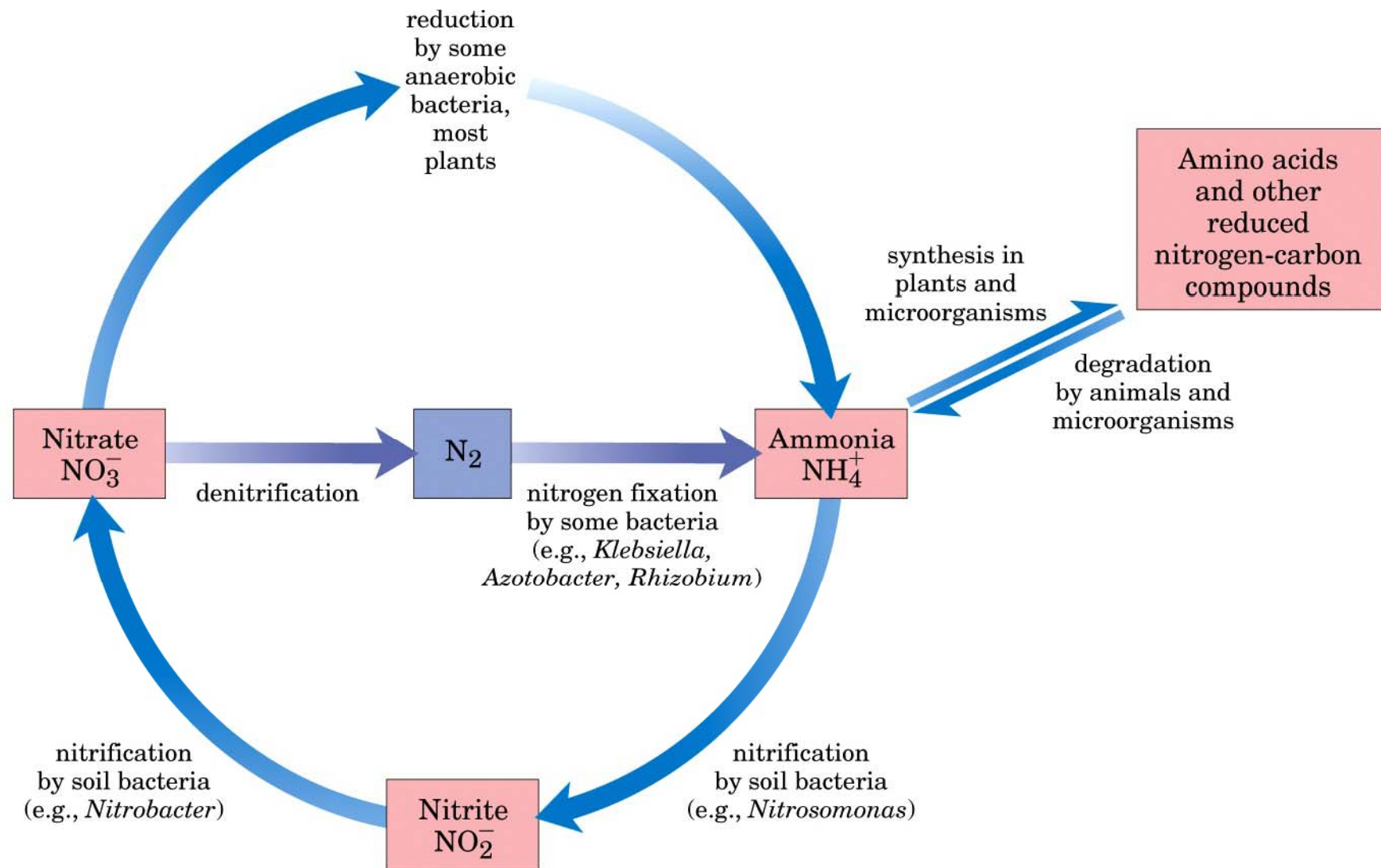
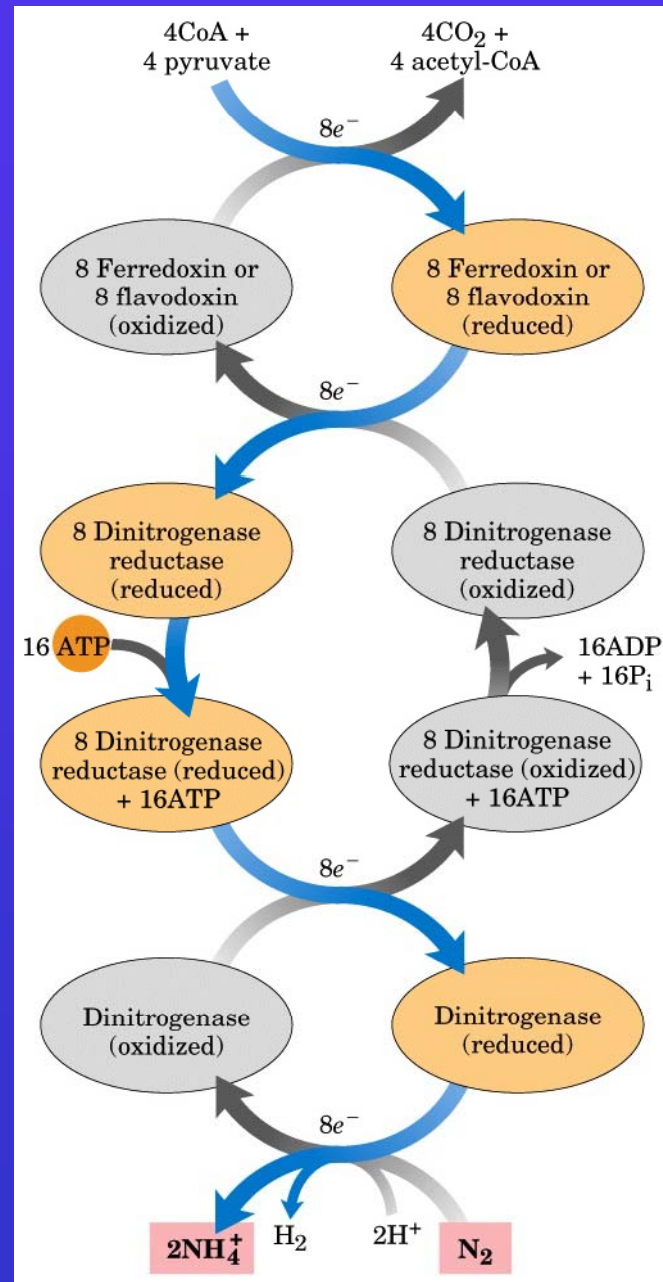
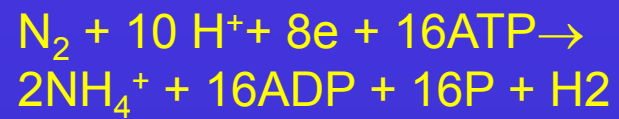


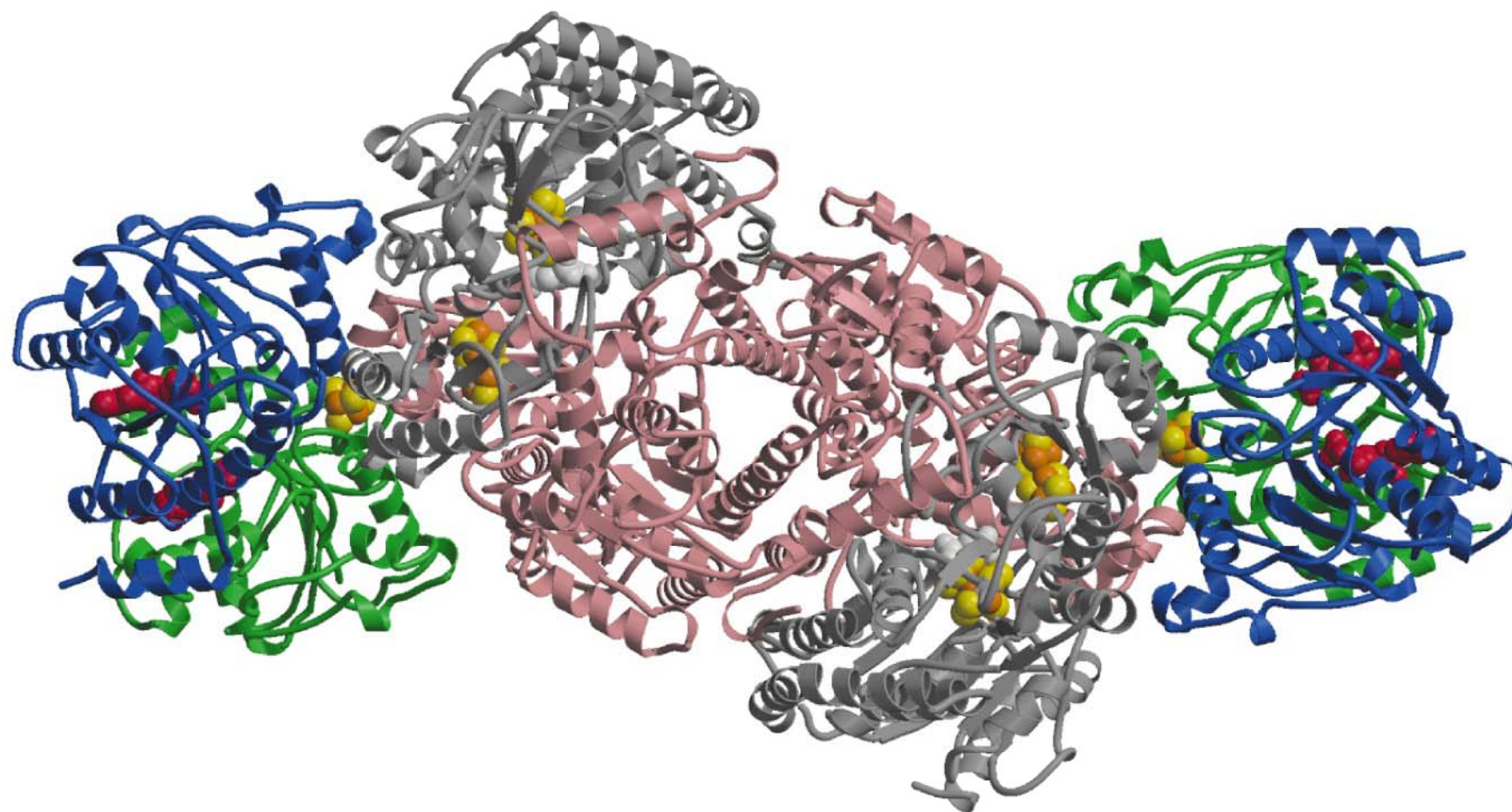
La fissazione dell'azoto



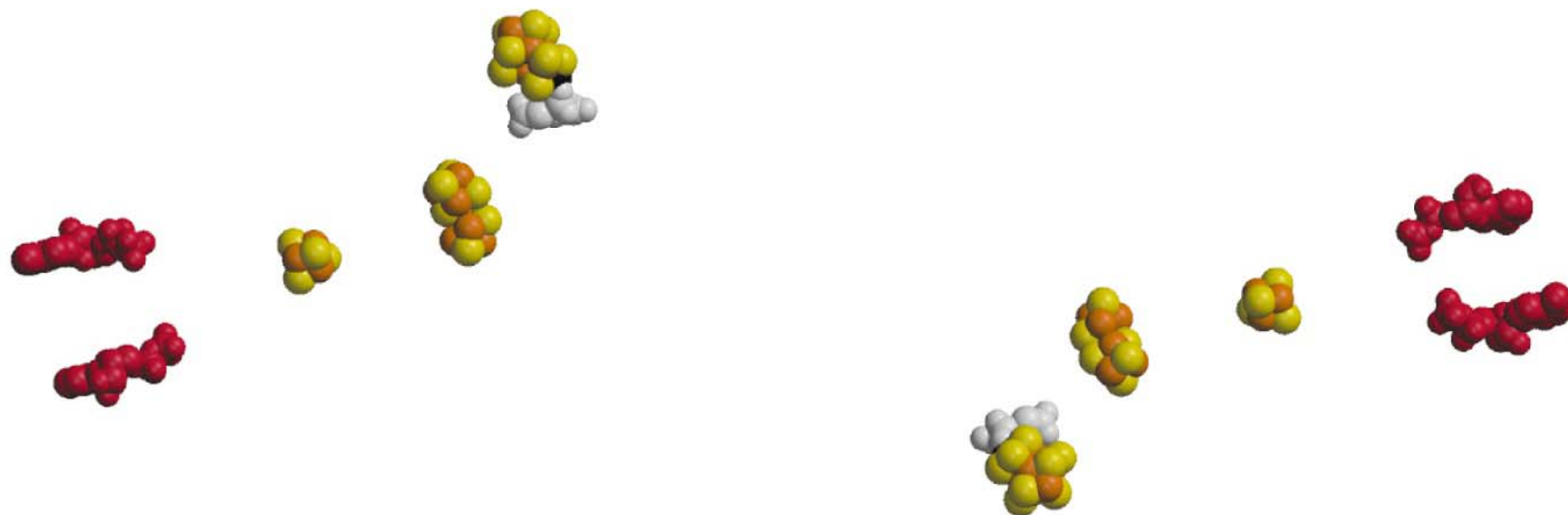


Complesso della nitrogenasi

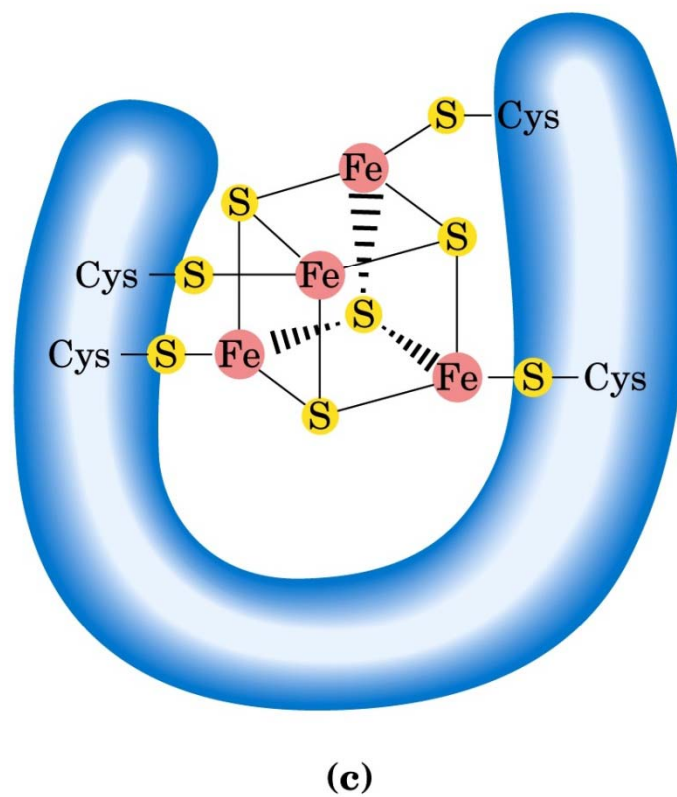
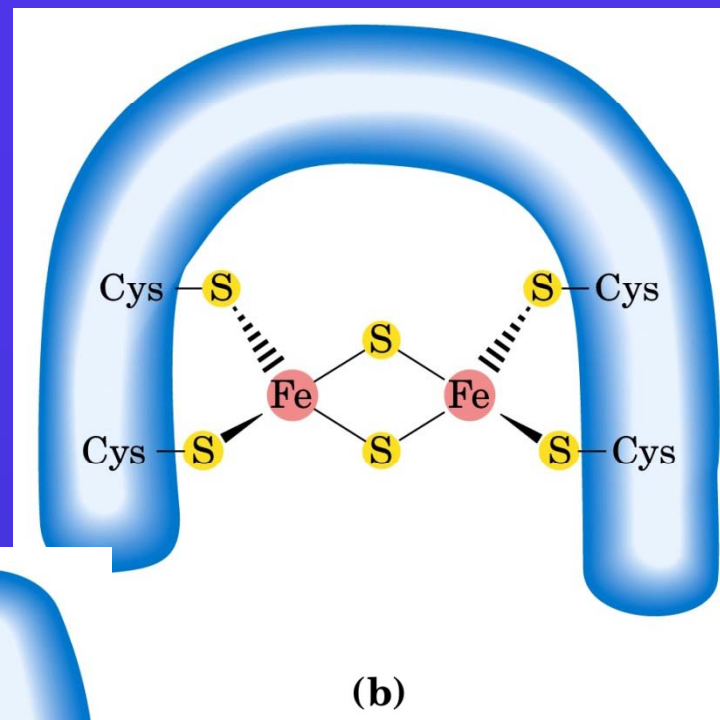
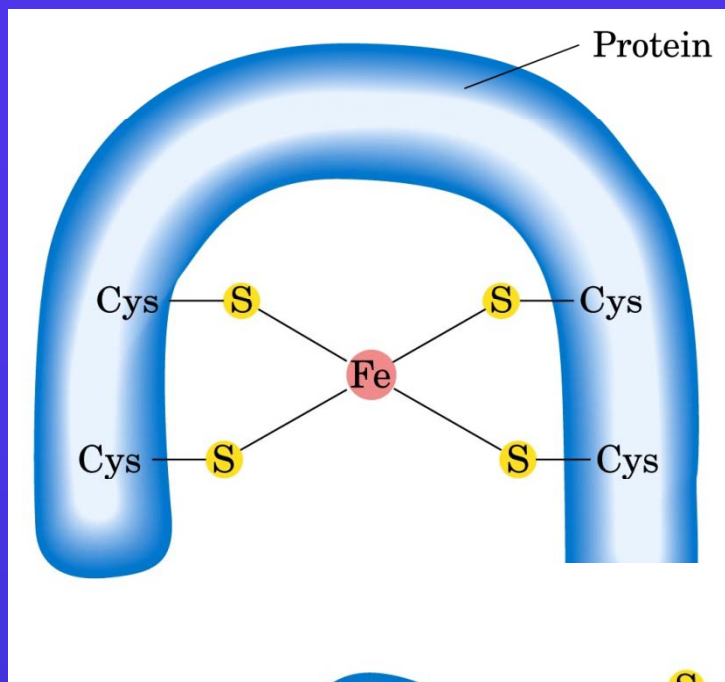


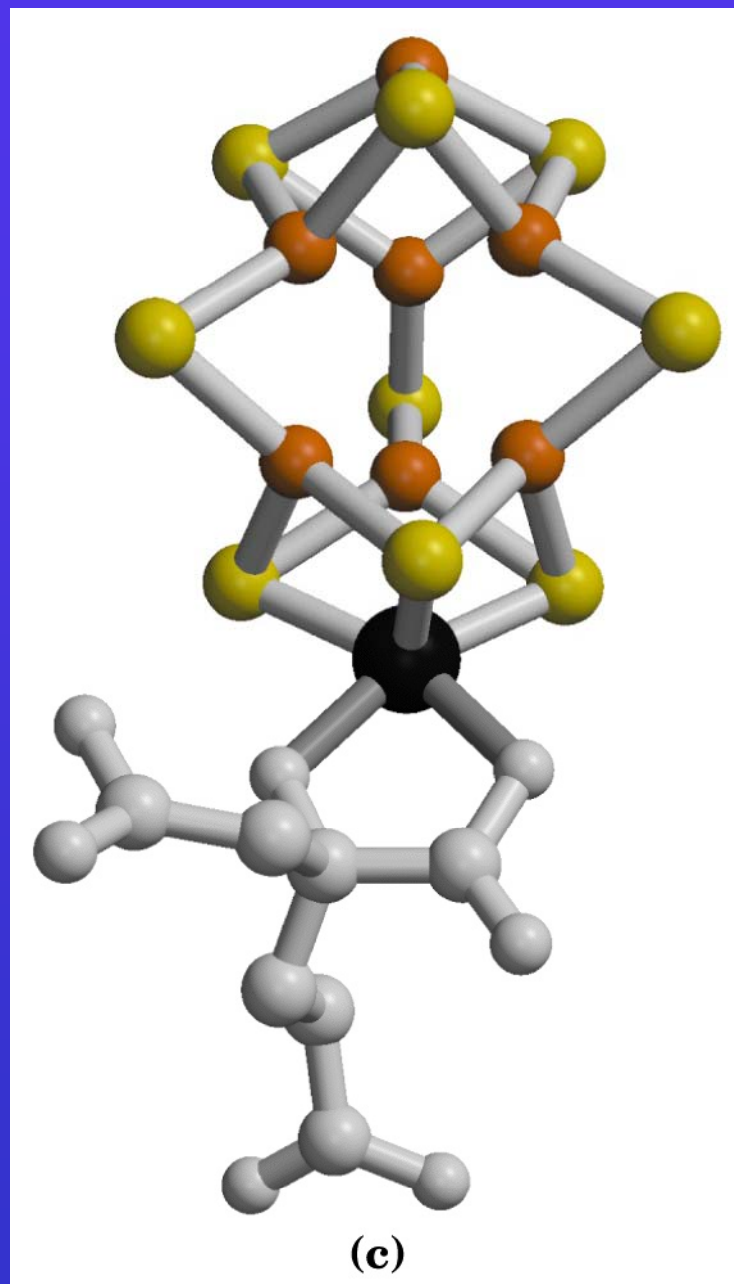


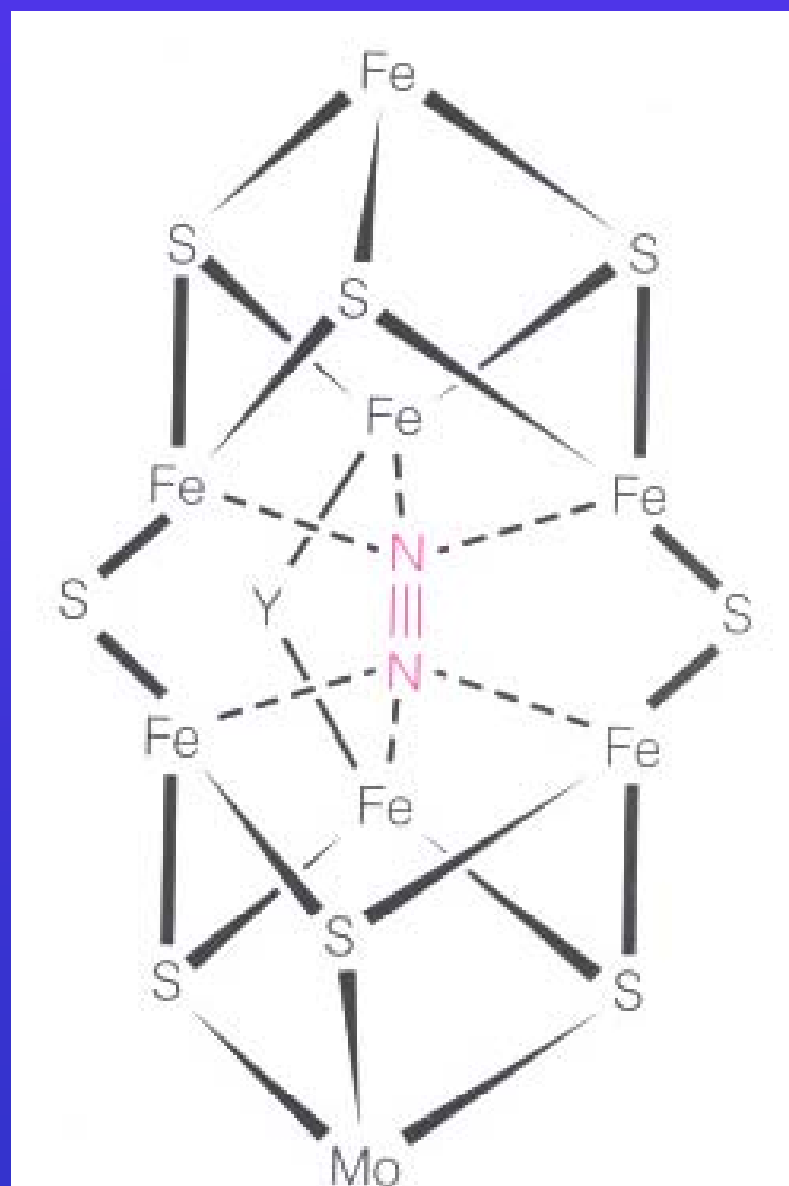
(a)



(b)

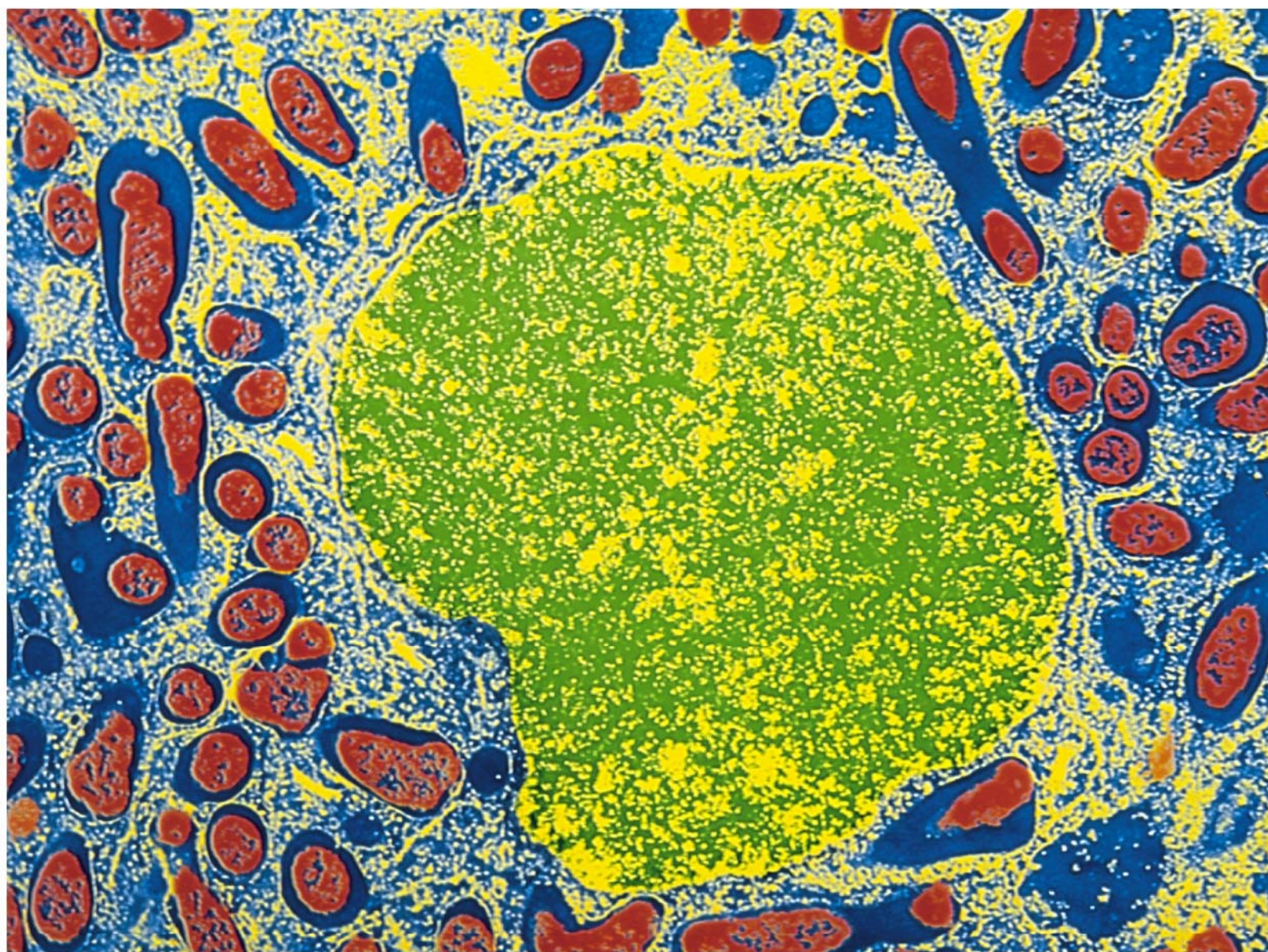






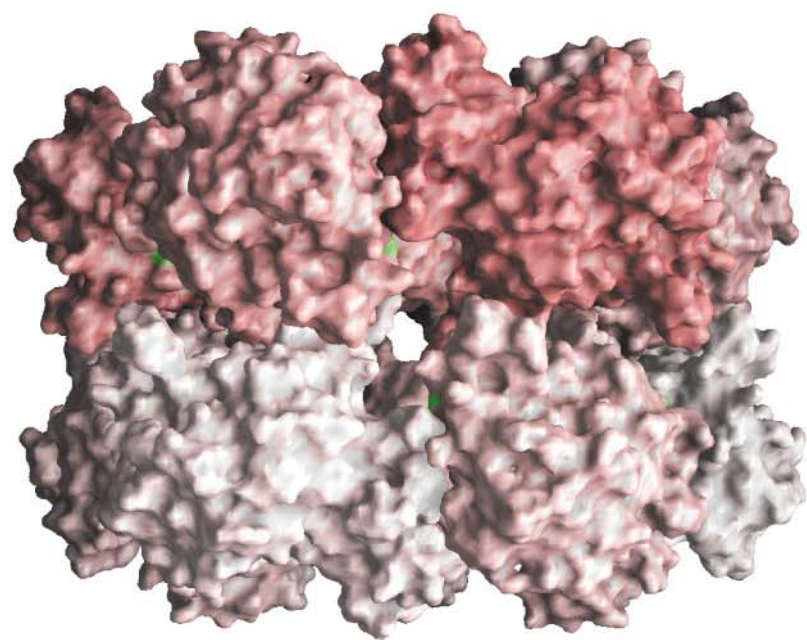


(a)

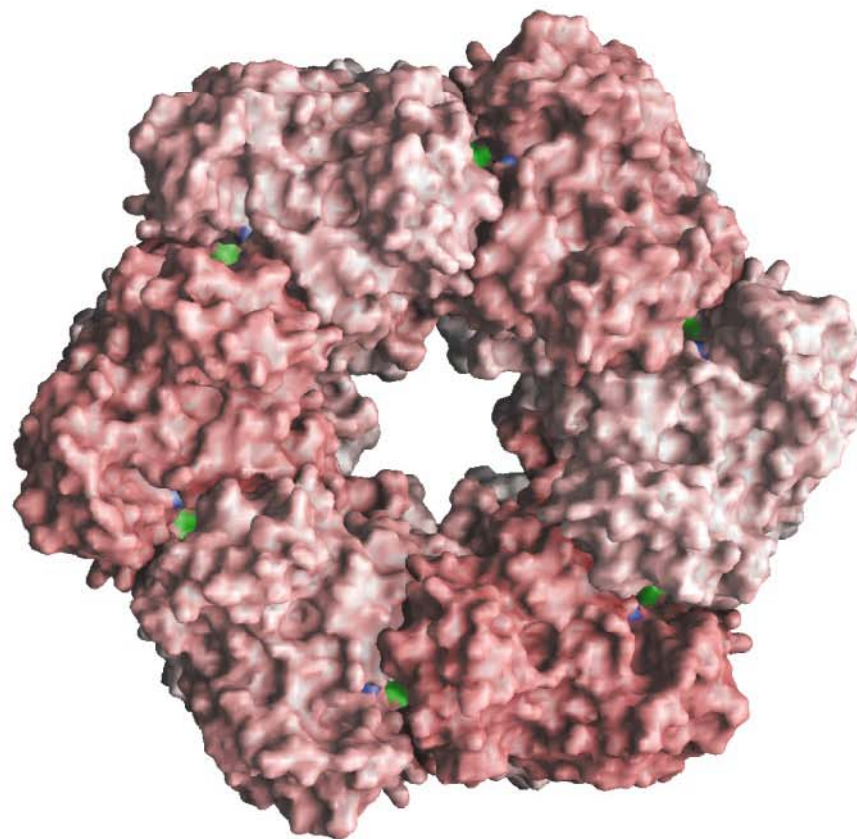


(b)

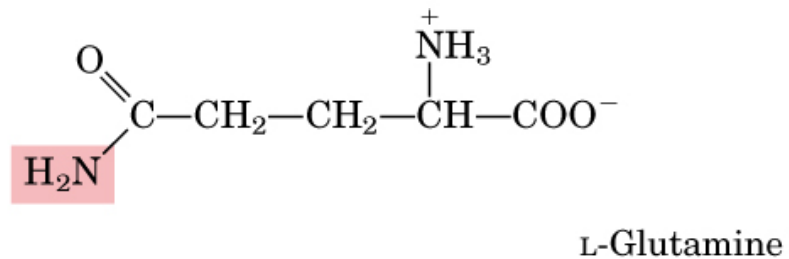
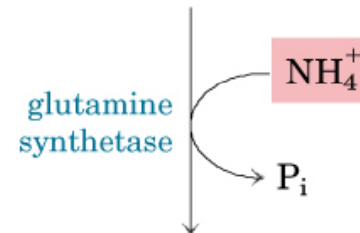
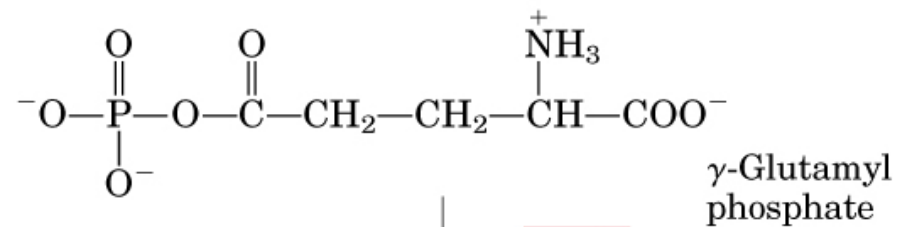
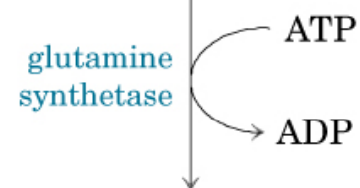
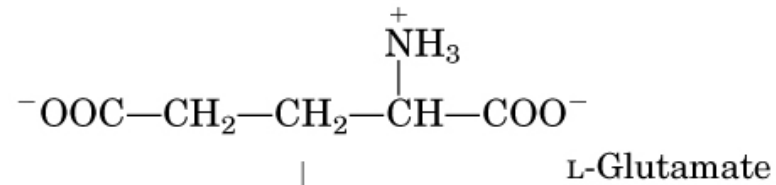
2 μm

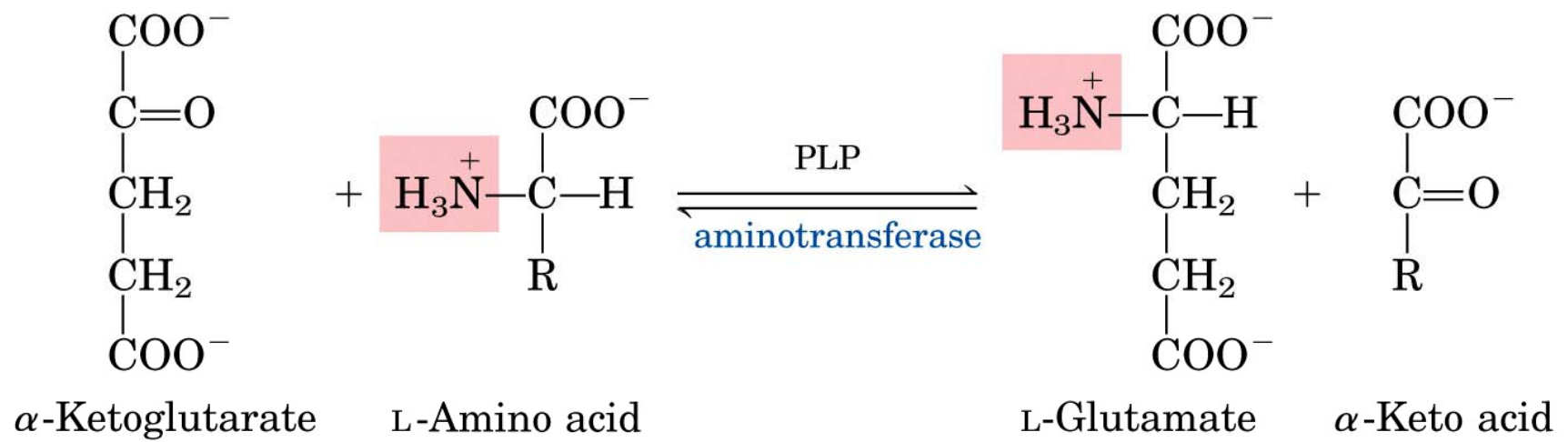


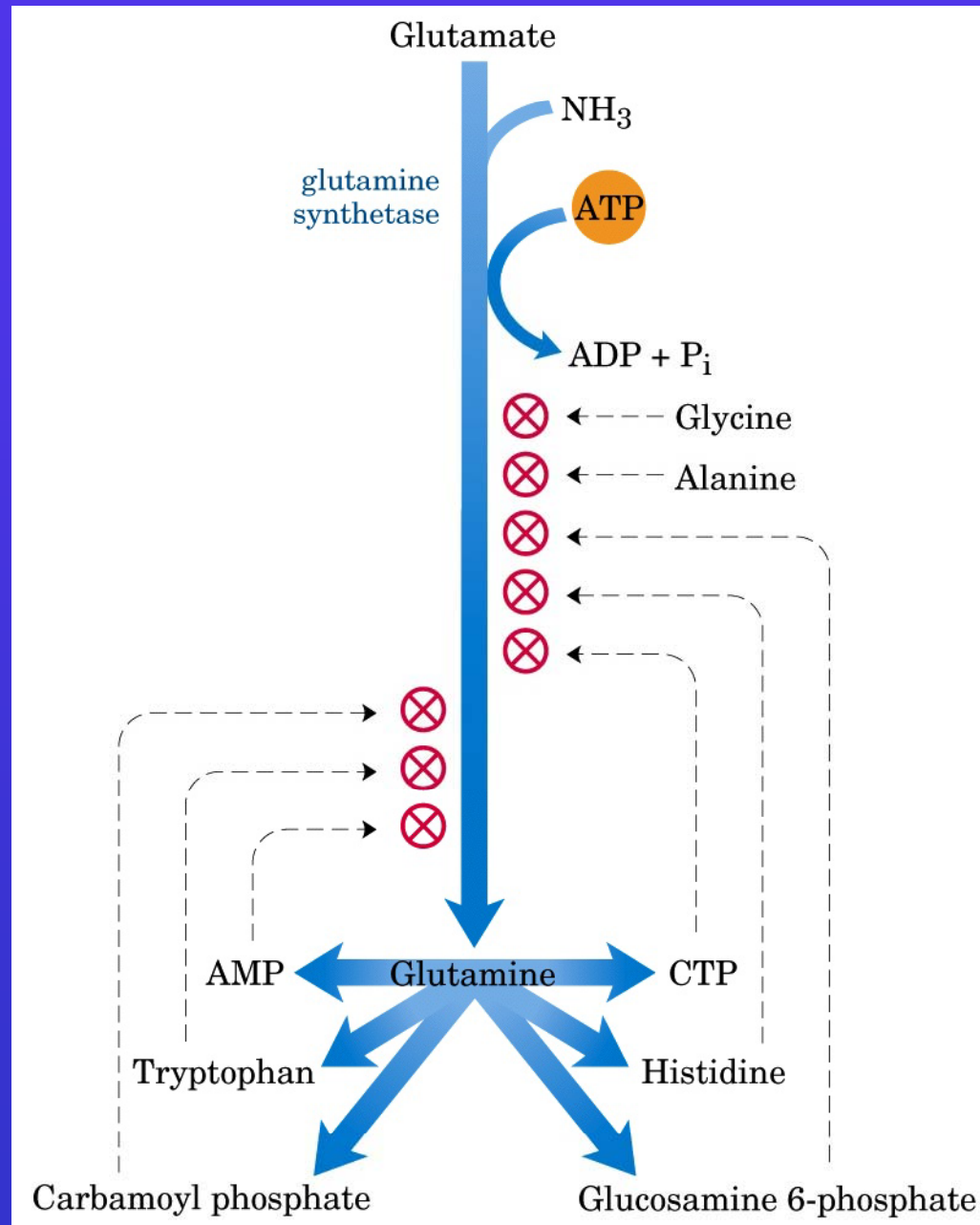
(a)



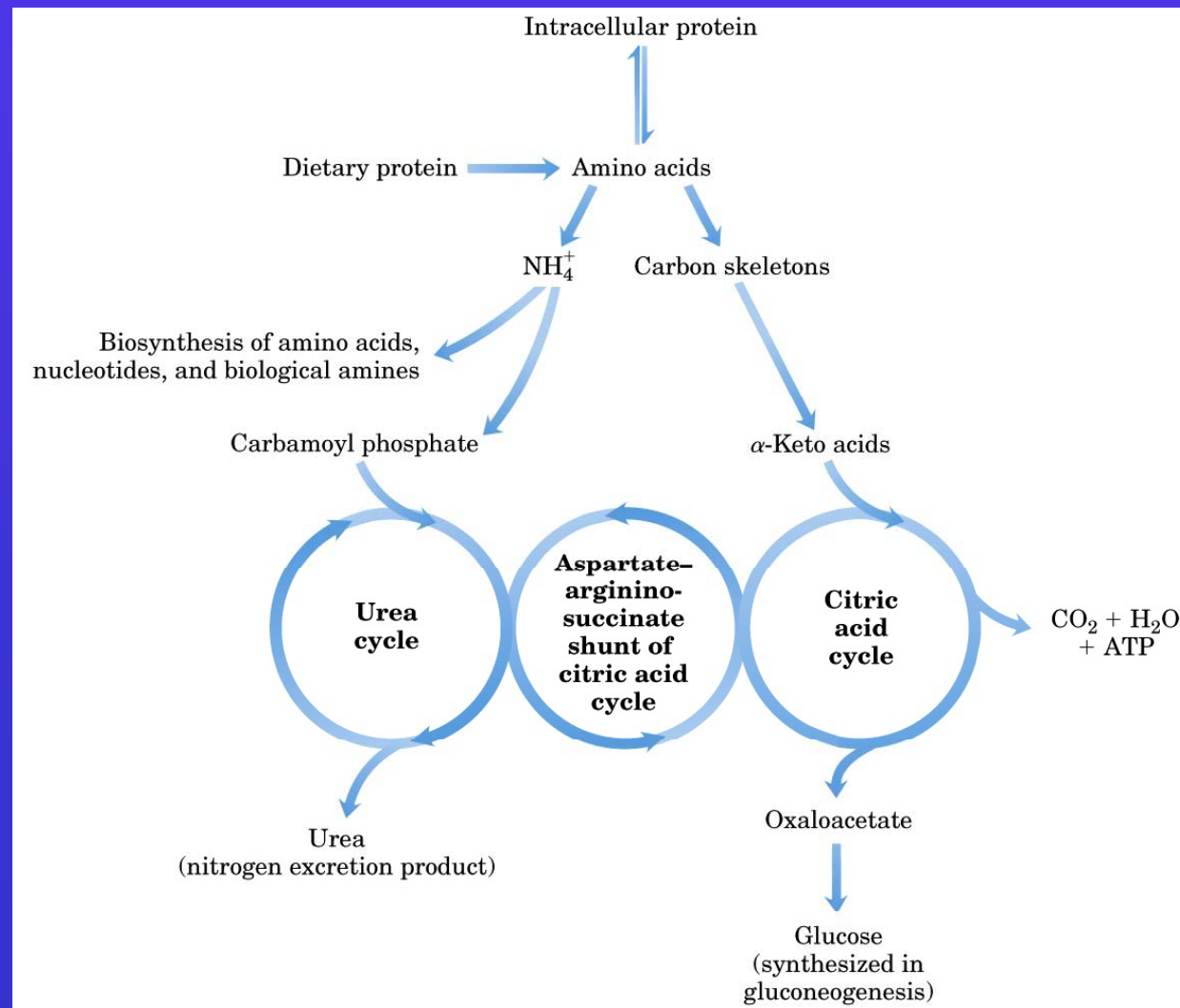
(b)







Metabolismo degli aminoacidi



Metabolismo degli aminoacidi

Gli aminoacidi introdotti in eccesso con la dieta vengono convertiti in composti precursori del glucosio, degli acidi grassi e dei corpi chetonici.

Degradazione delle proteine

- Le cellule sintetizzano continuamente proteine partendo da aminoacidi e le degradano ottenendo aminoacidi.
- Risparmio energetico
- Rimozione delle proteine danneggiate
- Regolazione del metabolismo cellulare

Degradazione degli aminoacidi

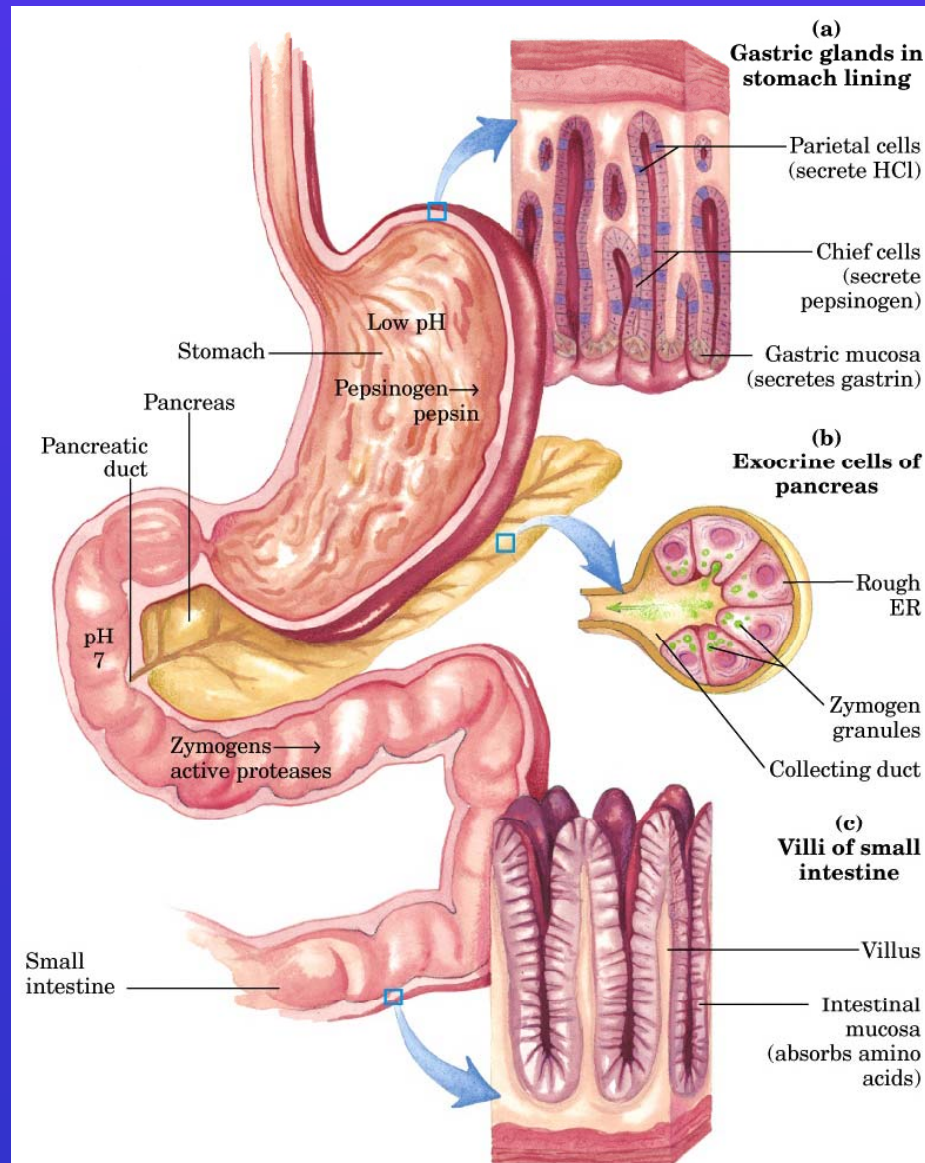
Gli aminoacidi vanno incontro a degradazione :

- 1.) per normale turnover delle proteine
- 2.) quando il loro apporto con la dieta sia particolarmente abbondante
- 3.) quando non siano disponibili gli zuccheri.

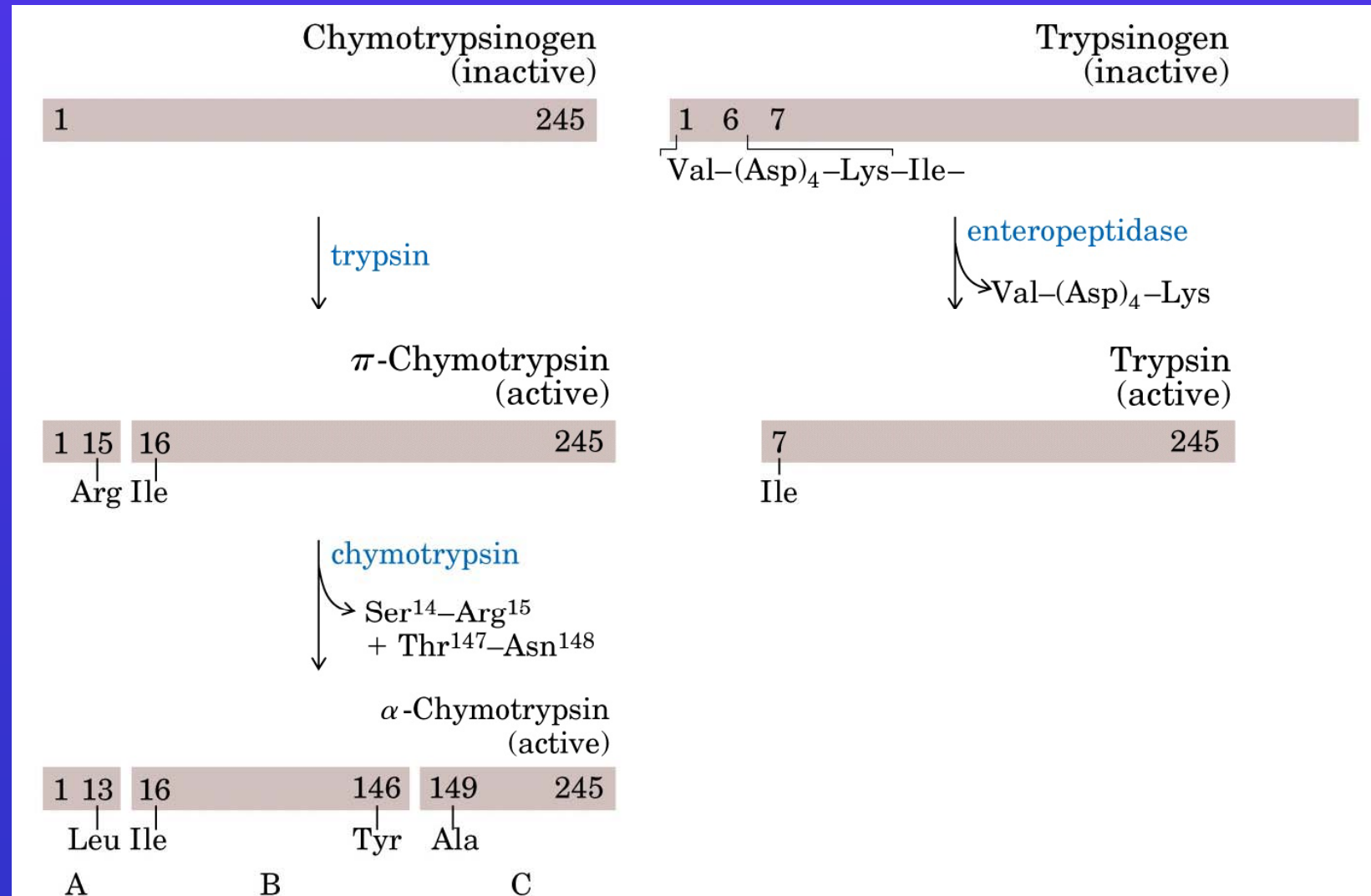
Degradazione delle proteine

- Le proteine sono caratterizzate da una diversa emivita
- Quelle che svolgono importanti funzioni regolative del metabolismo sono degradate più velocemente rispetto a quelle caratterizzate da un'attività catalitica costante in tutte le condizioni fisiologiche

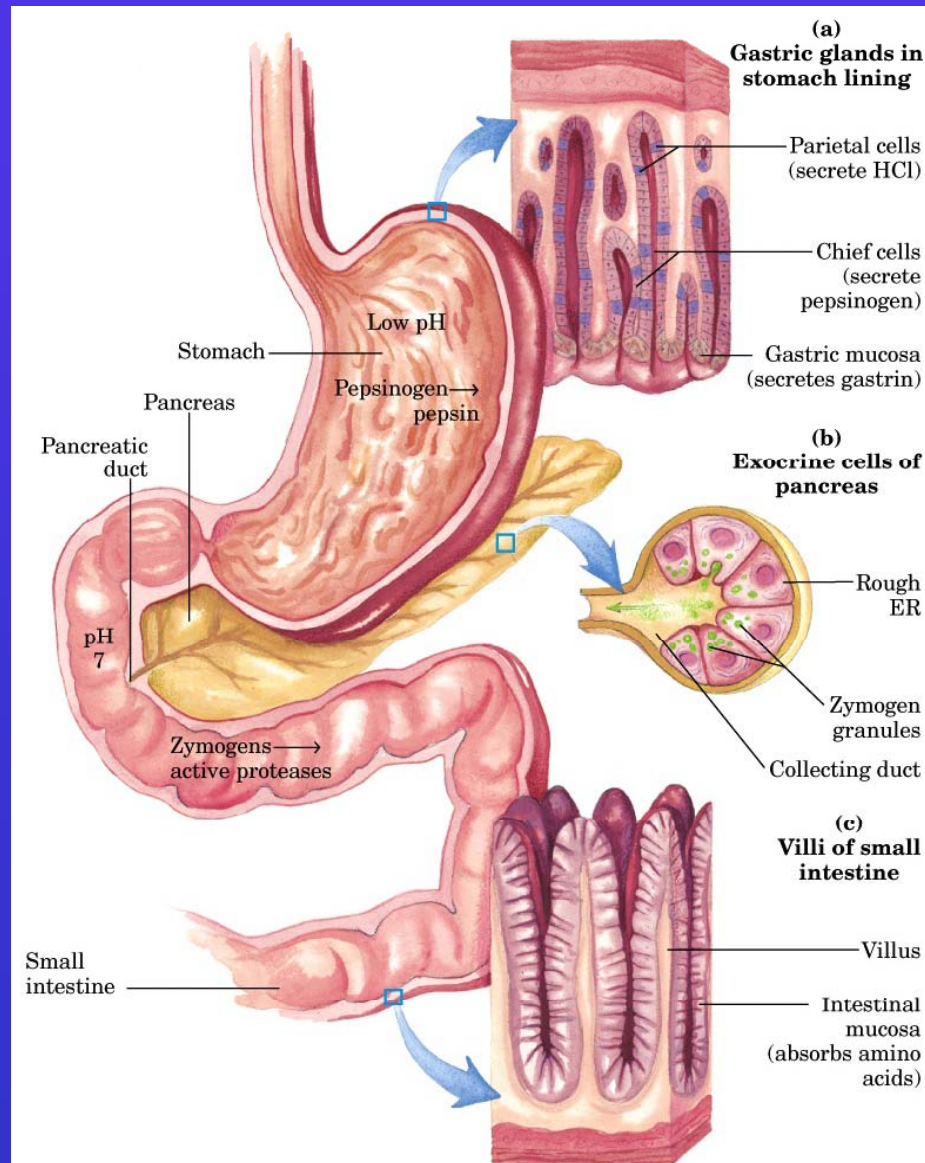
Degradazione delle proteine



Gli zimogeni



Degradazione delle proteine



Degradazione intracellulare delle proteine

- Degradazione lisosomale – 50 enzimi idrolitici, pH acido.
- È attiva sulle proteine assunte per endocitosi e, in generale, su tutti i costituenti cellulari racchiusi in vacuoli.
- La degradazione lisosomiale è non selettiva, ma in condizioni di digiuno prolungato vengono importate solo le proteine citosoliche contenenti il peptide KFERQ

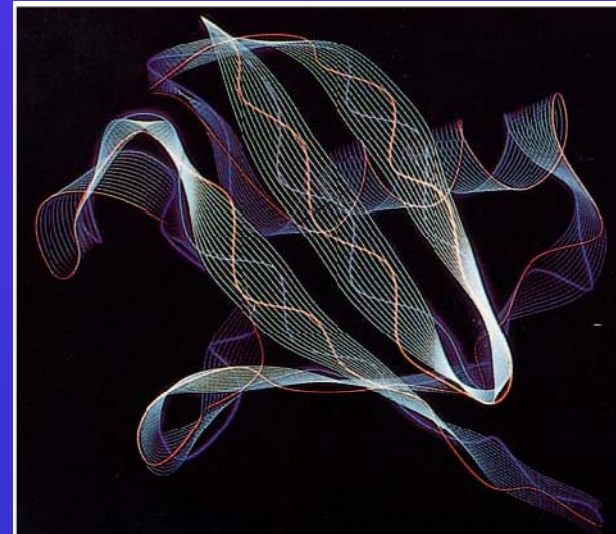
Degradazione intracellulare delle proteine ubiquitina-dipendente

La degradazione può avvenire
Tramite un processo che richiede ATP,
Indipendente dai lisosomi

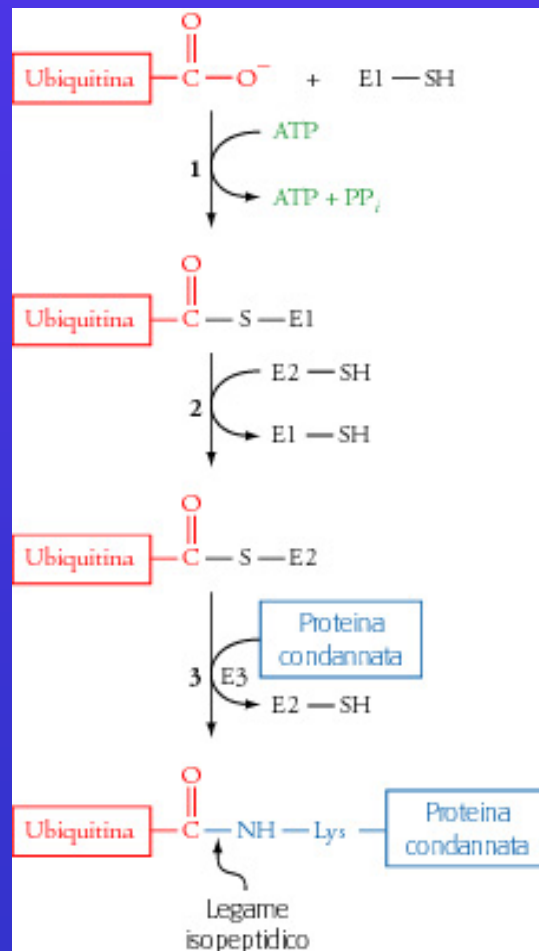
Ubiquitina – 76 residui

Le proteine sono marcate per essere
Degradate tramite un legame covalente
Con l'ubiquitina

Tutti gli eucarioti possiedono ubiquitina



Degradazione intracellulare delle proteine ubiquitina-dipendente



Più molecole di ubiquitina si legano formando delle lunghe catene (fino a 50 molecole), con legami tra la catena laterale del residuo lys 48 e il c-terminale dell'ubiquitina successiva

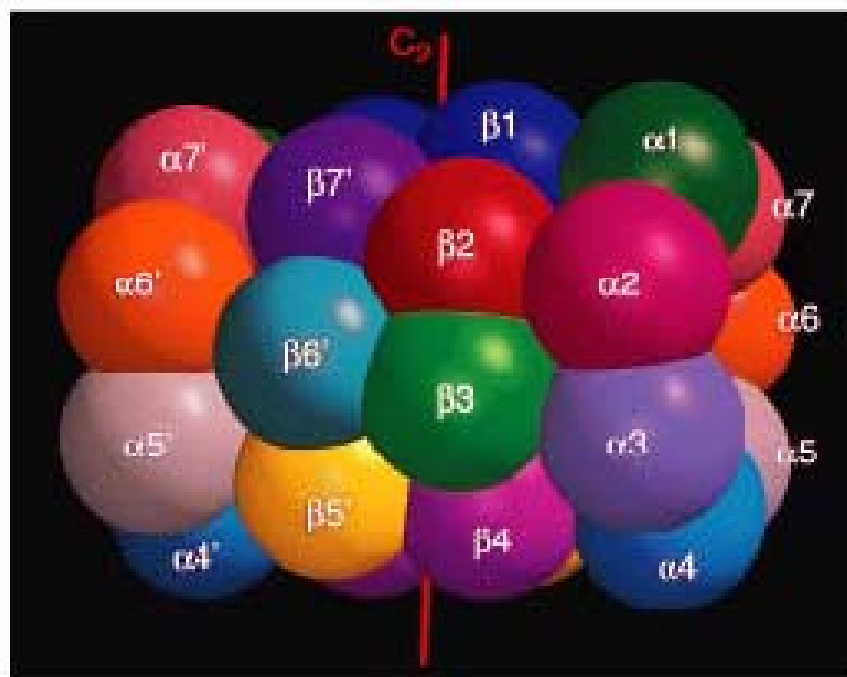
Il proteasoma

Le proteine ubiquitinate vengono degradate tramite un processo ATP-dipendente da un complesso proteico ad alto peso molecolare noto come proteasoma 26S (2000 kD, 26S). Si può riconoscere una struttura di base di forma cilindrica, cava, denominata proteasoma 20S.

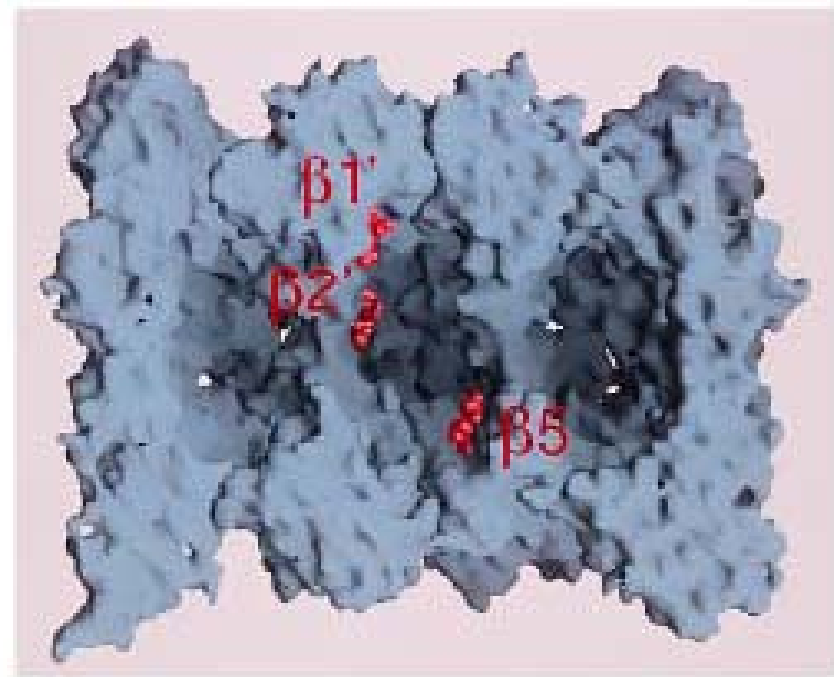
Questo è costituito da sette tipi di tipi di subunità α e da sette tipi di subunità β , dotate di attività proteolitica

Prodotti di circa 8 aminoacidi

Il proteasoma di lievito

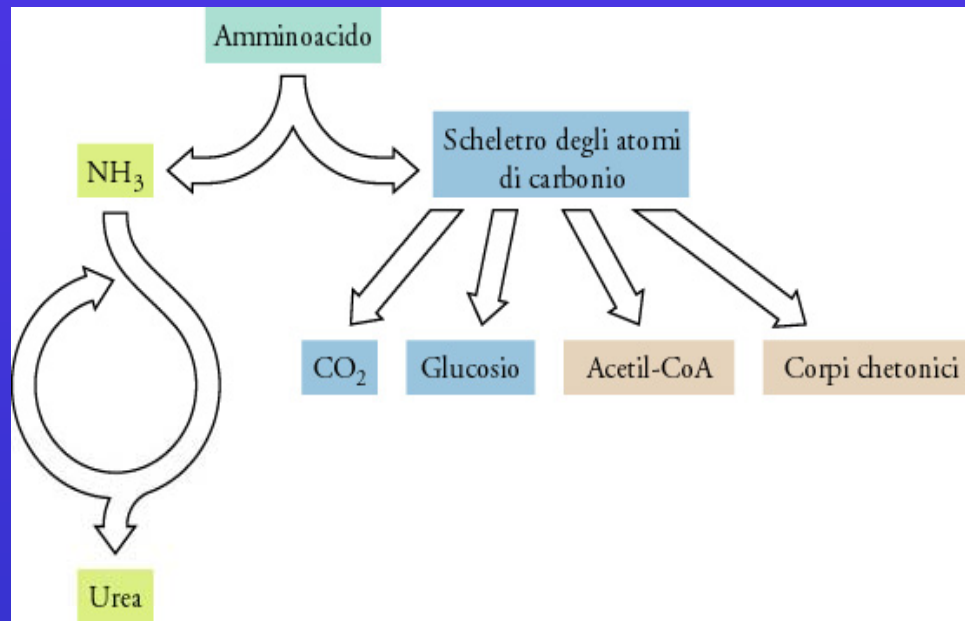


(a)



(b)

La degradazione degli aminoacidi

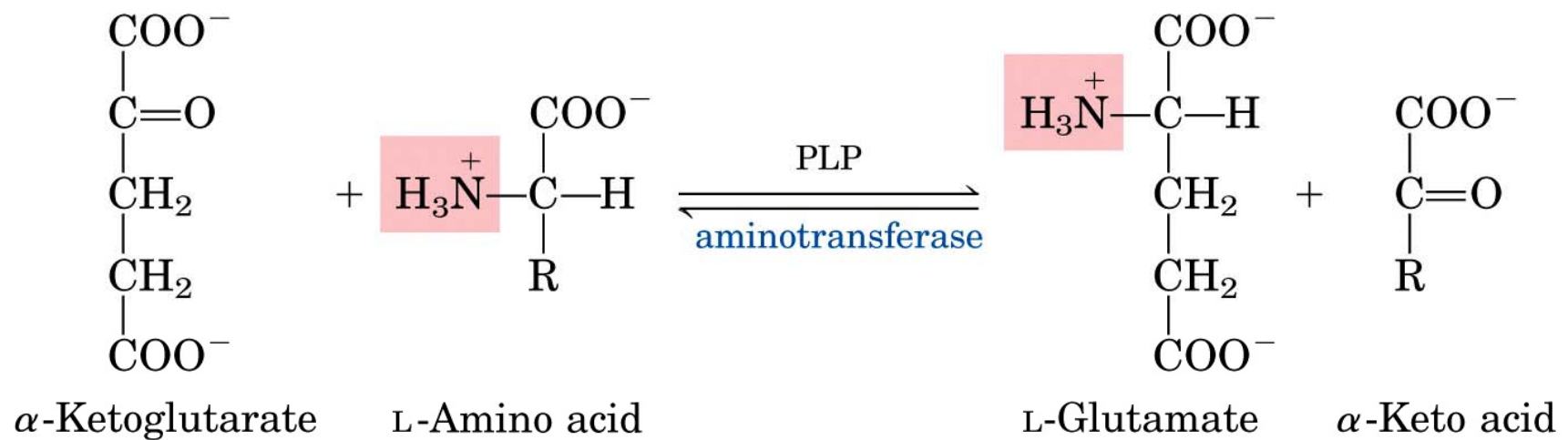


La via degradativa di tutti gli aminoacidi richiede l'allontanamento del gruppo aminico.

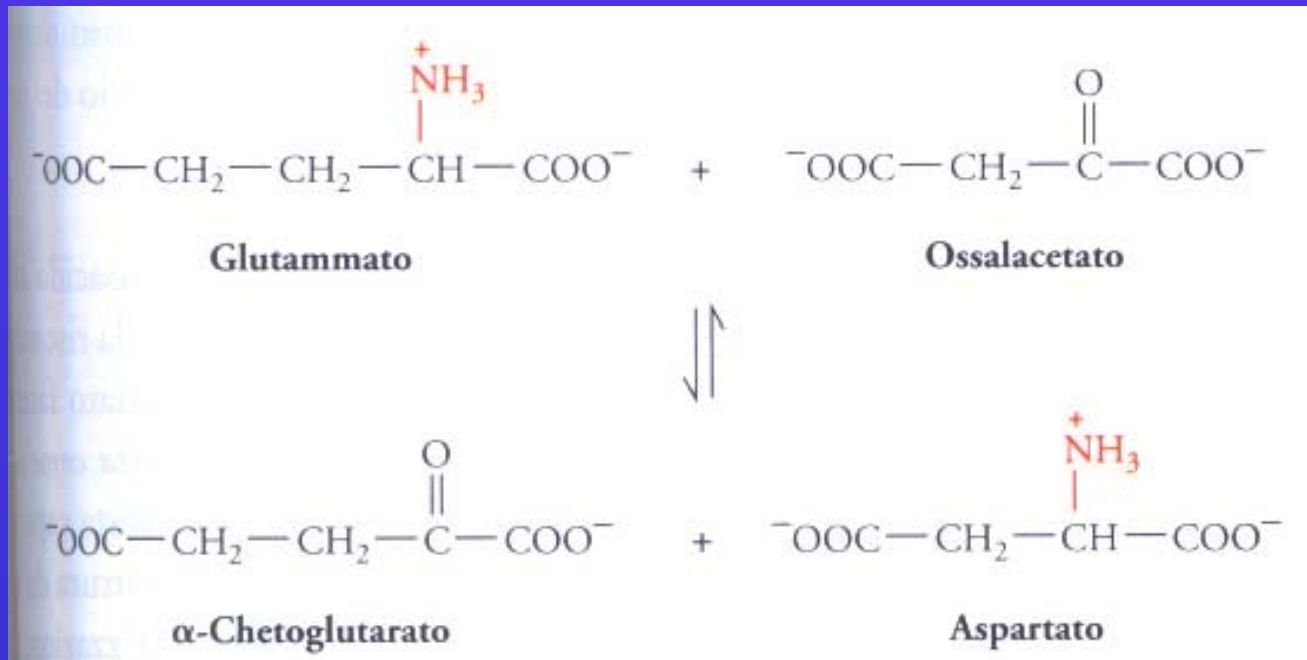
Lo scheletro carbonioso viene così utilizzato nel ciclo di Krebs o nella gluconeogenesi

Parte dell'azoto aminico viene riutilizzato in processi biosintetici; parte è escreta come tale a livello renale e parte sotto forma di urea.

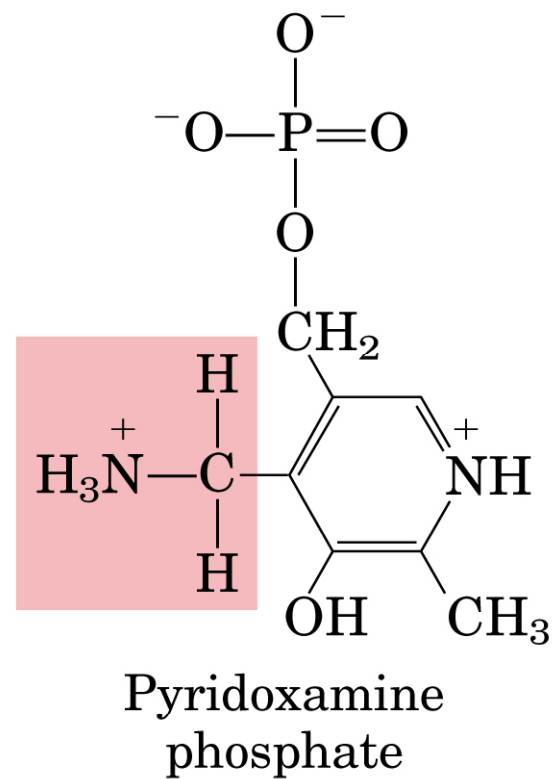
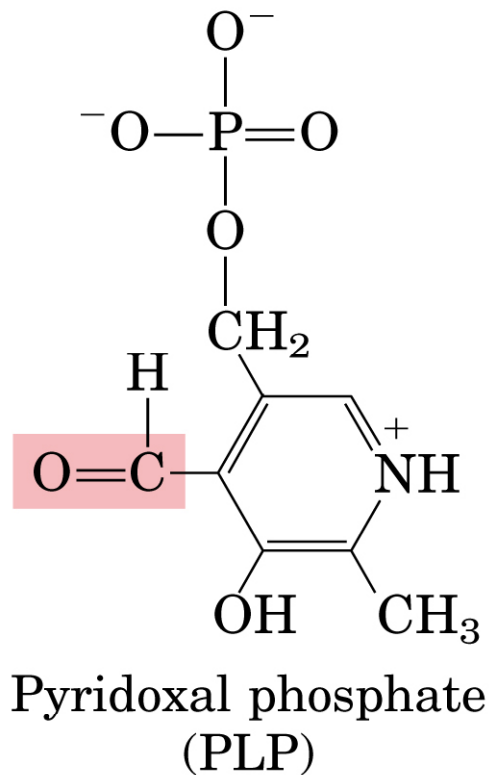
Reazioni di transaminazione



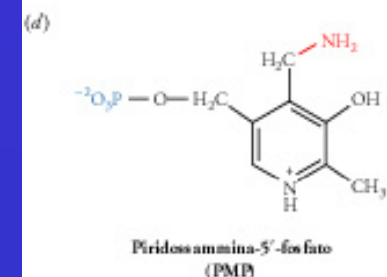
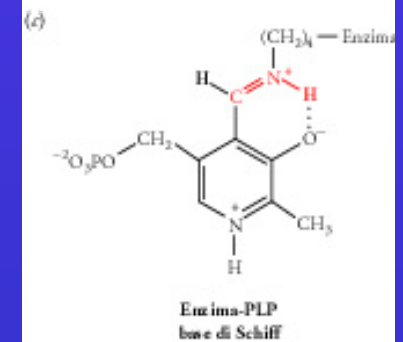
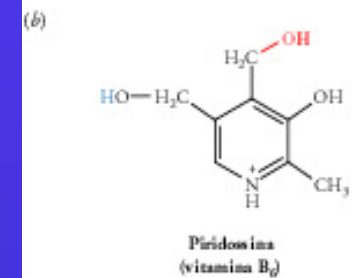
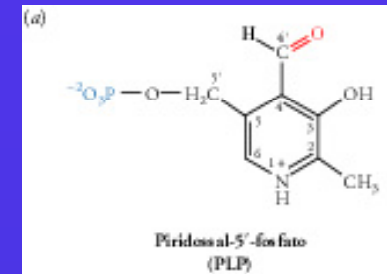
Reazioni di transaminazione



Il piridossal fosfato



(a)

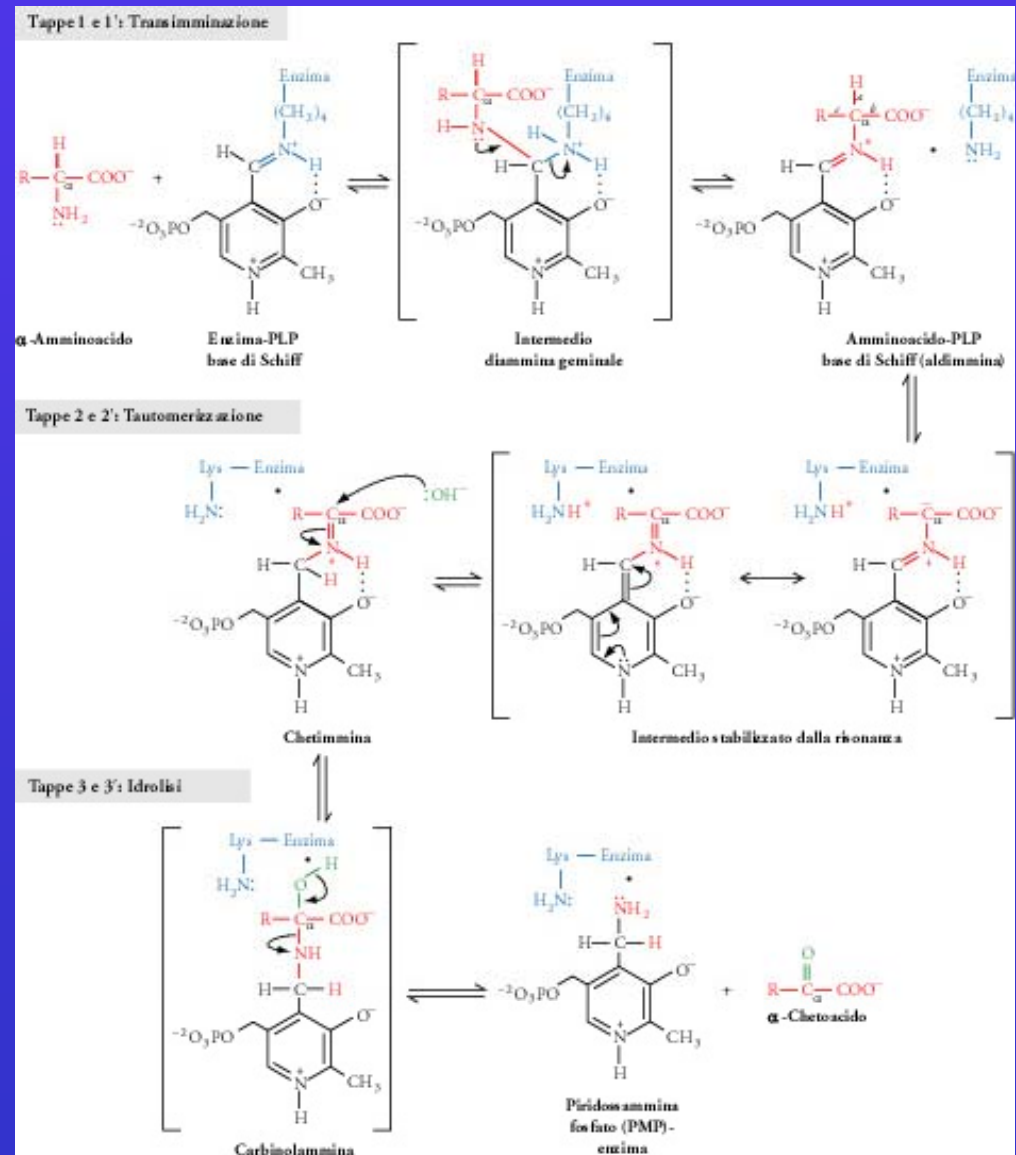


Meccanismo della transamminazione

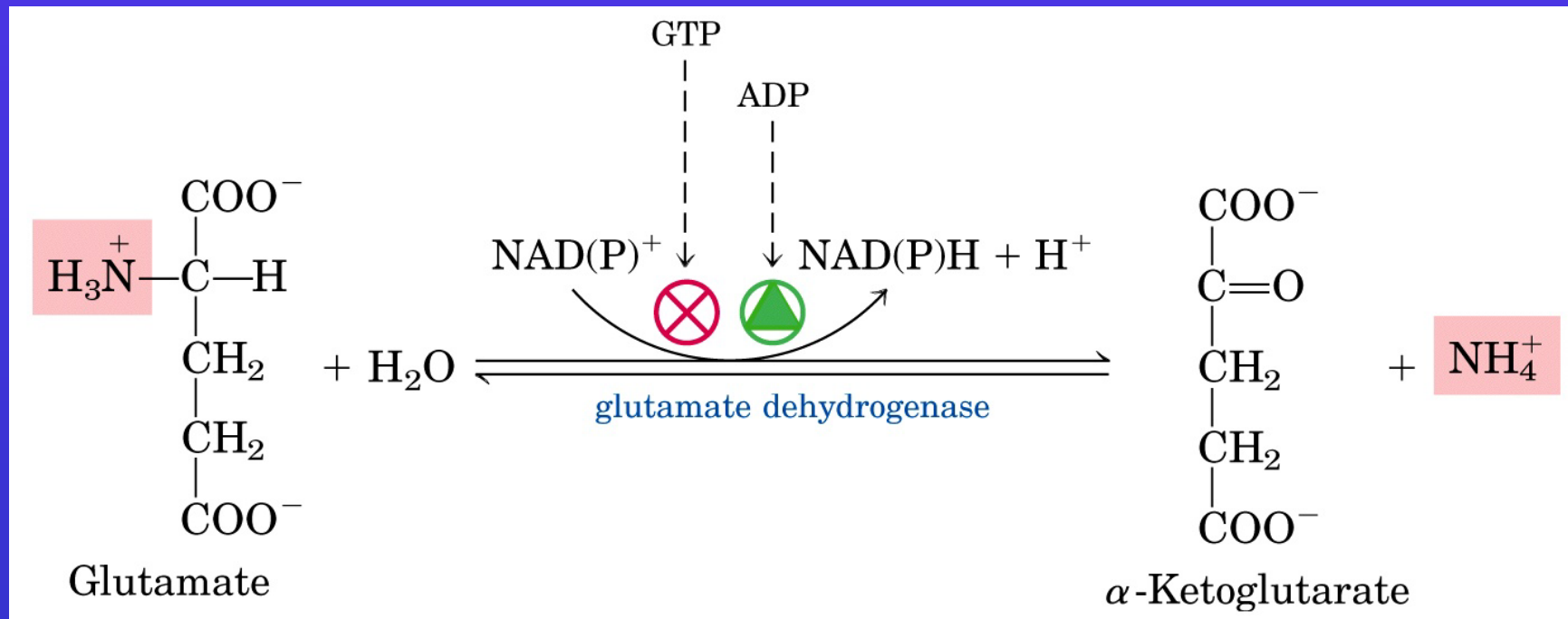
- Transimminazione

- Tautomerizzazione

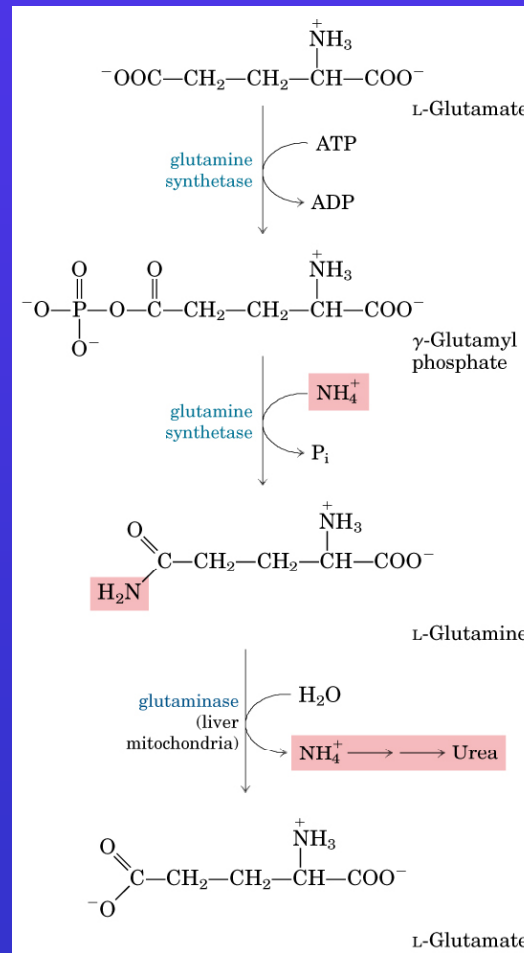
- idrolisi



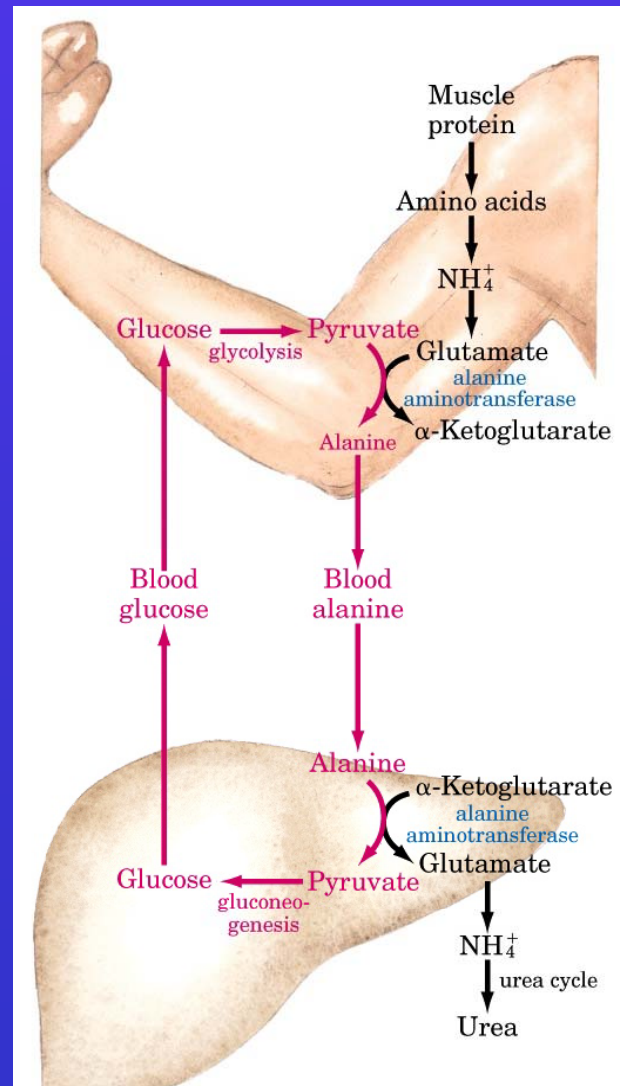
Deaminazione ossidativa



La glutammina trasporta ammoniaca attraverso il sangue



L'alanina trasporta l'ammoniaca dal muscolo al fegato

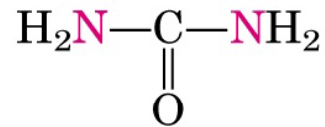


Escrezione dell'azoto



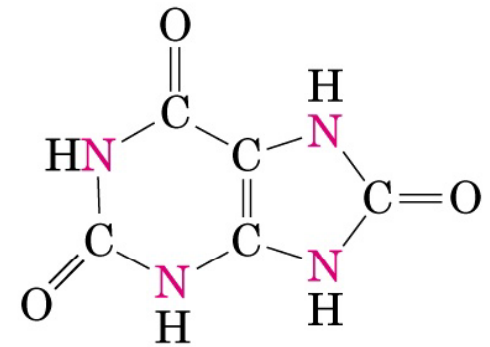
Ammonia (as ammonium ion)

Ammonotelic animals:
most aquatic vertebrates,
such as bony fishes and
the larvae of amphibia



Urea

Ureotelic animals:
many terrestrial
vertebrates; also sharks



Uric acid

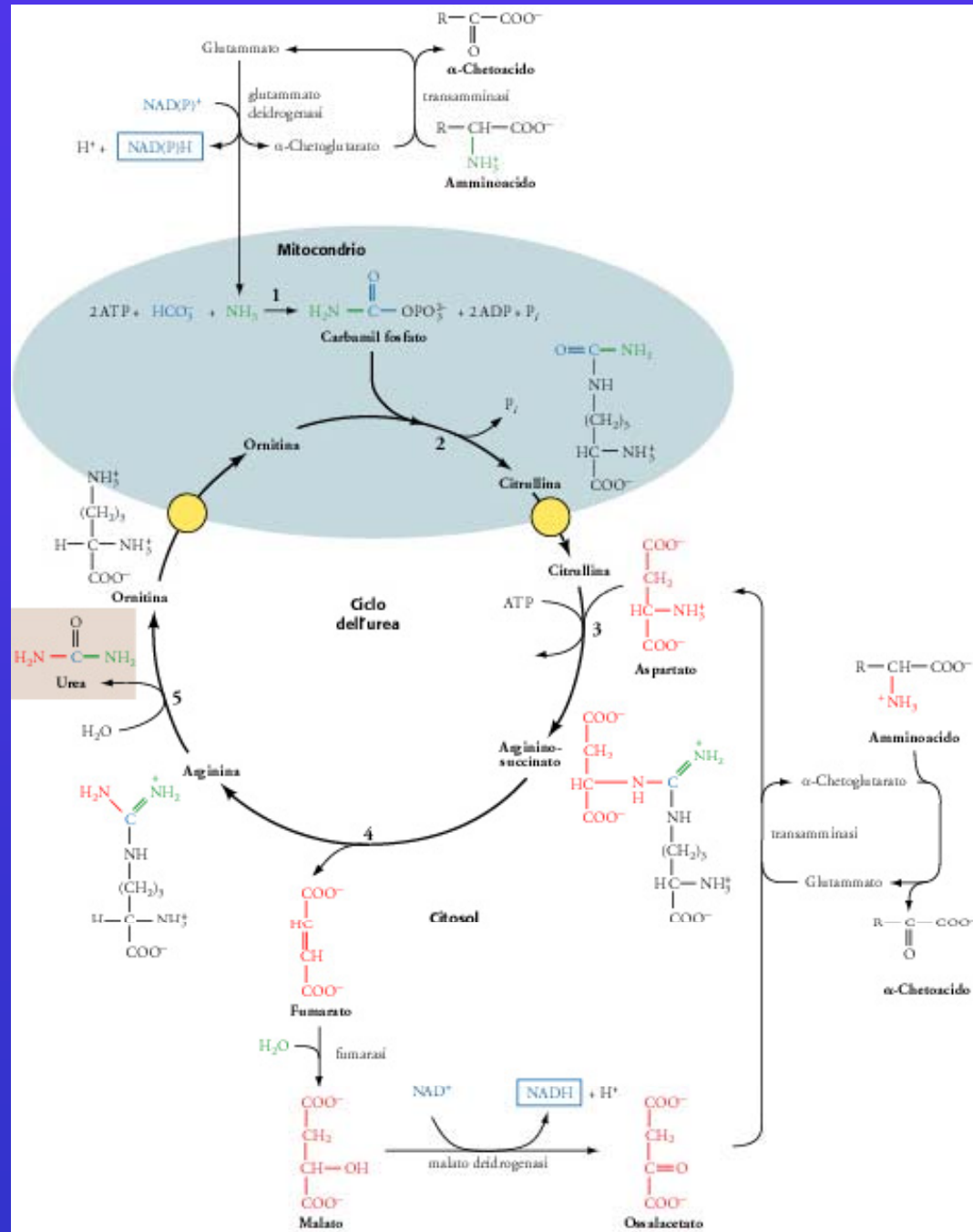
Uricotelic animals:
birds, reptiles

(b)

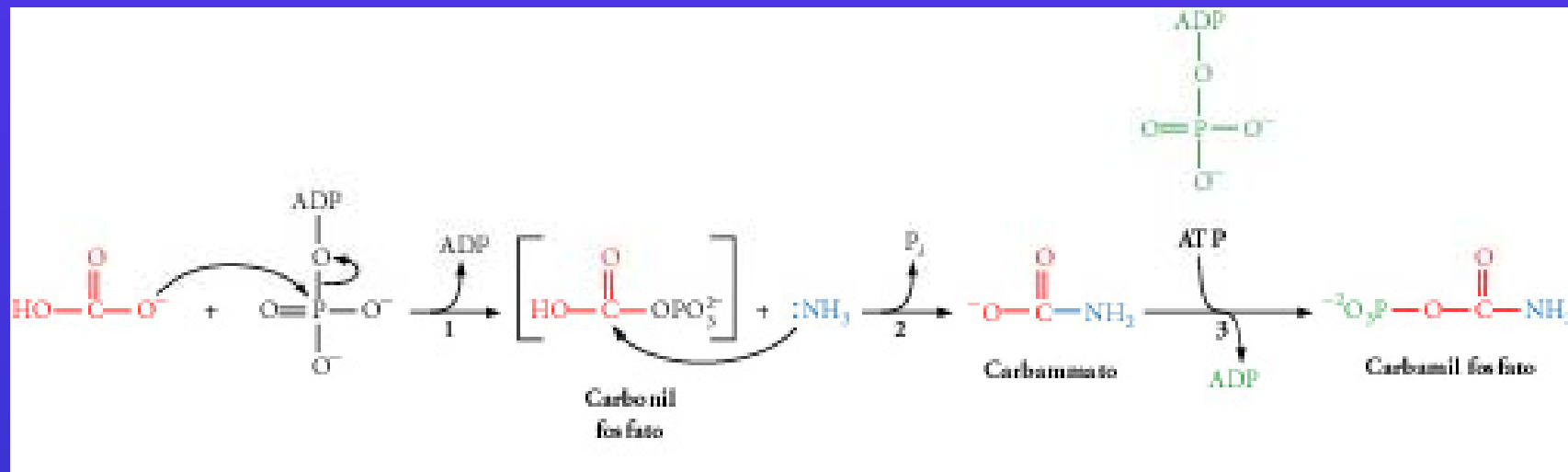
Il ciclo dell'urea

- L'urea viene sintetizzata nel fegato, secreta nel circolo sanguigno, sequestrata dai reni e poi escreta.
- Questo è stato il primo ciclo metabolico ad essere compreso (1932).
- E' composto da 5 reazioni (2 mitocondriali e 3 citoplasmatiche)
- $\text{NH}_3 + \text{HCO}_3^- + \text{aspartato} + 3\text{ATP} \rightarrow$
Urea + fumarato + 2 ADP + 1 AMP + 2Pi + PPI

I due atomi di azoto provengono dall'ammoniaca e dall'aspartato, il carbonio dal bicarbonato

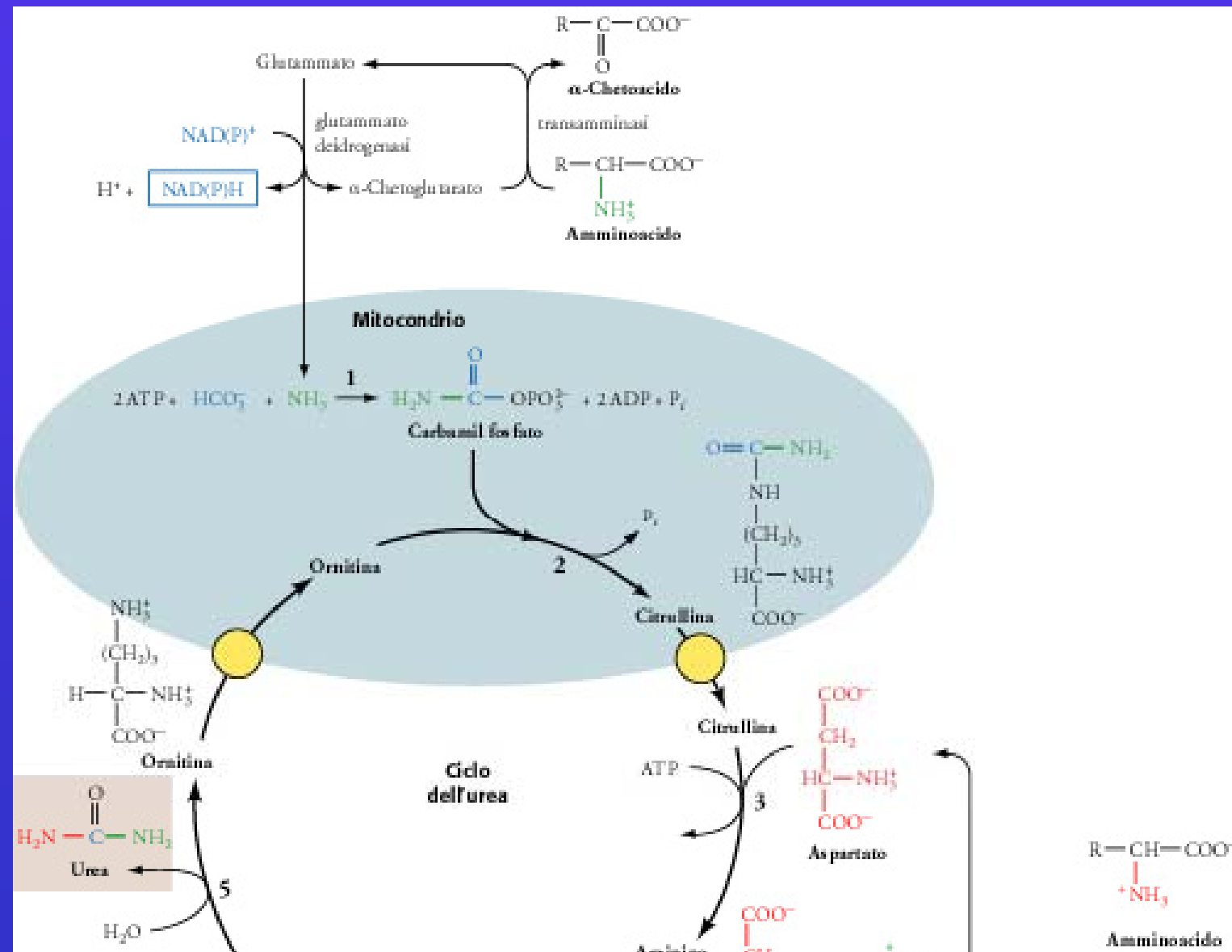


Carbamil fosfato sintetasi

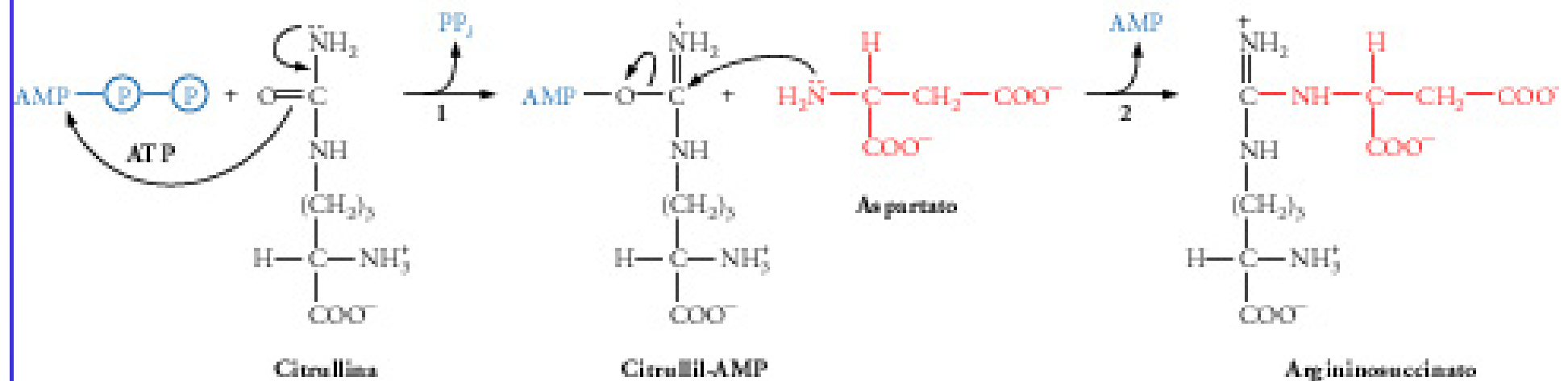


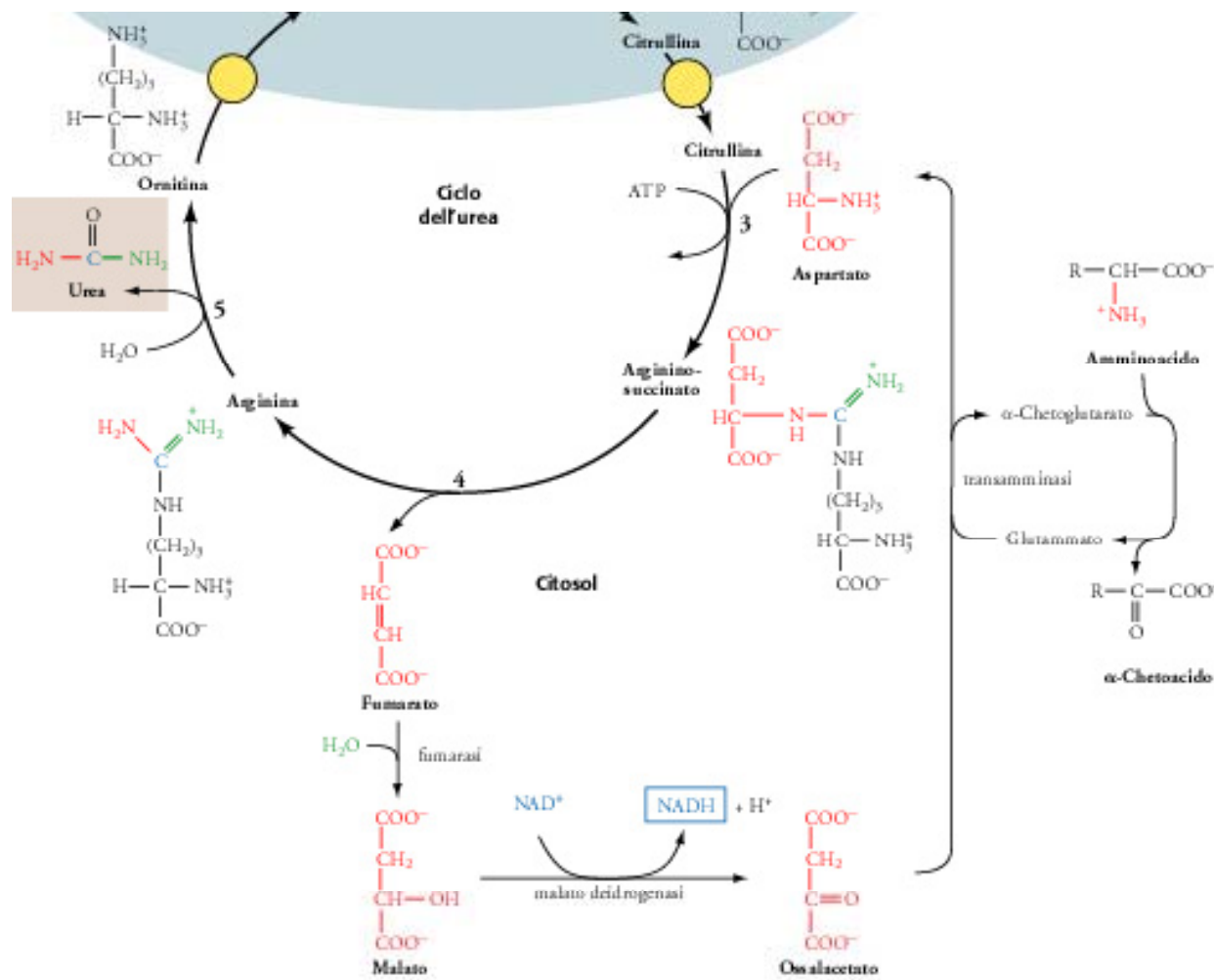
- Questo enzima è il principale sito di regolazione del ciclo (è stimolato da N-acetilglutammato)

Ornitina transcarbamilasi



Argininosuccinato sintetasi

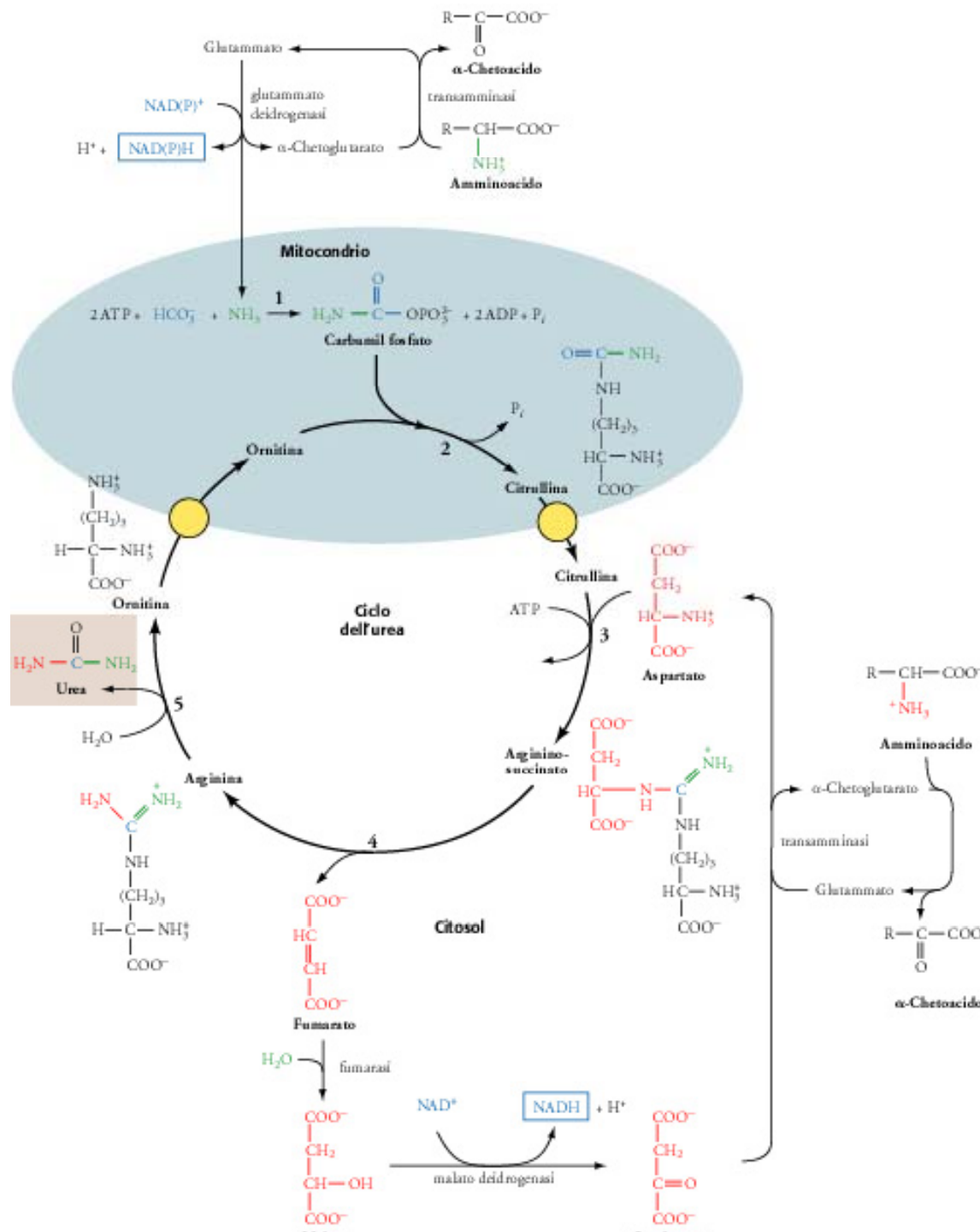




Argininosuccinasi

Arginasi

l'arginina è
il precursore
diretto
dell'urea

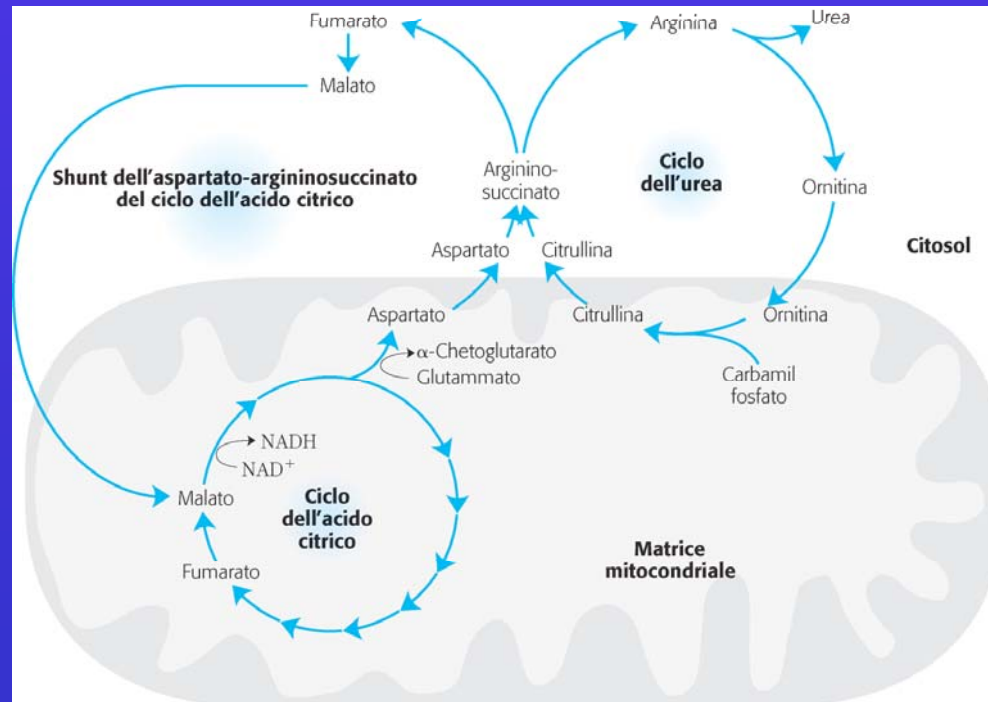


Qual'è il costo energetico del ciclo dell'urea?

Apparentemente:

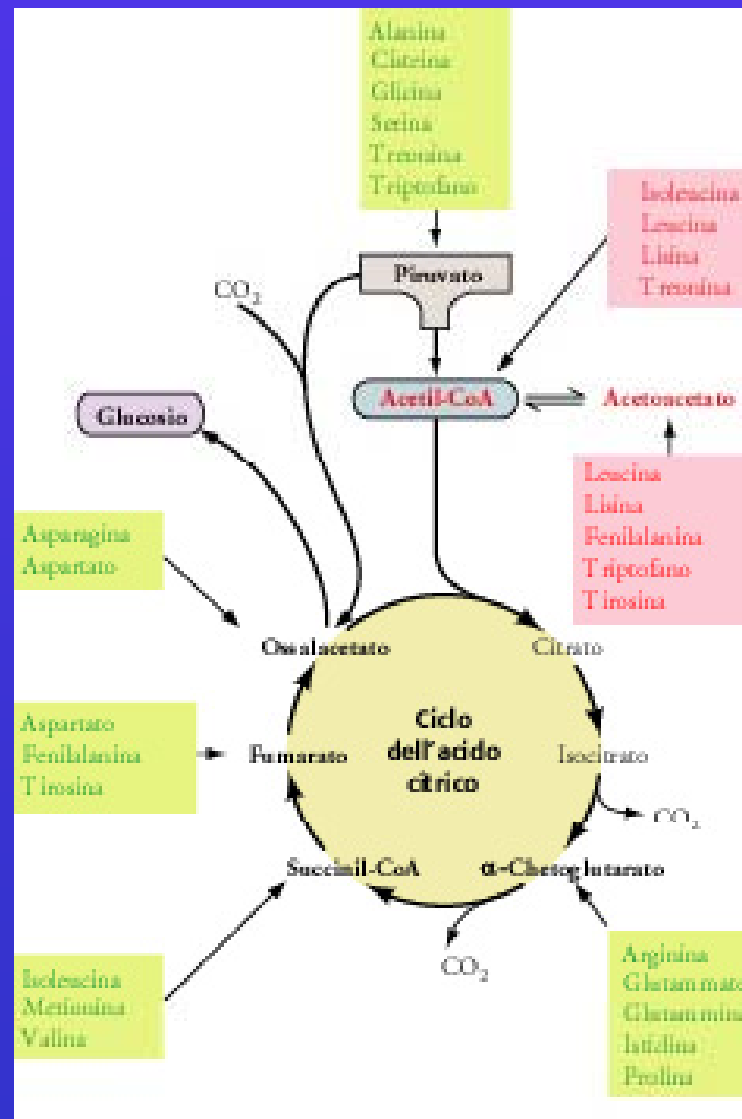


MA:



Inoltre: deaminazione ossidativa

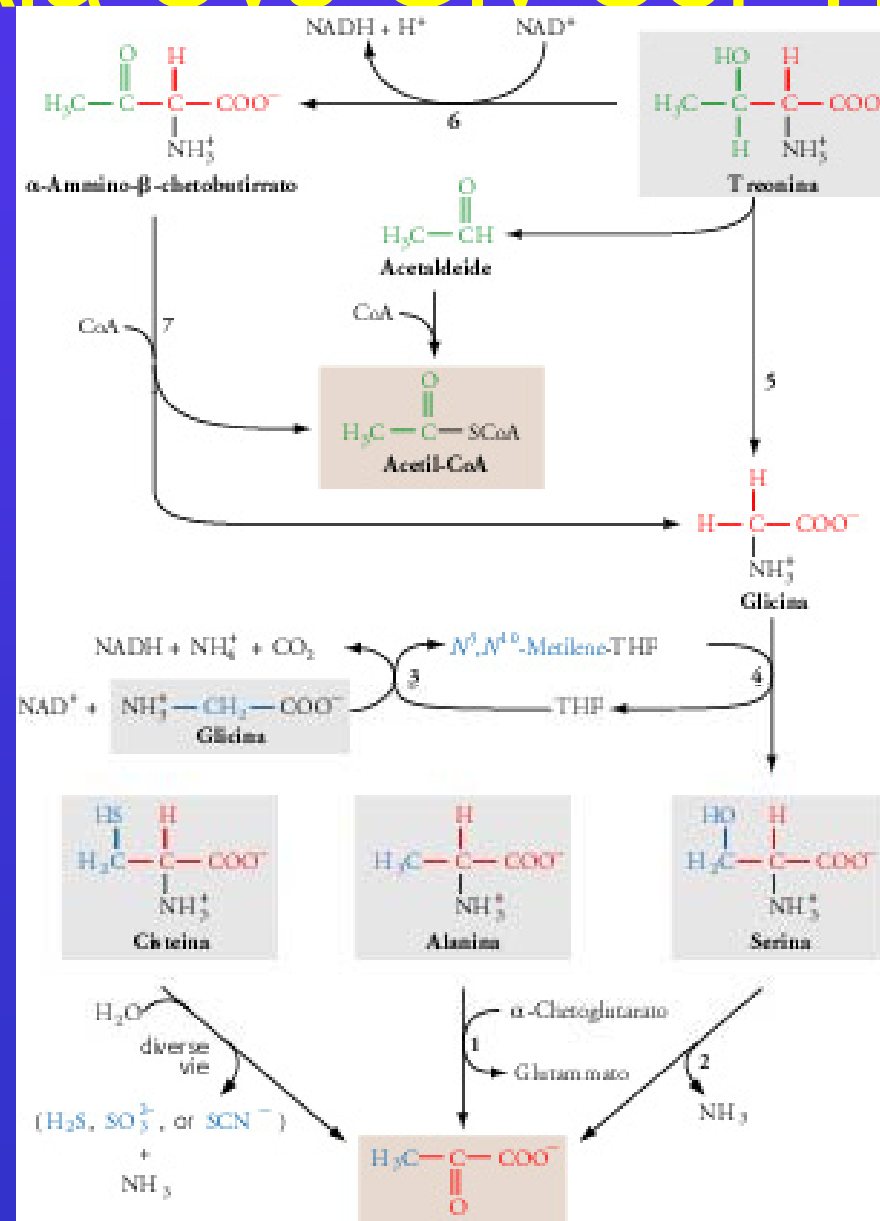
Degradazione degli aminoacidi



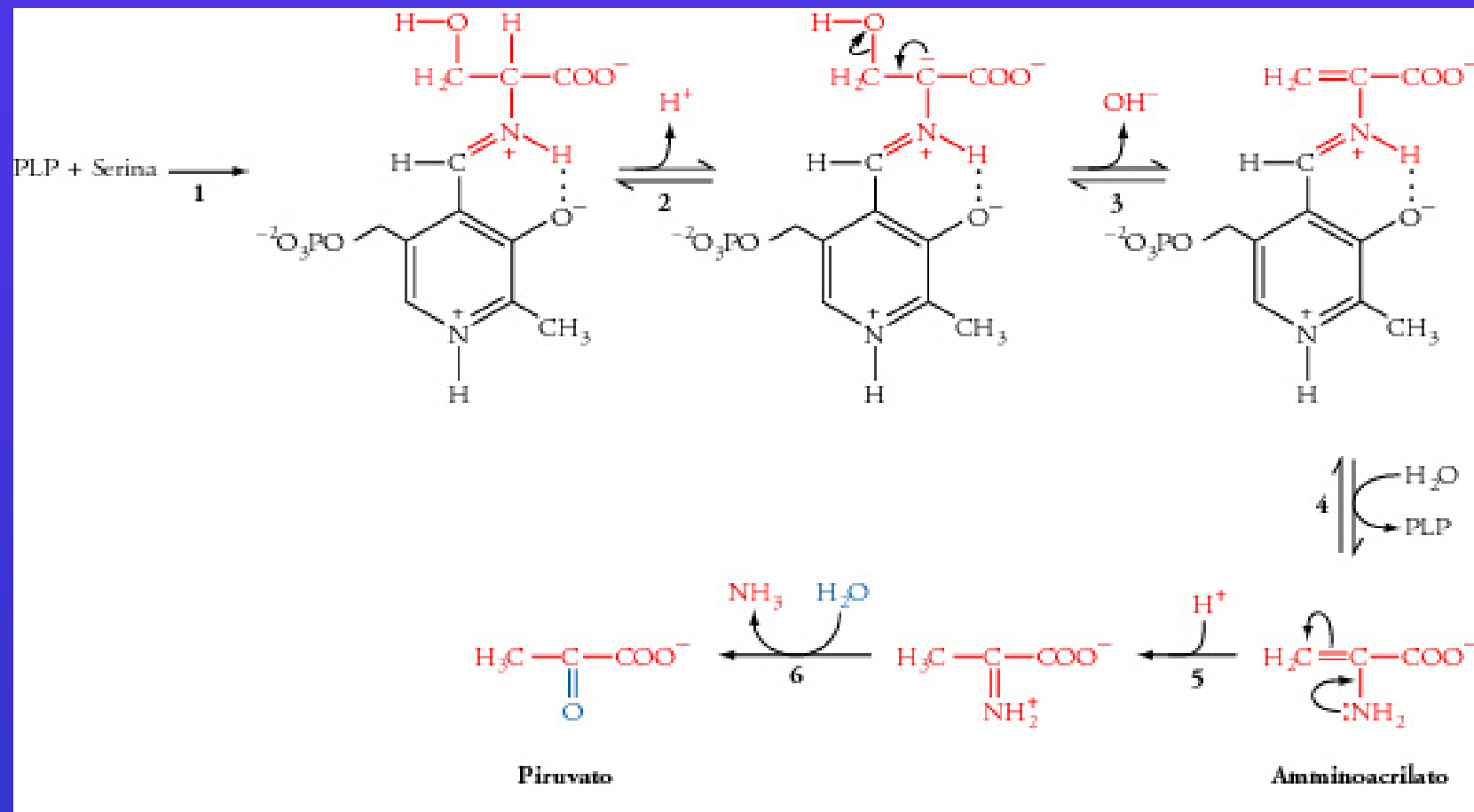
Glucogenici

chetogenici

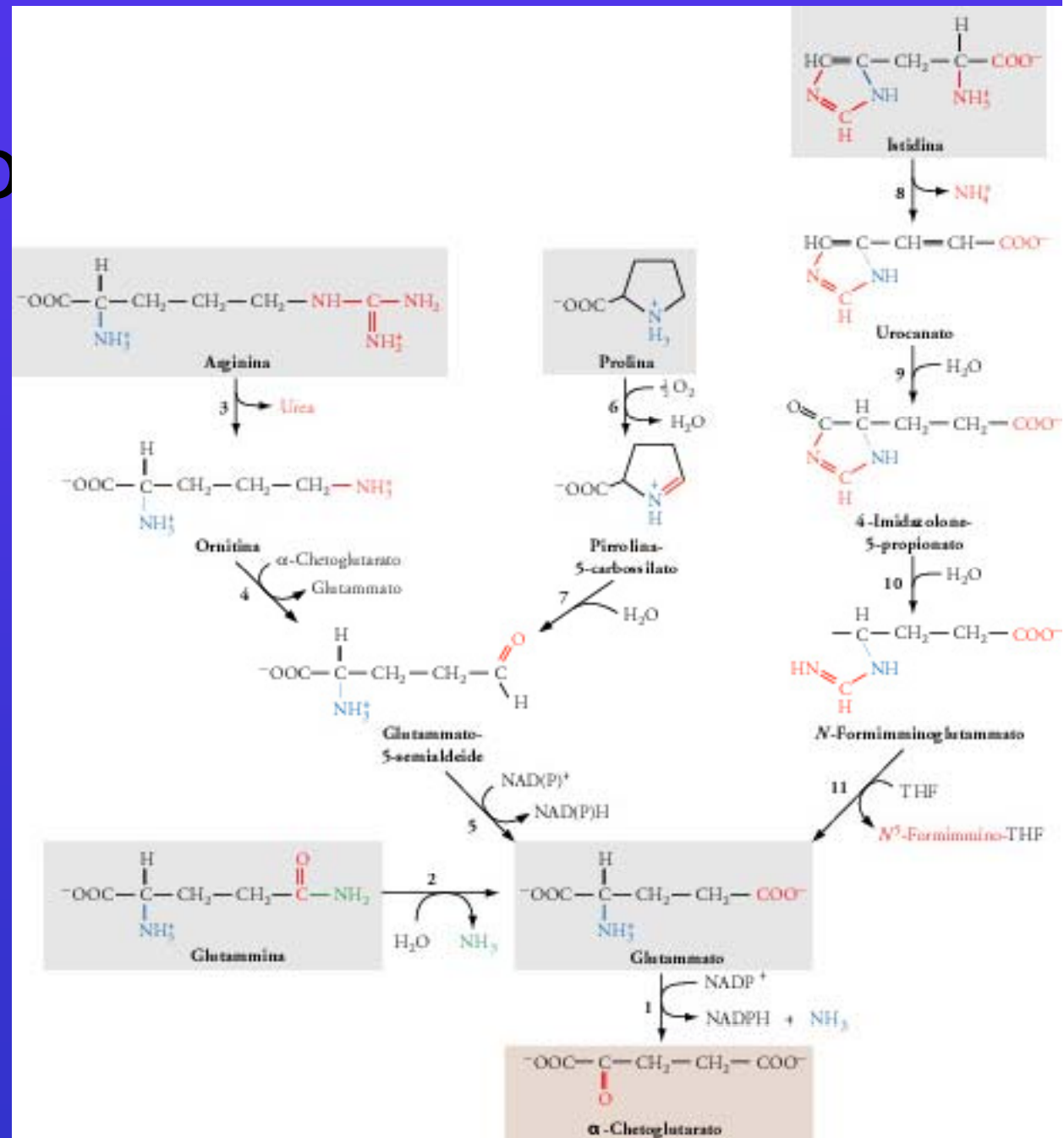
Ala Cys Gly Ser Thr



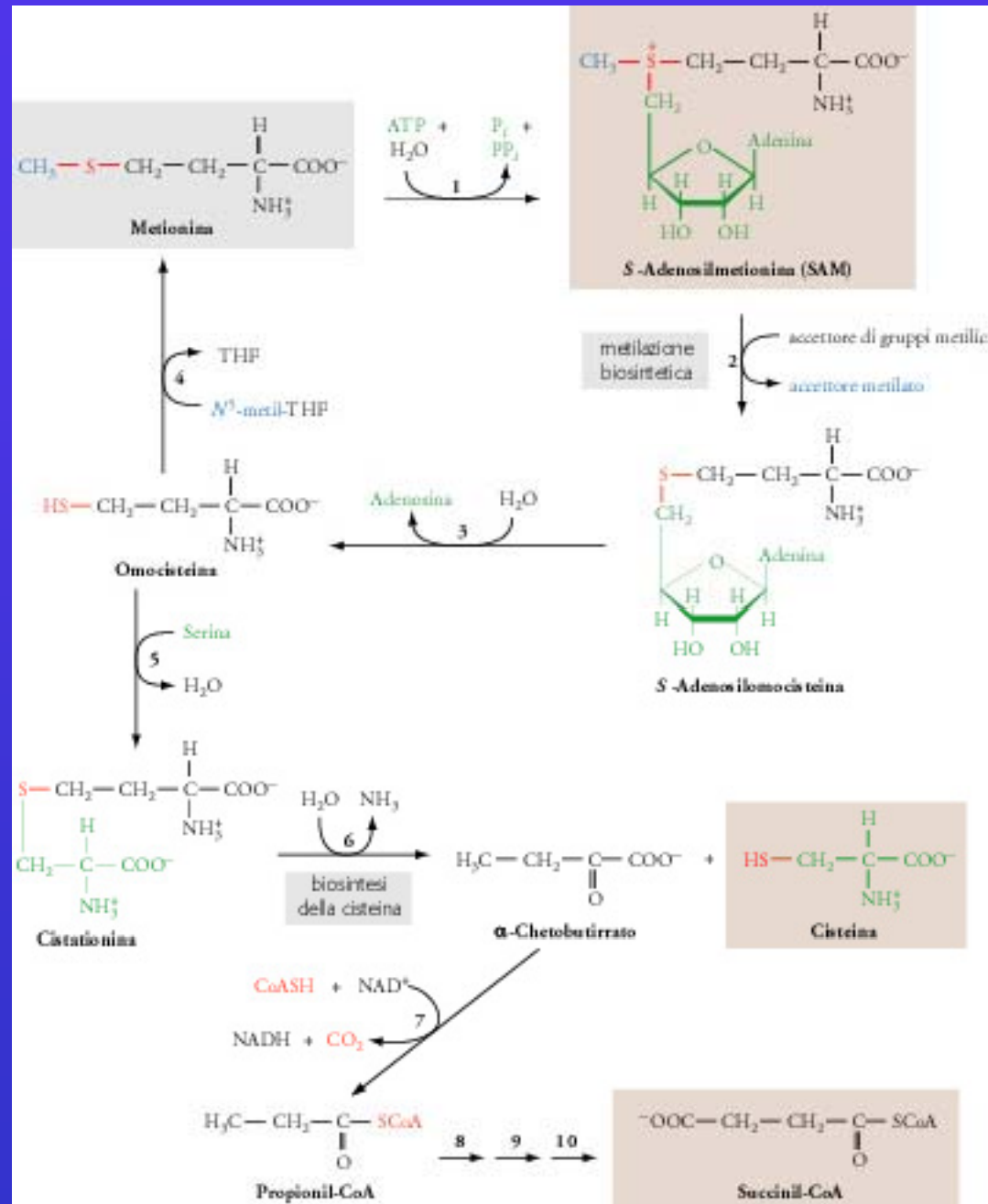
Serina deidratasi



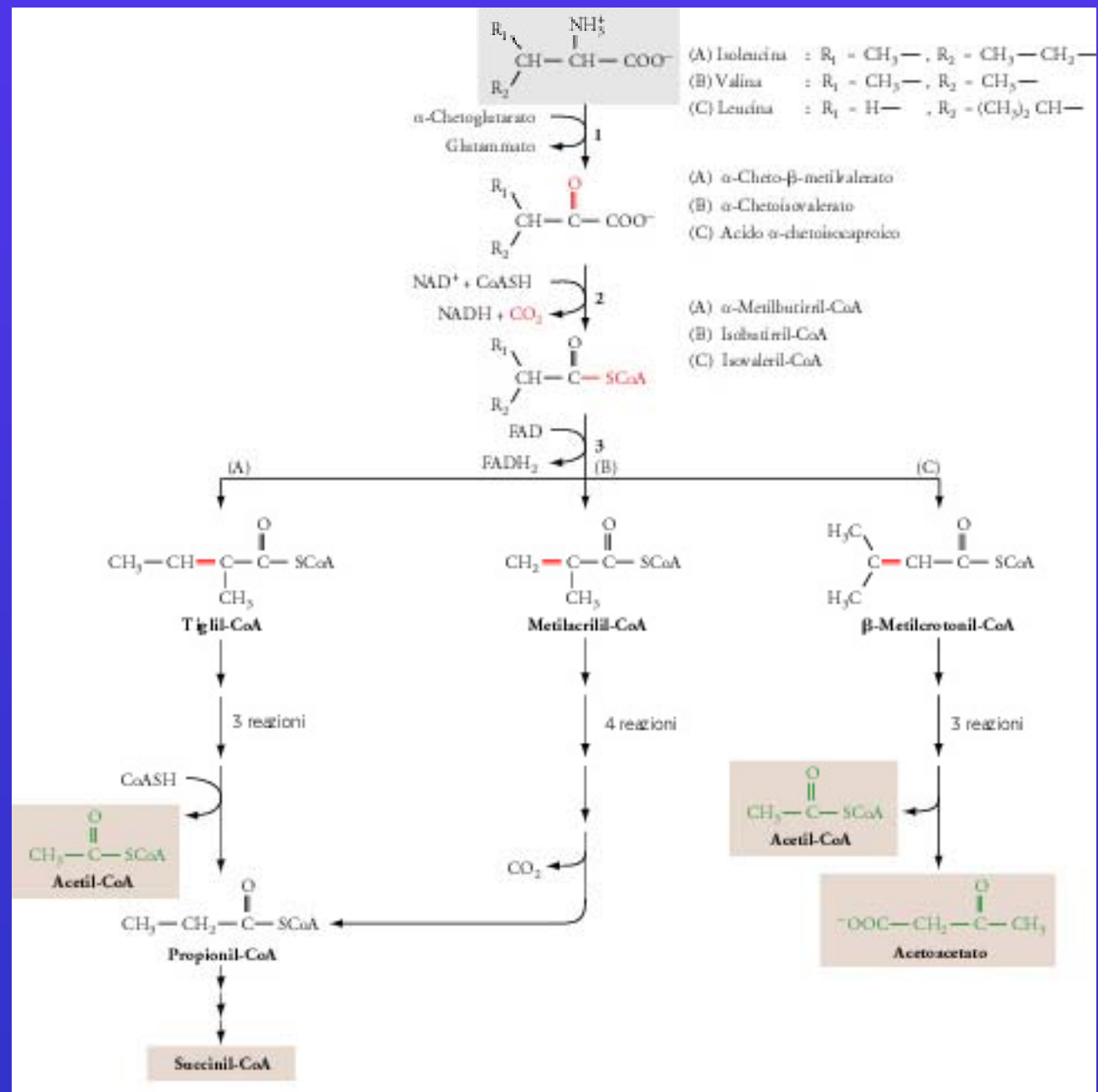
Arg, Glu, Gln, His, Pro



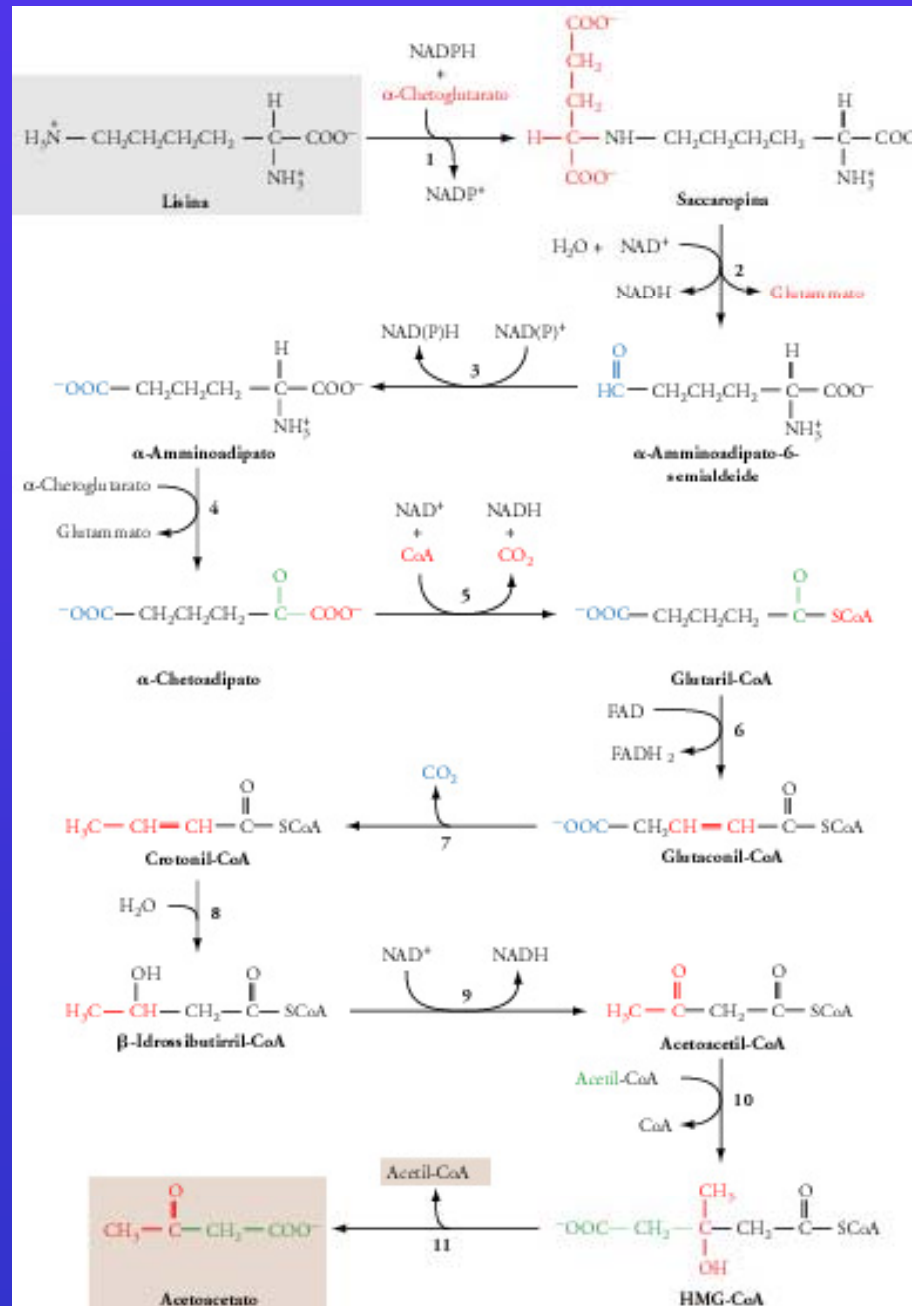
Met

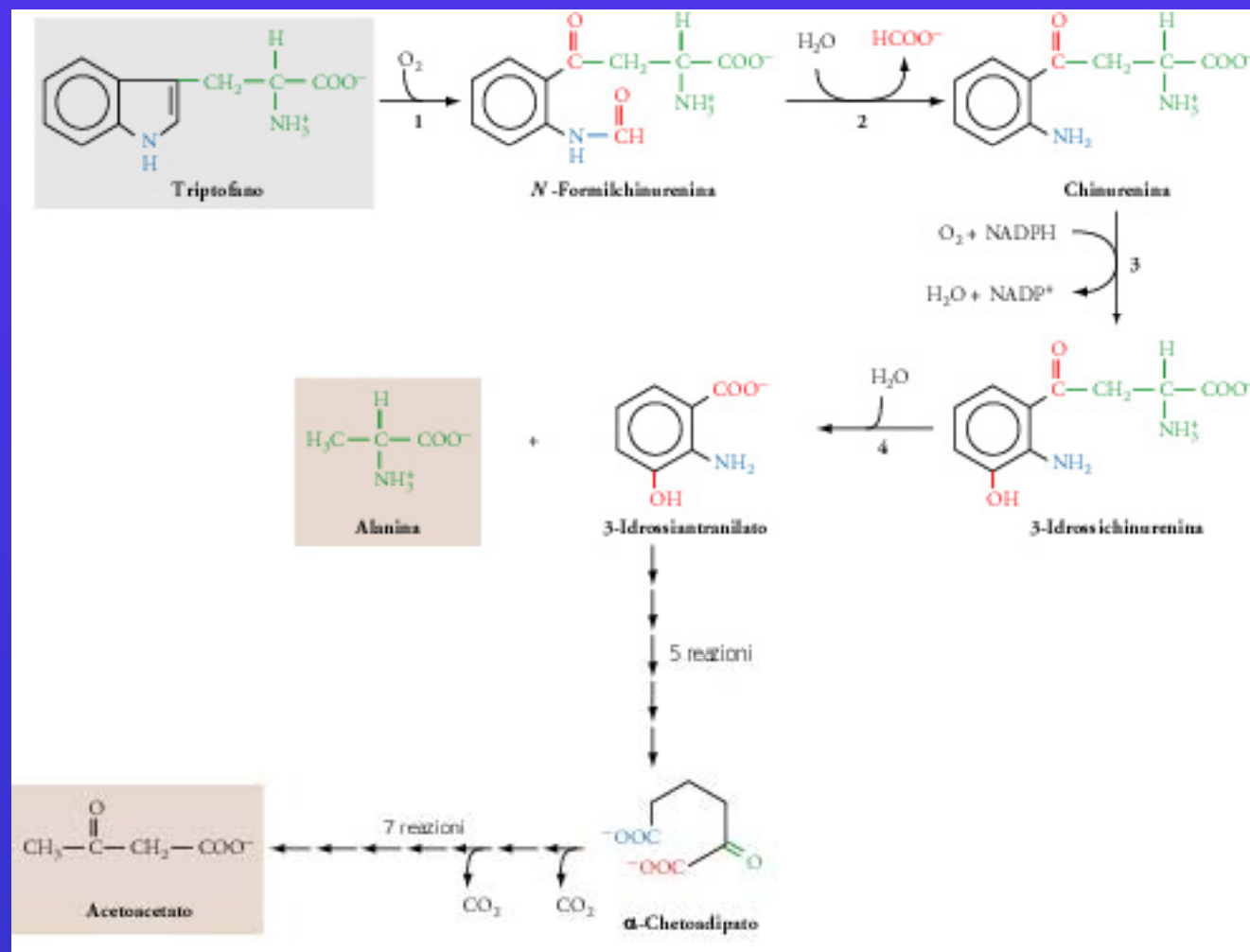


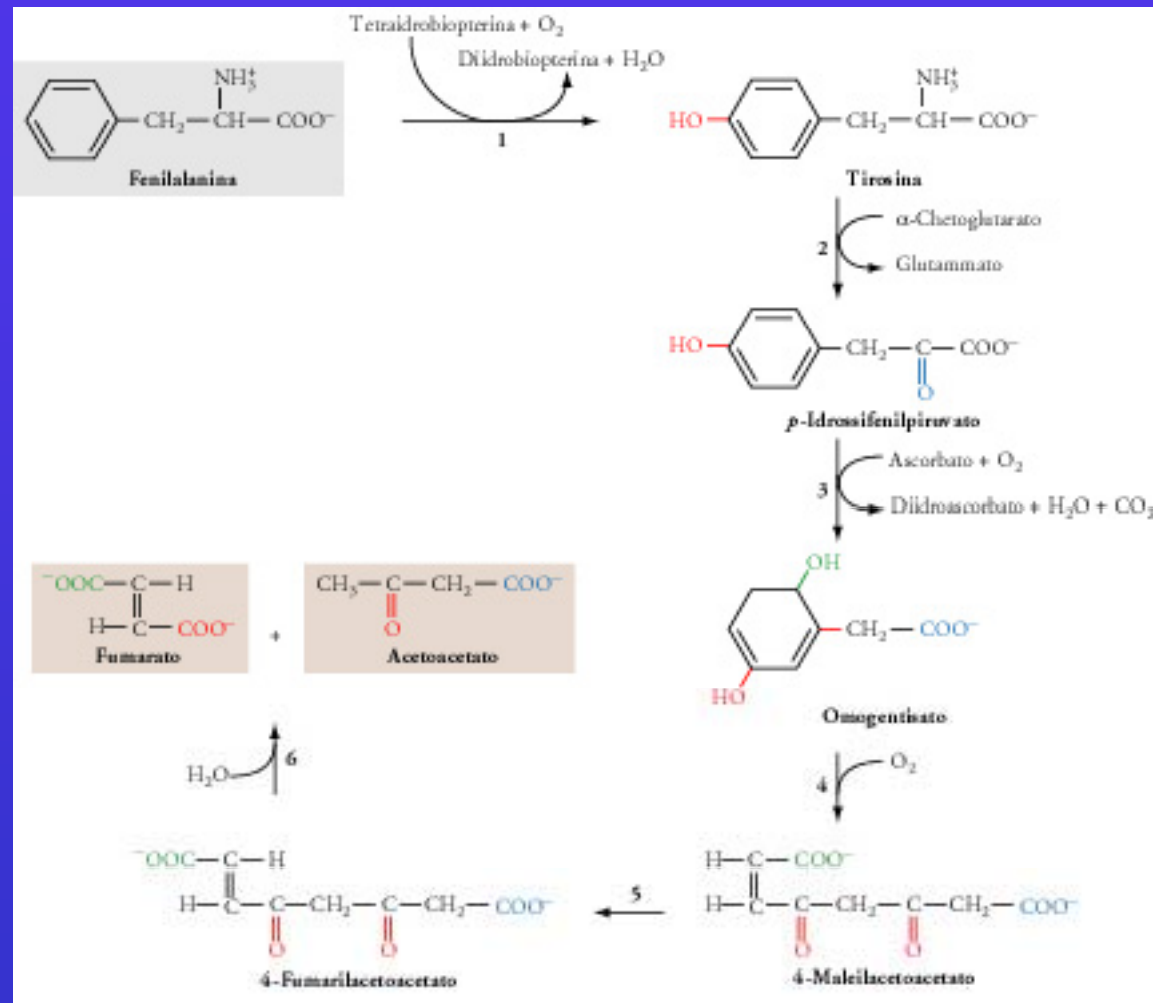
Catena ramificata



Lys e Leu







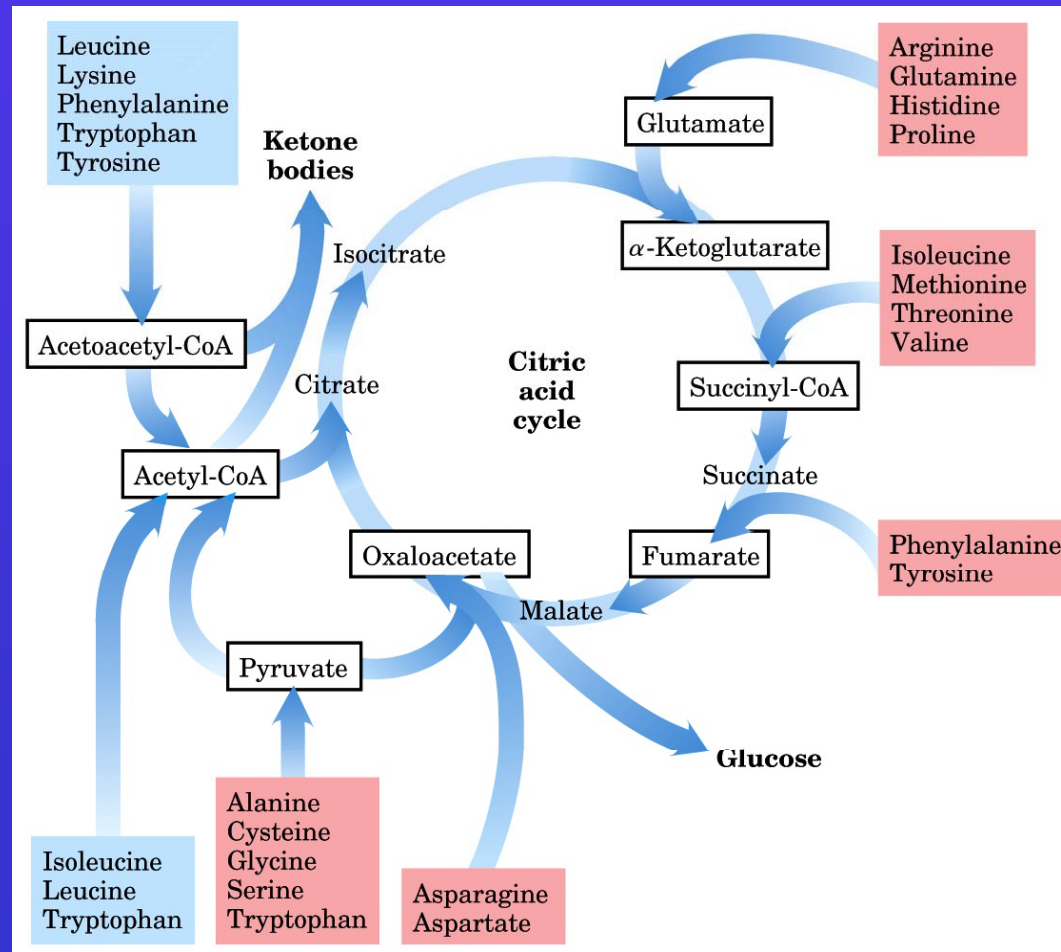


table 18–2

Some Human Genetic Disorders Affecting Amino Acid Catabolism

Medical condition	Approximate incidence (per 100,000 births)	Defective process	Defective enzyme	Symptoms and effects
Albinism	3	Melanin synthesis from tyrosine	Tyrosine 3-mono- oxygenase (tyrosinase)	Lack of pigmentation; white hair, pink skin
Alkaptonuria	0.4	Tyrosine degradation	Homogentisate 1,2-dioxygenase	Dark pigment in urine; late-developing arthritis
Argininemia	<0.5	Urea synthesis	Arginase	Mental retardation
Argininosuccinic acidemia	1.5	Urea synthesis	Argininosuccinate lyase	Vomiting, convulsions
Carbamoyl phosphate synthetase I deficiency	>0.5	Urea synthesis	Carbamoyl phosphate synthetase I	Lethargy, convulsions, early death
Homocystinuria	0.5	Methionine degradation	Cystathionine β -synthase	Faulty bone develop- ment, mental retardation
Maple syrup urine disease (branched- chain ketoaciduria)	0.4	Isoleucine, leucine, and valine degradation	Branched-chain α -keto acid dehydrogenase complex	Vomiting, convulsions, mental retardation, early death
Methylmalonic acidemia	<0.5	Conversion of propionyl- CoA to succinyl-CoA	Methylmalonyl-CoA mutase	Vomiting, convulsions, mental retardation, early death
Phenylketonuria	8	Conversion of phenyl- alanine to tyrosine	Phenylalanine hydroxylase	Neonatal vomiting; mental retardation