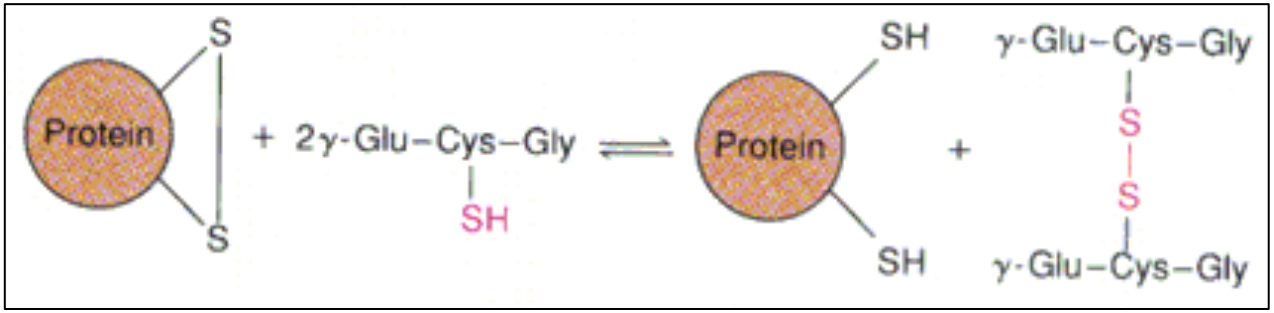
- Present in plants, animals and some bacteria
- It can be considered a redox buffer
- The oxidized form is composed by two molecules bound through a disulphide bond (GSSG)
- It helps in keeping protein cysteines reduced and heme iron in ferrous state ($Fe^{2+}$)
- It removes toxic peroxides



# D- AMINO ACIDS

- D-amino acids are found in bacterial cell walls and peptidic antibiotics.
- Peptidoglycans contain D-alanine and D-glutamate.
- They form from the corresponding L- amino acids.
- Amino acid racemase (PALP-dependent) is the enzyme involved in this isomerization reaction.
- These enzymes are target for antibiotic development, such as fluoroalanine andcycloserine.

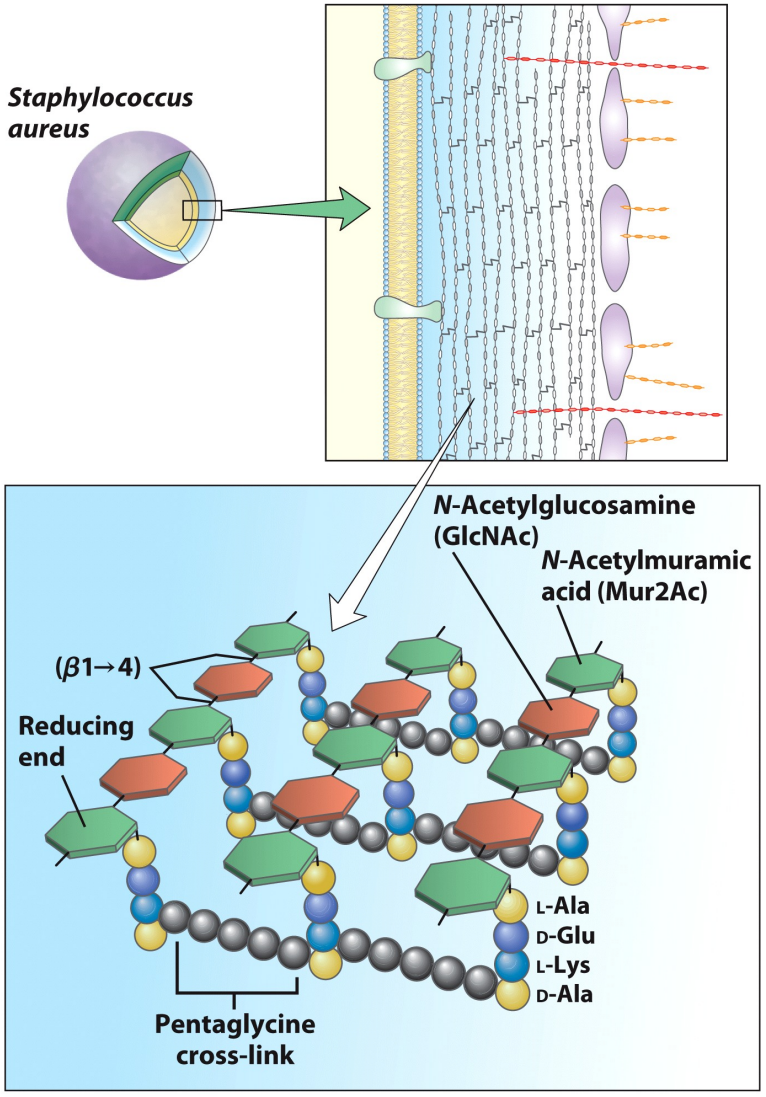



**Figure 20-30**
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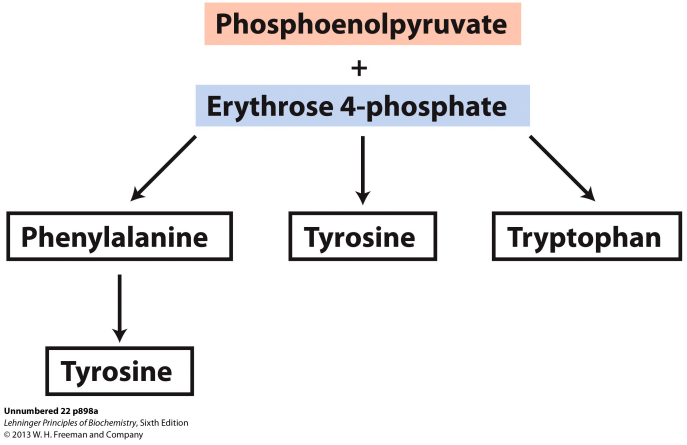
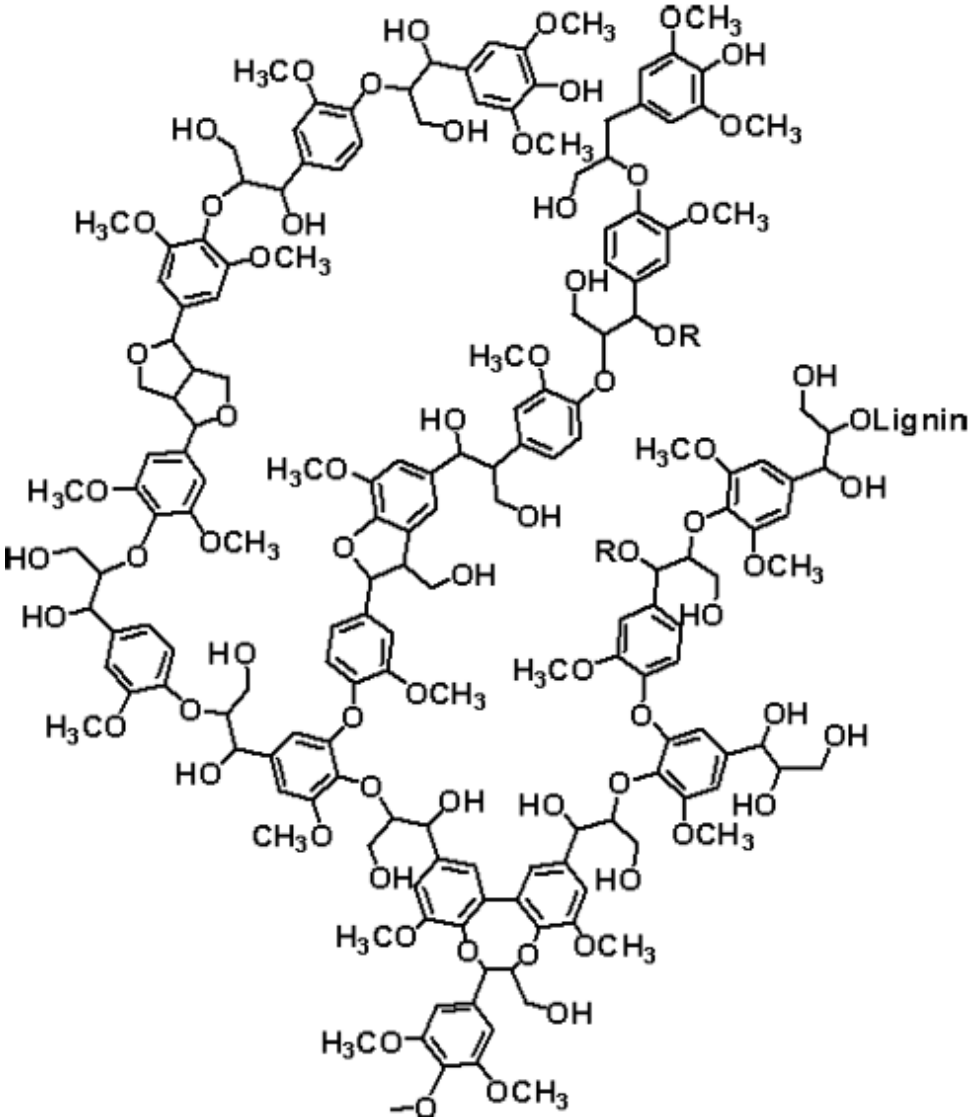
# LIGNIN




- The shikimic acid pathway leads to synthesis of nearly all aromatic compounds, including lignin.
- It is one of the most productive pathway in biology.



# NEUROTRANSMITTERS AND BIOLOGICAL REGULATORS

- Amino acids and their metabolites participate in signal transduction process - hormonal control and the synaptic transmission of nerve impulses.
- Some compounds, like epinephrine and histamine participate in both processes.
- Glycine and glutamate are amino acids that serve directly as neurotransmitters.
- Aminobutyric acid (**GABA**), the decarboxylation product of glutamate, is also a neurotransmitter.
- Amino acid metabolites that function in neurotransmission include **histamine** (from histidine), **serotonin** (from tryptophan), and **catecholamines** (epinephrine, dopamine, and norepinephrine), which are derived from tyrosine.
- **Serotonin** plays multiple roles in the nervous system, including neurotransmission. It is a precursor to **melatonin**, which is involved in the regulation of sleepiness and wakefulness.
- In the intestine, serotonin regulates intestinal peristalsis. Serotonin is also a potent vasoconstrictor, which helps regulate blood pressure.
- Catecholamines derive from tyrosine.

# BIOLOGICAL AMINES

Many important neurotransmitters are primary or secondary amines derived from amino acid precursors

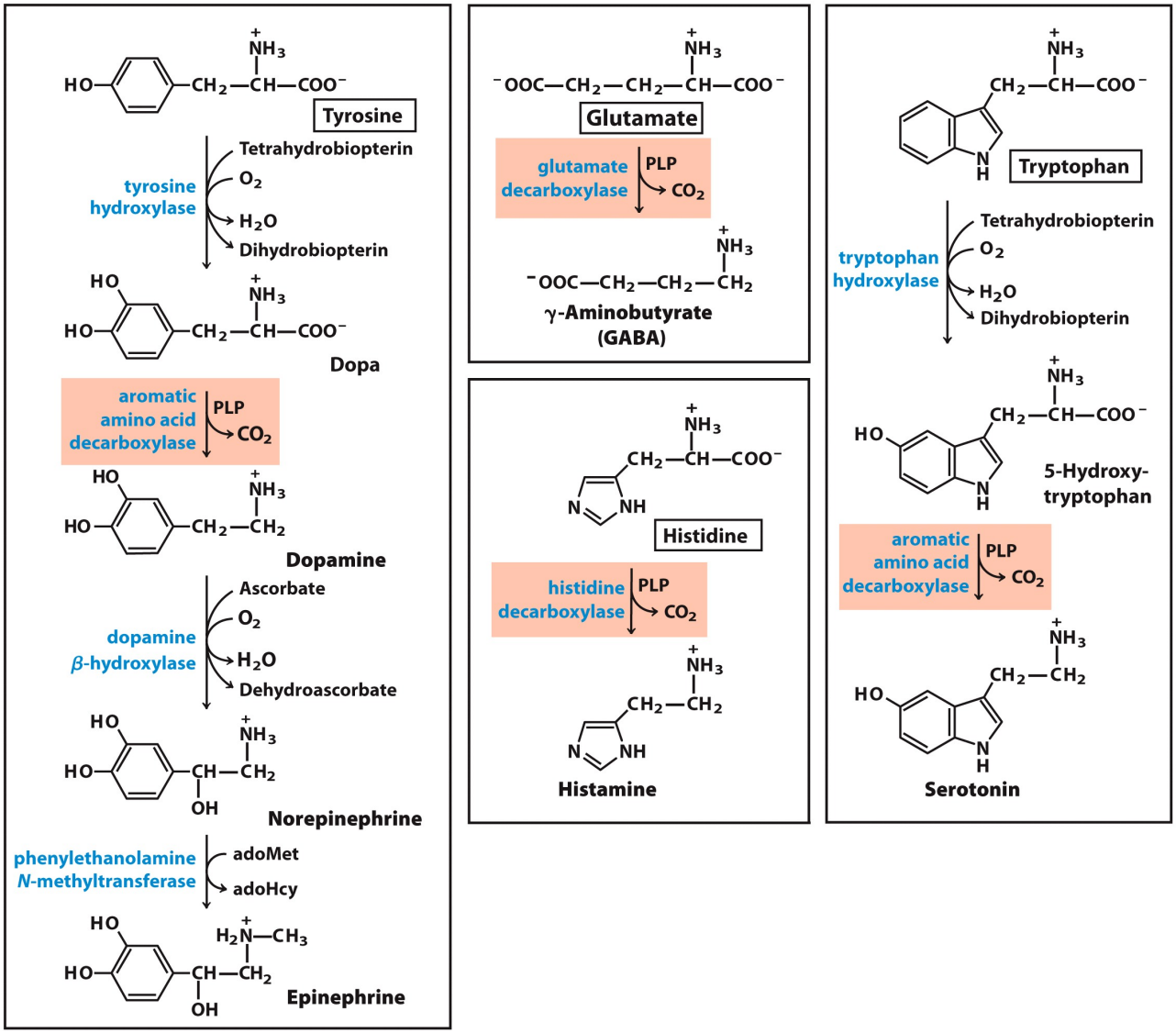



**Figure 22-31**
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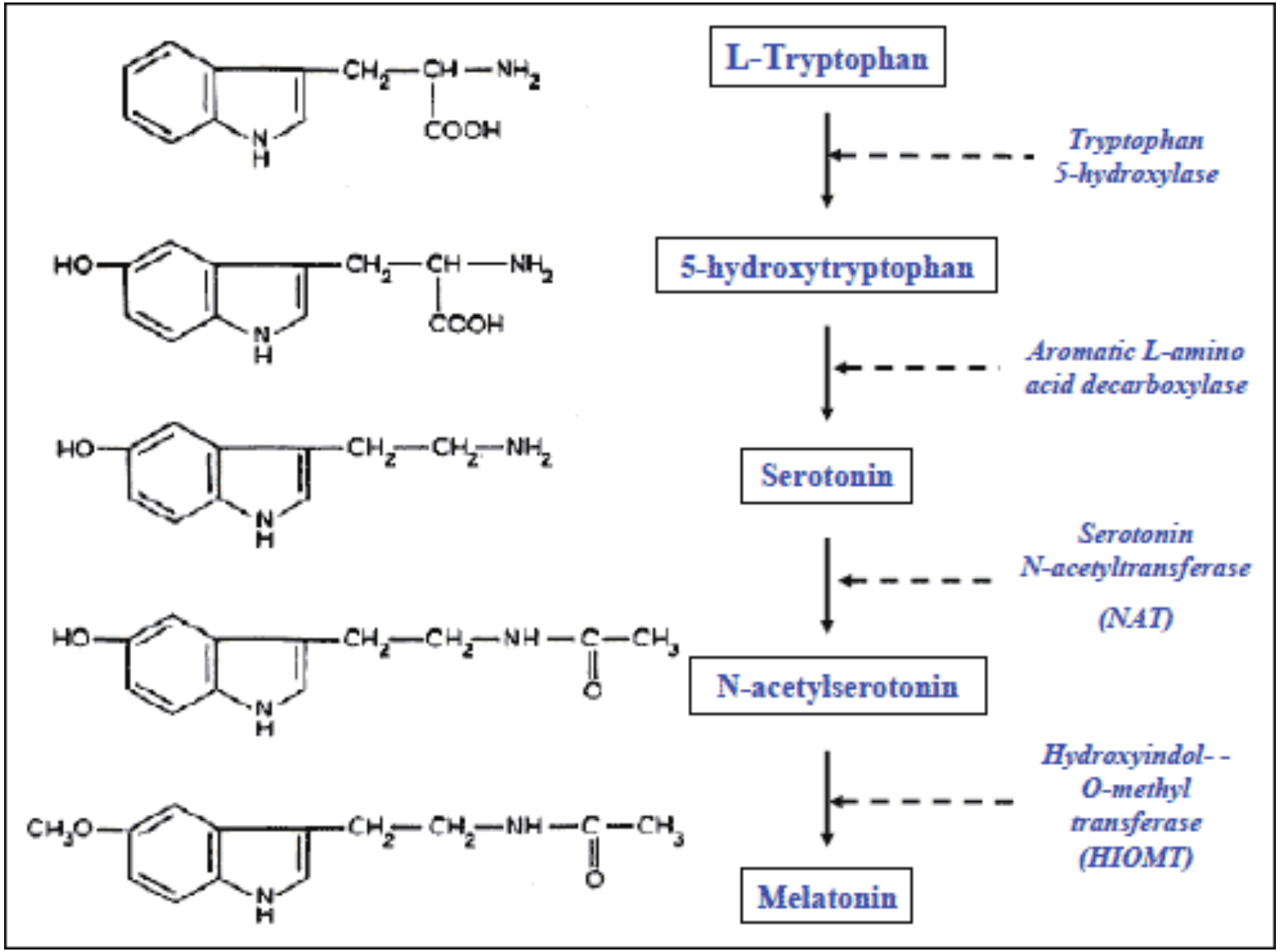
# BIOLOGICAL AMINES

Many important neurotransmitters are primary or secondary amines derived from amino acid precursors



# BIOLOGICAL AMINES

- PLP-dependent glutamic acid decarboxylase (GAD) converts glutamic acid into GABA.
- In mammals there are two forms, GAD65 and GAD67 (named according to their apparent molecular weights), which are the products of two different genes

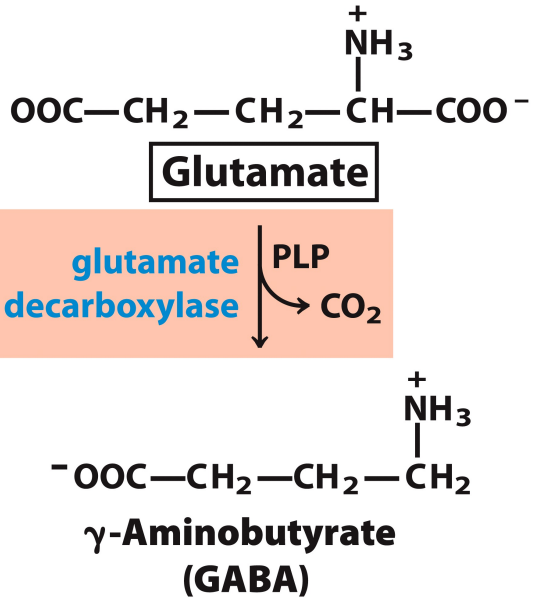



Figure 22-31 part 2
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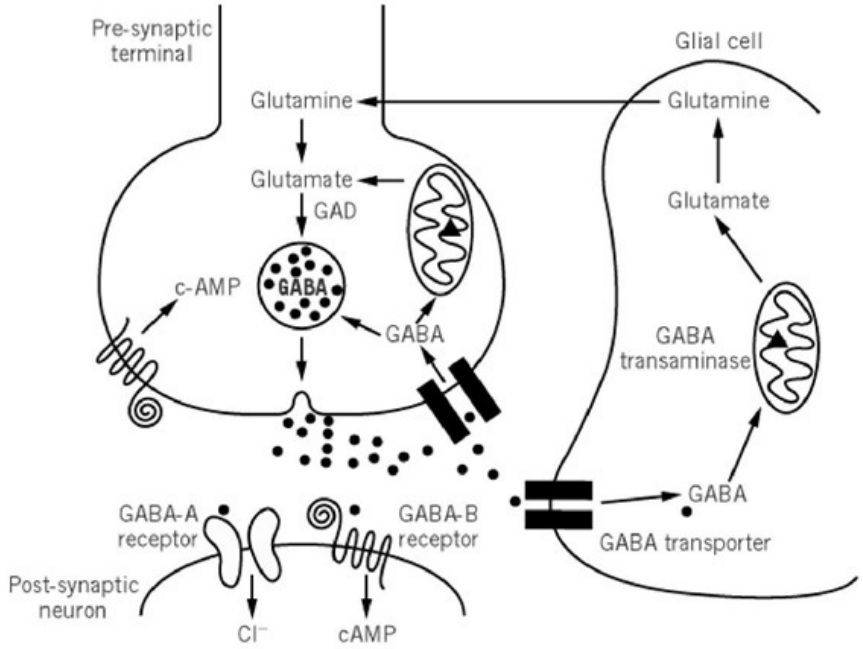
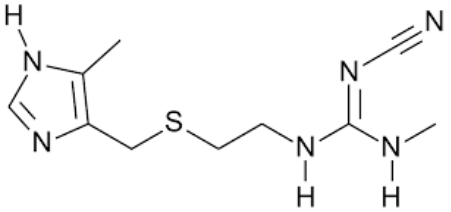



**A scheme of the vertebrate GABAergic synapse.**

- GABA (filled circles) is generated from glutamate by glutamic acid decarboxylase (GAD).
- When released from presynaptic vesicles into the synaptic cleft, it diffuses across and binds to postsynaptic GABAA and GABAB receptors. It may also bind to presynaptic GABAB receptors.
- GABA is removed from the synaptic cleft into surrounding glial cells or the presynaptic terminal by GABA transporters.
- It is directly recycled into synaptic vesicles or taken up by mitochondria, converted by GABA transaminase (filled triangle) to succinic semialdehyde, and enters the tricarboxylic acid pathway.

# BIOLOGICAL AMINES

- Decarboxylation of histidine yields histamine.
- In the stomach, histamine promotes secretion of hydrochloric acid and pepsin as digestion aids.
- Histamine is a potent vasodilator, released at sites of trauma, inflammation, or allergic reaction. Reddening of inflamed tissues is a result of local enlargement of blood capillaries.
- Antihistamines block binding of histamine to its receptors.



- Cimetidine is a structural analog of histamine

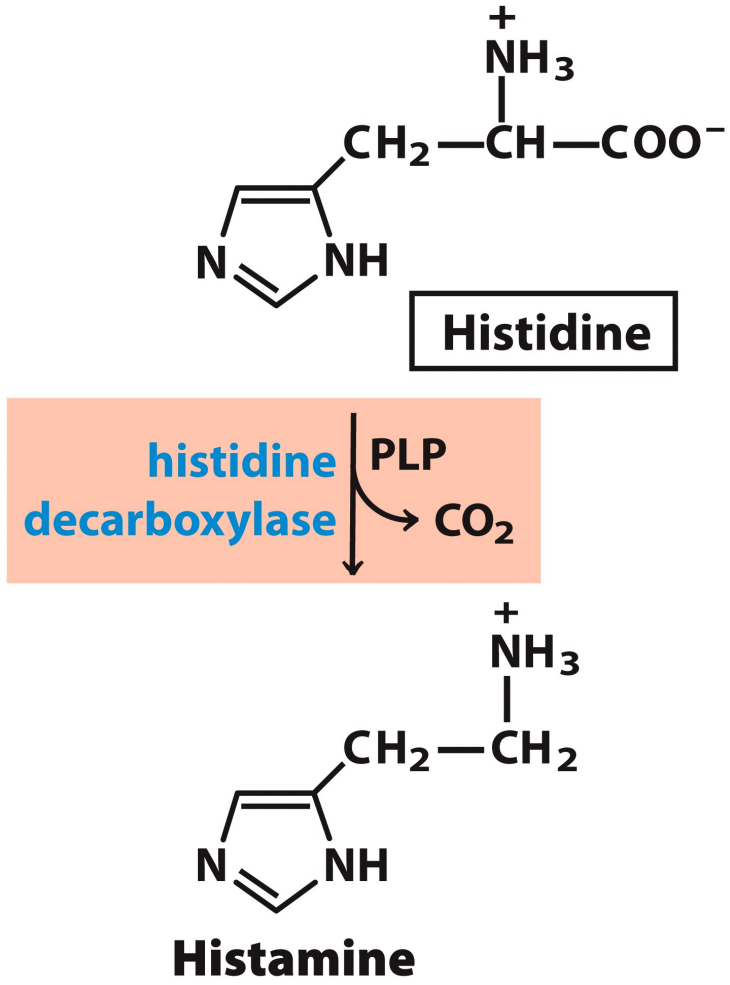



**Figure 22-31 part 3**
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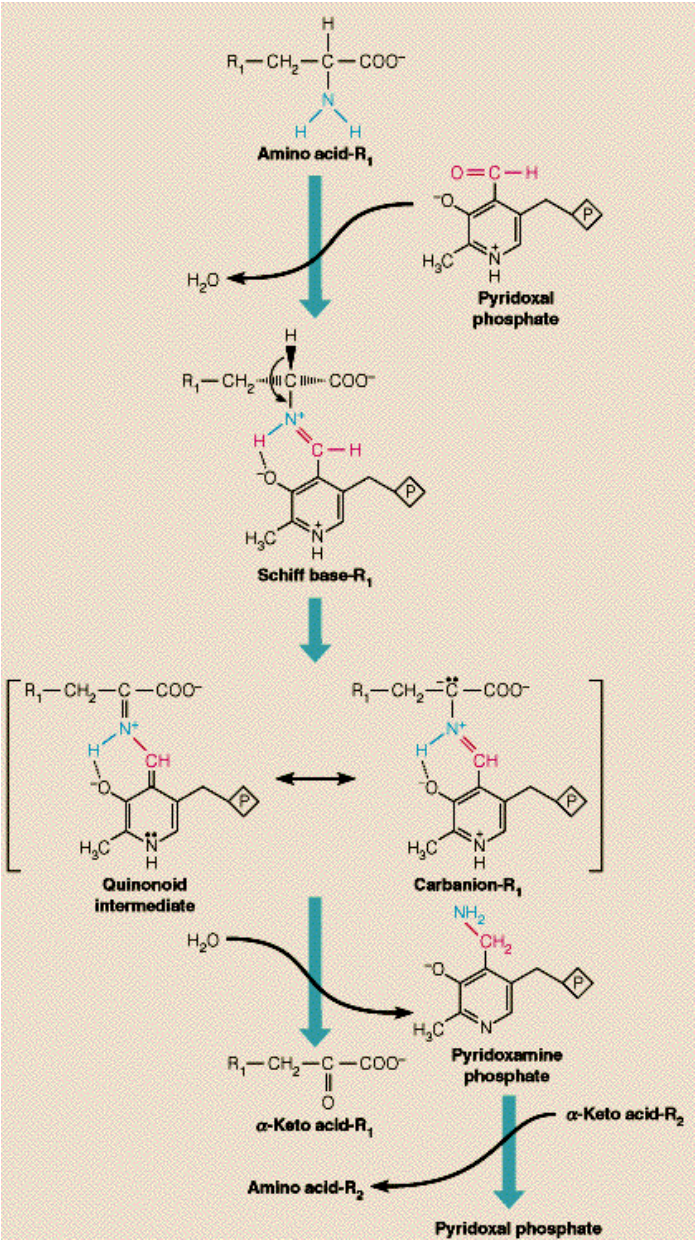
# PLP-DEPENDENT TRANSAMINATION

- Pyridoxal phosphate participates in transaminations, decarboxylations, racemizations, and numerous modifications of amino acid side chains.
- All pyridoxal phosphate-requiring enzymes act via the formation of a Schiff base between the amino acid and coenzyme.
- A cation (a metal or a proton) is essential to bridge the phenolate ion of the coenzyme and the imino nitrogen of the amino acid. This bridging maintains the planarity of the structure, which is essential for catalysis.
- The most important catalytic feature of the coenzyme is the electrophilic nitrogen of the pyridine ring, which acts as an electron sink, drawing electrons away from the amino acid and stabilizing a carbanion intermediate.
- All known reactions of PLP-containing enzymes can be described mechanistically in the same way- formation of a planar Schiff base or aldimine intermediate, followed by formation of a resonance-stabilized carbanion with a quinoid structure.
- Depending on the bond labilized, formation of the aldimine can lead to a transamination, to decarboxylation, to racemization, or to numerous side chain modifications.



# PLP-DEPENDENT REACTIONS

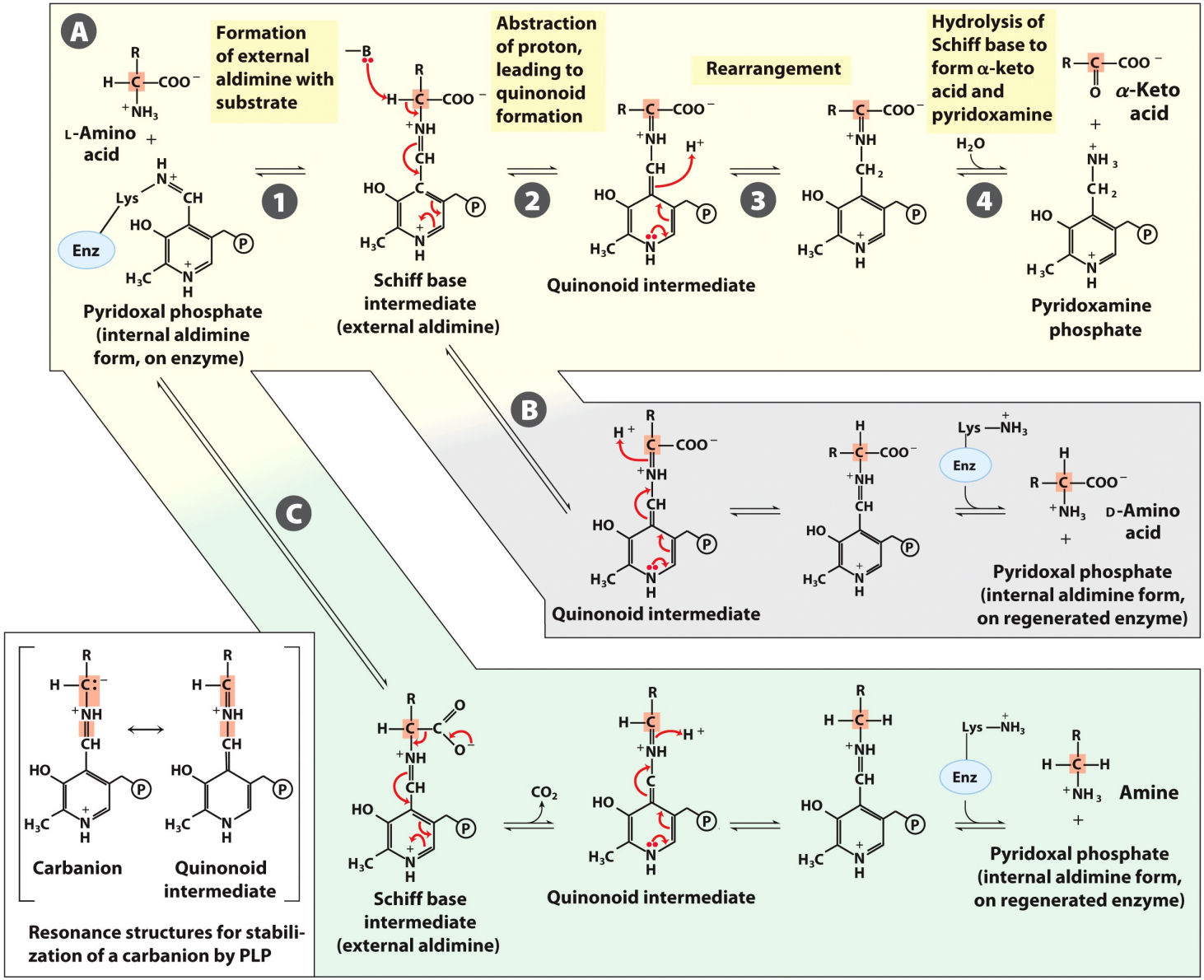



**Figure 18-6**

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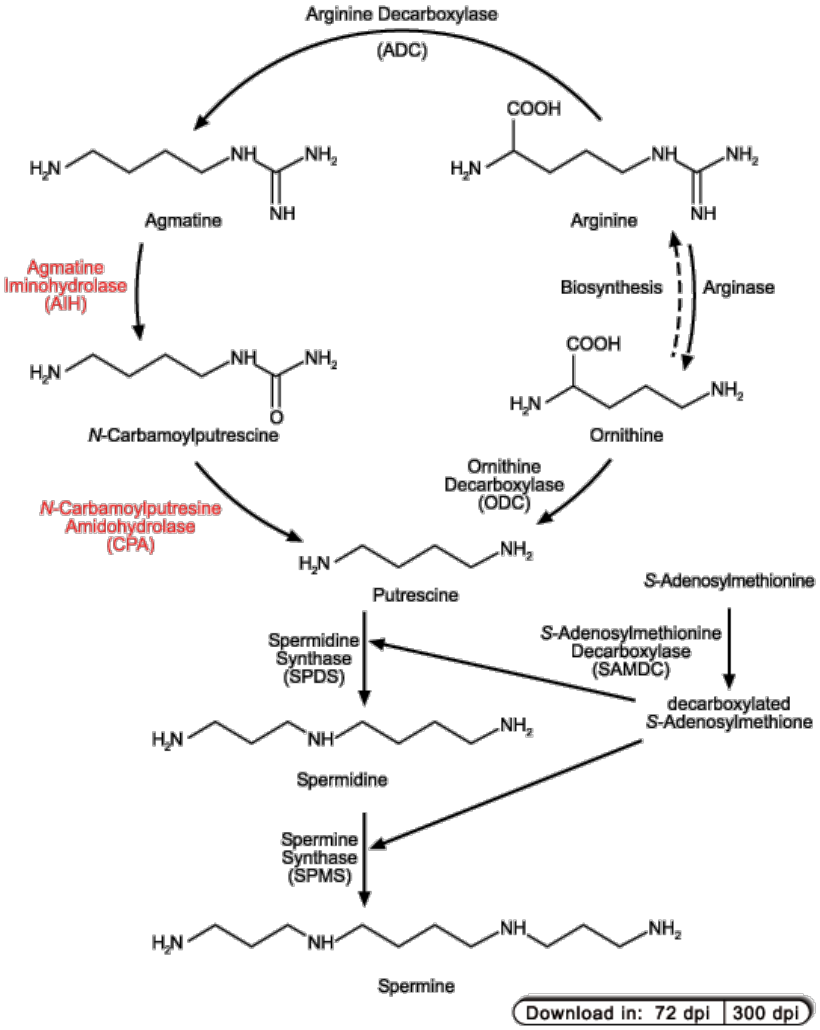
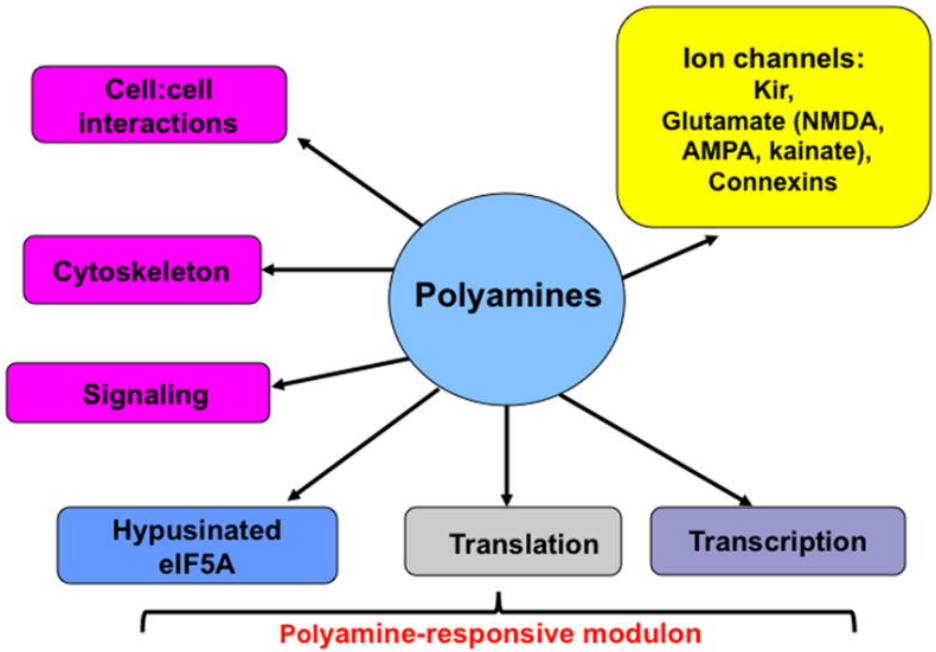
# BIOLOGICAL AMINES: POLYAMINES




Functions of polyamines. Polyamine levels affect ion channels, cell-cell interactions, the cytoskeleton, signaling via phosphorylation and other mechanisms, activity of eIF5A via the role of spermidine as a precursor for its hypusination, transcription and mRNA translation. The effects on transcription and translation (both direct and indirect) alter the cellular levels of many proteins making up the polyamine-responsive modulon.

From Pegg, IUBMB Life. 2009 Sep; 61(9): 880–894.

# BIOLOGICAL AMINES

Some polyamines derive from methionine and ornithine

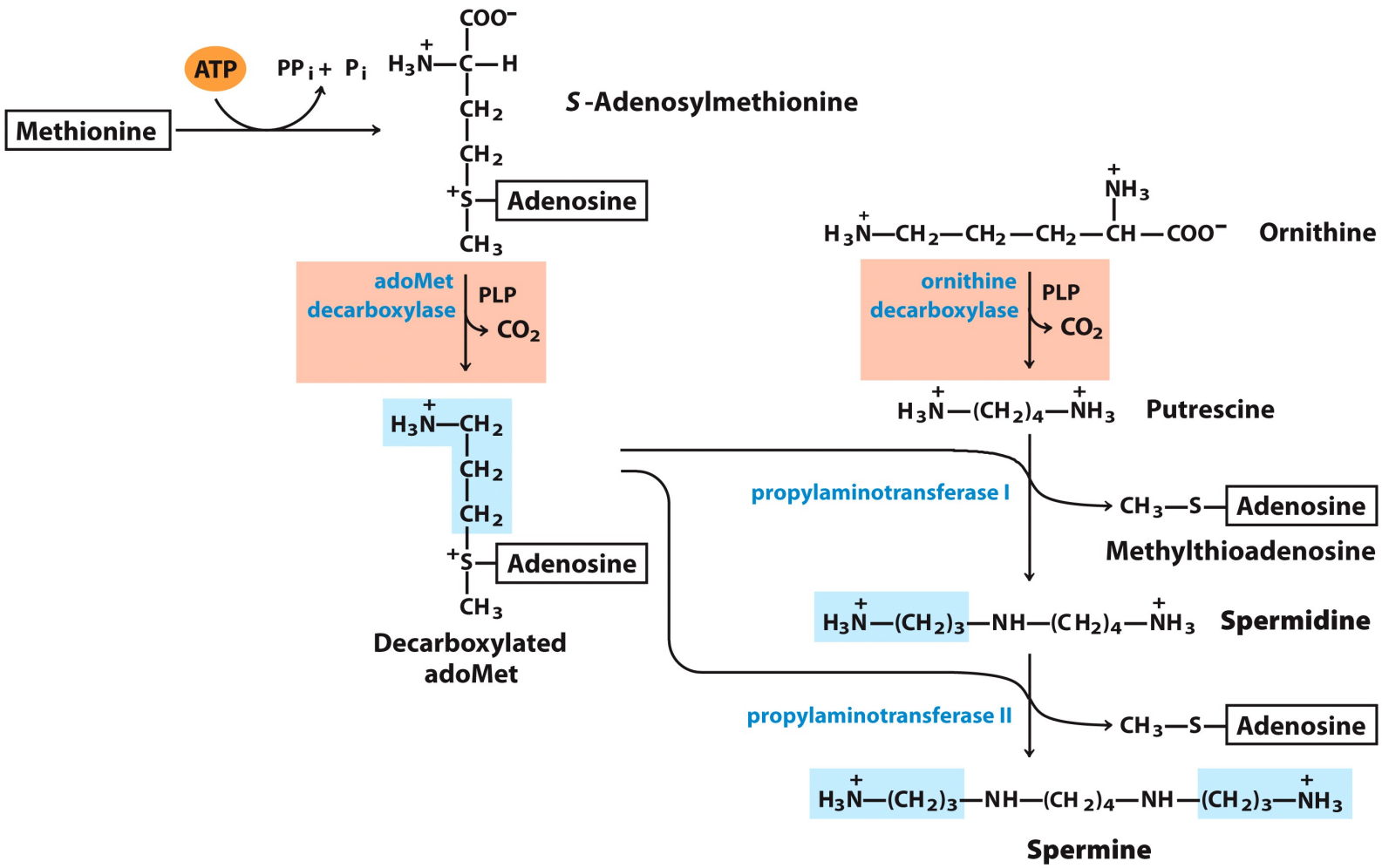



**Figure 22-32**
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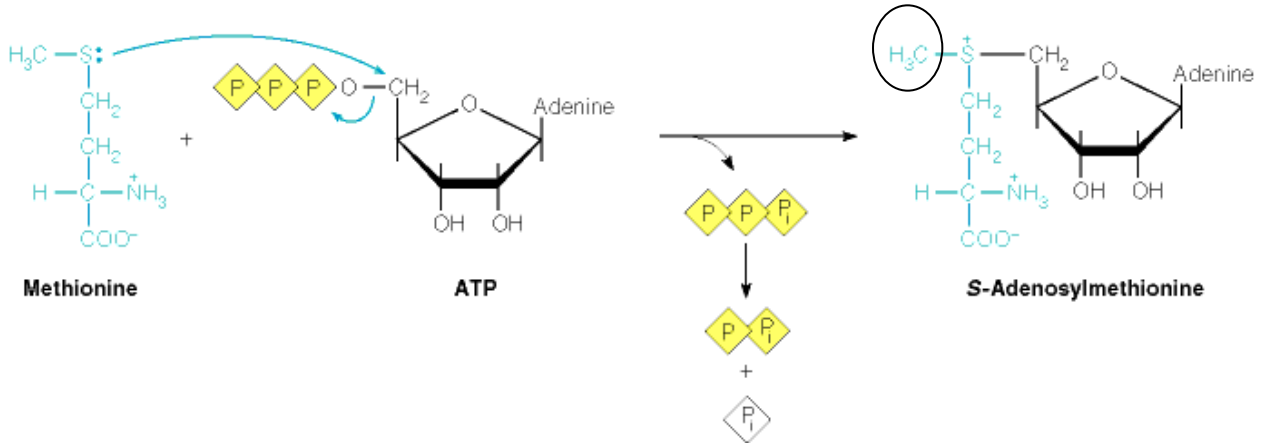
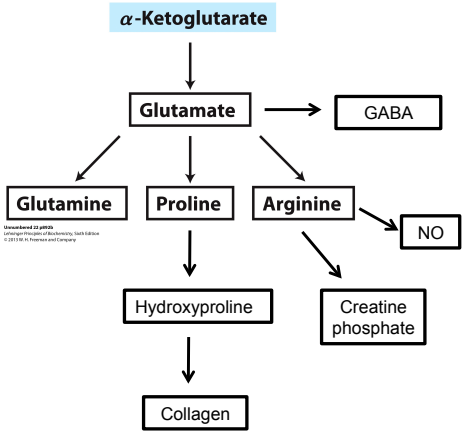
# *S*-ADENOSYLMETHIONINE (AdoMet)

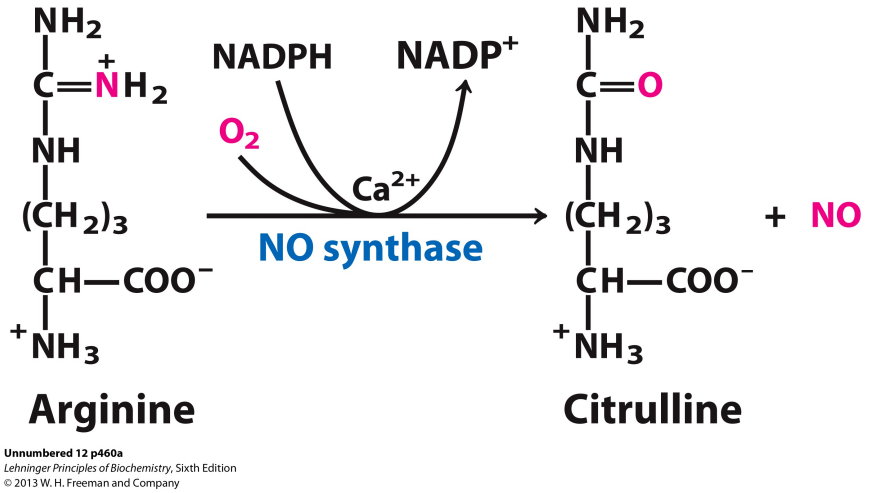



- S-Adenosylmethionine (AdoMet) is a metabolically activated form of methionine capable of donating a methyl group.
- Transfer of a methyl group from AdoMet to a target molecule converts AdoMet to S-Adenosylhomocysteine (AdoHcy).
- Substrates range from small metabolites, such as norepinephrine, to polymers, such as DNA, RNA, or proteins.
- In proteins, targets for methylation include lysine, arginine, and residues containing free carboxyl groups.
- Histones (chromatin proteins), for example, become methylated at specific arginine and lysine residues at particular times in the cell cycle.
- Except for a few reactions in bacteria, the only known methyl group transfer in cells that does not involve AdoMet is the synthesis of methionine itself.

| Methyl Group Acceptor | Methylated Product |
|---|---|
| Norepinephrine | Epinephrine |
| Guanidinoacetic acid | Creatine |
| Phosphatidylethanolamine | Phosphatidylcholine |
| DNA-adenine or -cytosine | DNA-*N*-methyladenine or 5-methylcytosine |
| tRNA bases | Methylated tRNA bases |
| Nicotinamide | $N^1$-Methylnicotinamide |
| Protein amino acid residues | Methylated amino acid residues |

# ARGININE IS THE PRECURSOR OF THE SECOND MESSENGER NO




- Nitric oxide is produced from arginine in an unusual five-electron oxidation that also yields citrulline
- The enzyme catalyzing the reaction, nitric oxide synthase, contains bound FMN, FAD, non-heme iron, and tetrahydrobiopterin.
- Nitric oxide, is is a signal-transducing agent in the vasodilation of endothelial vascular cells and underlying smooth muscle.
- It is also involved in signaling decreases in blood pressure, and inhibiting platelet aggregation.
- In the inflammatory and immune responses, an inducible form of nitric oxide synthase produces nitric oxide at levels sufficient to be toxic to pathogenic organisms.
- It can act in neurotransmission in the central nervous system and stimulate erection of the penis.
- Nitric oxide is a gas so it can diffuse rapidly into neighboring cells and control their metabolism.
- It is also unstable, with a half-life of 1 to 5 seconds, so its effects are short-lived. In the cell, nitric oxide acts primarily **by stimulating cyclic GMP synthesis**.
- The drug, Viagra, acts by inhibiting cyclic GMP breakdown, thereby prolonging the effect of nitric oxide.

# AMINO ACIDS DEGRADATION

Step 1. Removal of amino group

Step 2. Carbon skeleton oxidize to intermediates of Krebs cycle

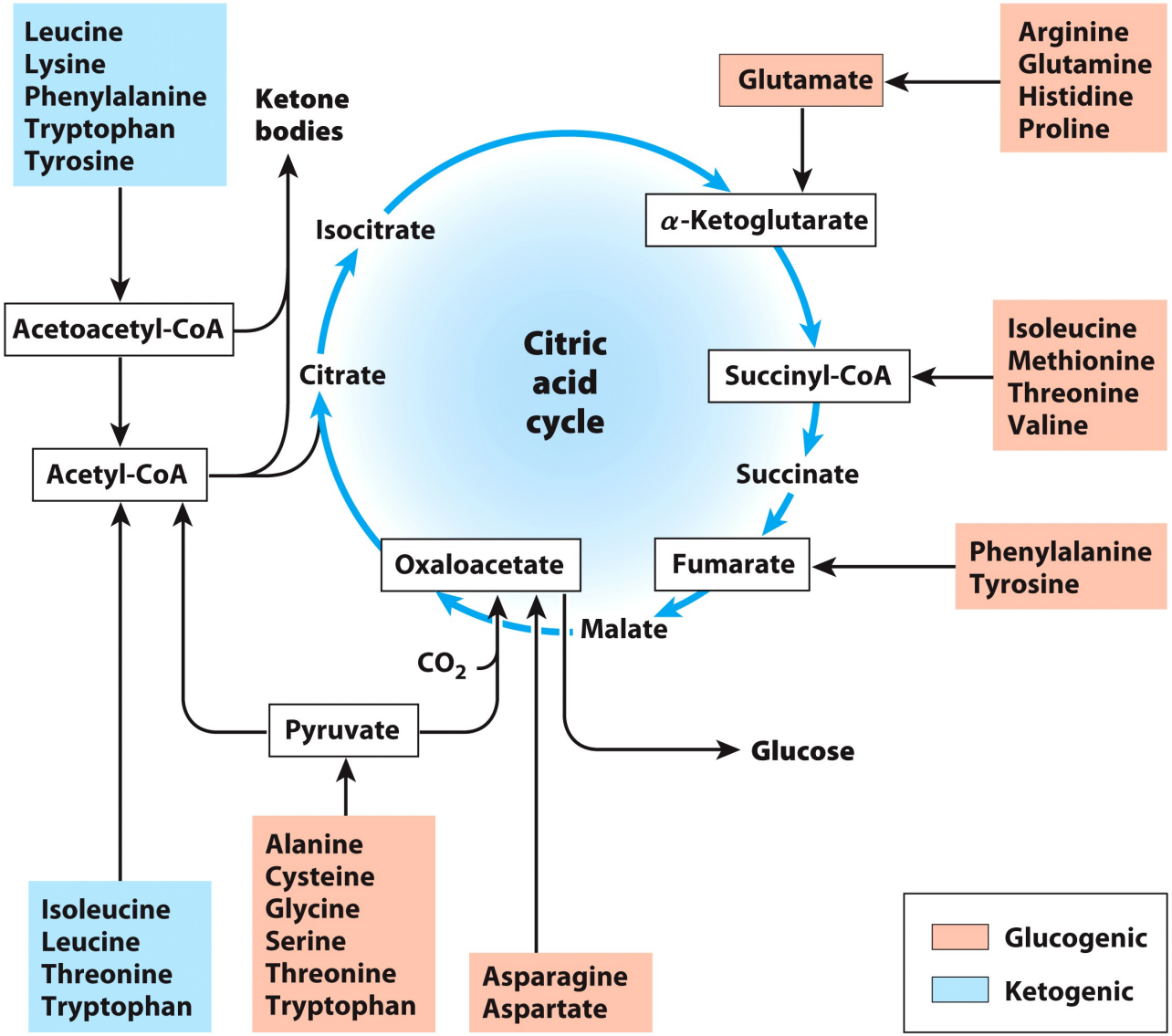



**Figure 18-15**
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# AMINO ACIDS DEGRADATION

**Glucogenic Amino Acids**

- Glucogenic amino acids can be degraded to pyruvate or an intermediate in the Krebs Cycle.
- They are named glucogenic because they can produce glucose under conditions of low glucose.
- This process is also known as gluconeogenesis, or the production of "new glucose."
- Amino acids form glucose through degradation to pyruvate or an intermediate in the Krebs Cycle.

- Step 1. Removal of amino group
- Step 2. Carbon skeleton oxidize to intermediates of Krebs cycle
- These reactions require a number of cofactors for transfer of monocarbon units.

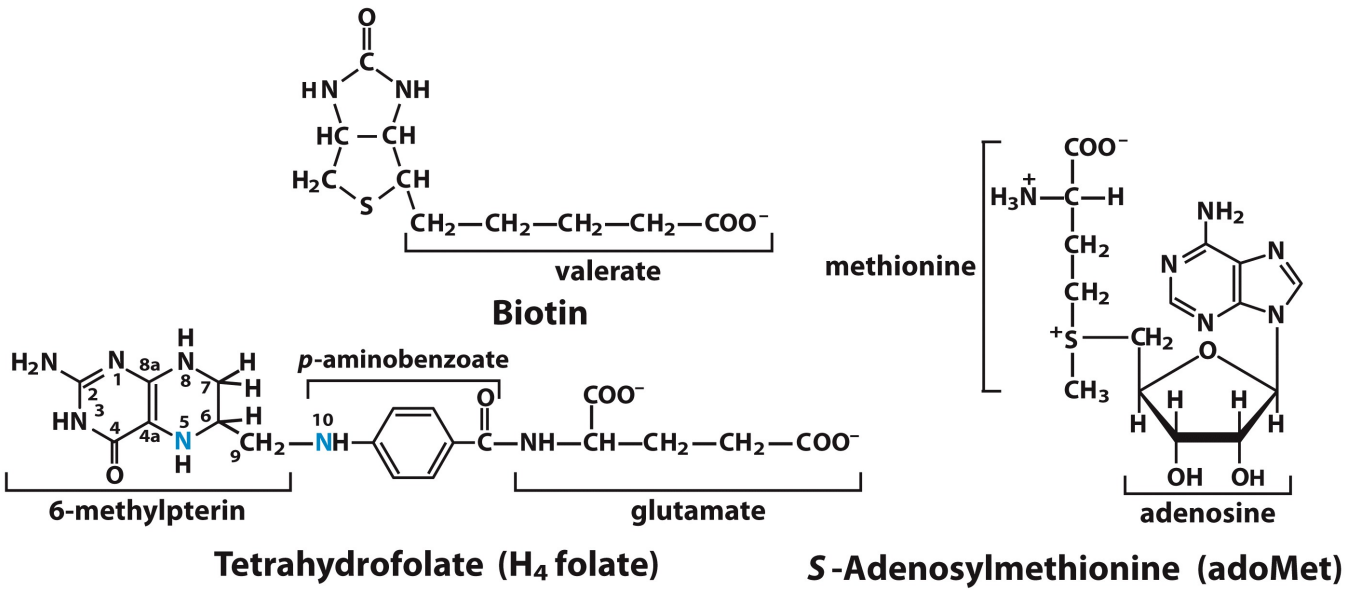


**Figure 18-16**
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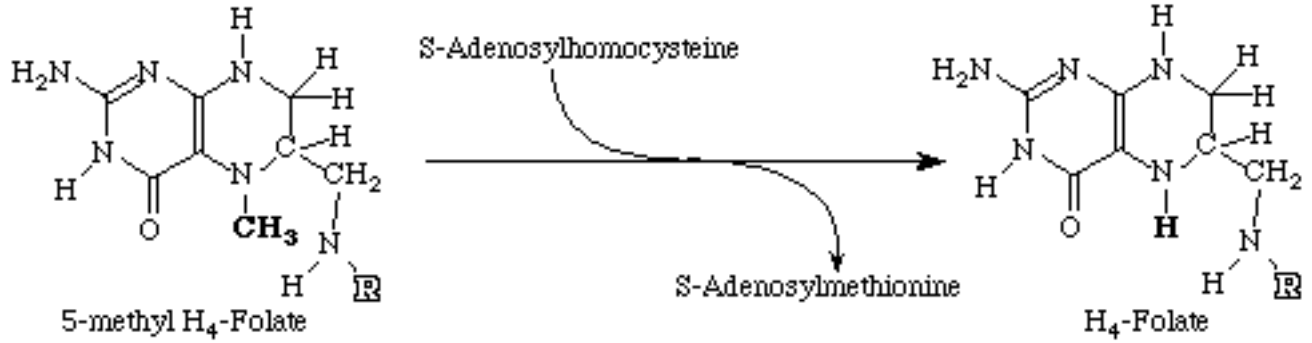
# AMINO ACIDS DEGRADATION



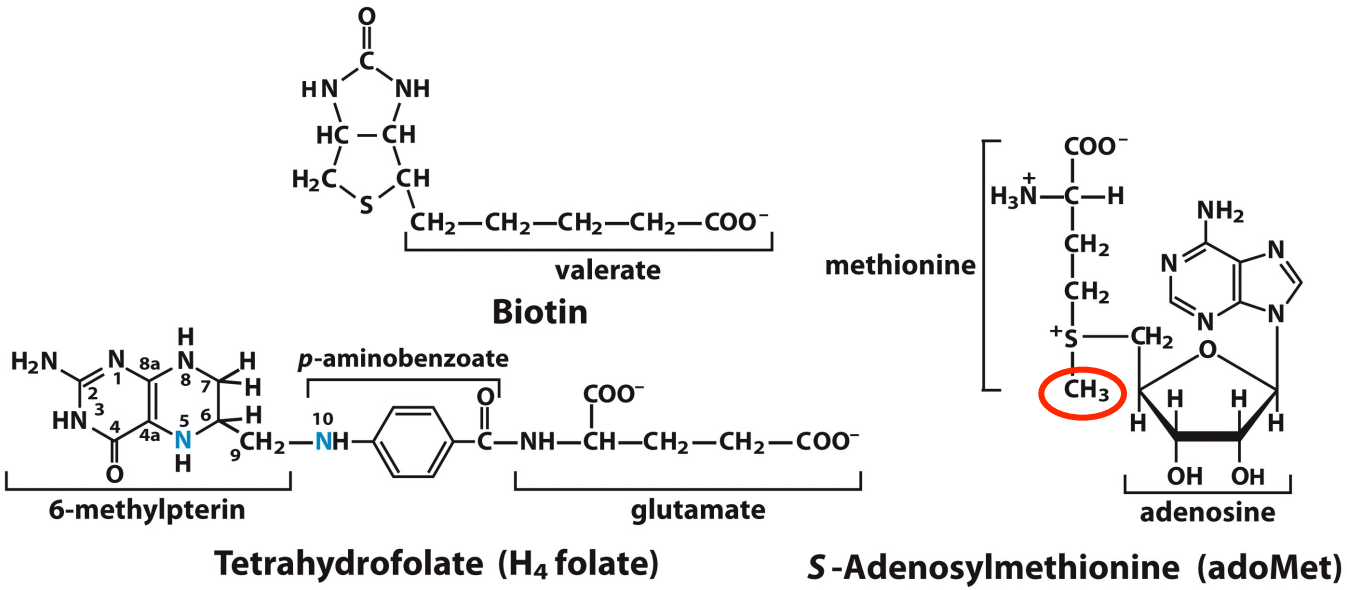




**Figure 18-16**
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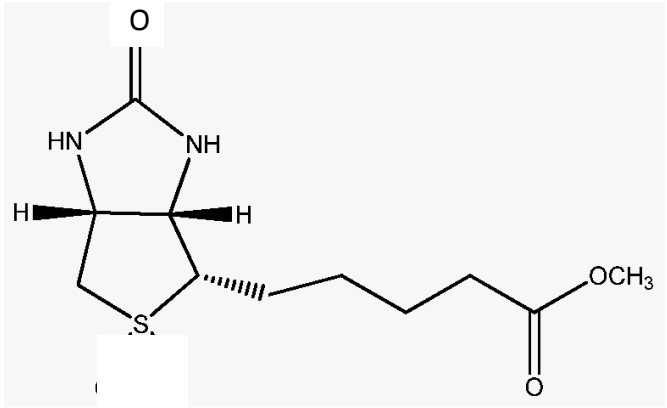
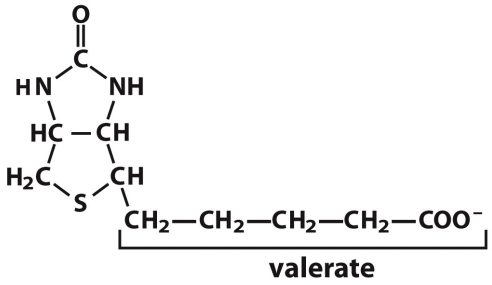
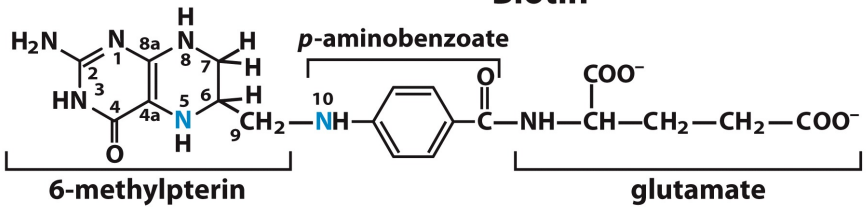
# AMINO ACIDS DEGRADATION

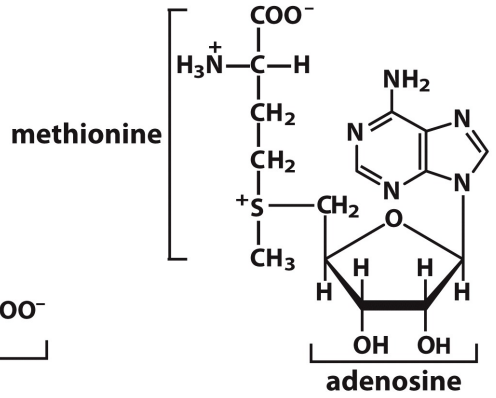



**Biotin**




**Tetrahydrofolate ($H_4$ folate)**




***S*-Adenosylmethionine (adoMet)**

**Figure 18-16**
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# AMINO ACIDS DEGRADATION

**Ketogenic Amino Acids**

- Ketogenic amino acids can produce ketones when energy sources are low.
- Some of these amino acids are degraded directly to ketone bodies such as acetoacetate. They include leucine, lysine, phenylalanine, tryptophan, and tyrosine.
- The other ketogenic amino acids can be converted to acetyl-CoA. Acetyl-CoA has several different fates, one of which is the conversion to acetoacetate.
- Although not a preferential energy source, acetoacetate can be metabolized by the brain and muscle for energy when blood glucose is low.

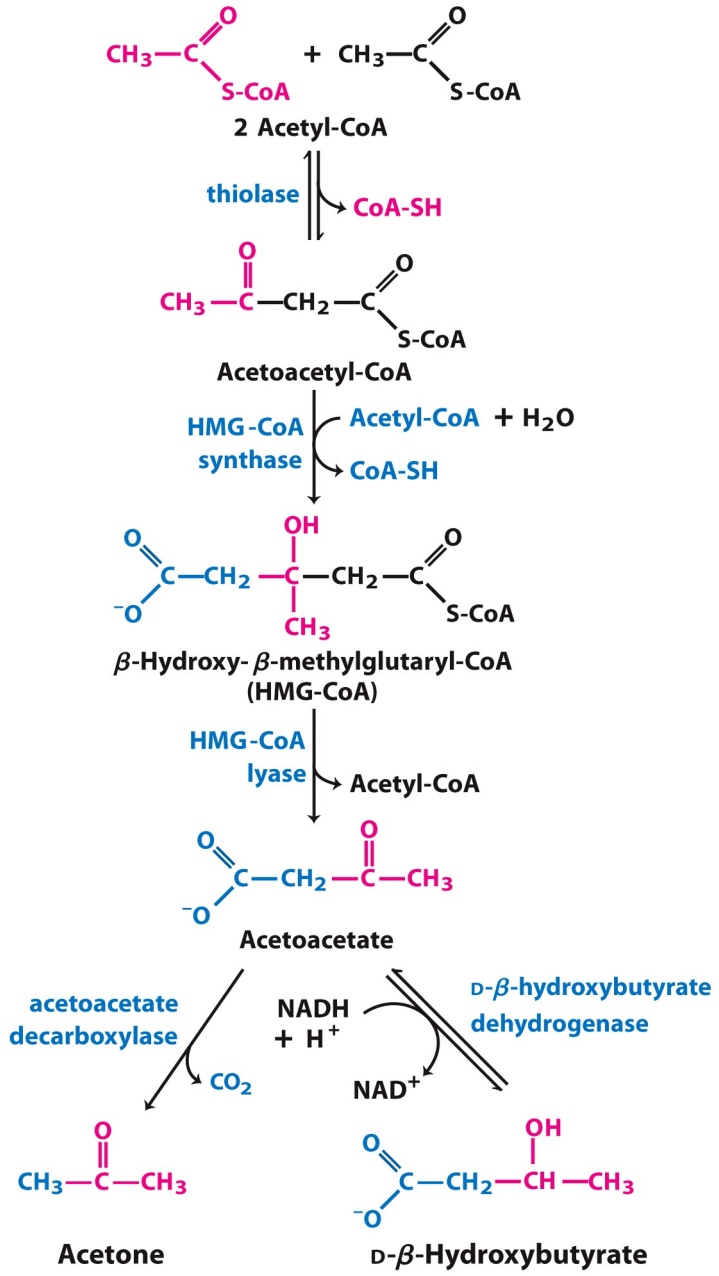


**Figure 17-19**
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