Faculty of Pharmacy
Biochemistry-2

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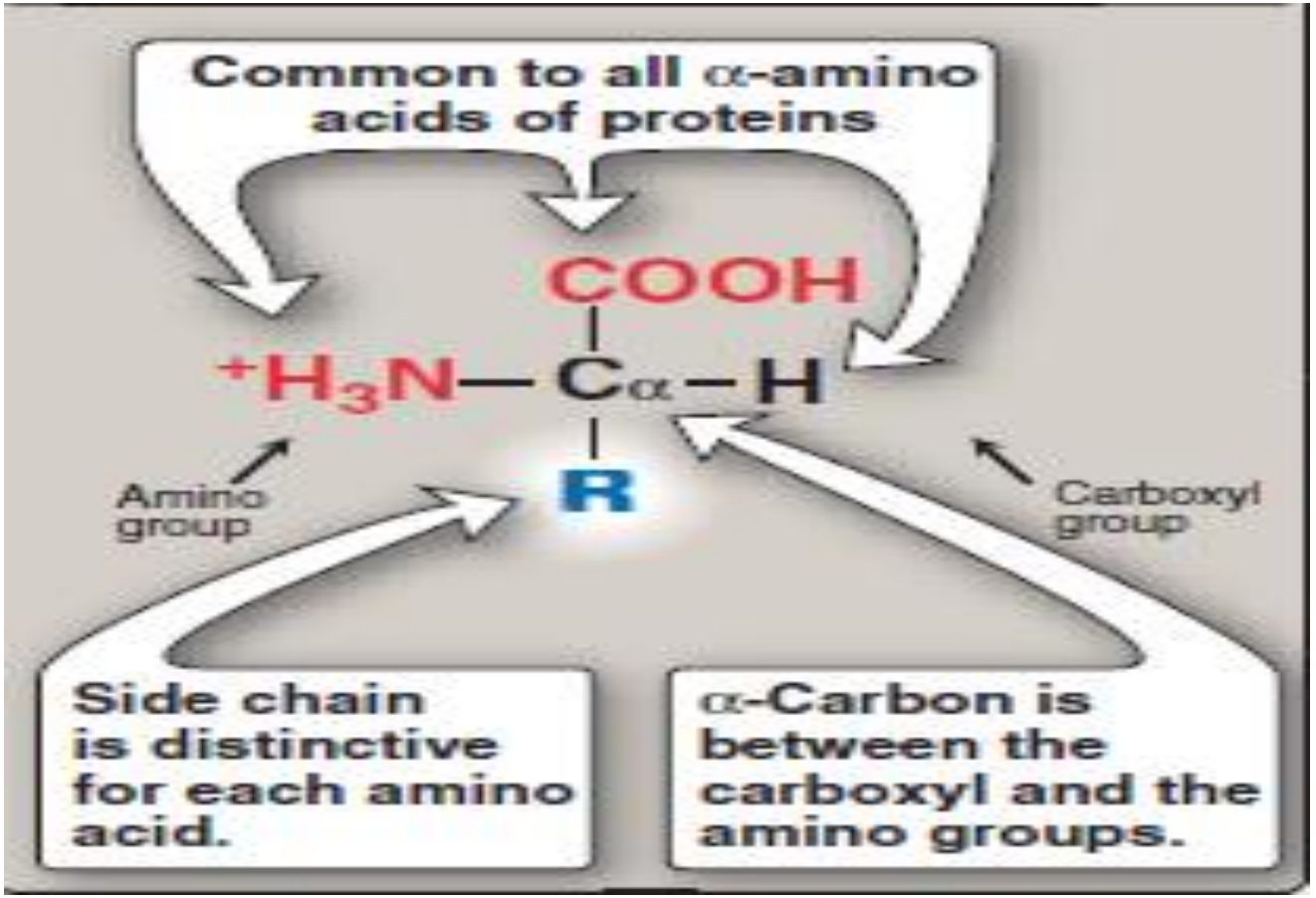
Lecturer of Biochemistry

Lecture 5

WHAT IS PROTEIN?

- Proteins are a sequence of amino acids
- Protein consists of 20 amino acids, 10 are essential amino acids, and 10 are non-essential
- There are also 4 amino acids that can be considered semiessential as arginine , histidine , tyrosine and cysteine

General structure of amino acids



Essential	Semi-essential	Non essential
Tryptophan	Arginine	Alanine
Phenylalanine	Histidine	Glycine
Methionine	Tyrosine	Serine
Threonine	Cysteine	Cysteine
Valine		Cystine
Isoleucine		Glutamic
Leucine		Aspartic
Lysine		Tyrosine
		Proline
		Hydroxyproline

Metabolism of the carbon skeleton

Glucogenic amino acid

- **It** is an amino acid that can be converted into glucose through gluconeogenesis.
- These amino acids being converted to Pyruvate, Oxaloacetic acid, α-ketoglutarate, fumarate or succinyl CoA and then to glucose, with both processes occurring in the liver.

Ketogenic amino acids

- It is an amino acid that can be degraded to acetoacetate or one of its precursors (acetyl CoA or acetoacetyl CoA)
- Their carbon skeletons are not substrates for gluconeogenesis and, therefore, cannot give rise to formation of glucose.

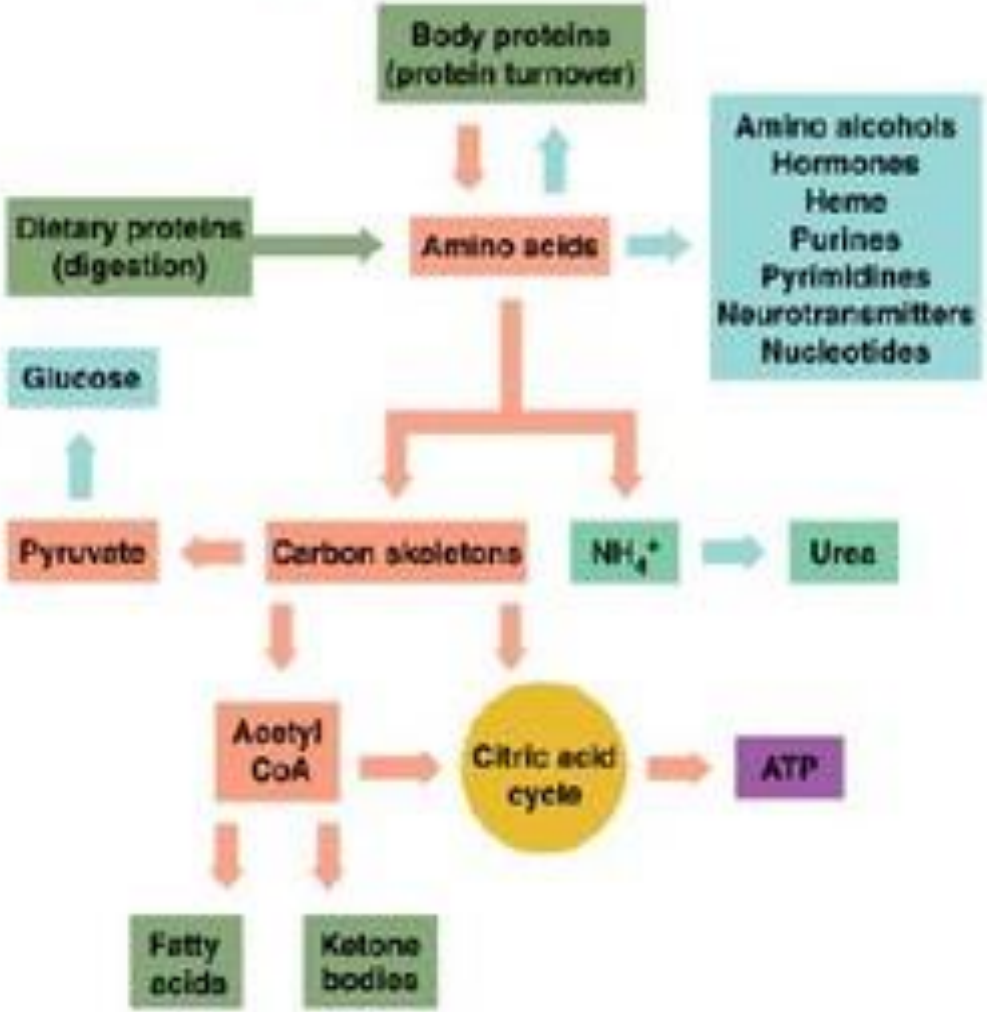
Glucogenic and Ketogenic Amino Acids

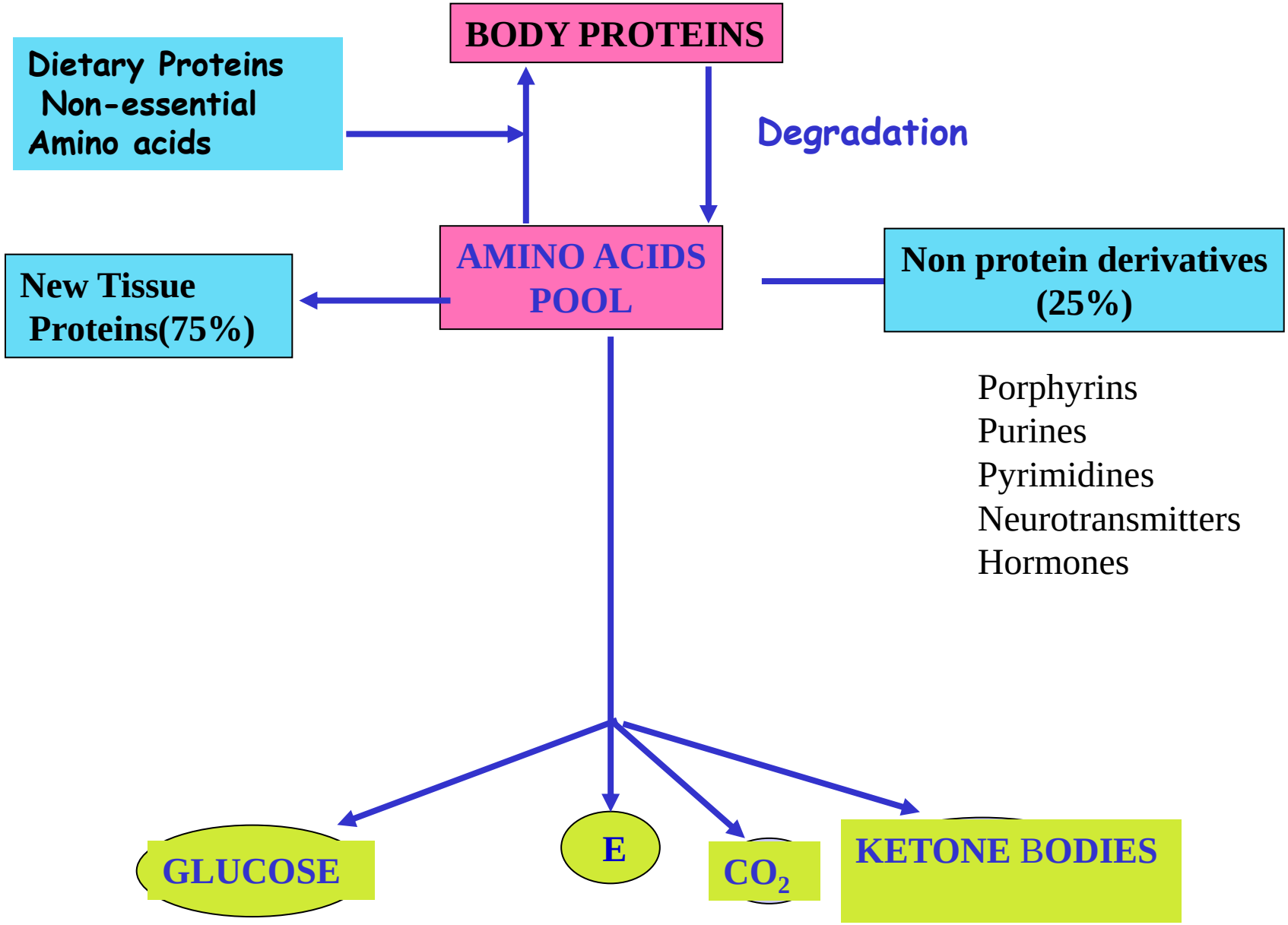
Glucogenic	*Glucogenic and Ketogenic*	*Ketogenic*
Alanine	Isoleucine	Leucine
Arginine	Phenylalanine	Lysine
Asparagine	Threonine	
Aspartate	Tryptophan	
Cysteine	Tyrosine	
Glutamine		
Glutamate		
Glycine		
Histidine		
Hydroxyproline		
Methionine		
Proline		
Serine		
Valine		

Proteins in the Body

Proteins provide:

- Amino acids for protein synthesis.
- Nitrogen atoms for nitrogen-containing compounds.
- Energy when carbohydrate and lipid resources are not available.




BODY PROTEINS
Dietary Proteins
Non-essential
Amino acids
Degradation
AMINO ACIDS
POOL
New Tissue
Proteins(75%)
Non protein derivatives
(25%)
Porphyrins
Purines
Pyrimidines
Neurotransmitters
Hormones
GLUCOSE
E
CO_2
KETONE BODIES

Amino acid metabolism

- About 75% of all amino acids are used for the production of protein.
- Amino acids can come from the protein we eat or from degraded proteins in the body.
- This degradation is a continuous process as proteins in the body are constantly being replaced - protein turnover.
- How often a protein is replaced by the body can vary greatly.

Protein turnover examples

Protein	turnover rate (halflife)	
enzymes	7-10 minutes	Extracellular
in liver	10 days	
in plasma	10 days	
hemoglobin	120 days	Intracellular
muscle	180 days	
collagen	1000 days	

- In humans, no mechanism for storage of amino acids or proteins.
- Healthy adults can hydrolyze & re-synthesize 125 to 220 g of body protein/day.
- **Amino acids are obtained either from:**

1. Diet.
2. Liver
3- Body protein degradation.

- The *Recommended Dietary Allowance* (RDA) is 65 g of protein per day for a 70 kg man.

NITROGEN BALANCE

- Excess nitrogen derived form the amino group not required for growth is excreted in the urine
- In normal, healthy adult, the amount of nitrogen ingested in the diet over a given period of time equals that excreted in the urine and feces as excretory products.
- This is known as “Nitrogen balance” or “Nitrogen Equilibrium”.

- Positive: synthesis > degradation (e.g., Growth, Body building).
- Negative: synthesis < degradation (e.g., Starvation, Trauma, Sever diseases, Cancer, Hepatitis, AIDS).

- ***Positive Nitrogen Balance:***
- Pregnancy, Infancy, Childhood, During the recovery phase from a severe illness or surgery.
- ***Negative Nitrogen Balance:***
- During starvation, Immediately following Severe trauma, Surgery, or Acute stress as Infectious hepatitis, Cancers, or AIDS.
- **Nitrogen balance is controlled:**
- Positive nitrogen balance is associated with growth hormone, insulin and with testosterone and other anabolic steroids.
- Negative nitrogen balance is associated with glucocorticoid.

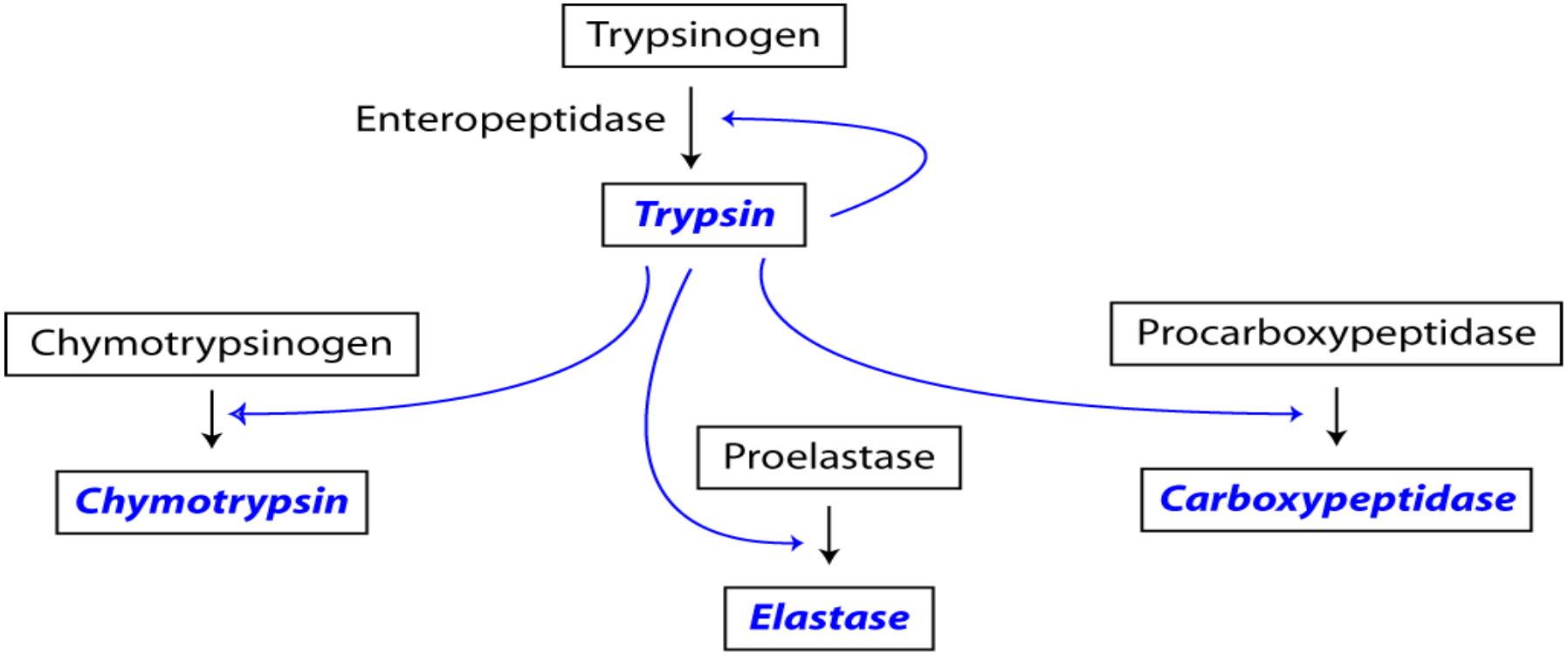
Protein Digestion

Proteolytic enzyme

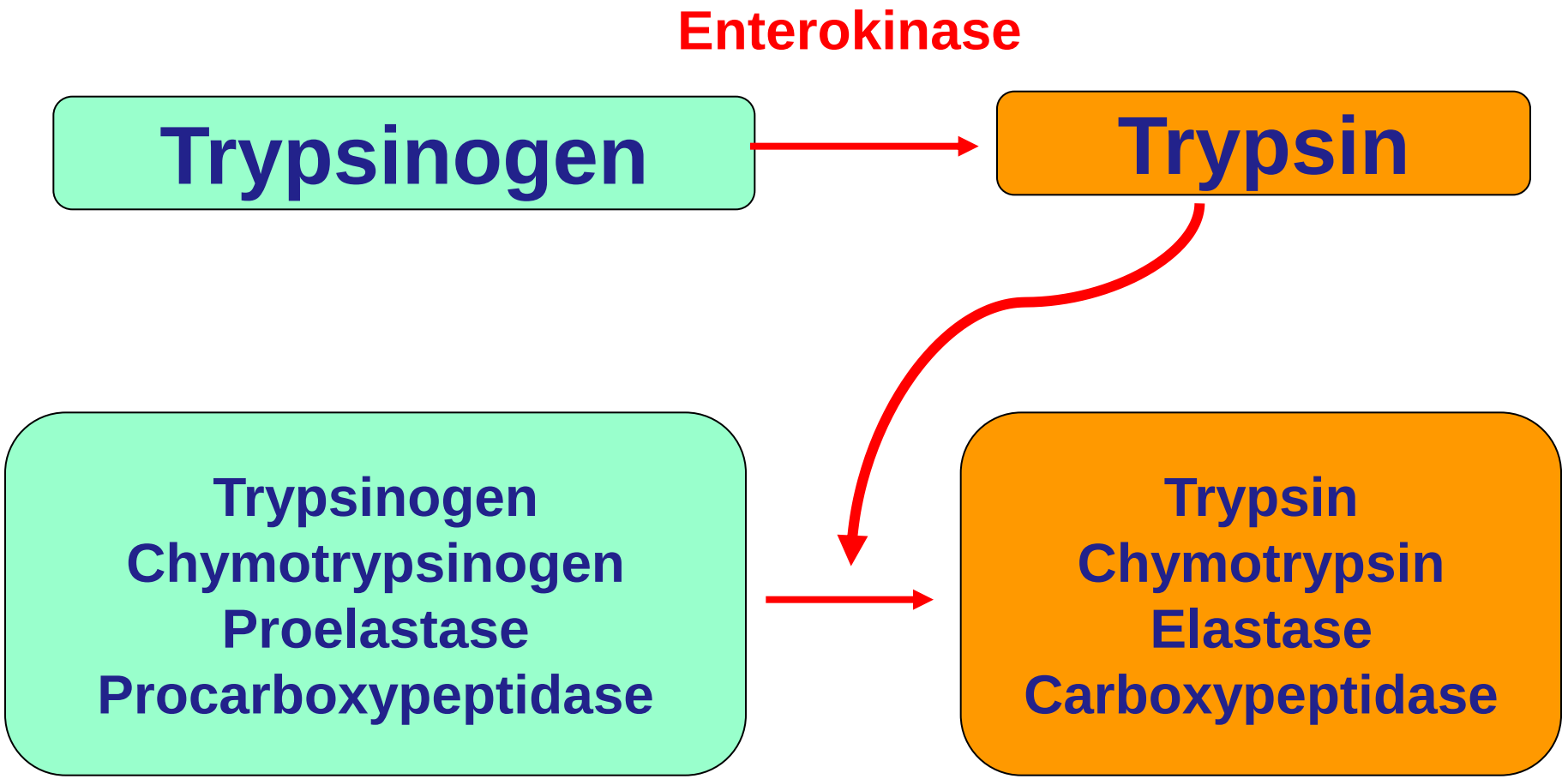
Gastric juice	Pancreatic Juice	Intestinal juice
Pepsin	Trypsin	Aminopeptidase
HCl	Chymotrypsin	dipeptidase
	Carboxypeptidase	Tripeptidase

Activation of proteolytic enzymes

The duodenum secretes **enteropeptidase**, a protease that specifically activates several protealytic zymogens released from the pancreas. One of these proteases is the pancreatic zymogen **trypsinogen** which is cleaved to form the endopeptidase **trypsin** which cleaves numerous pancreatic zymogens, including **chymotrypsinogen**, and **procarboxypepetidases** A and B



Activation of pancreatic proteases



DIGESTION

- No digestion of protein takes place in the mouth, it begins in the stomach
- Hydrochloric acid denatures protein and also converts pepsinogen to pepsin
- Pepsin breaks the protein down into peptides of various lengths and some amino acids
- Pepsin completes ~ 10-20% of digestion

DIGESTIN

- Pancreas makes trypsinogen and chymotrypsinogen (proenzymes) in response to protein in the small intestine
- They will be activated to trypsin and chymotrypsin

  Proteases break down polypeptides into smaller peptides (very few peptides have been broken down to amino acids at this stage)

DIGESTION

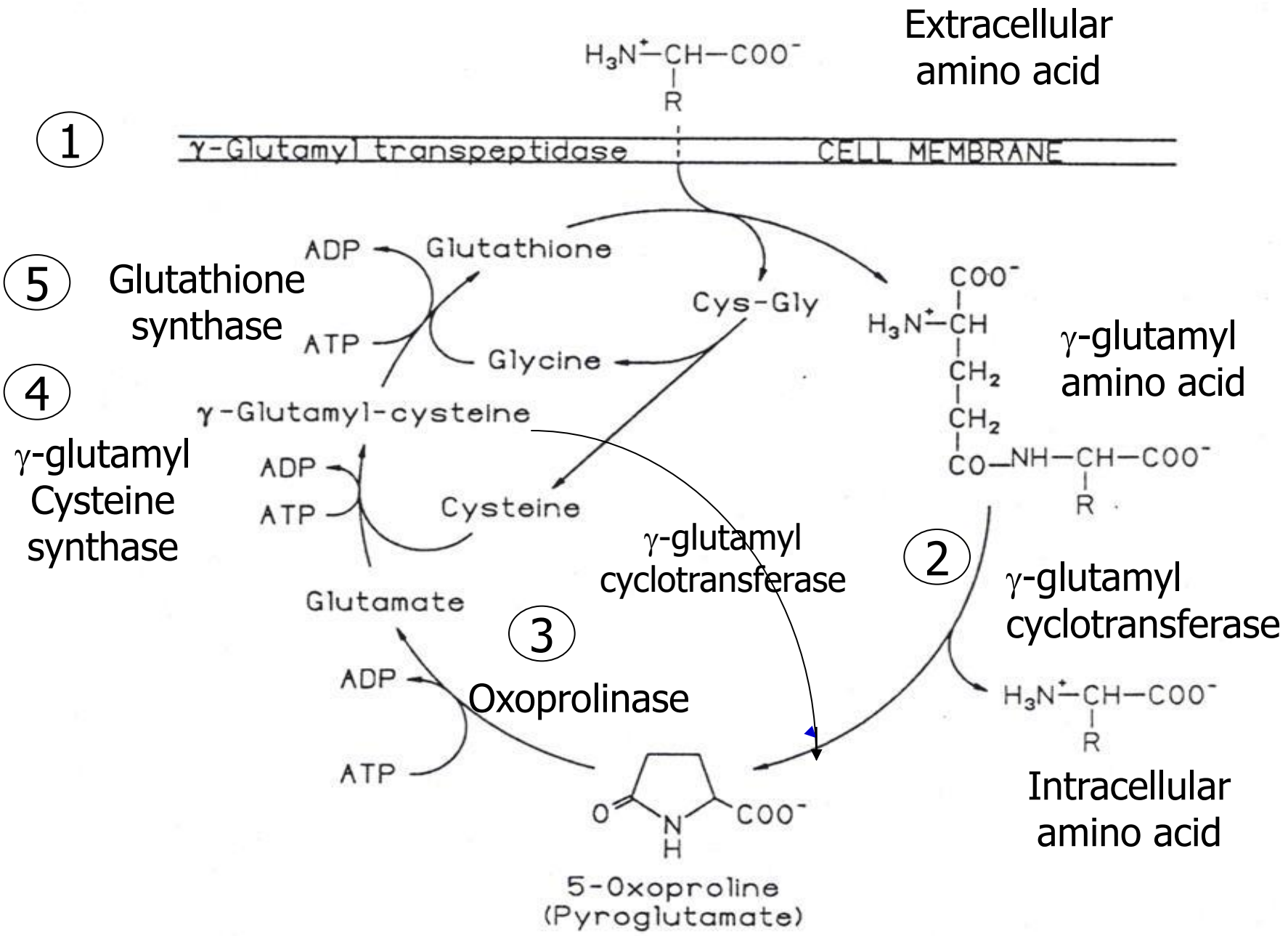
- The intestinal wall produces peptidases which continue to split the remaining polypeptides into tripeptides, dipeptides, and some amino acids
- These smaller units are transported into the enterocytes

AMINO ACID ABSORPTION

Six active transport carrier mechanisms:

1. Small neutral amino acids.
2. Large neutral amino acids.
3. Basic amino acids.
4. Acidic amino acids.
5. Proline.
6. *The γ-Glutamyl Cycle.*

Amino acid transport across the cell membrane (Meister cycle)



Oxoprolinuria

It is a genetic disease due to deficiency of glutathione synthase, leading to accumulation of oxoproline & its excretion into urine.

Amino acid catabolism

- Amino acids cannot be stored by the body.
- If there is an excess of amino acids or a lack of other energy sources, the body will use them for energy production.
- Unlike fats and carbohydrates, amino acids require the removal of the amine group.
- It must then be disposed of as it is toxic to the body.

Amino acid degradation

Metabolism of the carbon skeleton

Removal of amino group

Catabolism of amino acids

Removal of α-amino group.

A two step process.

Transamination reaction

Aminotransferase moves the amine to α-ketoglutarate producing glutamate or to oxaloacetate, producing aspartate.

Oxidative deamination

Removal of the amine from glutamate producing an ammonium ion.

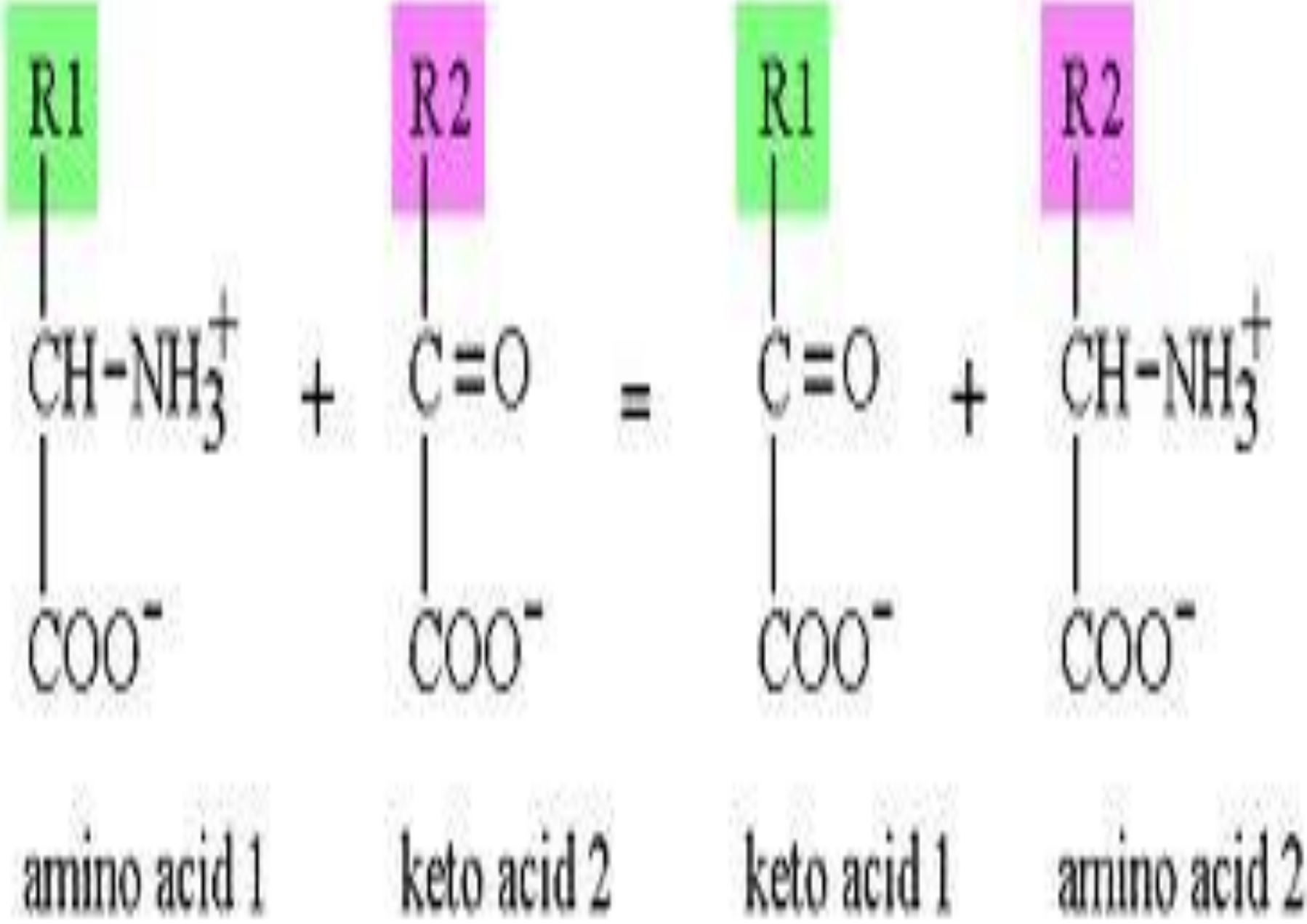
Removal of the amino group

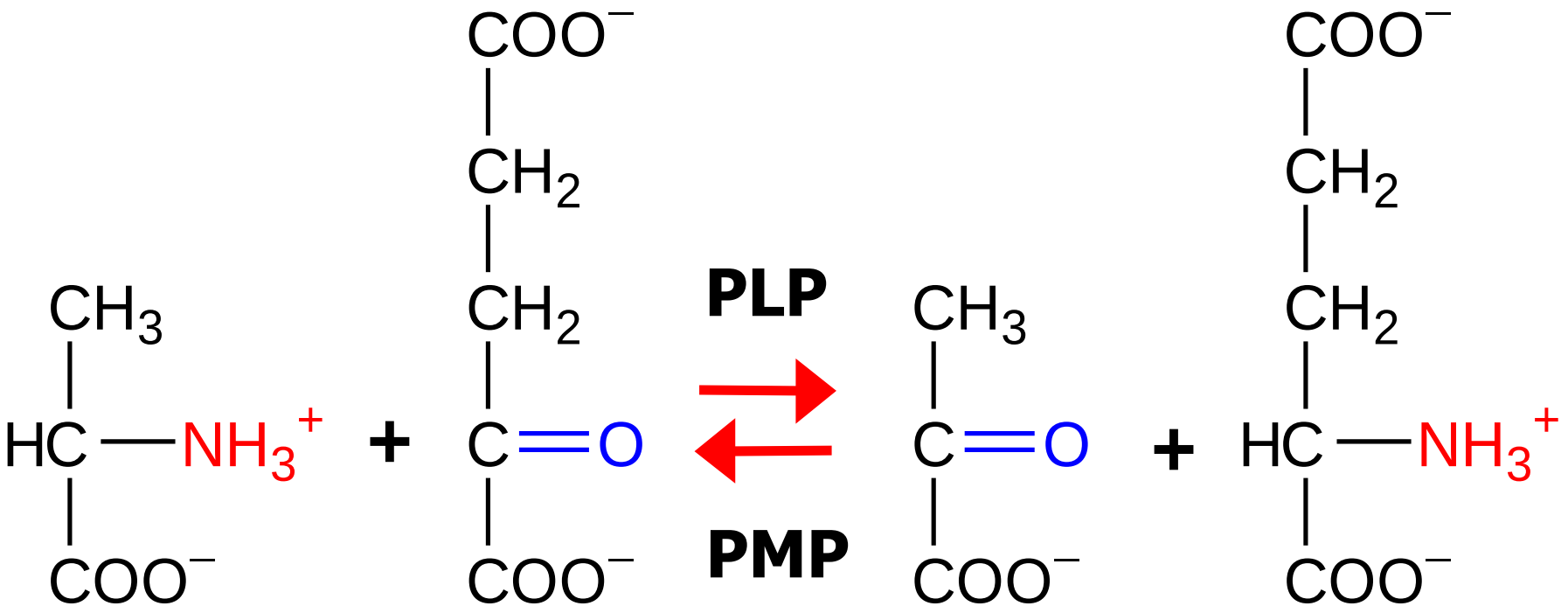
a. Transamination

The enzymes involved are called transaminases (aminotransferases).

Transaminase enzymes (Aminotransferase) catalyze the reversible transfer of an amino group between a-amino acid & a-keto acid and use the cofactor, pyridoxal phosphate (vitamin B6).

The purpose of transamination is transfer the amino groups to one species of amino acid (glutamate) that can be used for further nitrogen metabolism, either synthesis of other amino acid or elimination of NH_4^+.

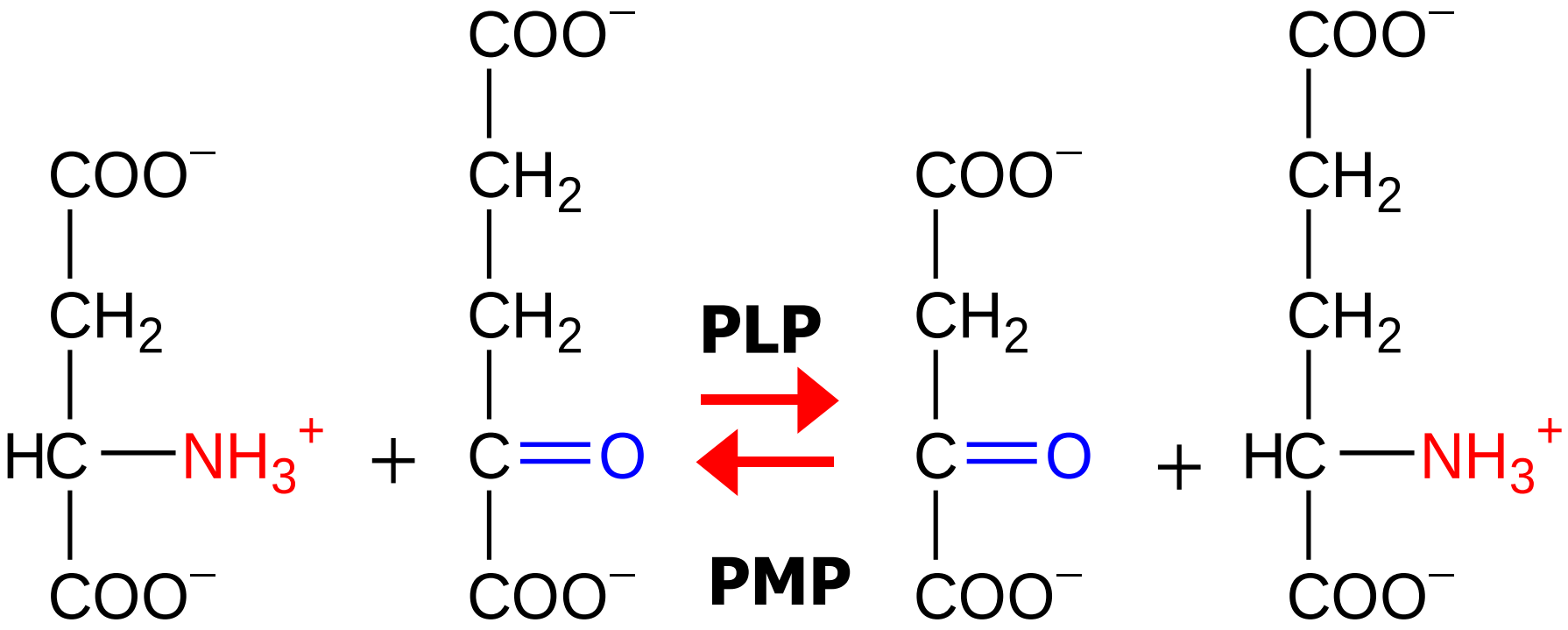

R1
CH-NH3+
COO-
amino acid 1
+
R2
C=O
COO-
keto acid 2
=
R1
C=O
COO-
keto acid 1
+
R2
CH-NH3+
COO-
amino acid 2



alanine α-ketoglutarate pyruvate glutamate

Aminotransferase (Transaminase)

(ALT, ALAT, sGPT)



aspartate α-ketoglutarate oxaloacetate glutamate

Aminotransferase (Transaminase)

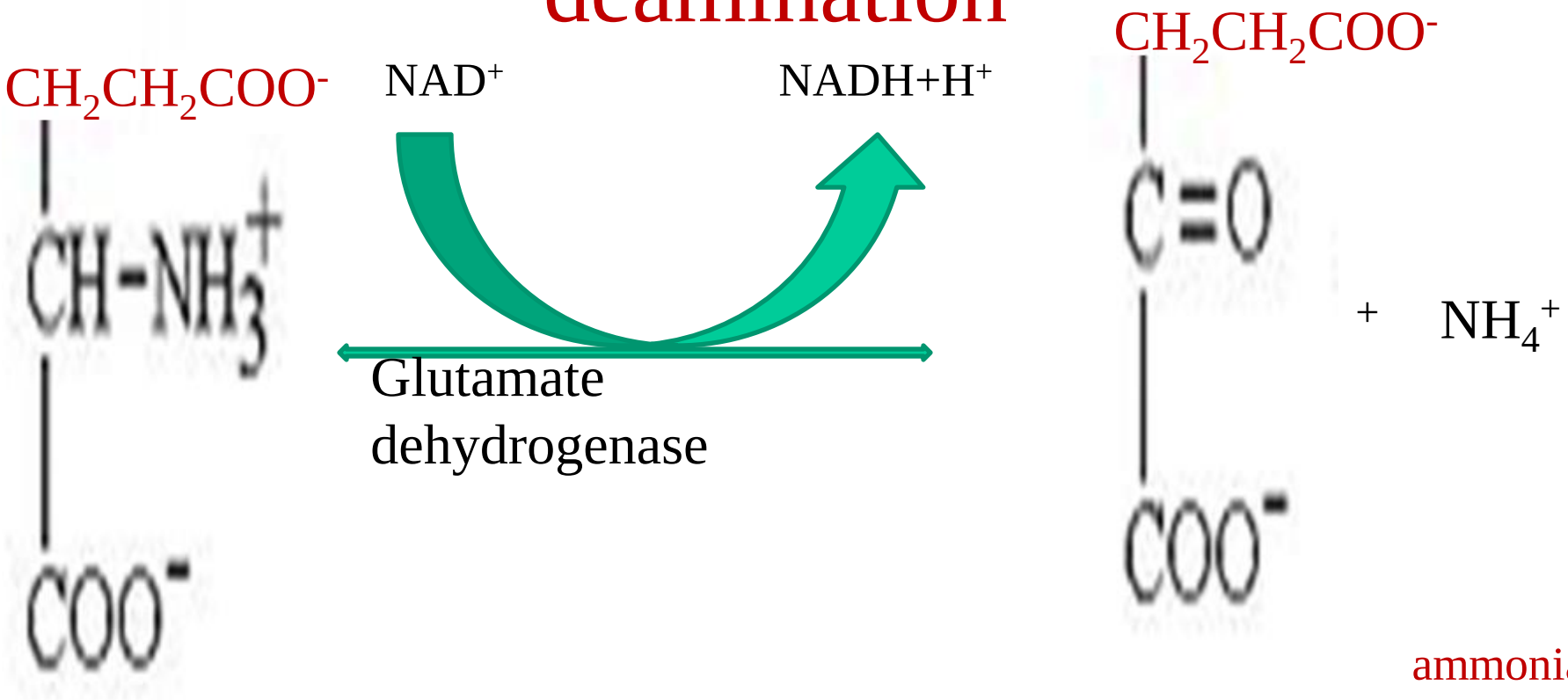
(AST, ASAT, sGOT)

b. Oxidative deamination

Glutamate is the only amino acid that undergoes rapid oxidative deamination by glutamate dehydrogenase.

This is the reason that aminotransferases commonly transfer α-amino groups to α-ketoglutarate to form glutamate.

Conversion of glutamate to α-ketoglutarate by oxidative deamination



Glutamate

α-Ketoglutarate

ammonia

to the urea cycle

Excretion of Nitrogen

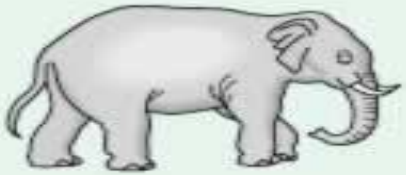
Proteins

Nucleic acids

Amino acids

Nitrogenous bases

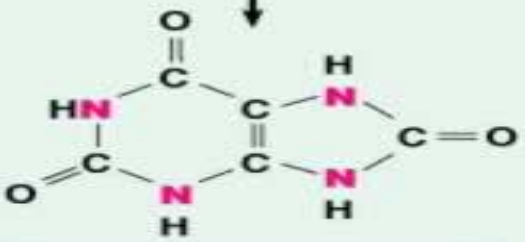
$-NH_2$
Amino groups



Most aquatic animals, including many fishes

Mammals, amphibians, sharks, some bony fishes

Birds, insects, many reptiles, land snails



Ammonia

Urea

Uric acid