Protein and amino acid metabolism

Protein-rich products

Essential amino acids

- valine, leucine, isoleucine, lysine, methionine, threonine, tryptophan, phenylalanine

Semiessential amino acids

- **arginine** and **histidine**

Proteases

Serine proteases

Cysteine proteases

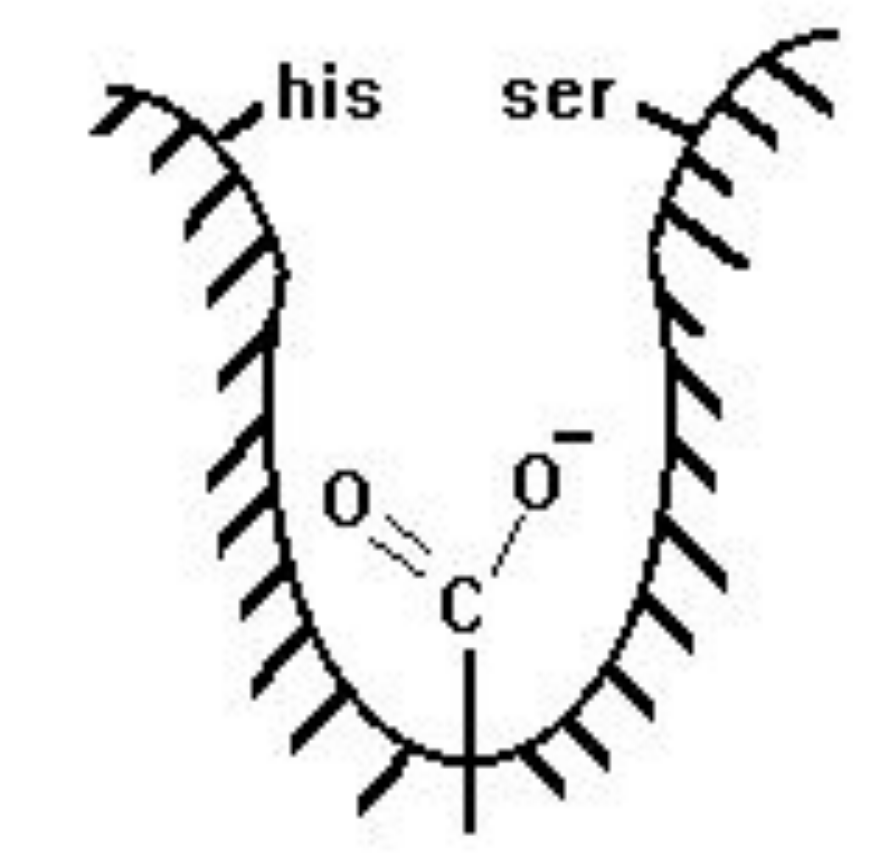
Aspartic proteases

Metalloproteases

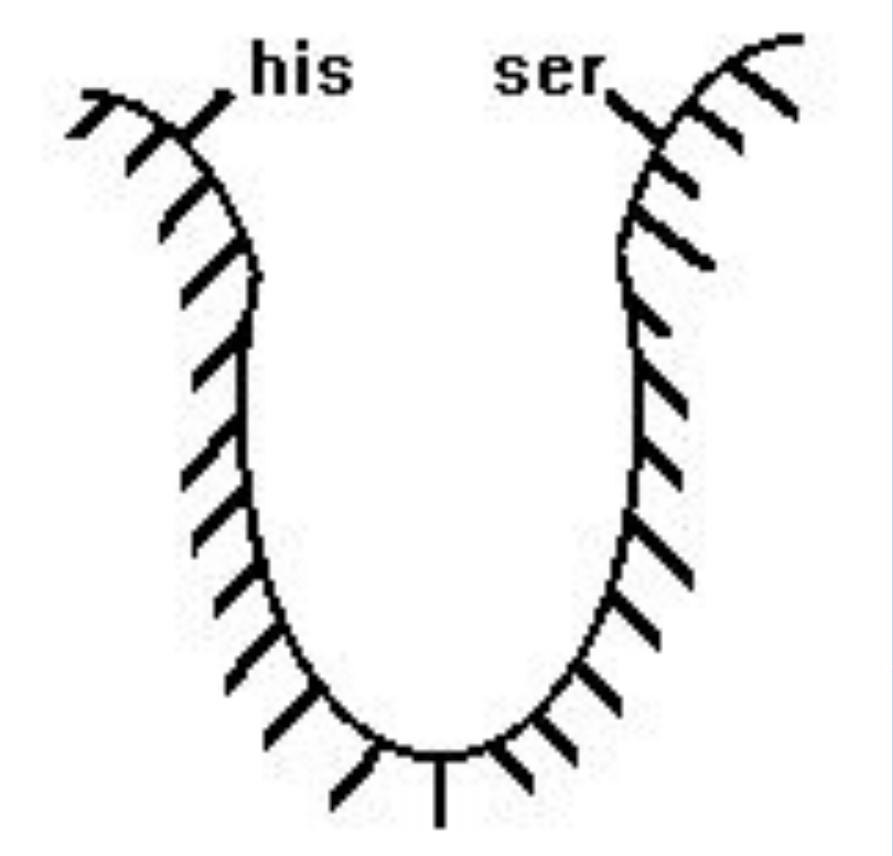
Treonine proteases

Glutamic proteases

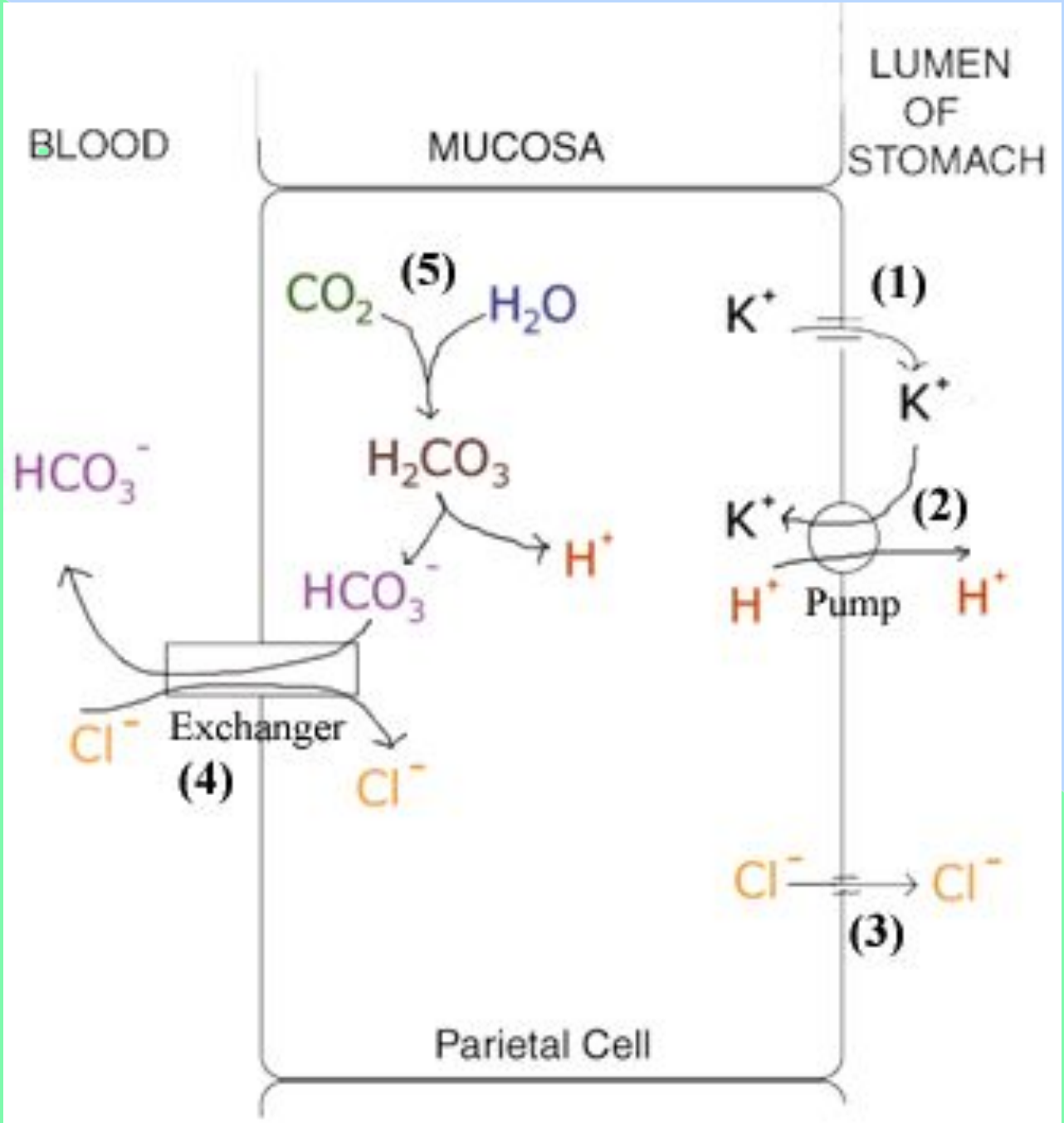
Active site of tripsin



Active site of chymotripsin



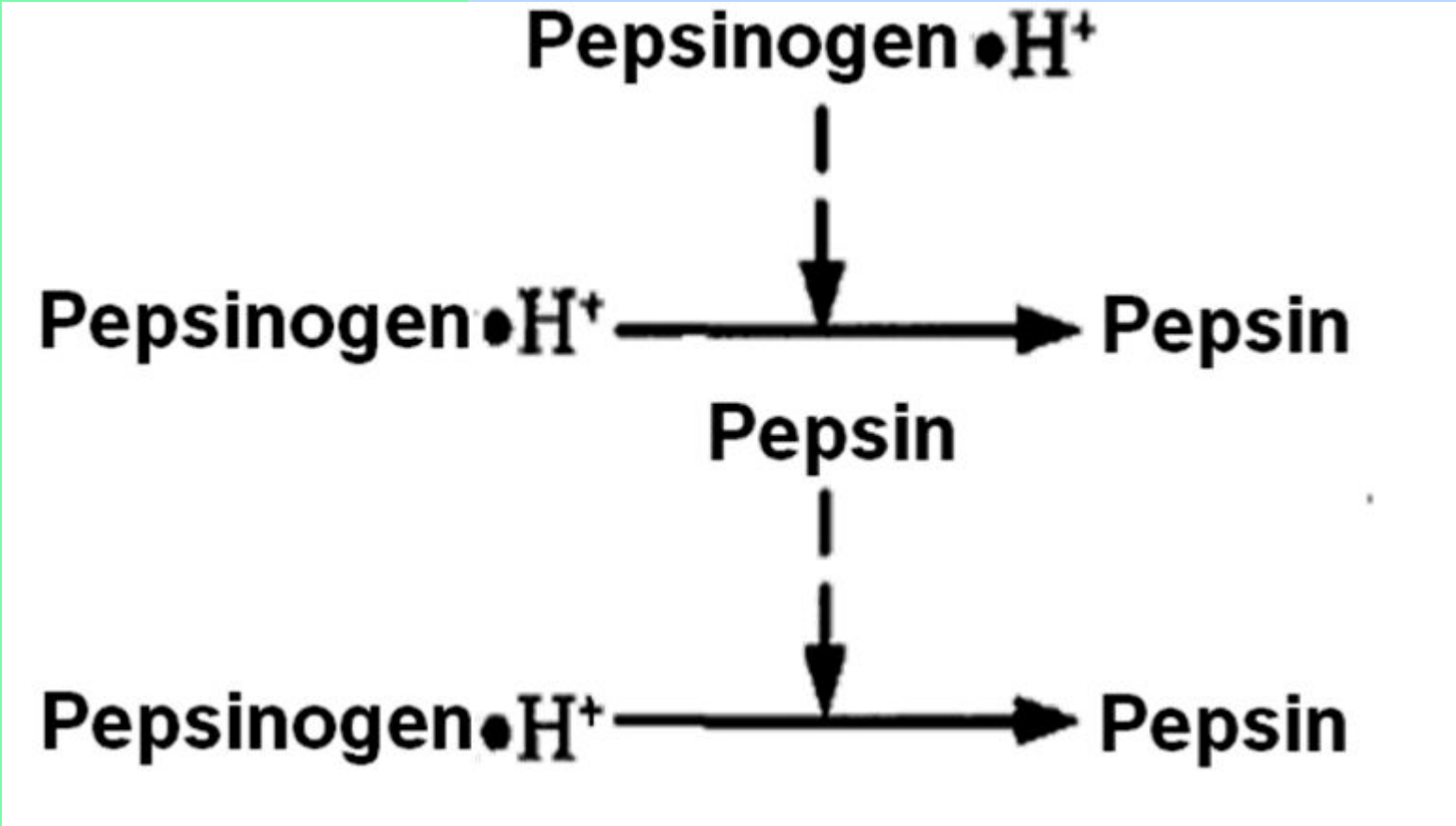
HCL secretion



Pepsinogen activation

Pepsinogen + H^+ → Pepsinogen • H^+

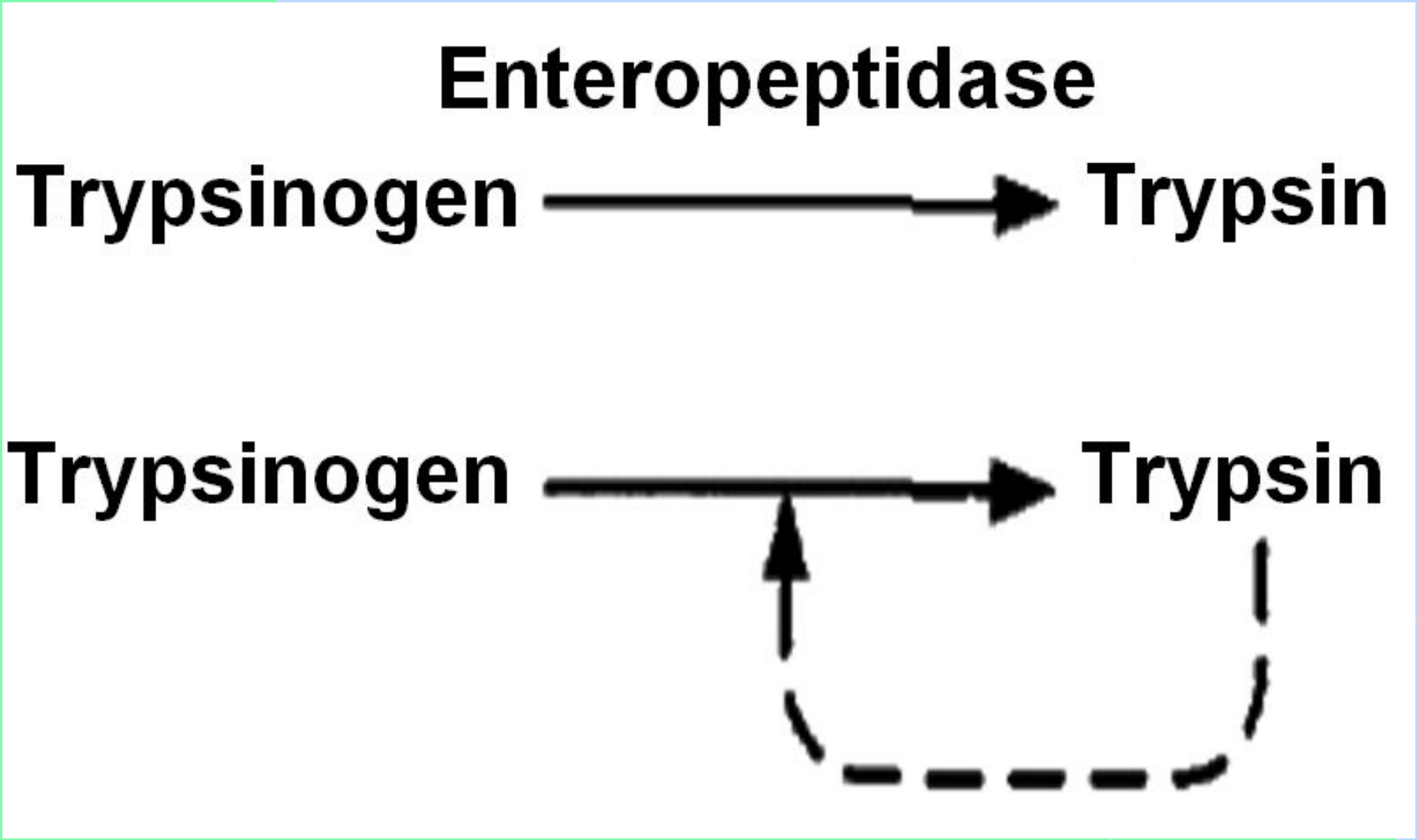
(inactive) (slightly active)



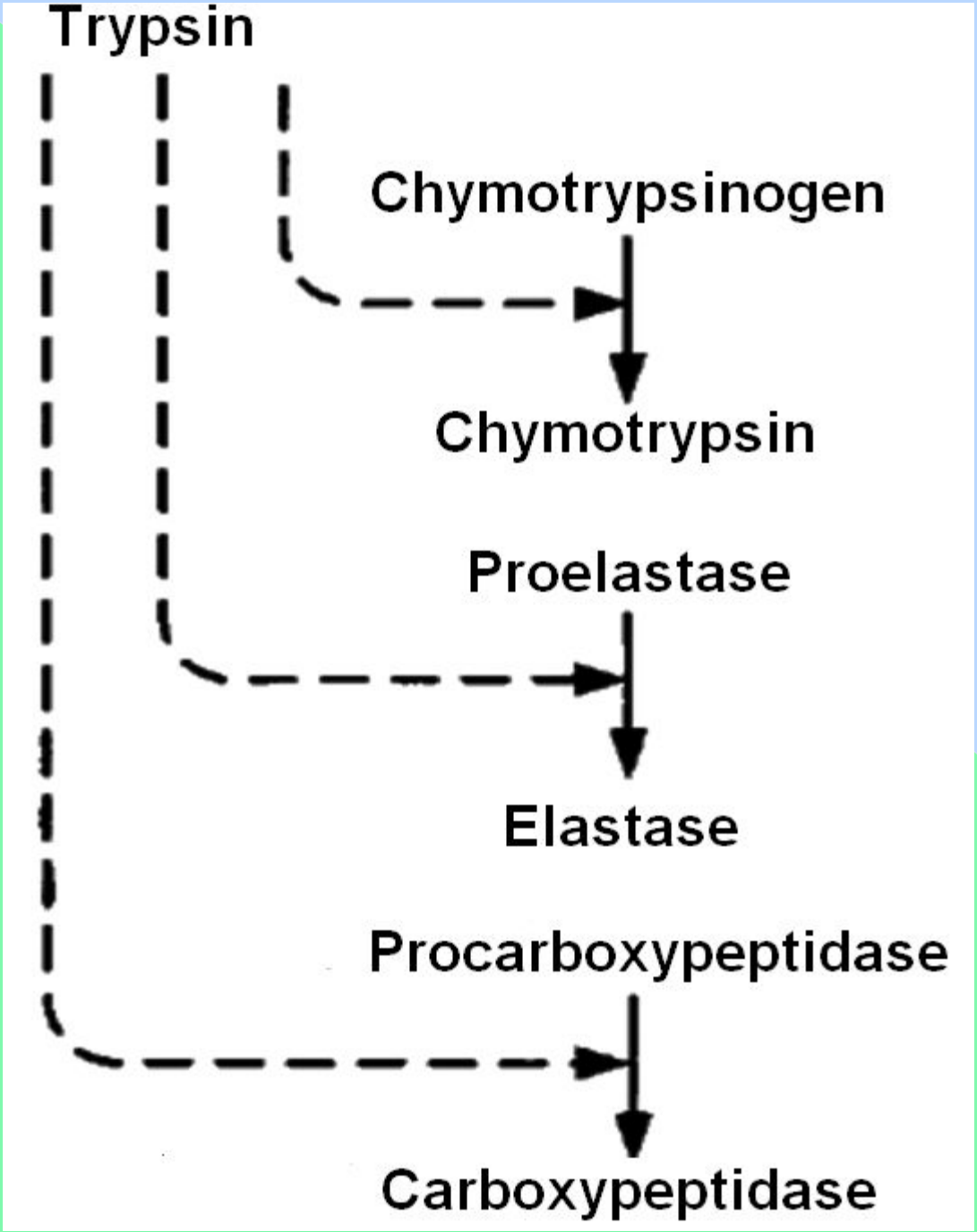
The selectivity of pepsin

Enzyme	Splittable peptide bonds
Pepsin	phenylalanine, tyrosine, glutamic acid

Trypsinogen activation



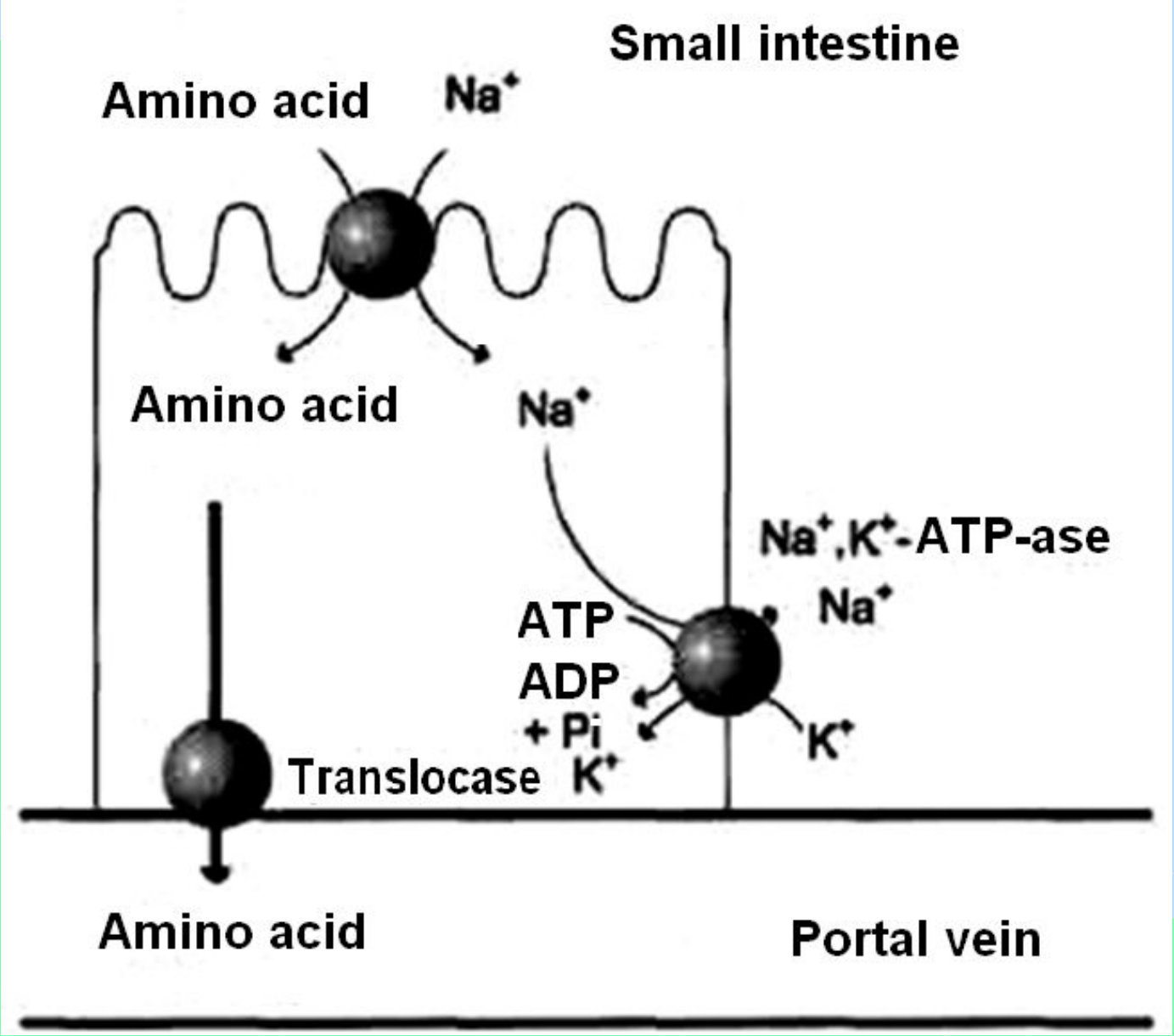
Activation of intestinal proteases



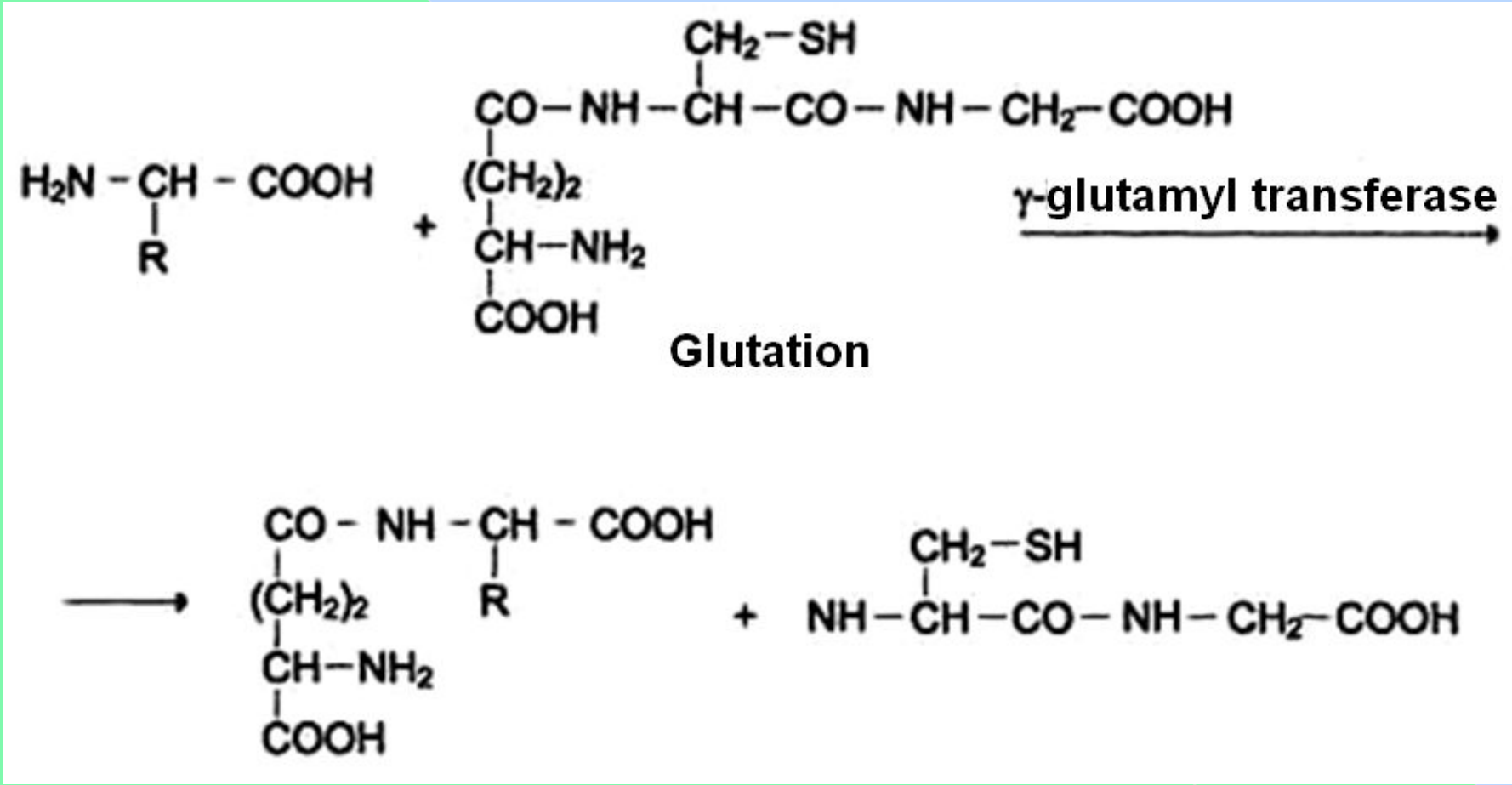
The selectivity of peptidases

Enzyme	Splittable peptide bonds
Trypsin	lysine, arginine
Chymotrypsin	tryptophan, phenylalanine, tyrosine
Elastase	alanine, serine, glycine
Carboxypeptidase A	alanine, leucine, valine
Carboxypeptidase B	lysine, arginine

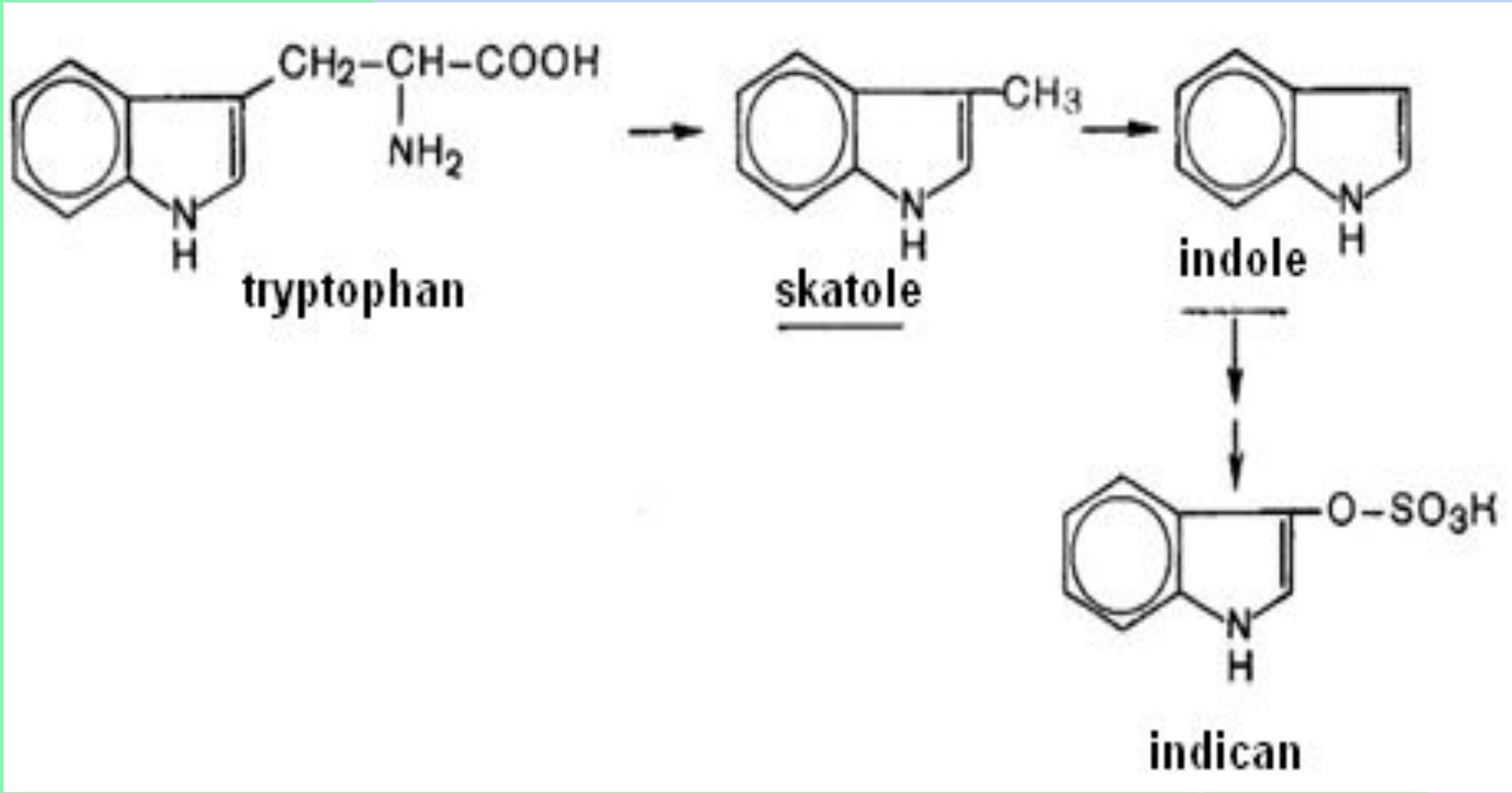
Amino acid absorption



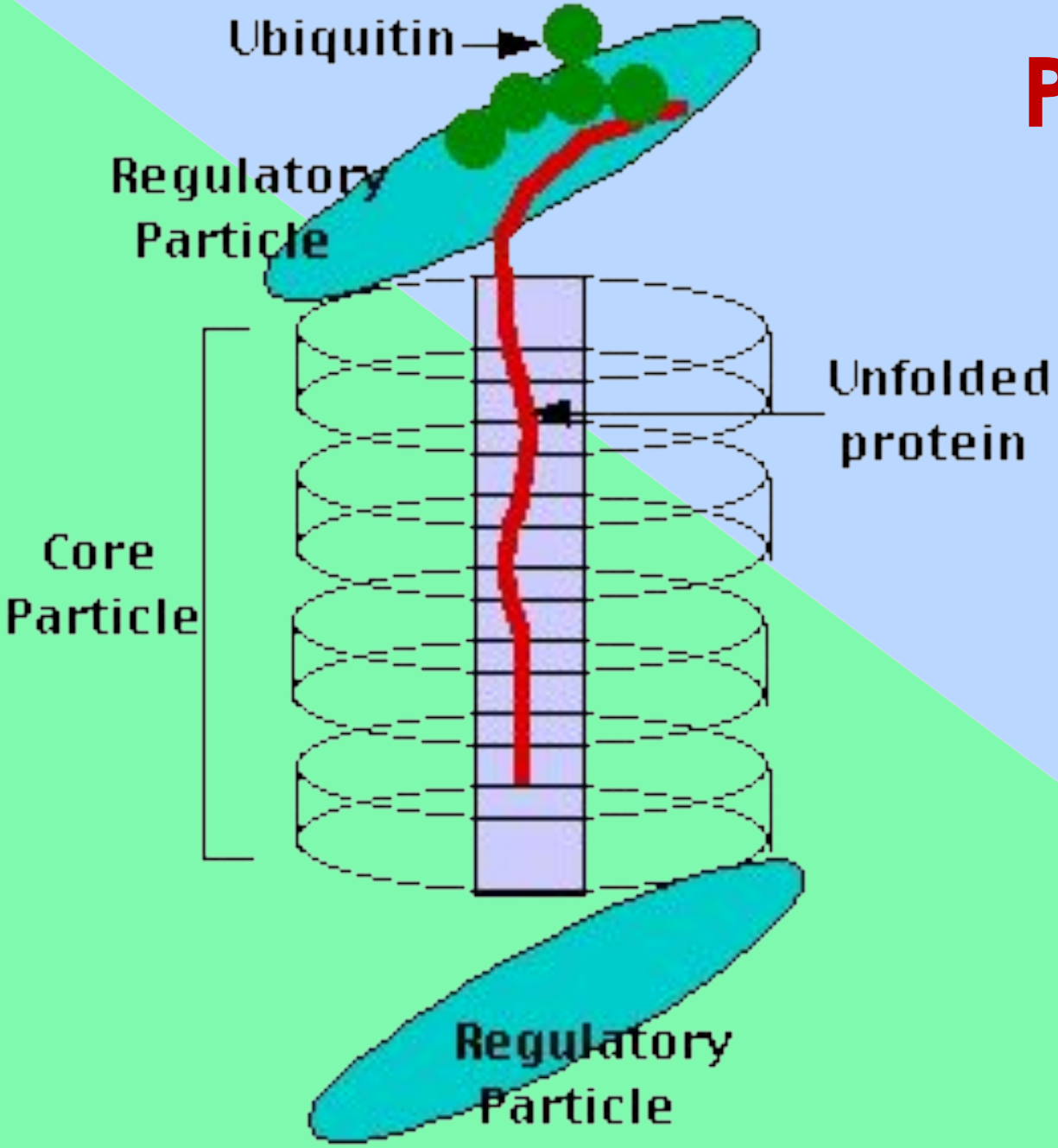
Transport
Catalytic cycle of GGT

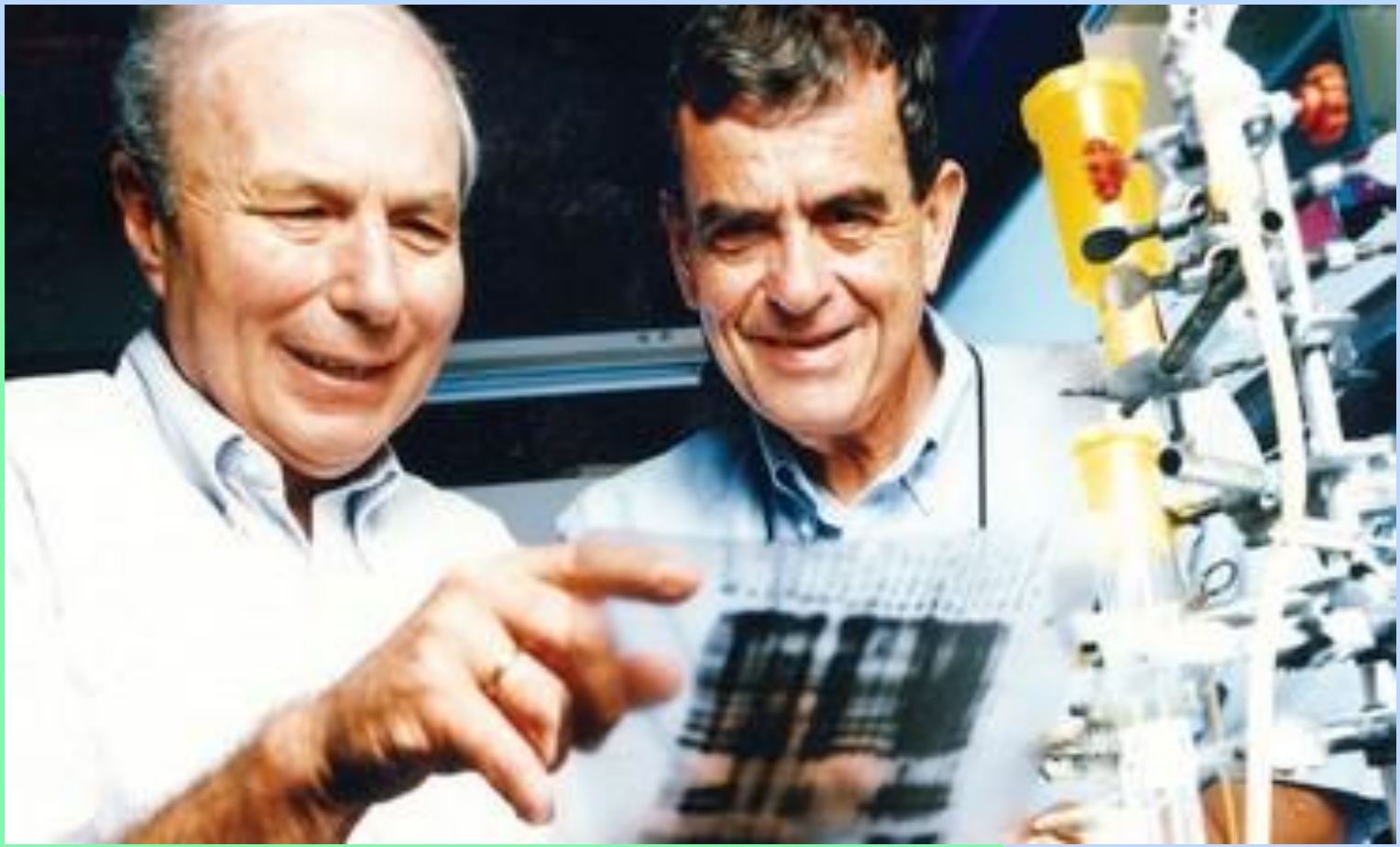


Conversion of amino acids under the action of intestinal microflora



Proteolysis in tissues

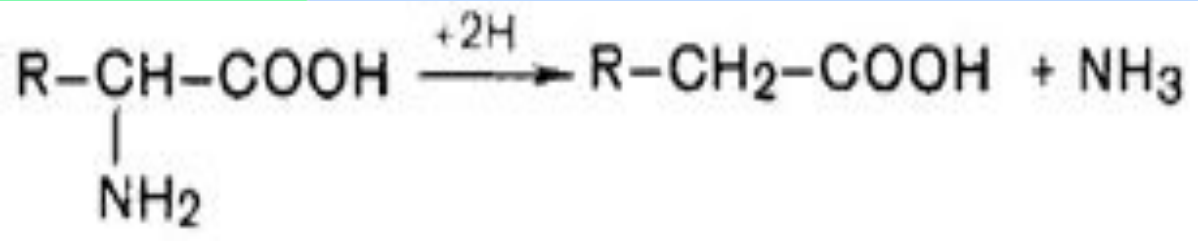




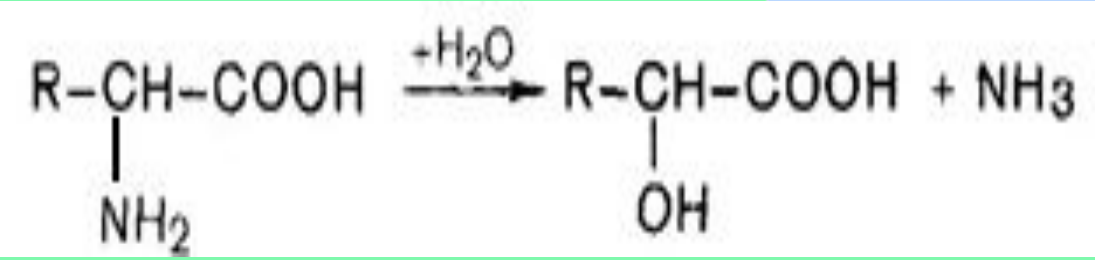
Avram Hershko,
Aaron Ciechanover and Irwin Rose
Nobel Prize in Chemistry, 2004

Reactions of amino group

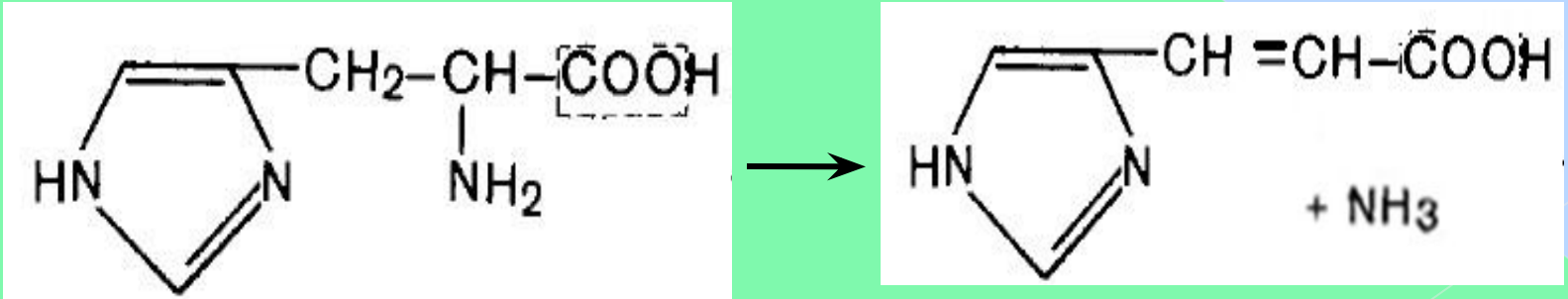
Reductive deamination



Hydrolytic deamination



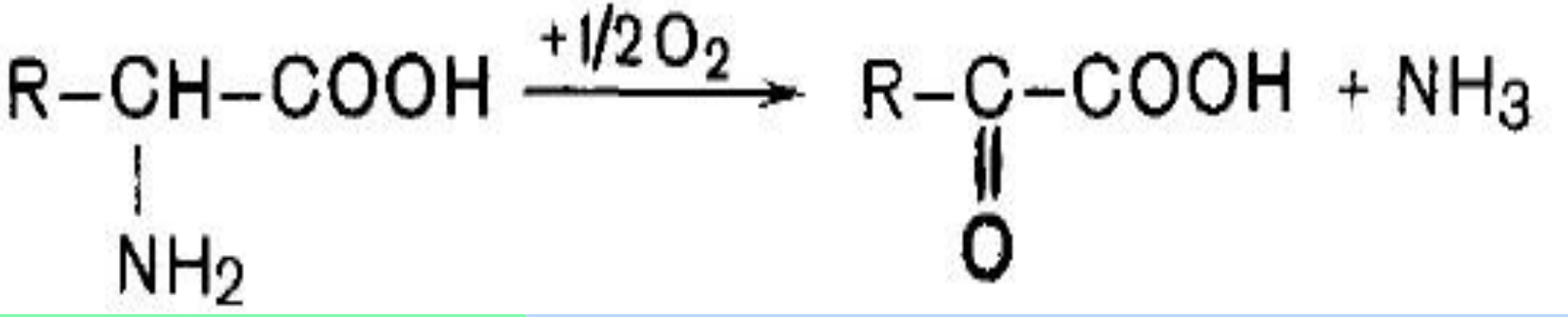
Intramolecular deamination

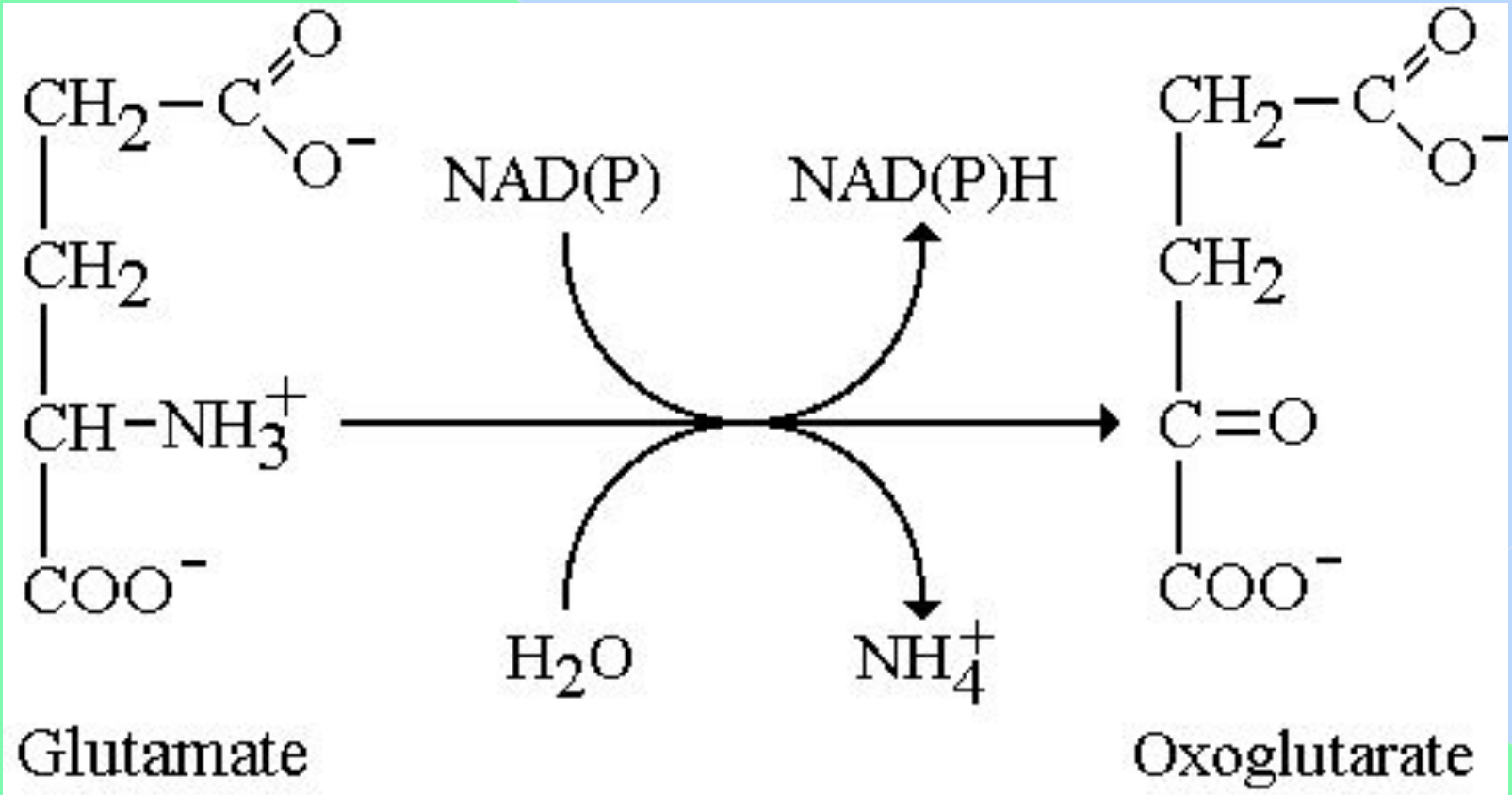


histidine

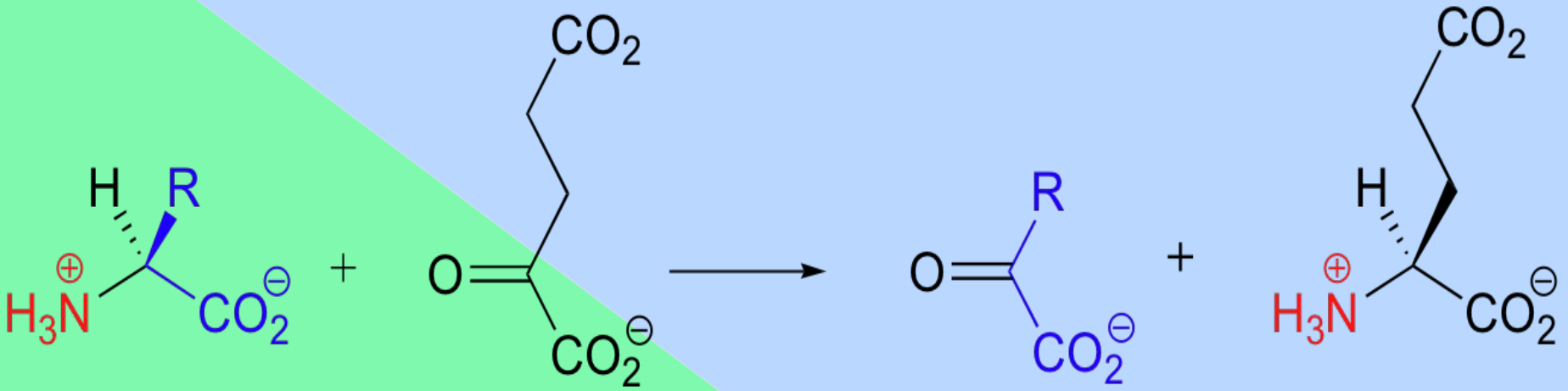
urocanic acid

Oxidative deamination

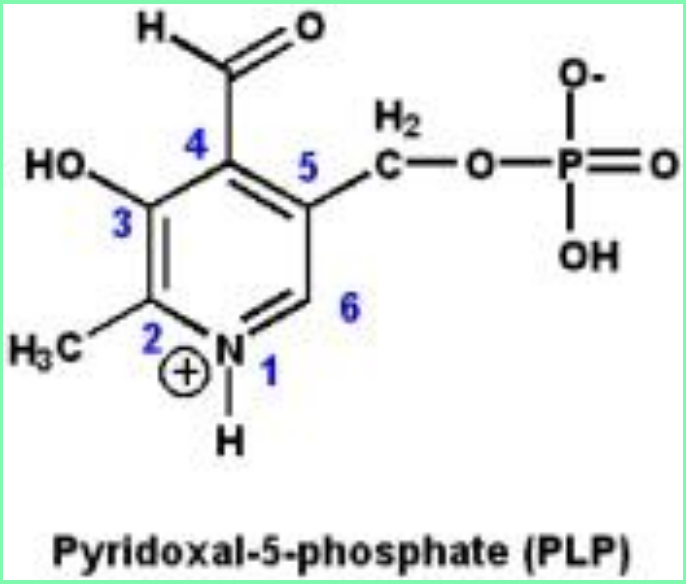




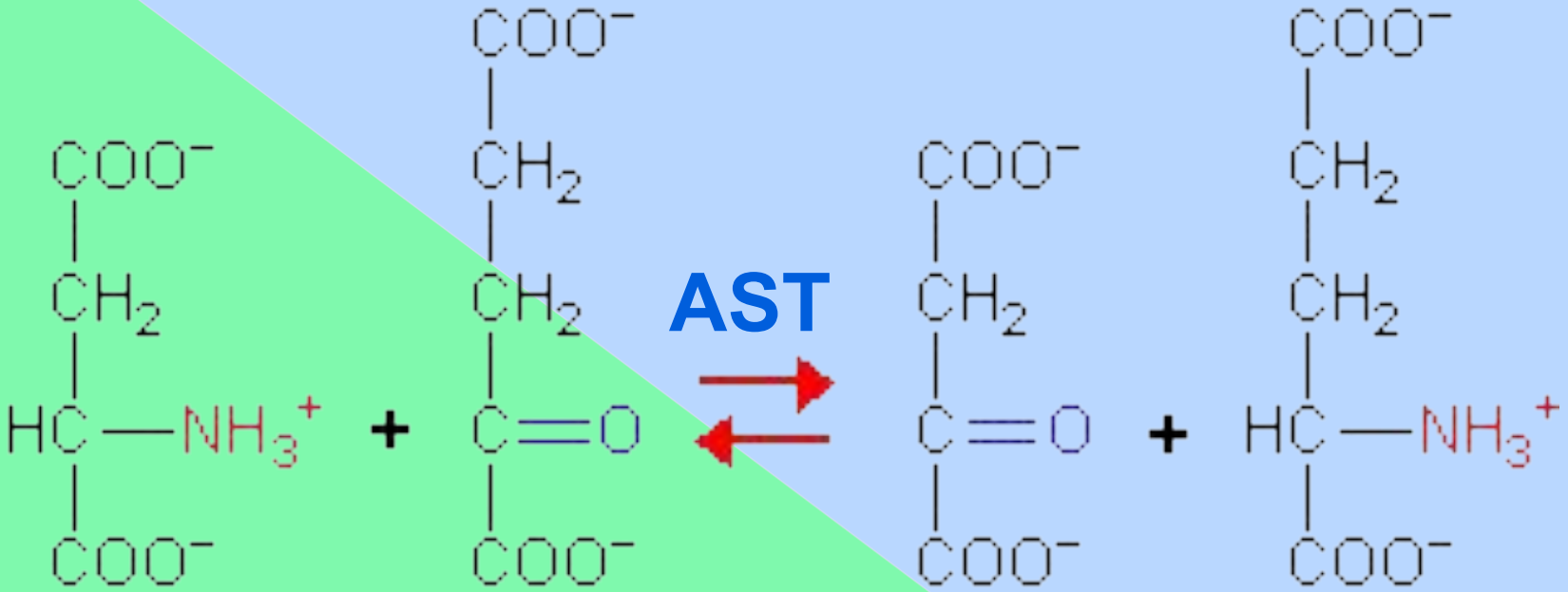
Transamination



NH_3 eliminated



Evaluation of transaminase activity



aspartate α-ketoglutarate oxaloacetate glutamate

Aminotransferase (Transaminase)

Alanine + α-ketoglutarate $\xrightarrow{\text{ALT}}$ **→ pyruvate + glutamate**

Transaminases in human tissues (U/g protein)

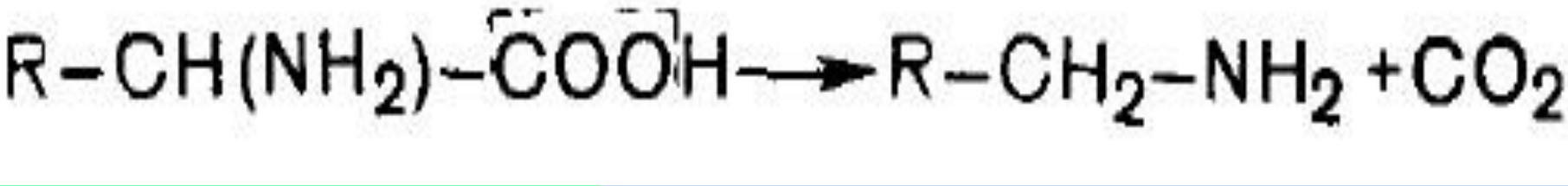
Tissues	AST	ALT
Heart	1166	66
Liver	612	358
Cerebral cortex	1230	8
Skeletal muscle	357	33
Pancreas	86	20

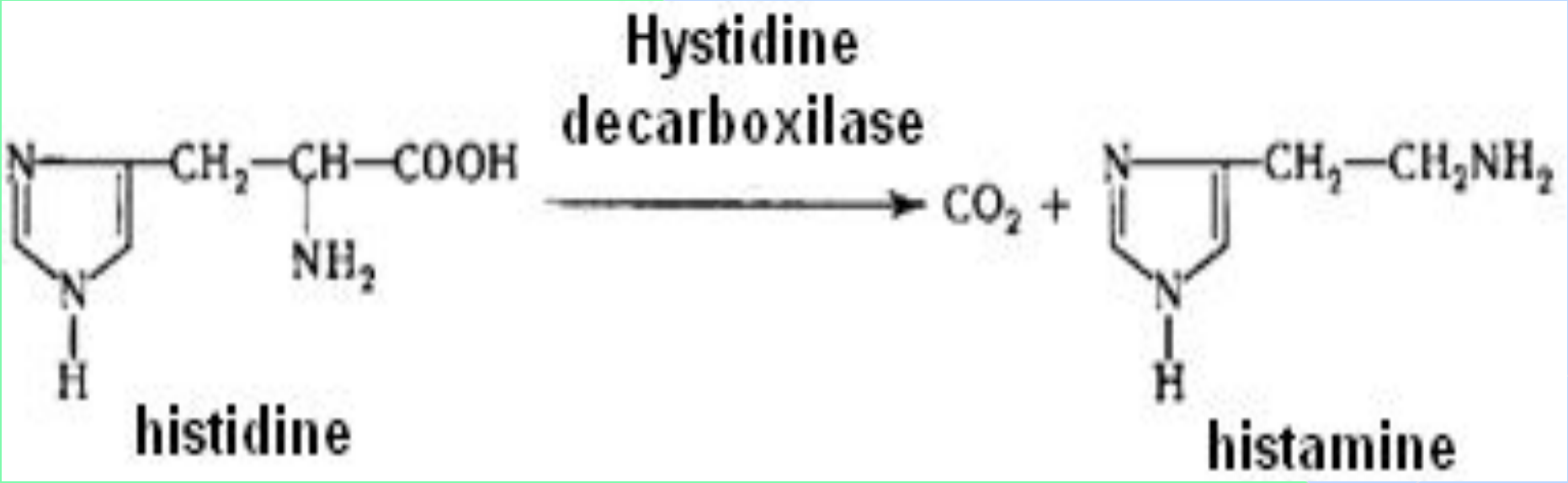
$$\text{de Ritis ratio} = \frac{\text{AST}}{\text{ALT}}$$

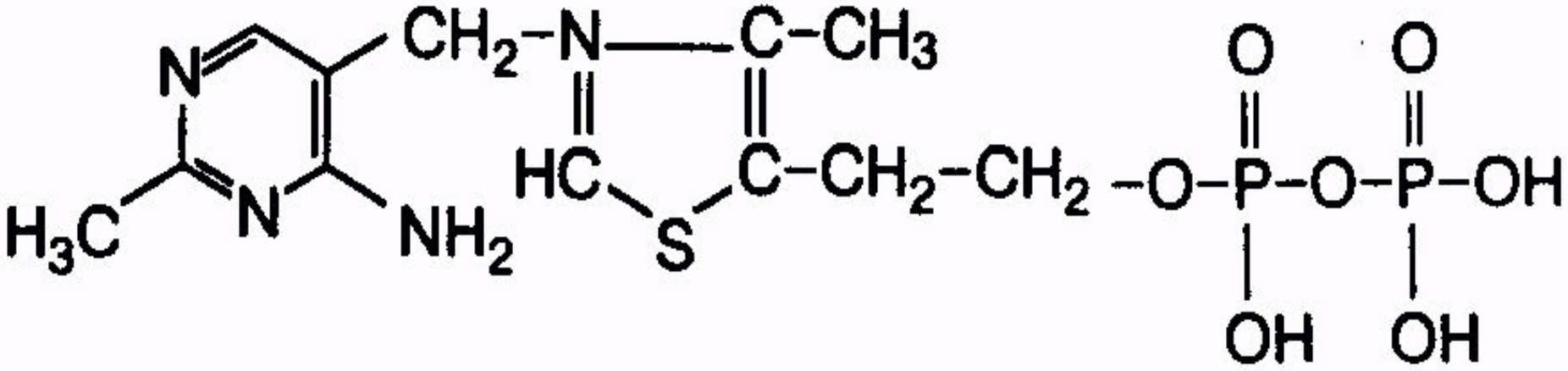
Myocardial infarction DRr > 1,3

Viral hepatitis DRr < 1

Decarboxylation

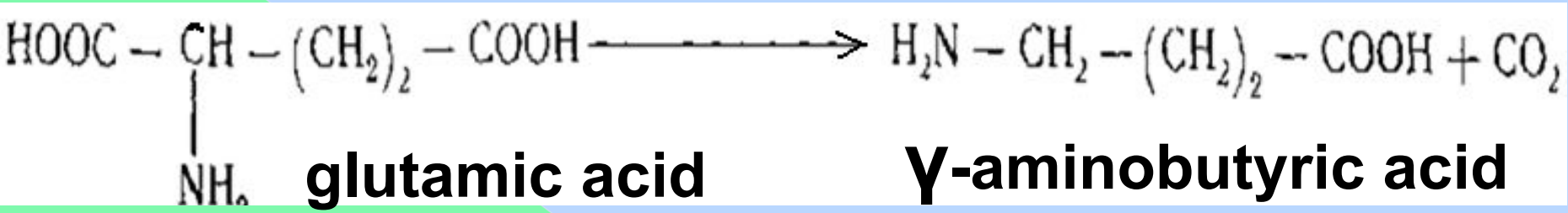






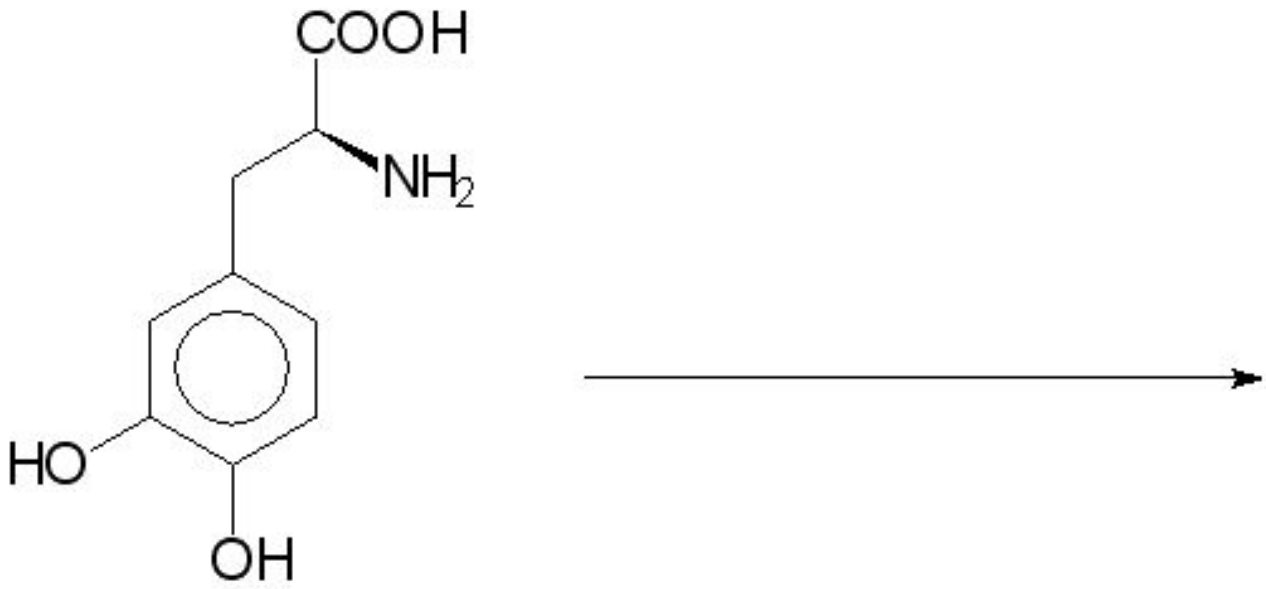
thiamine pyrophosphate

Decarboxylation

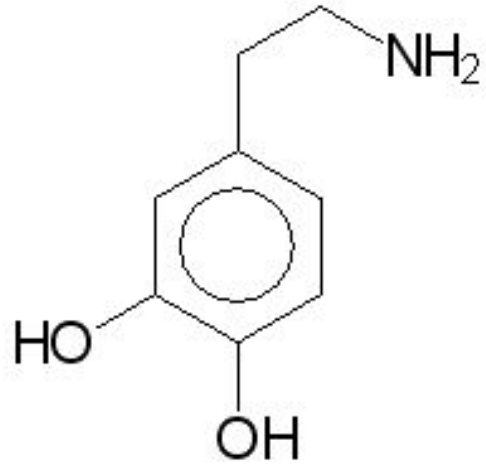


glutamic acid

γ-aminobutyric acid



L-Dopa



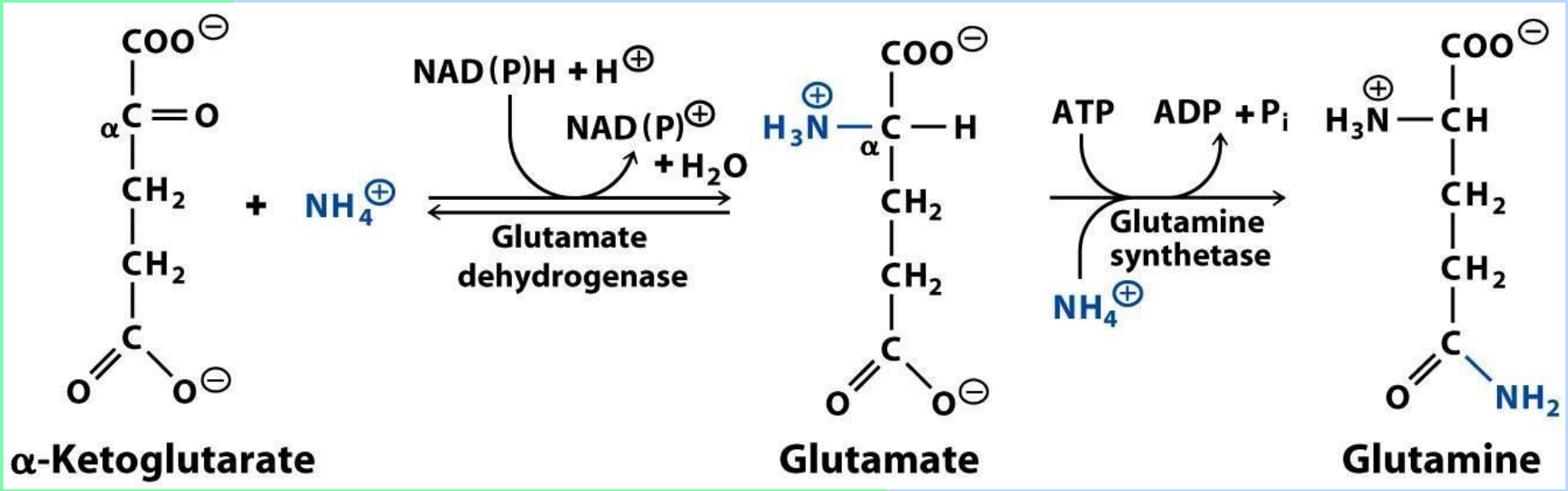
DA

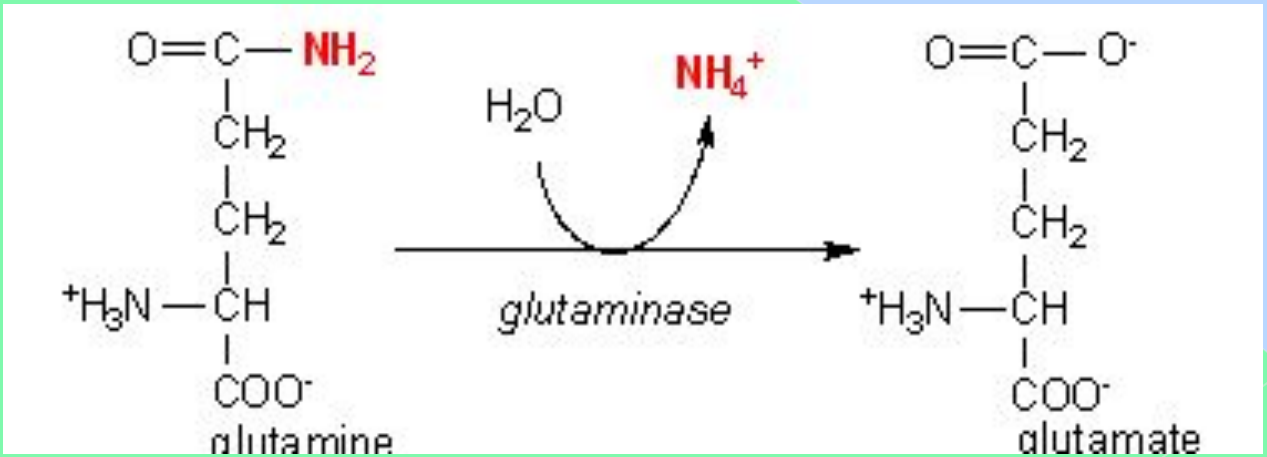
Oxidative deamination of biogenic amines

$$R\text{-}CH_2\text{-}NH_2 + E\text{-}FAD + H_2O \rightarrow R\text{-}CHO + NH_3 + E\text{-}FAD \cdot H_2$$

$$E\text{-}FAD \cdot H_2 + O_2 \rightarrow E\text{-}FADH_2 + H_2O_2$$

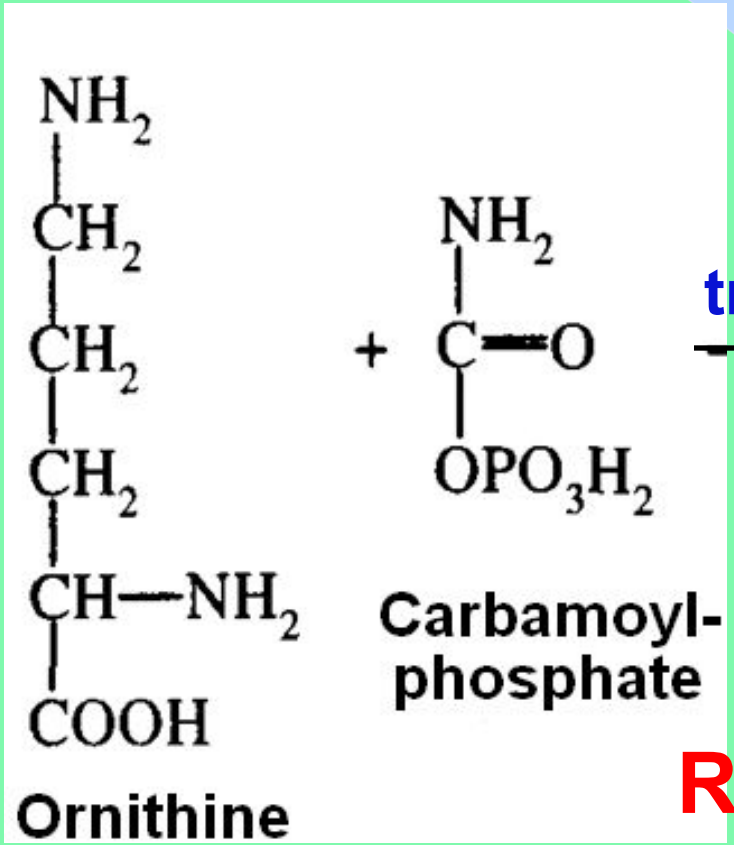
Ammonia neutrralisation



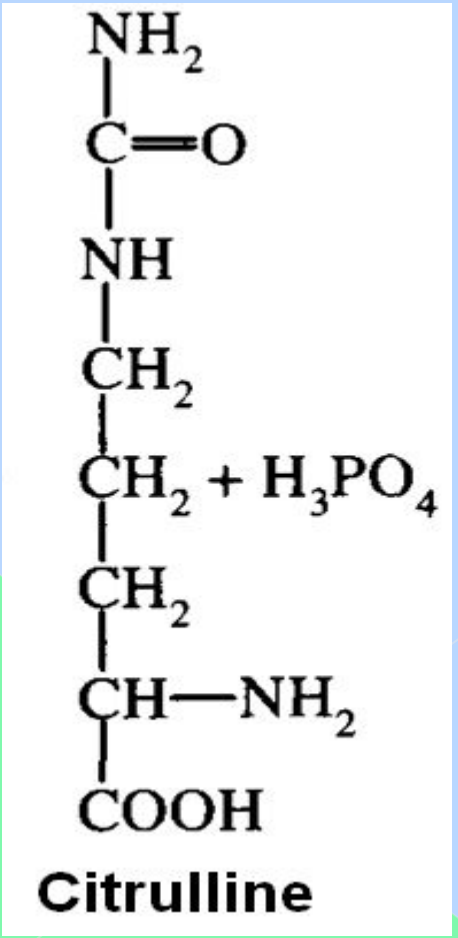


Urea cycle. Reactions 1, 2

$NH_3 + CO_2 + 2\,ATP + H_2O$ —(Carbamoylphosphate synthetase)→ $H_2N\text{-}CO\text{-}OPO_3H_2 + 2\,ADP + H_3PO_4$

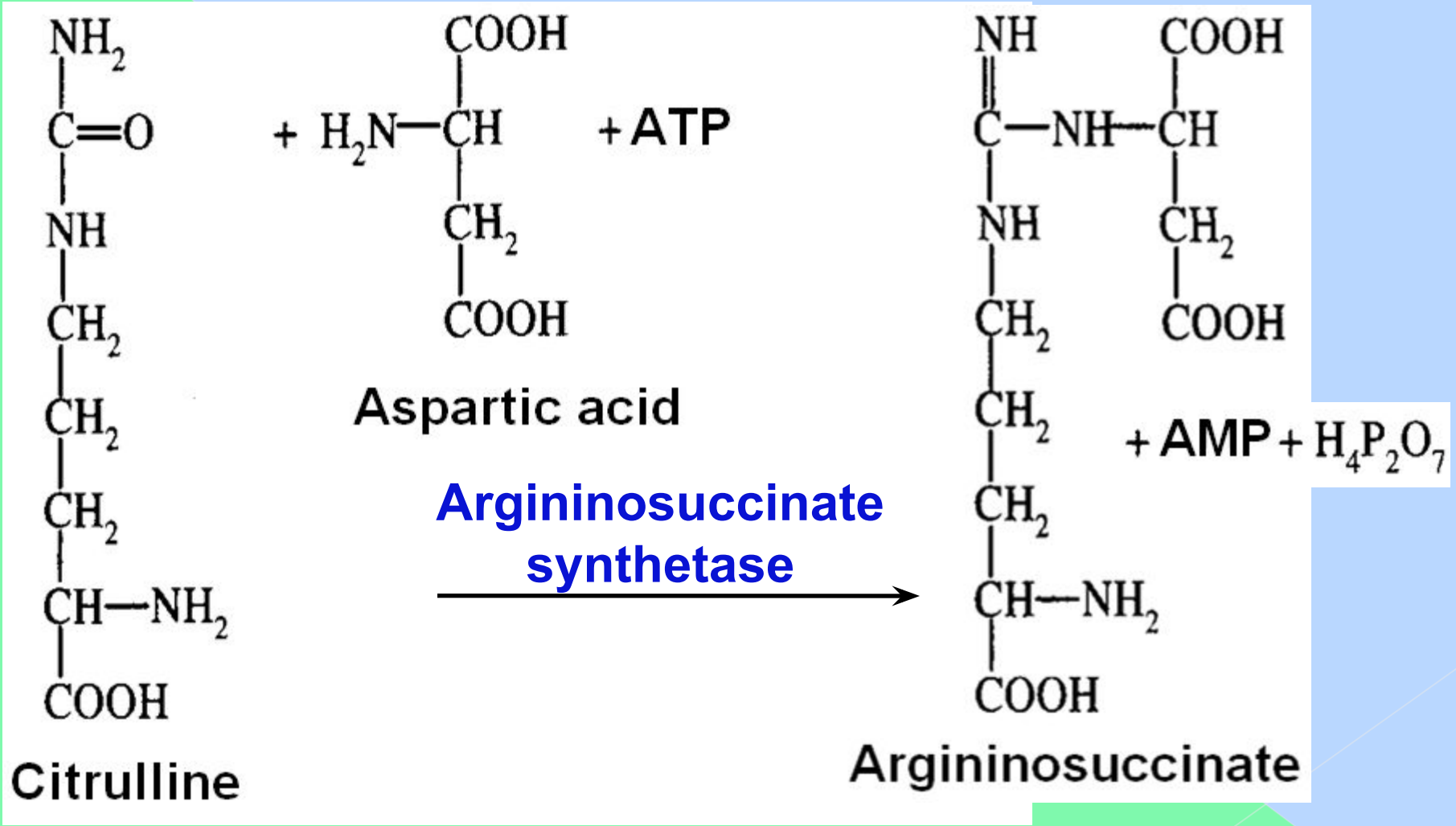


Ornithine transcarbamoilase

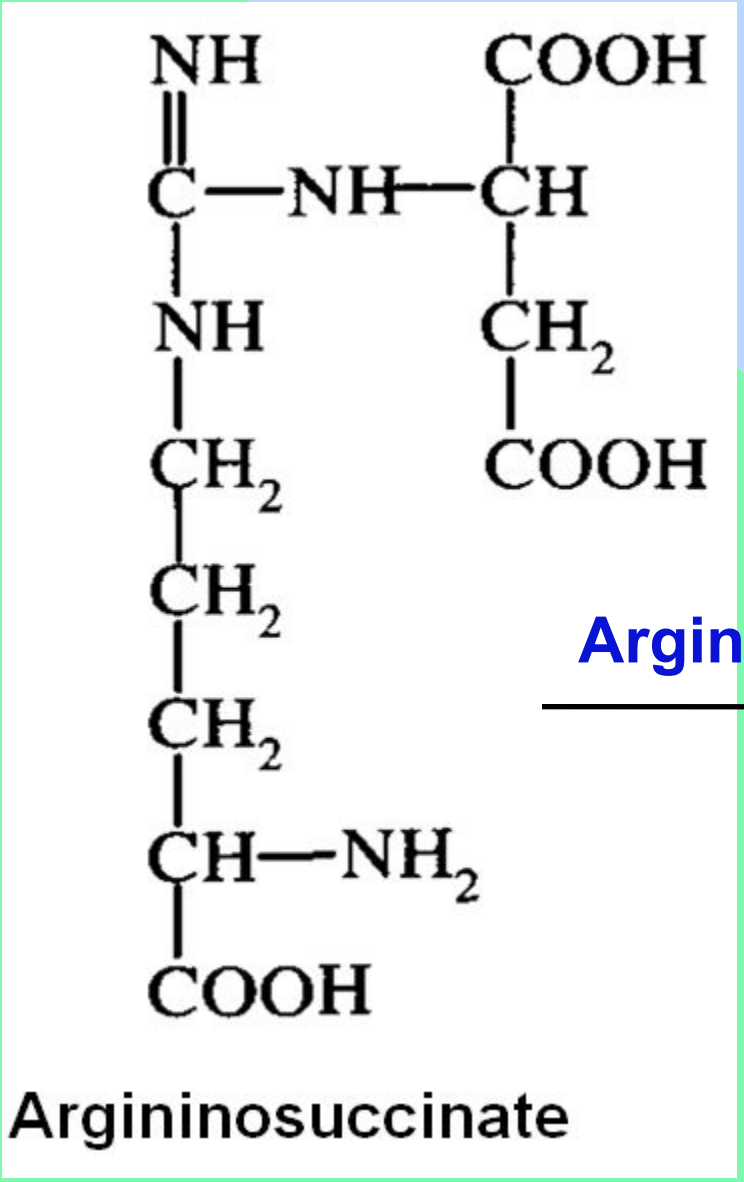


Rate-limiting!

Urea cycle. Reaction 3

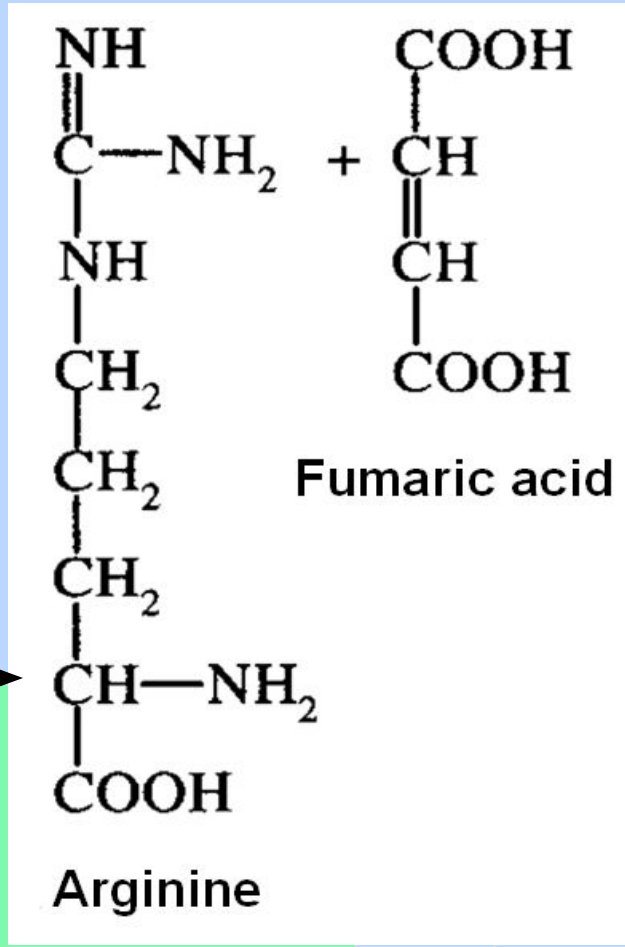


Urea cycle. Reaction 4



Argininosuccinate

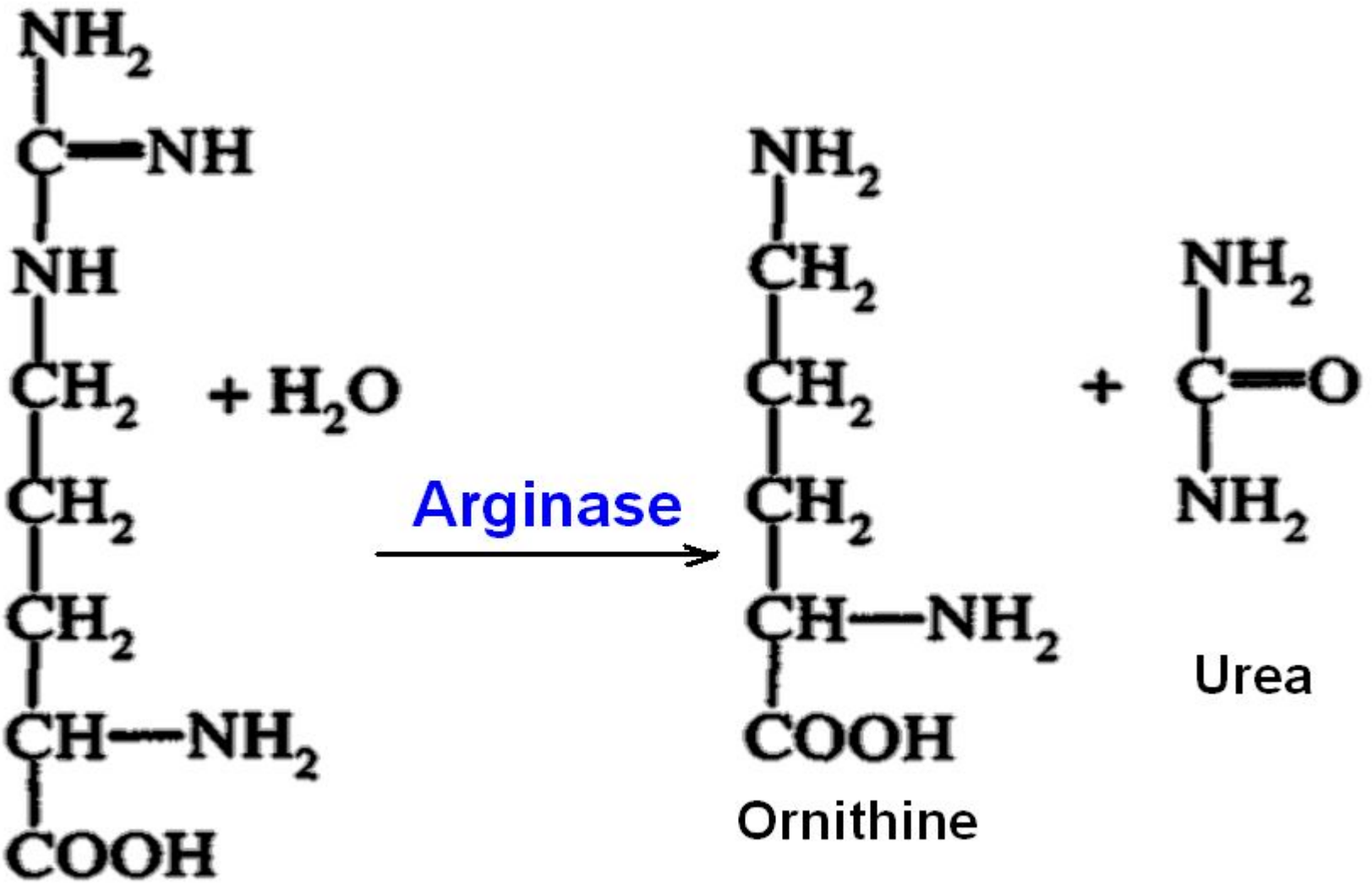
Argininosuccinase



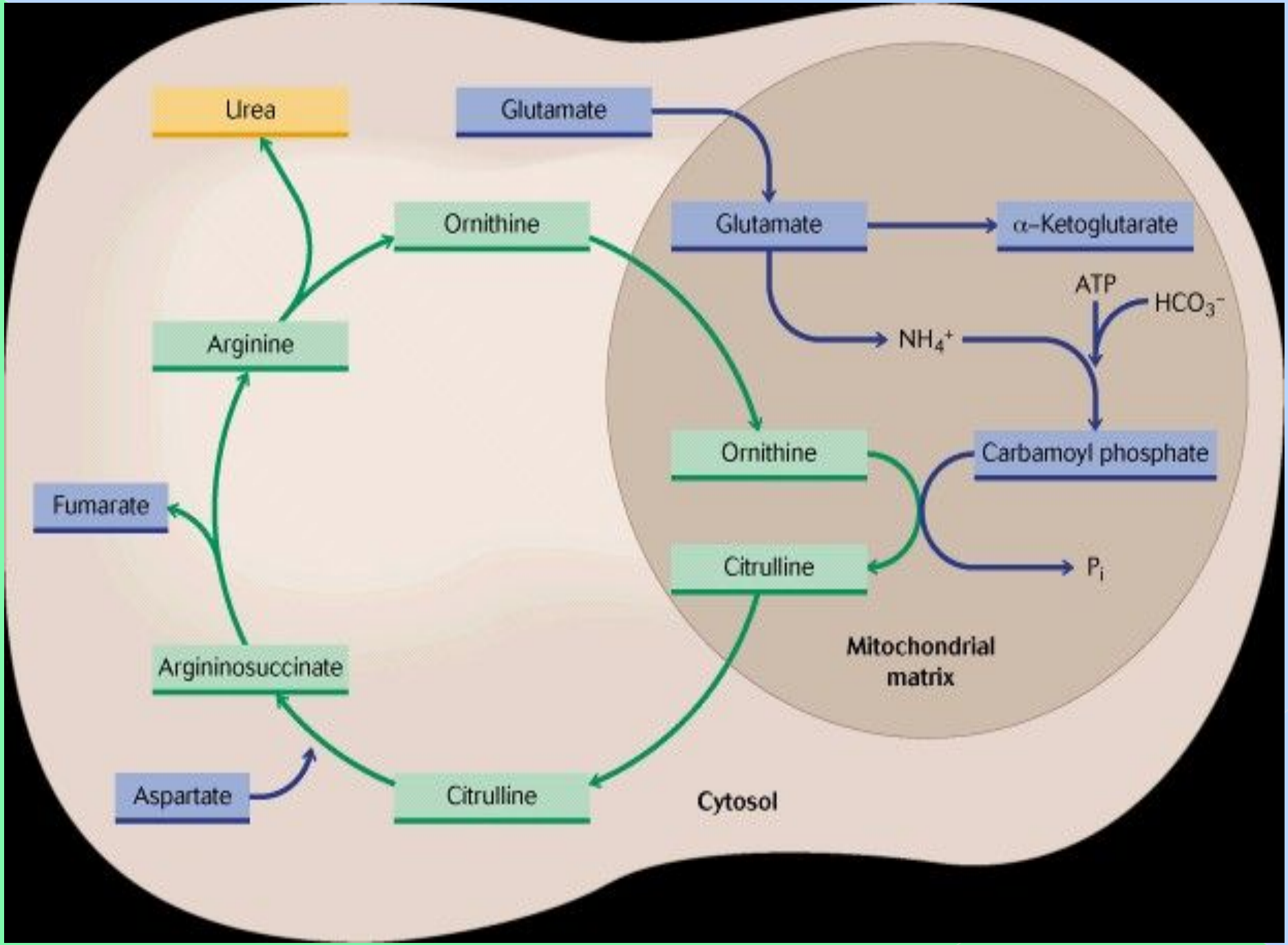
Fumaric acid

Arginine

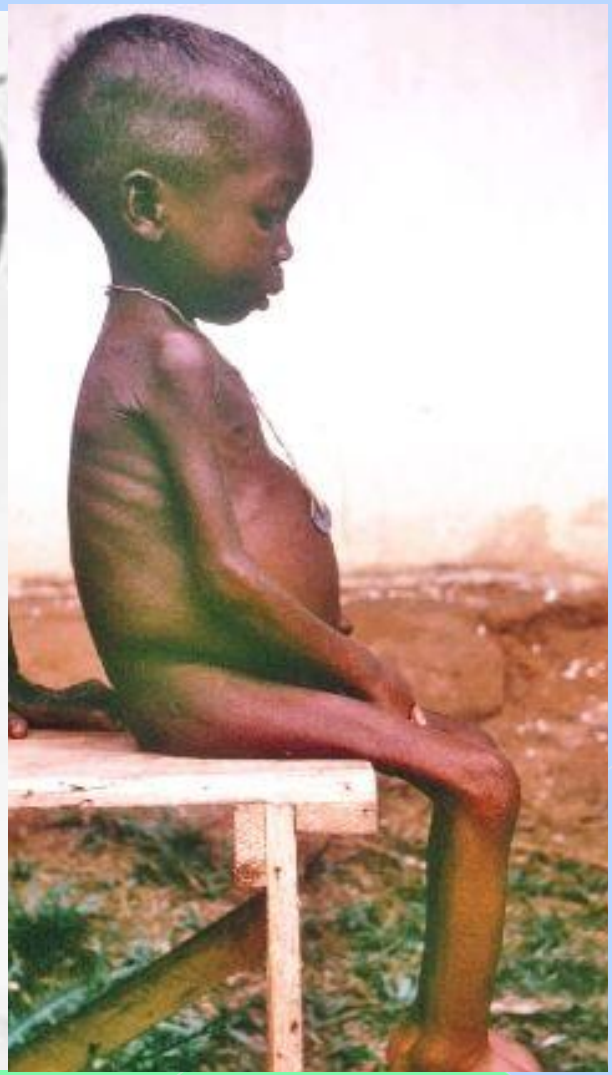
Urea cycle. Reaction 5

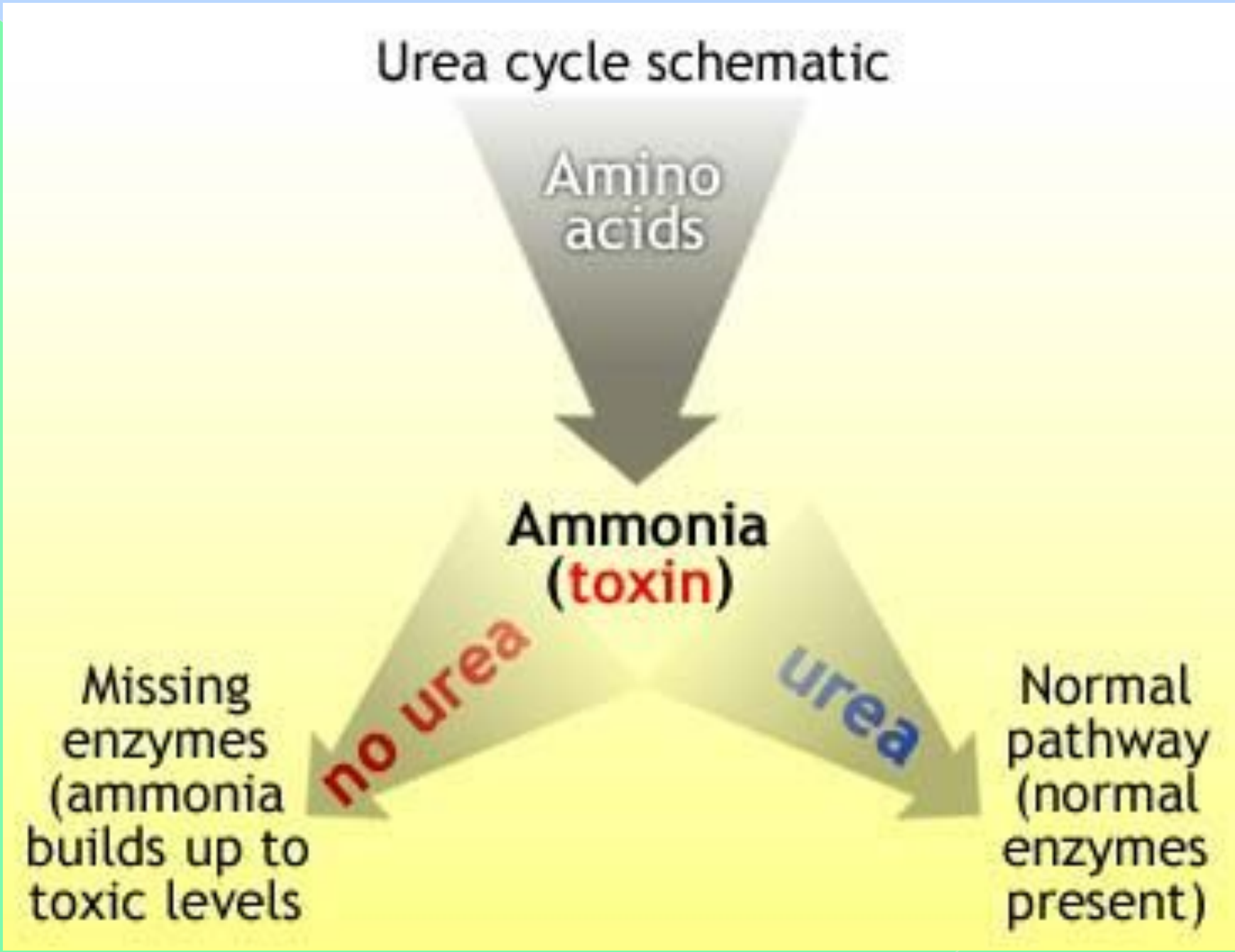


Rate-limiting!


Urea
Glutamate
Ornithine
Glutamate
α-Ketoglutarate
ATP
HCO_3^-
NH_4^+
Arginine
Ornithine
Carbamoyl phosphate
Fumarate
Citrulline
P_i
Mitochondrial matrix
Argininosuccinate
Aspartate
Citrulline
Cytosol

Kwashiorkor




Urea cycle schematic
Amino acids
Ammonia (toxin)
no urea
urea
Missing enzymes (ammonia builds up to toxic levels
Normal pathway (normal enzymes present)

Hereditary disorders of Urea cycle

Disease	Enzyme	Mode of inheritance	Clinical presentations	Blood metabolites
Hyper-ammonemia, type I	Carbamoyl phosphate synthetase I	Autosomal recessive	Coma, and death within 24-48 hours after birth	Gln Ala NH_3
Hyper-ammonemia, type II	Ornithine carbamoyl-transferase	X-linked	Hypotension, reduced tolerance to proteins	Gln Ala NH_3