Amino Acid Catabolism

- Dietary Proteins
- Turnover of Protein
- Cellular protein
- Deamination
- Urea cycle
- Carbon skeletons of amino acids

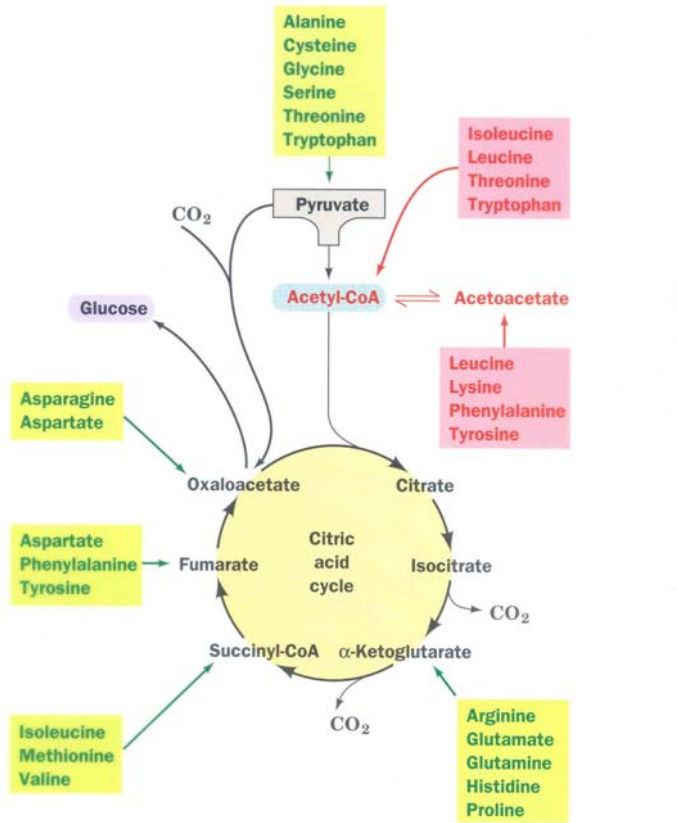


Figure 24-8. The degradation of amino acids to seven common metabolic intermediates.

Amino Acid Metabolism

- Metabolism of the 20 common amino acids is considered from the origins and fates of their:
  - (1) Nitrogen atoms
  - (2) Carbon skeletons

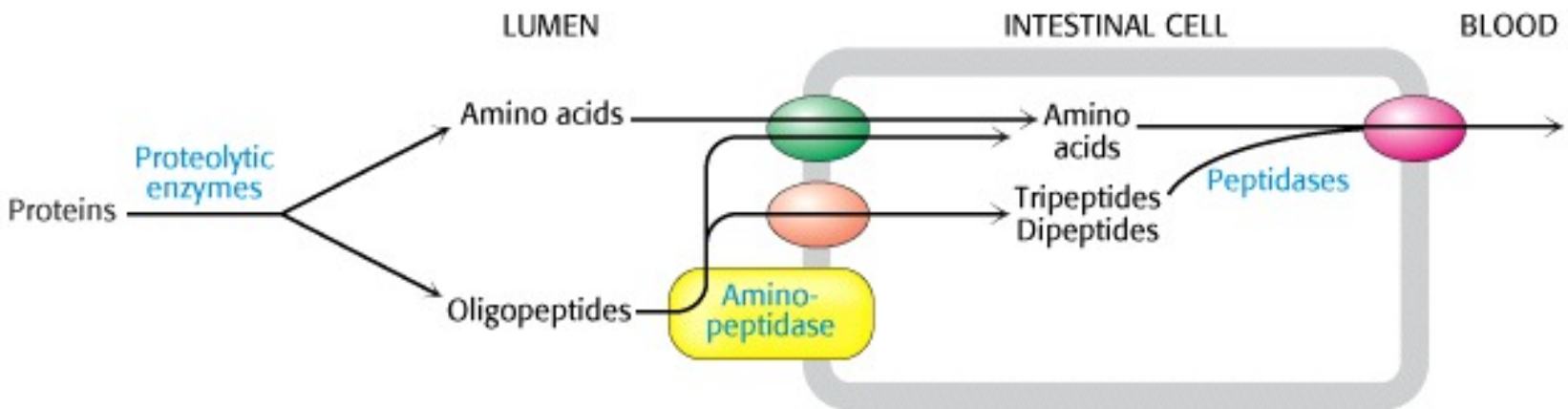
- For mammals:
  Essential amino acids must be obtained from diet
  Nonessential amino acids - can be synthesized

Amino Acid Catabolism

- Amino acids from degraded proteins or from diet can be used for the biosynthesis of new proteins
- During starvation proteins are degraded to amino acids to support glucose formation
- First step is often removal of the α-amino group
- Carbon chains are altered for entry into central pathways of carbon metabolism

Dietary Proteins

- Digested in intestine
- by peptidases
- transport of amino acids
- active transport coupled with Na+



Protein Turnover

- Proteins are continuously synthesized and degraded (turnover) (half-lives minutes to weeks)
- Lysosomal hydrolysis degrades some proteins
- Some proteins are targeted for degradation by a covalent attachment (through lysine residues) of **ubiquitin** (C terminus)
- **Proteasome** hydrolyzes ubiquitinated proteins

Turnover of Protein

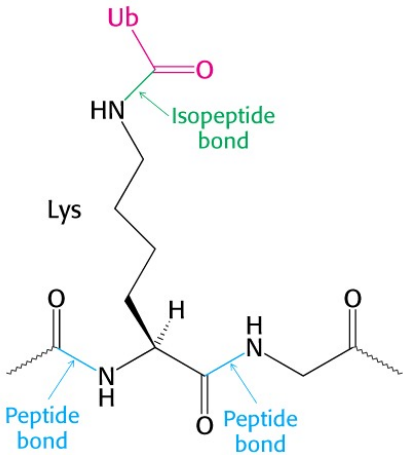
- **Cellular protein**
- **Proteasome degrades protein with Ub tags**
- **T 1/2 determined by amino terminus residue**
- **stable: ala, pro, gly, met greater than 20h**
- **unstable: arg, lys, his, phe 2-30 min**

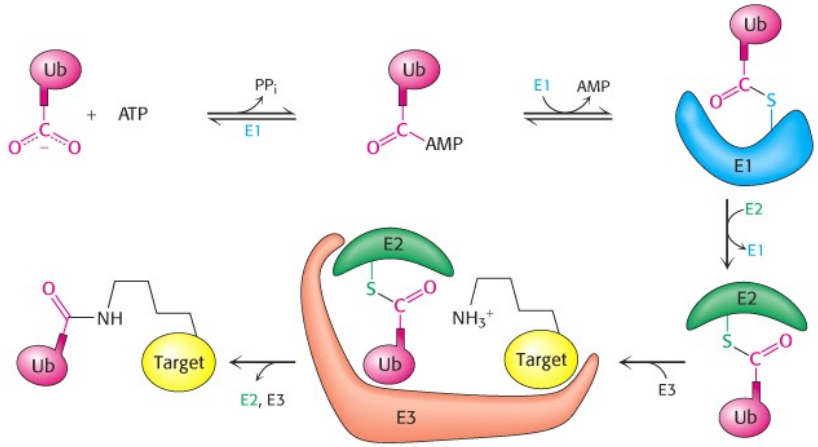
TABLE 23.1 Dependence of the half-lives of cytosolic yeast proteins on the nature of their amino-terminal residues

Highly stabilizing residues			
($t_{1/2}$ > 20 hours)			
Ala	Cys	Gly	Met
Pro	Ser	Thr	Val
Intrinsically destabilizing residues			
($t_{1/2}$ = 2 to 30 minutes)			
Arg	His	Ile	Leu
Lys	Phe	Trp	Tyr
Destabilizing residues after chemical modification			
($t_{1/2}$ = 3 to 30 minutes)			
Asn	Asp	Gln	Glu

Source: J. W. Tobias, T. E. Schrader, G. Rocap, and A. Varshavsky. *Science* 254(1991):1374.

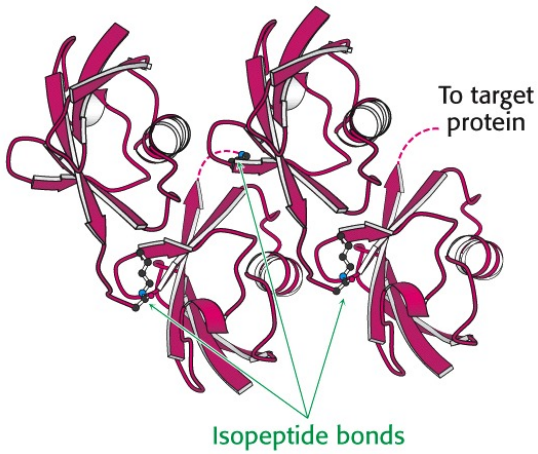
Ubibiquitin

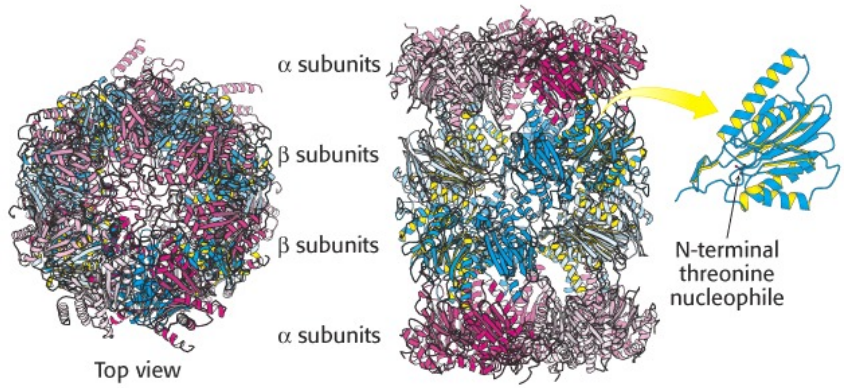




- **Ubiquitin protein, 8.5 kD**
- **highly conserved in yeast/humans**
- **carboxy terminal attaches to ε-lysine amino group**
- **Chains of 4 or more Ub molecules target protein for destruction**

Degradation-- Proteasome

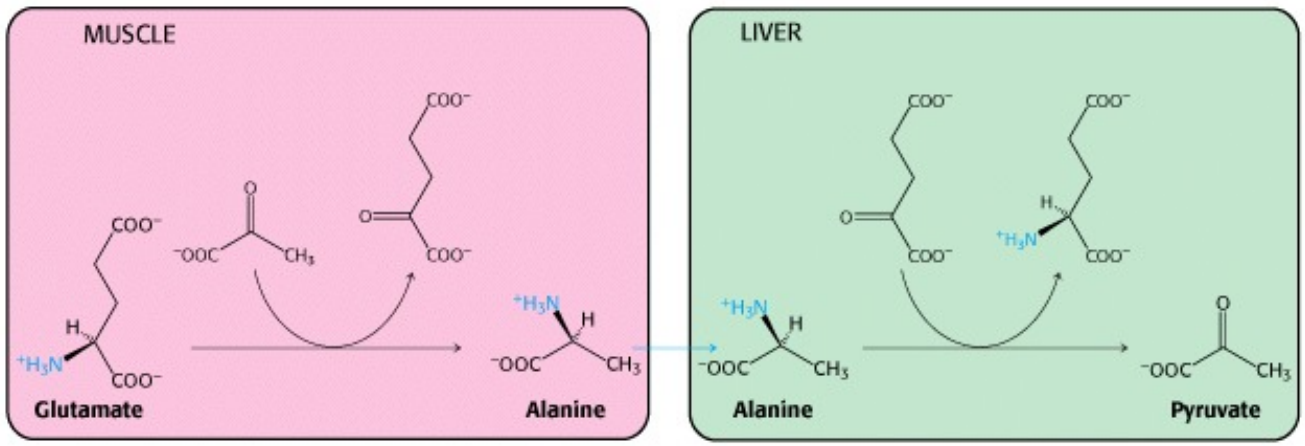




- **Proteasome degrades protein with Ub tags**
- 26s: two subunits, 20s (catalytic) and 19s (regulatory)
- Releases peptides 7-9 units long

Deamination

- Collect NH_3 from tissues
- alanine from muscle
- glutamine from other tissues
- glutamate from liver



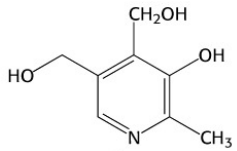
Transamination Reactions

- Transfer of an amino group from an **α-amino acid** to an **α-keto acid**
- In amino acid biosynthesis, the amino group of glutamate is transferred to various α-keto acids generating α-amino acids
- In amino acid catabolism, transamination reactions generate glutamate or aspartate

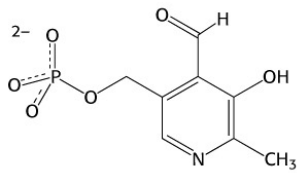
Transamination

- **cytosol of liver**
- **collect in glutamate**
- **glutamate transferred to mitochondria**

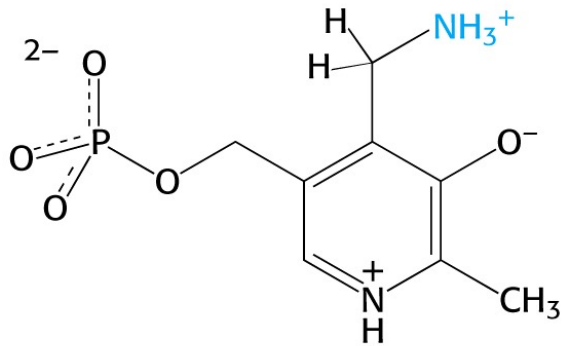
Mechanism



Pyridoxine
(Vitamin B_6)



Pyridoxal phosphate
(PLP)

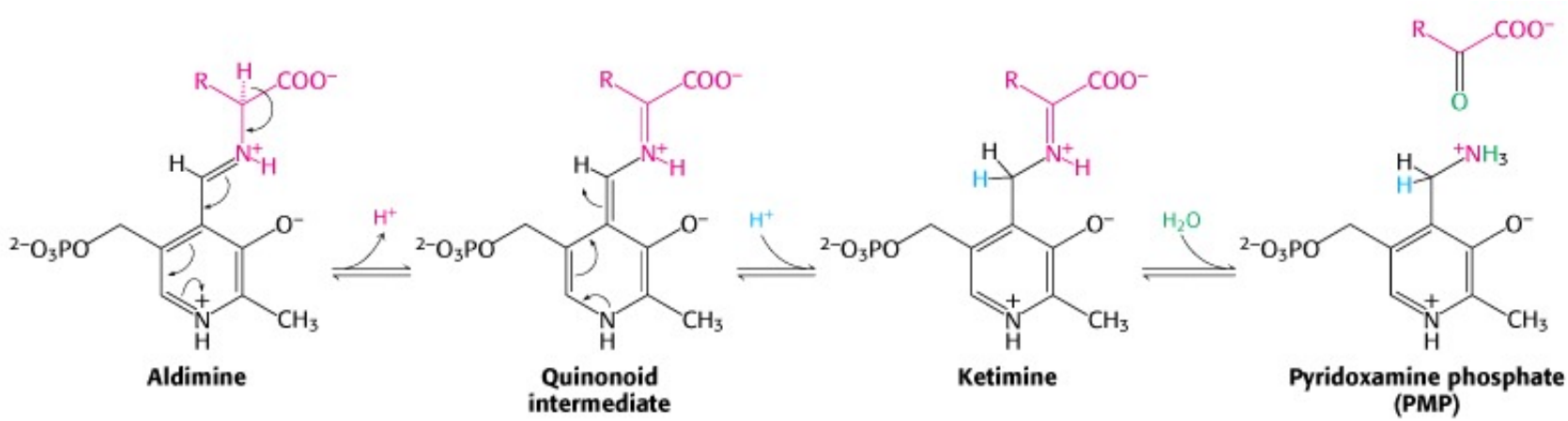


Pyridoxamine phosphate
(PMP)

- **Pyridoxal phosphate co-factor**

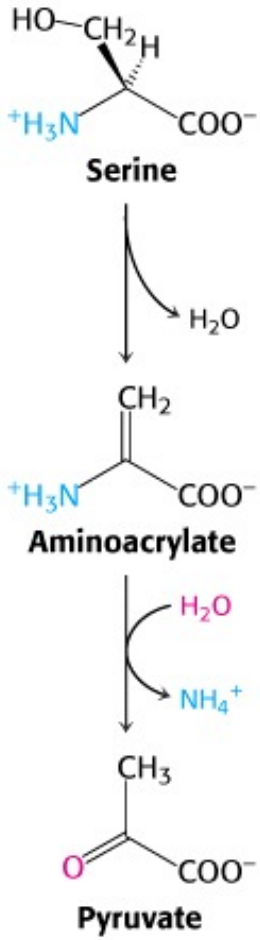
Schiff base

- **Ping pong**
- **Keto acid**



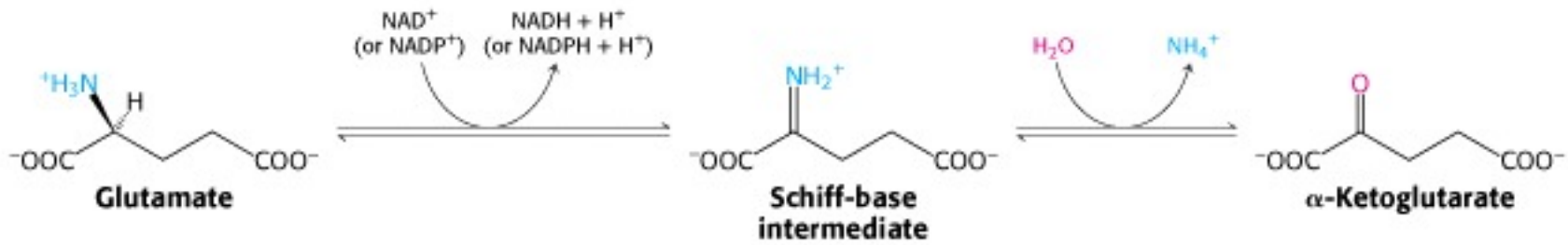
Serine & Threonine deamination

- Dehydratase reaction
- Remove H_2O first
- Serine → pyruvate
- Threonine →α-ketobutyrate



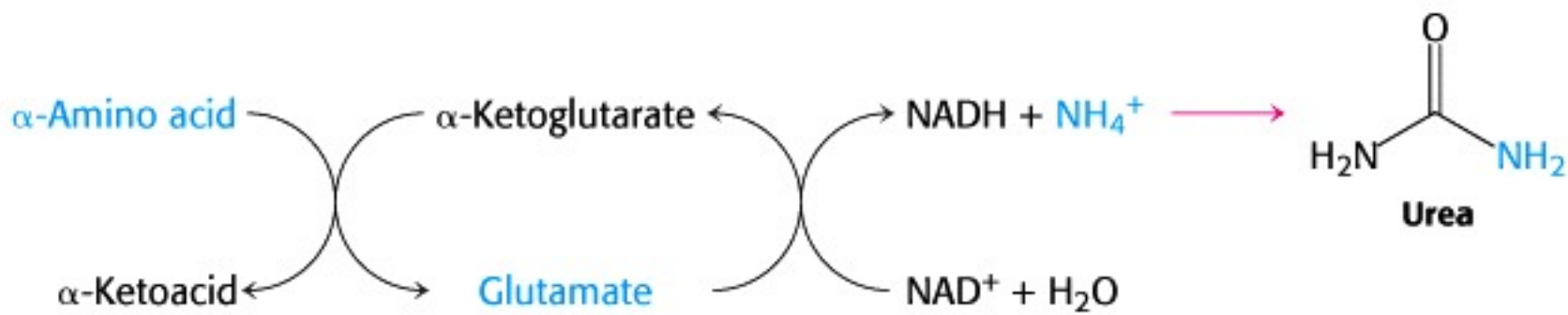
Oxidative deamination

- glutamate transferred to mitochondria
- Glutamate dehydrogenase



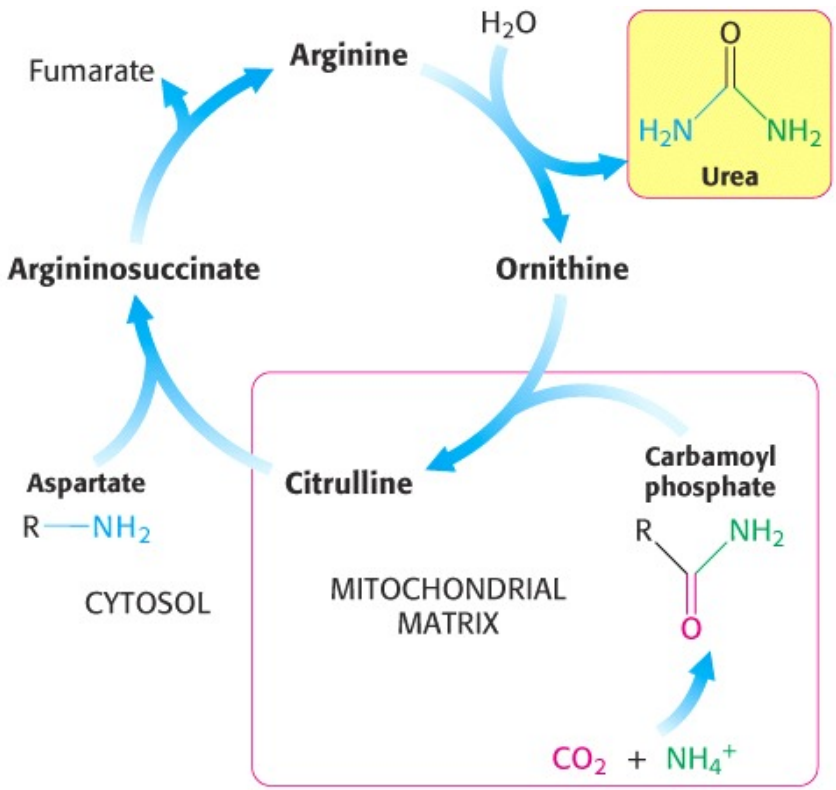
Urea cycle

- In Liver
- Glutamate dehydrogenase
- CPS I
- bicarbonate and ammonia react
- In mitochondria: reactions
- cytosolic reactions
- arginase releases urea
- remove waste products
- tied to TCA cycle

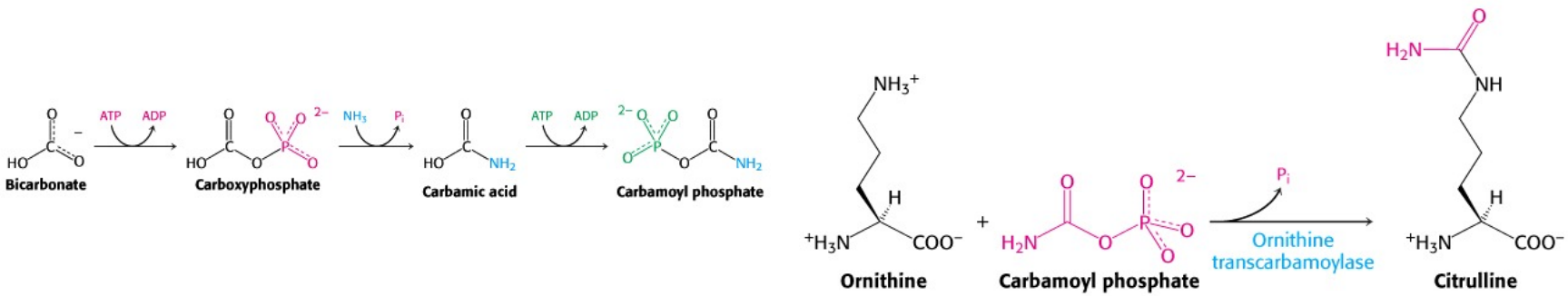


Urea cycle

- **Mitochondria reactions**
- **Cytosolic reactions**

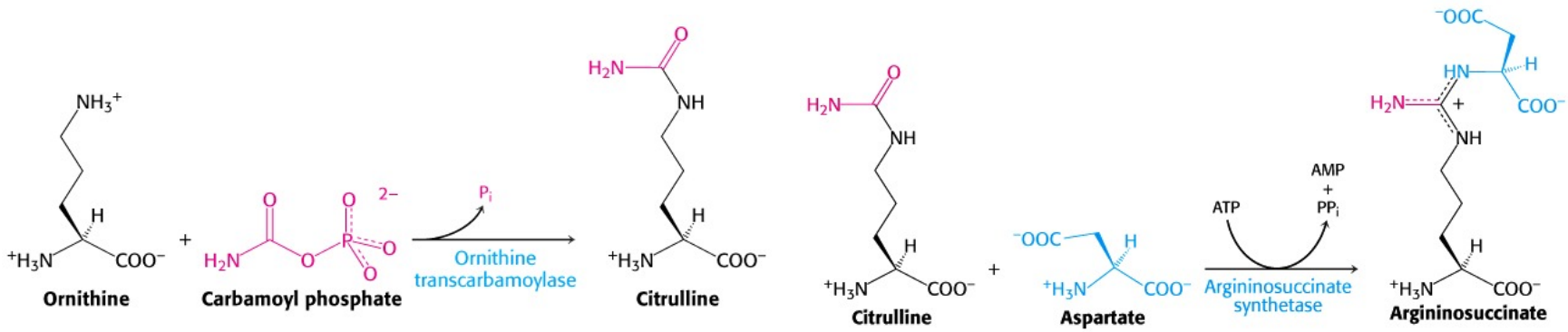


Mitochondrial Reactions



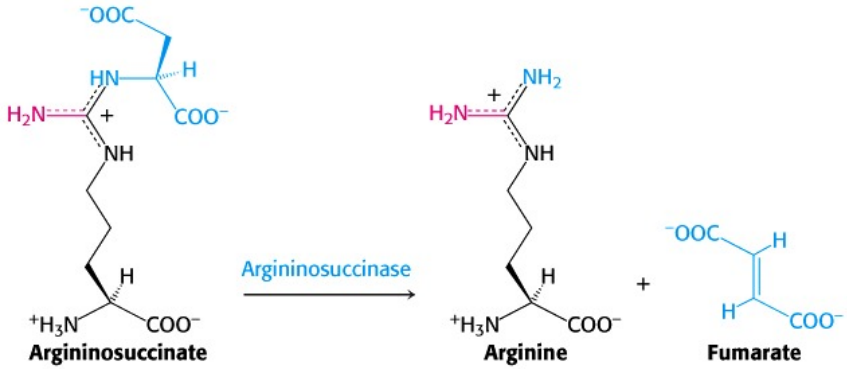
- **CPS I**
- **Bicarbonate and ammonia react**
- **Orinithine transcarbamolyse**
- **Citrulline transported to cytosol**

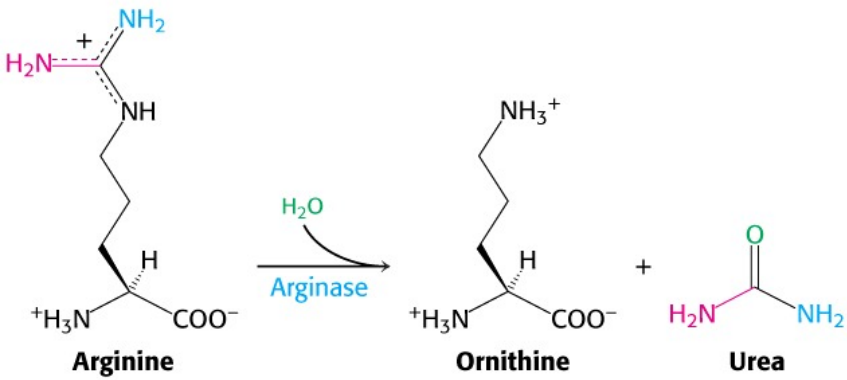
Cytosolic reactions

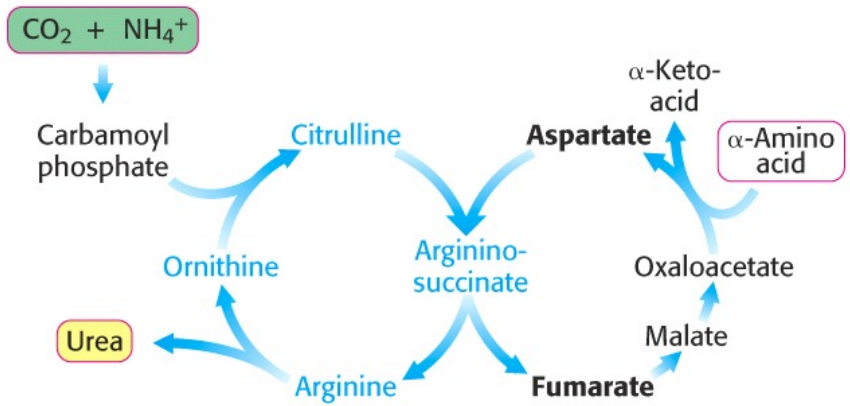


- Arginase releases urea
- remove waste products: ammonia/bicarbonate
- tied to TCA cycle

Urea cycle and TCA cycle





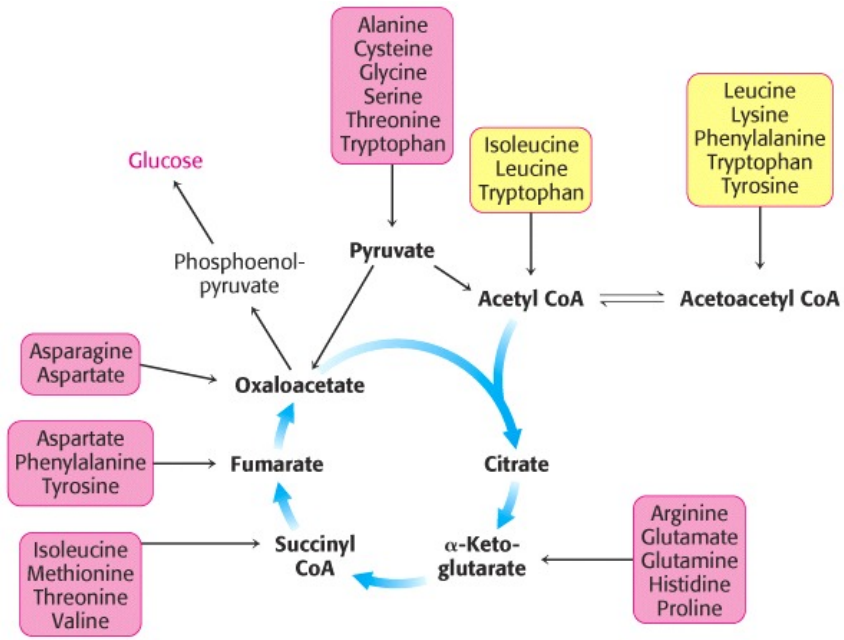


Glucogenic vs ketogenic amino acids

- Glucogenic amino acids can supply gluconeogenesis pathway via pyruvate or citric acid cycle intermediates
- Ketogenic amino acids can contribute to synthesis of fatty acids or ketone bodies
- Some amino acids are both glucogenic and ketogenic

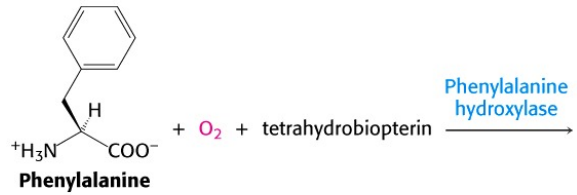
Carbon skeletons of amino acids

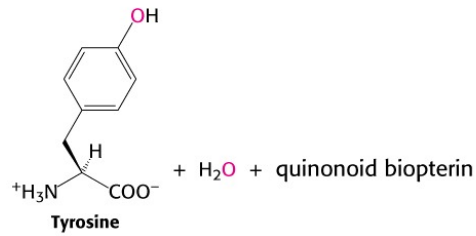
- glucogenic
- ketogenic
- Phenylalanine example
- Autosomal genetic defect



Phenylalanine Metabolic defect

- Genetic defect
- Recessive
- Hydroxylase defect
- Minor pathway produce Phenylpyruvic acid





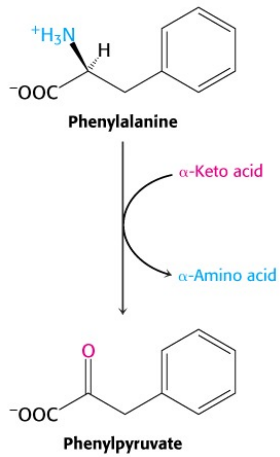


TABLE 23.3 Inborn errors of amino acid metabolism

Disease	Enzyme deficiency	Symptoms
Citrullinema	Arginosuccinate lyase	Lethergy, siezures, reduced muscle tension
Tyrosinemia	Various enzymes of tyrosine degradation	Weakness, self-mutilation, liver damage, mental retardation
Albinism	Tyrosinase	Absence of pigmentation
Homocystinuria	Cystathionine β-synthase	Scoliosis, muscle weakness, mental retardation, thin blond hair
Hyperlysinemia	α-Aminoadipic semialdehyde dehydrogenase	Seizures, mental retardation, lack of muscle tone, ataxia