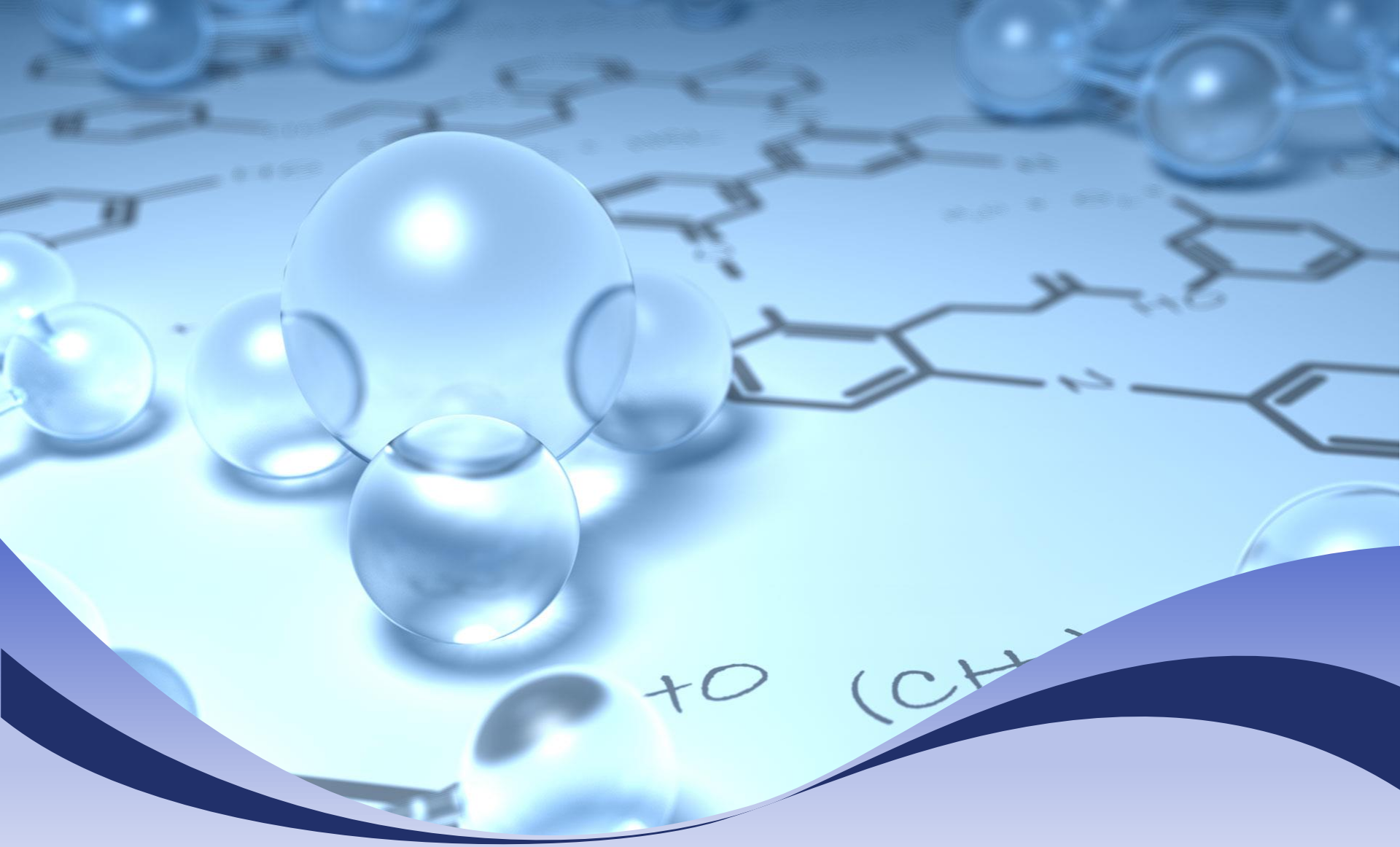
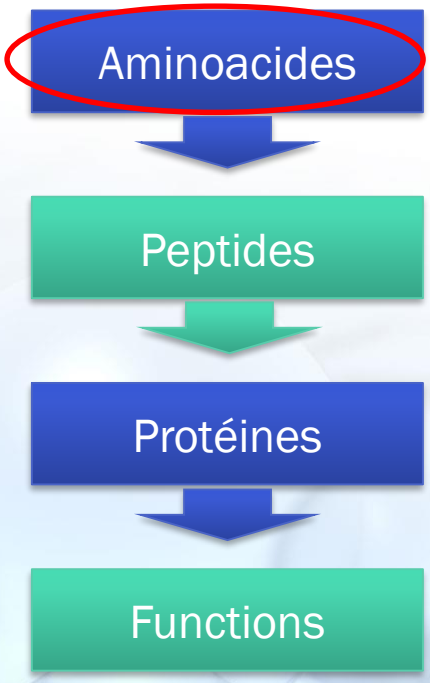


CHMI 3226E

Metabolism of Proteins/Aminoacids

Laurentian University
Université Laurentienne

Proteins: **Structure & Functions**



Composition of an adult (70Kg)

1. H20 ----- 42 Kg
2. Proteins----12 Kg
3. Lipides-----12 Kg
4. Minerals---3.5 Kg
5. Carbohydrates-----0,5 Kg

Digestion of Proteins

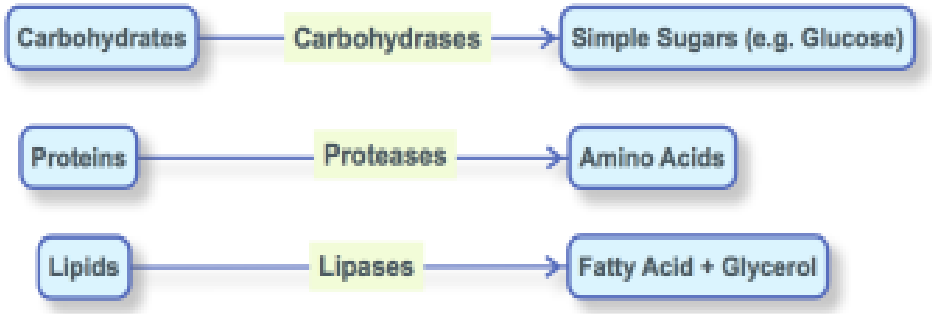
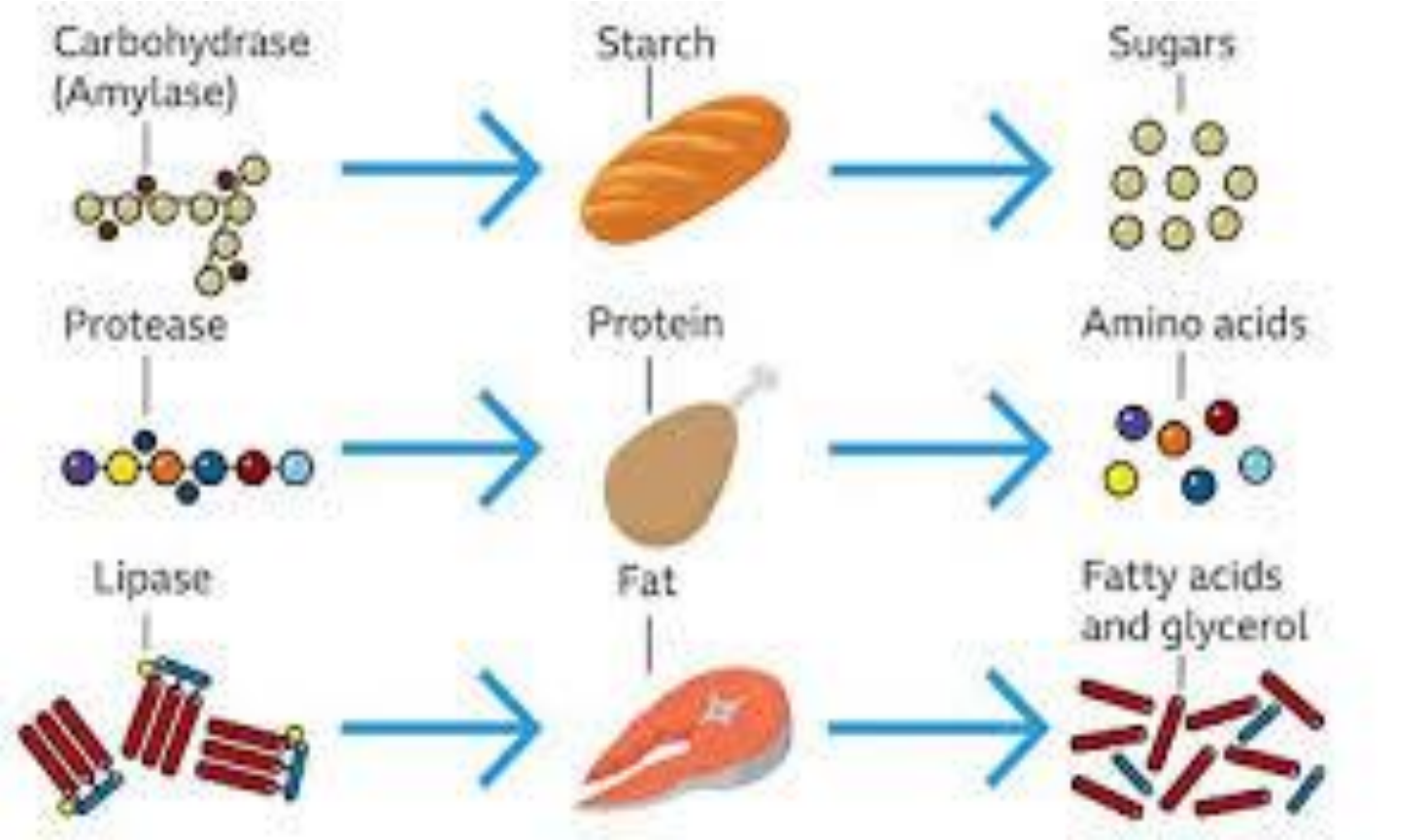


Fig 6. The Enzymes Involved in Digestion.

Digestion


Carbohydrase (Amylase)
Starch
Sugars
Protease
Protein
Amino acids
Lipase
Fat
Fatty acids and glycerol

Protein into amino-acids

Pepsin-Stomach

Trypsin-Pancreatic fluid

Chymotrypsin-Pancreatic fluid

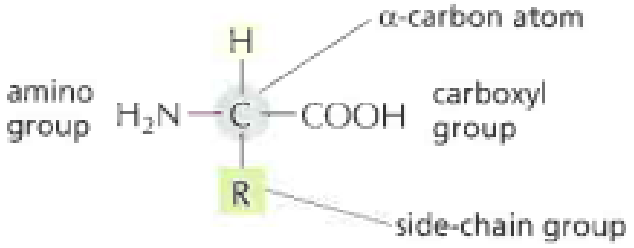
Etc----------= Amino acids

Amino acids

AMINO ACID		
Aspartic acid	Asp	D
Glutamic acid	Glu	E
Arginine	Arg	R
Lysine	Lys	K
Histidine	His	H
Asparagine	Asn	N
Glutamine	Gln	Q
Serine	Ser	S
Threonine	Thr	T
Tyrosine	Tyr	Y

AMINO ACID		
Alanine	Ala	A
Glycine	Gly	G
Valine	Val	V
Leucine	Leu	L
Isoleucine	Ile	I
Proline	Pro	P
Phenylalanine	Phe	F
Methionine	Met	M
Tryptophan	Trp	W
Cysteine	Cys	C

Structure



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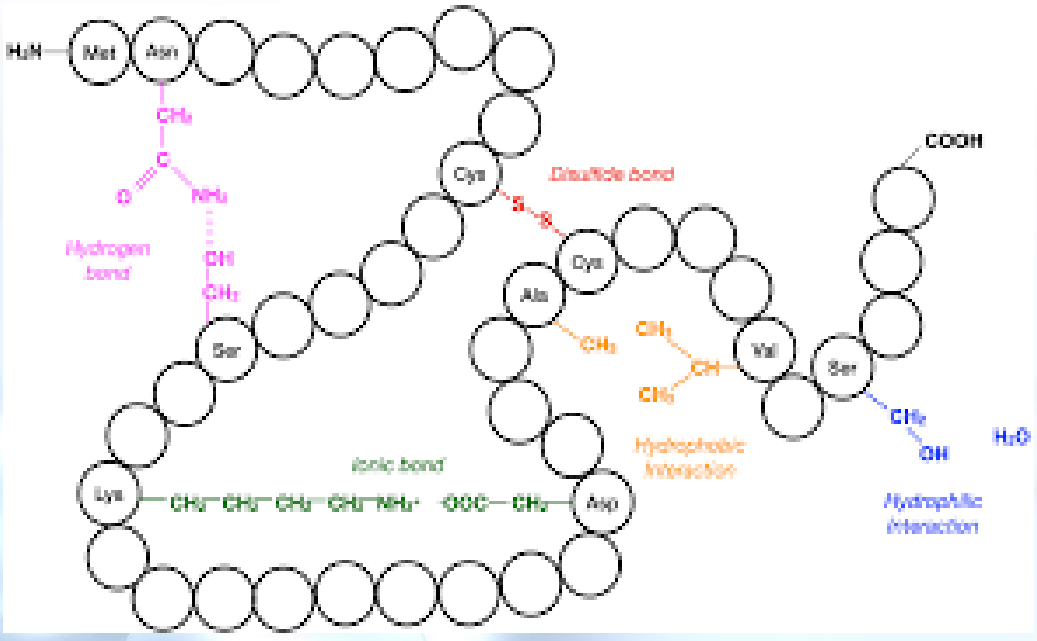
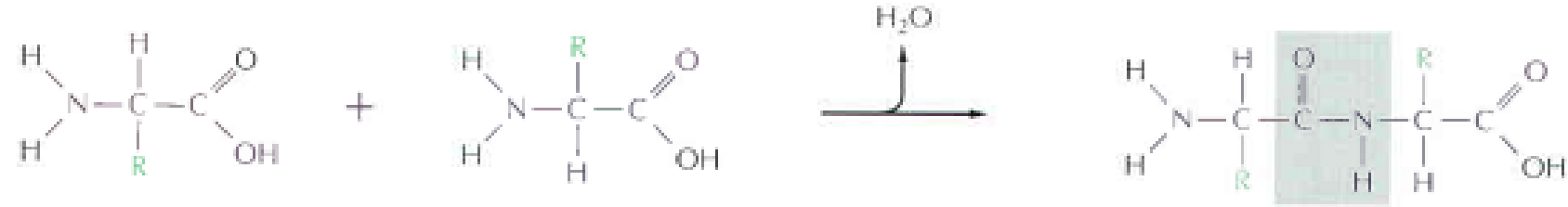
Amino-Acids

Essential	Conditionally Non-Essential	Non-Essential
Histidine	Arginine	Alanine
Isoleucine	Asparagine	Asparatate
Leucine	Glutamine	Cysteine
Methionine	Glycine	Glutamate
Phenylalanine	Proline	
Threonine	Serine	
Tryptophan	Tyrosine	
Valine		
Lysine		

Primary Structure



Polypeptides:



- Dipeptides, tripeptides, tetrapeptides, etc.

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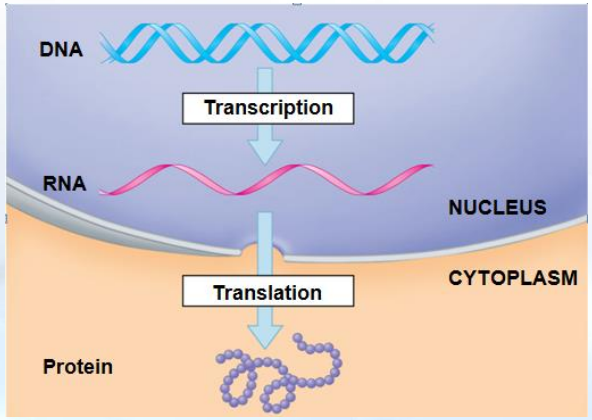
Polypeptides/Proteins



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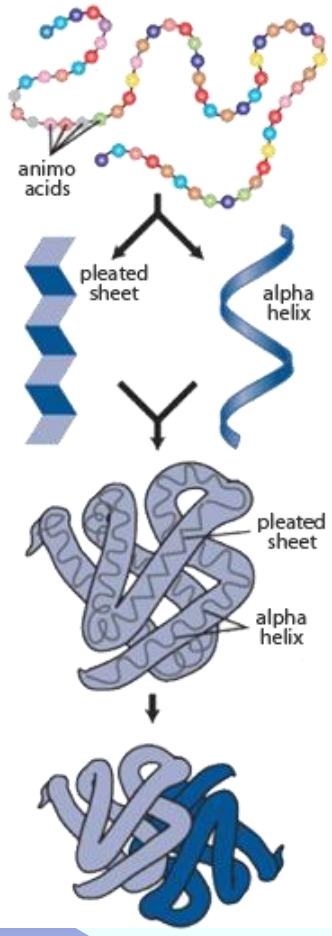
Proteins



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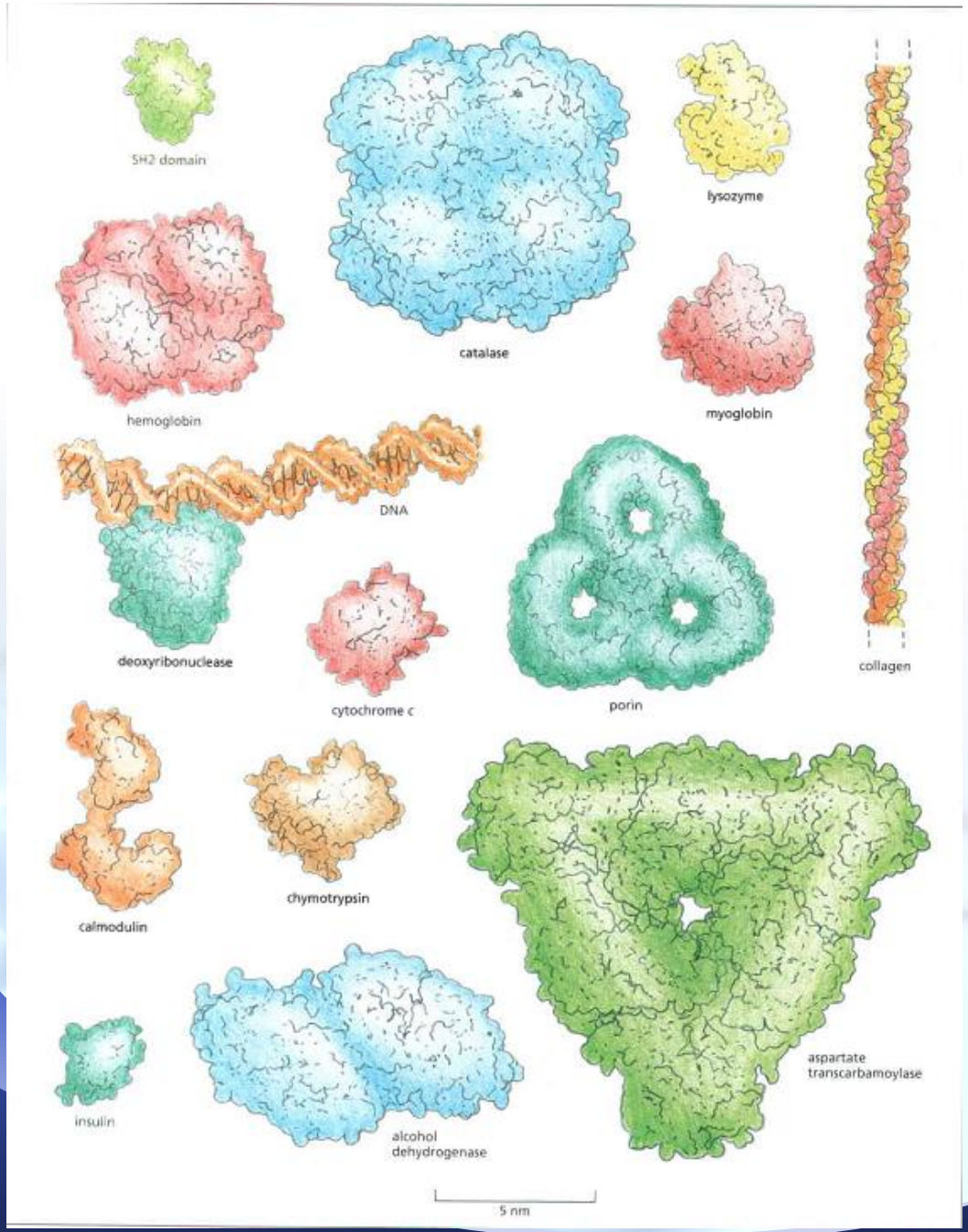
Proteins



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Protein-conjugated

Glycoproteins------protein+carbohydrates

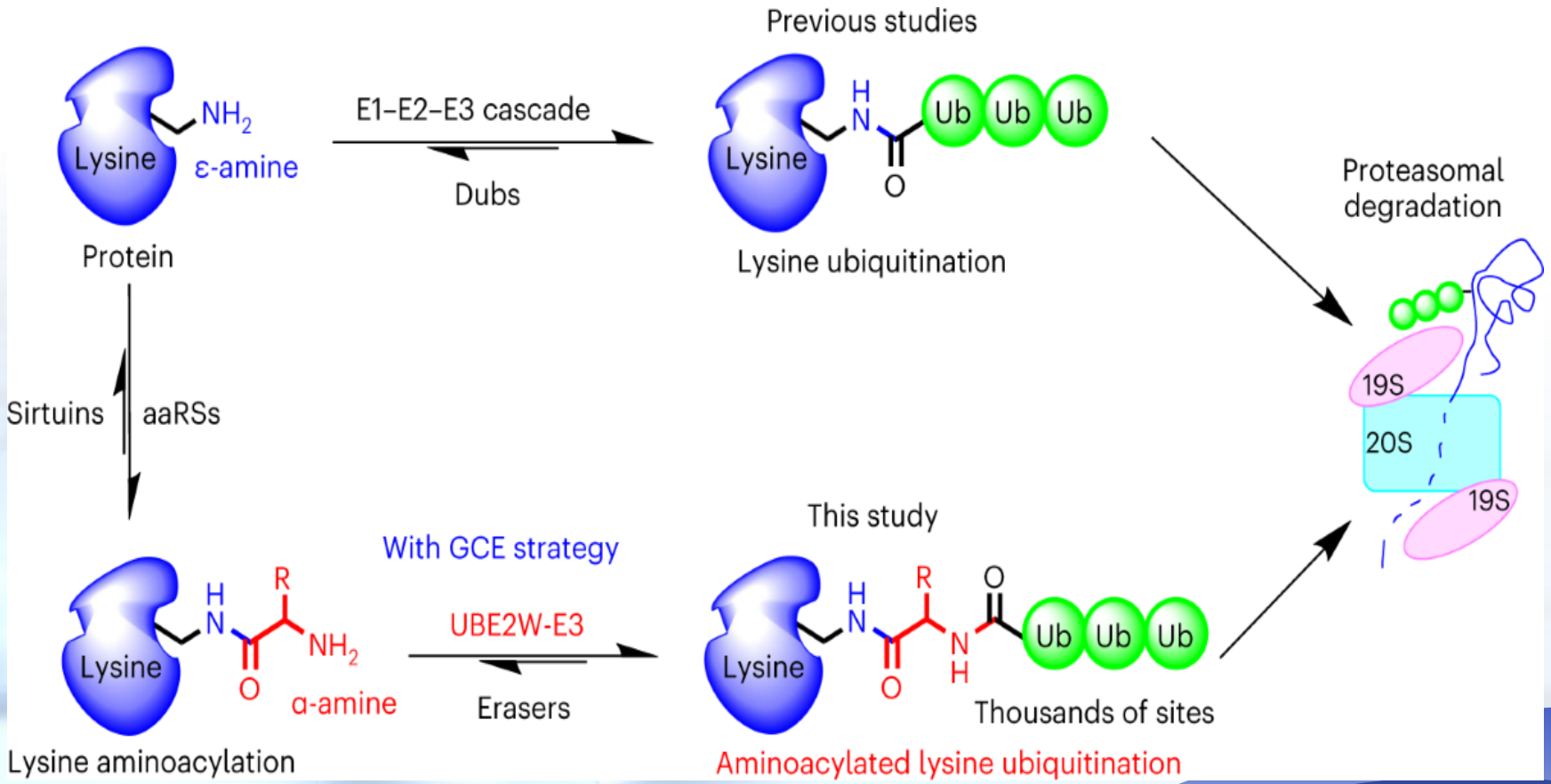
Transferrine, ceruloplasmine, membranes etc

Lipoproteins------protein + lipids

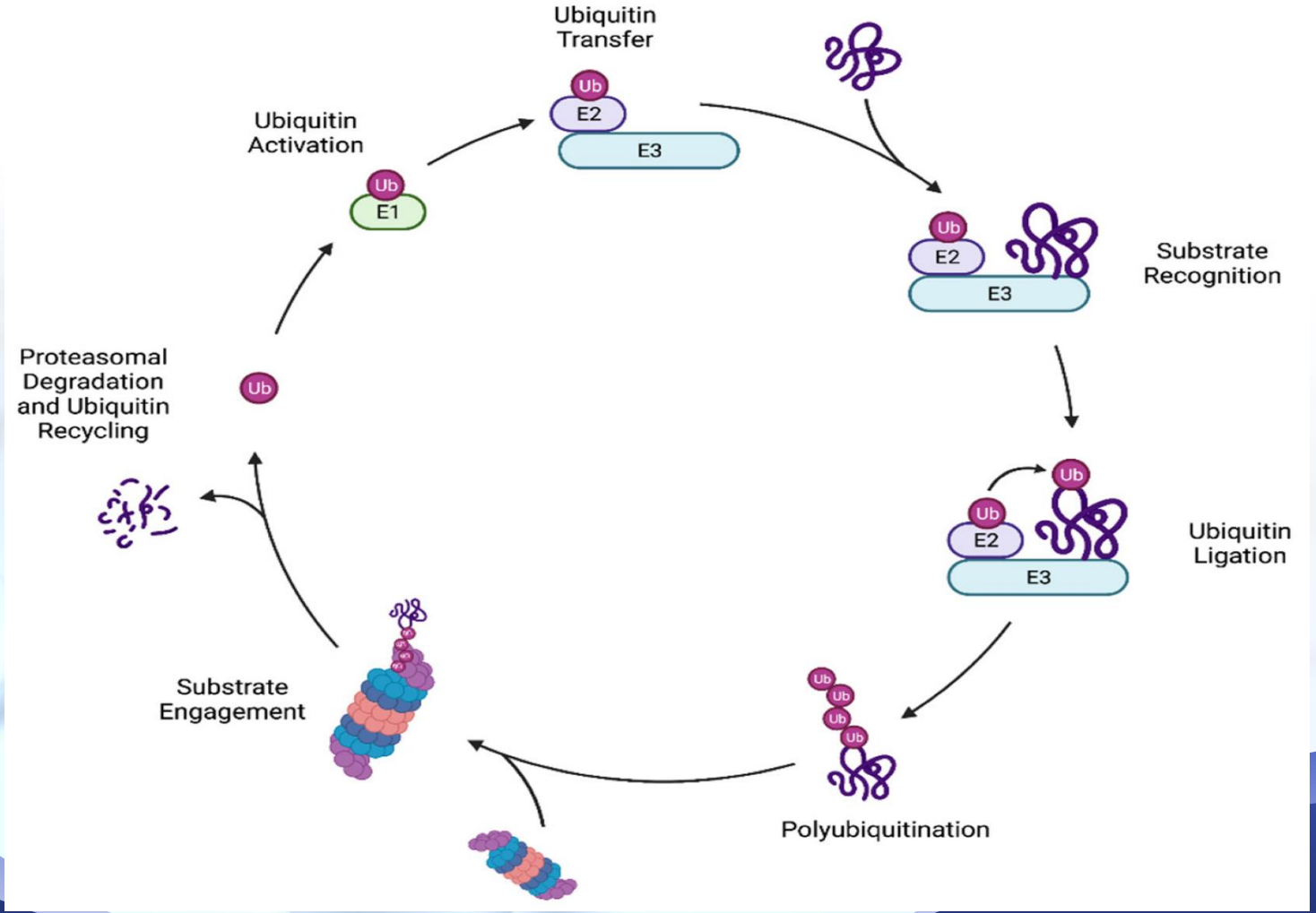
Intracellular protein degradation

1. Regulation of Protein Levels:
2. Removal of Damaged or Misfolded Proteins:-Ubiquitin system
3. Recycling of Amino Acids:
4. Control of Cellular Processes:
5. Response to Environmental Stress:
6. **Energy Production:**

Ubiquitin binding to damaged proteins



Intracellular Protein Degradation



Intracellular Protein Degradation

1. Regulation of Protein Levels:
2. Removal of Damaged or Misfolded Proteins:-Ubiqutin system
3. Recycling of Amino Acids:
4. Control of Cellular Processes & all physiological responses
5. Response to Environmental Stress:
6. Energy Production:

Digestion/degradation of proteins

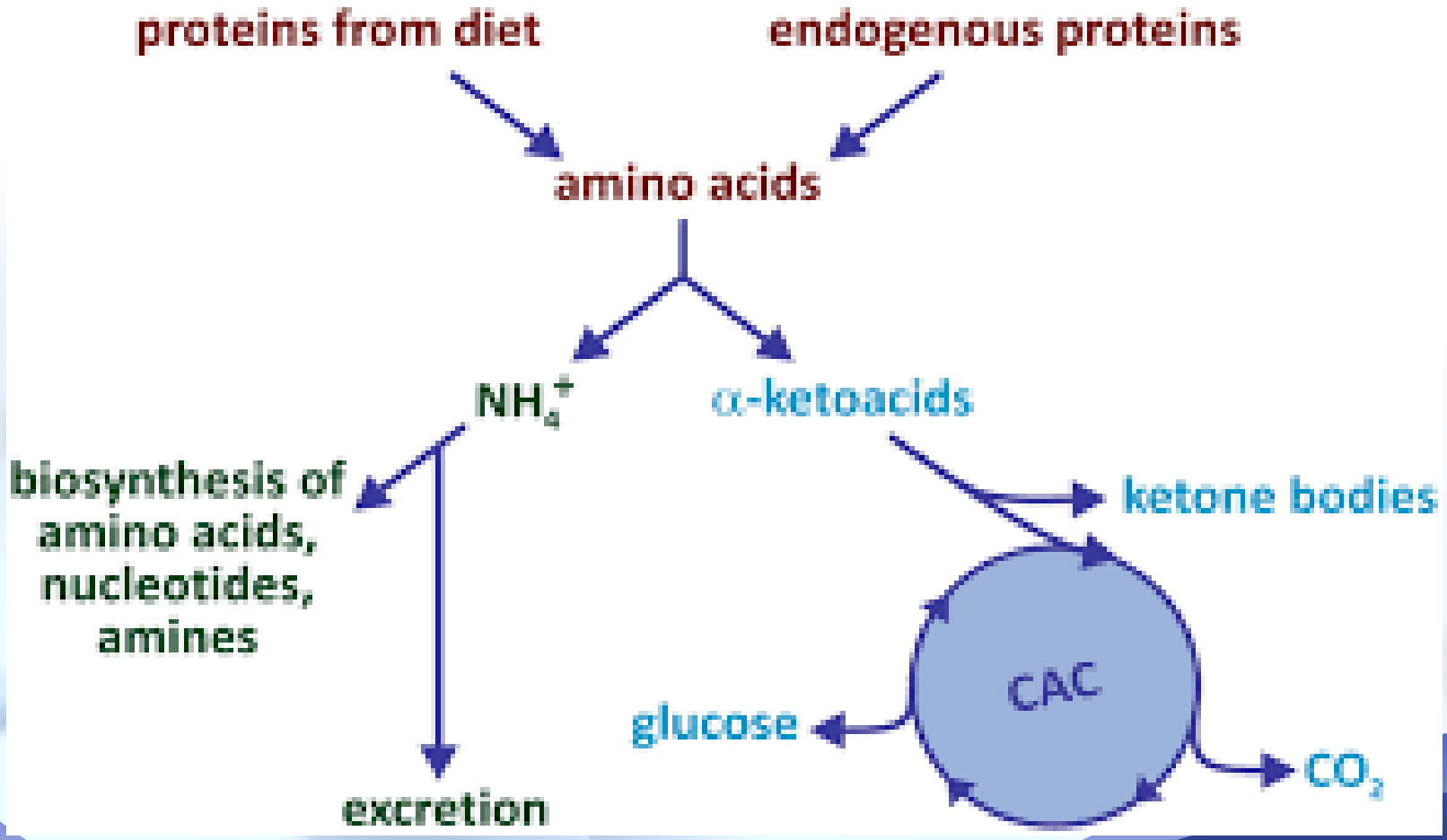
Proteins---------proteases= amino-acids

Pepsin

Trypsin

Chymotrypsin

Proteins-ATP production



N-terminal rule and protein degradation Met-Stable, Lys/Arg/aromatic a.a-unstable

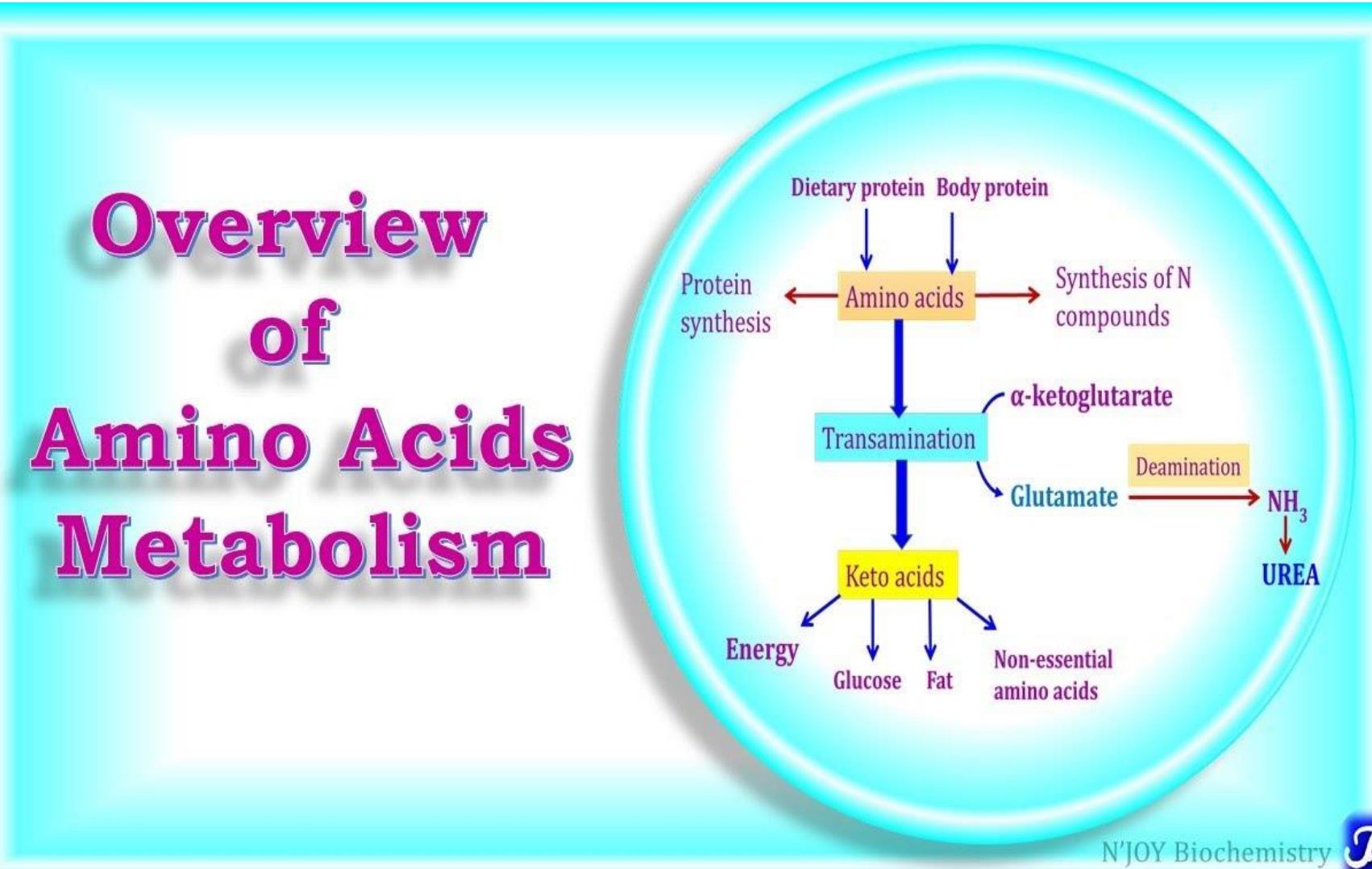
Table 10.2 N-Terminal Rule for Protein Stability

N-Terminal Residue	Approximate Half-Life (Minutes)
Met, Gly, Ala, Ser, Thr, Val	120
Ile, Glu, Tyr	30
Gln, Pro	10
Leu, Phe, Asp, Lys, Arg	2–3

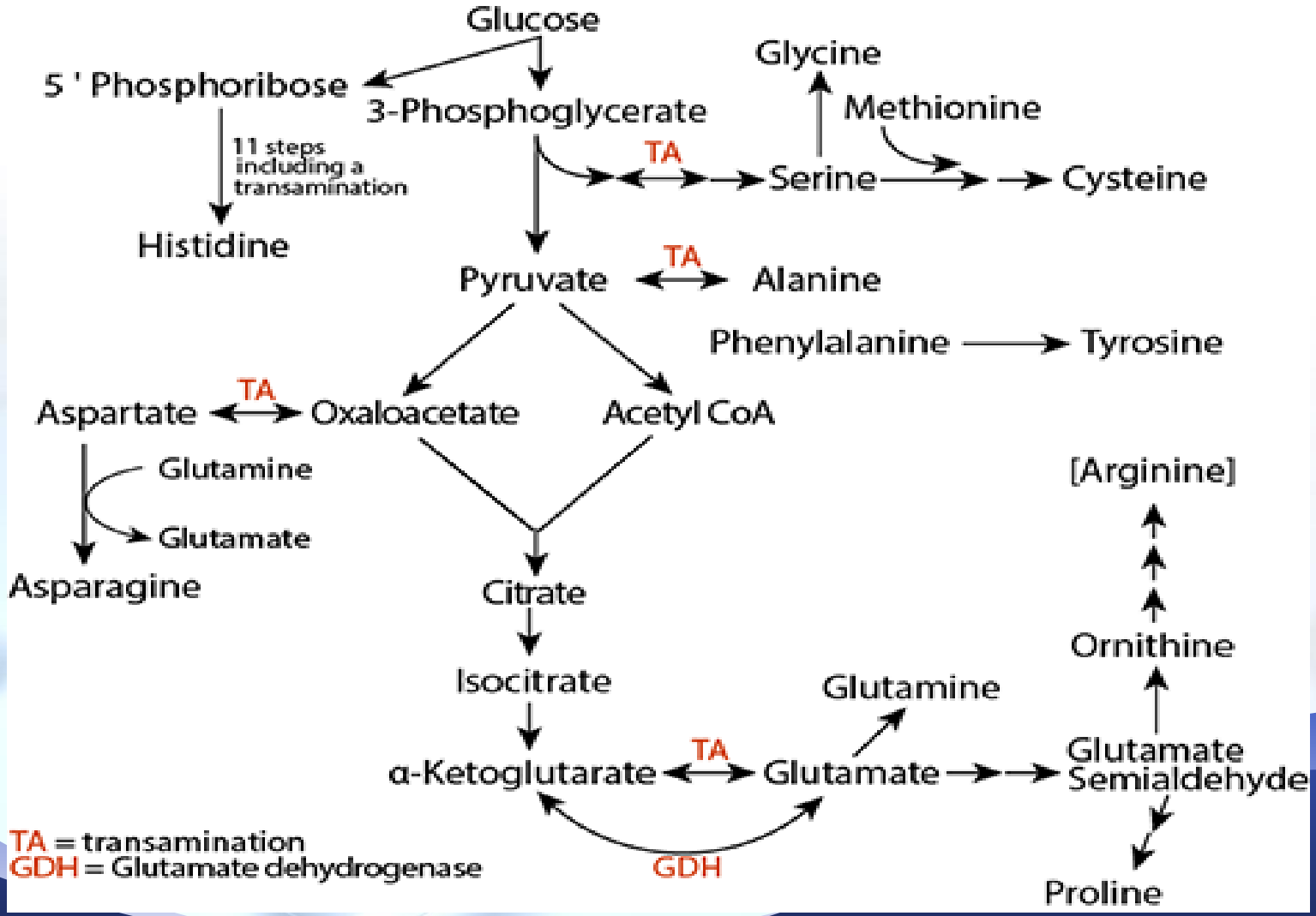
Stability of Proteins

•**Methionine (Met)** at the N-terminus generally provides long-lasting stability.
•**Phenylalanine (Phe)** and **Leucine (Leu)** promote fast degradation half-lives measured in minutes.
•**Arginine (Arg)** and **Lysine (Lys)**, though not as fast as the hydrophobic

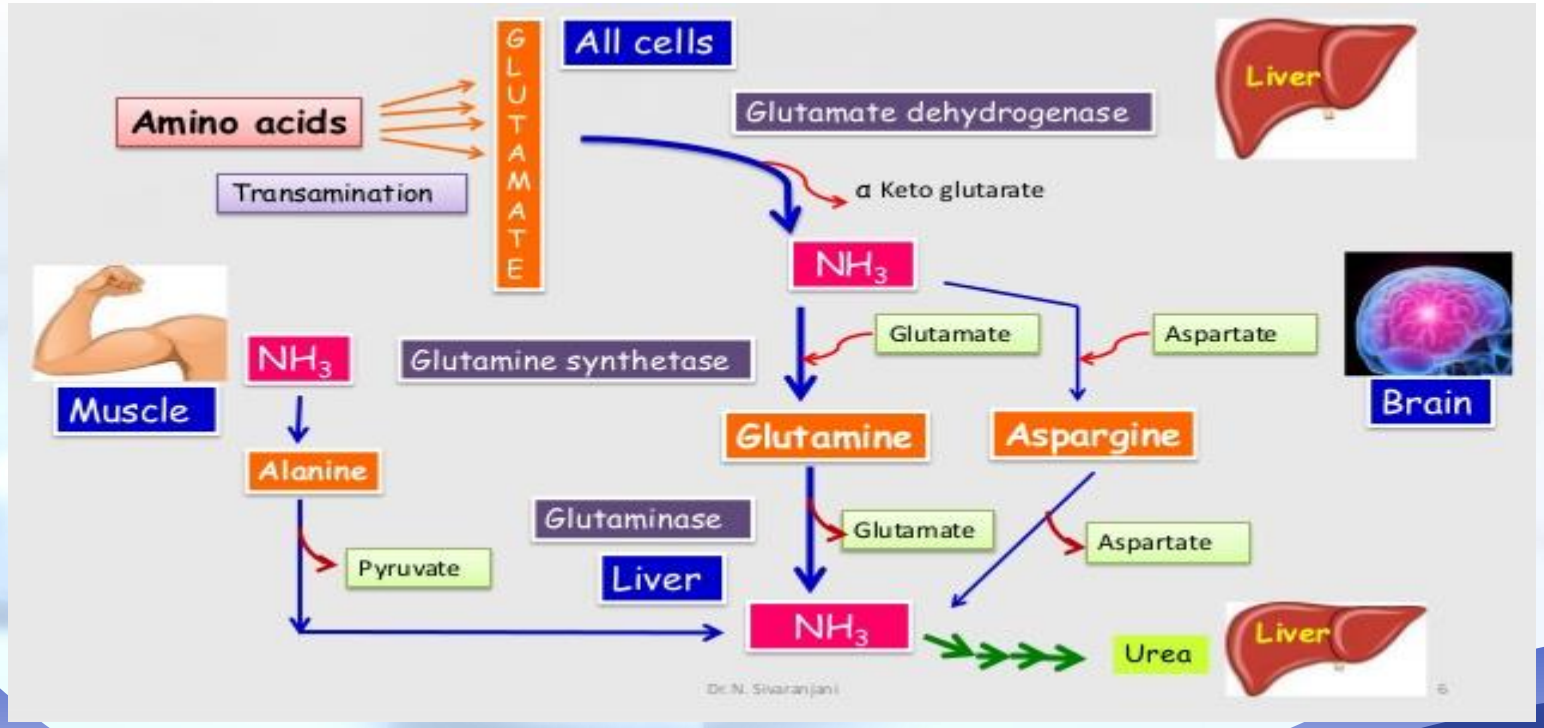
Proteins to Aminoacids



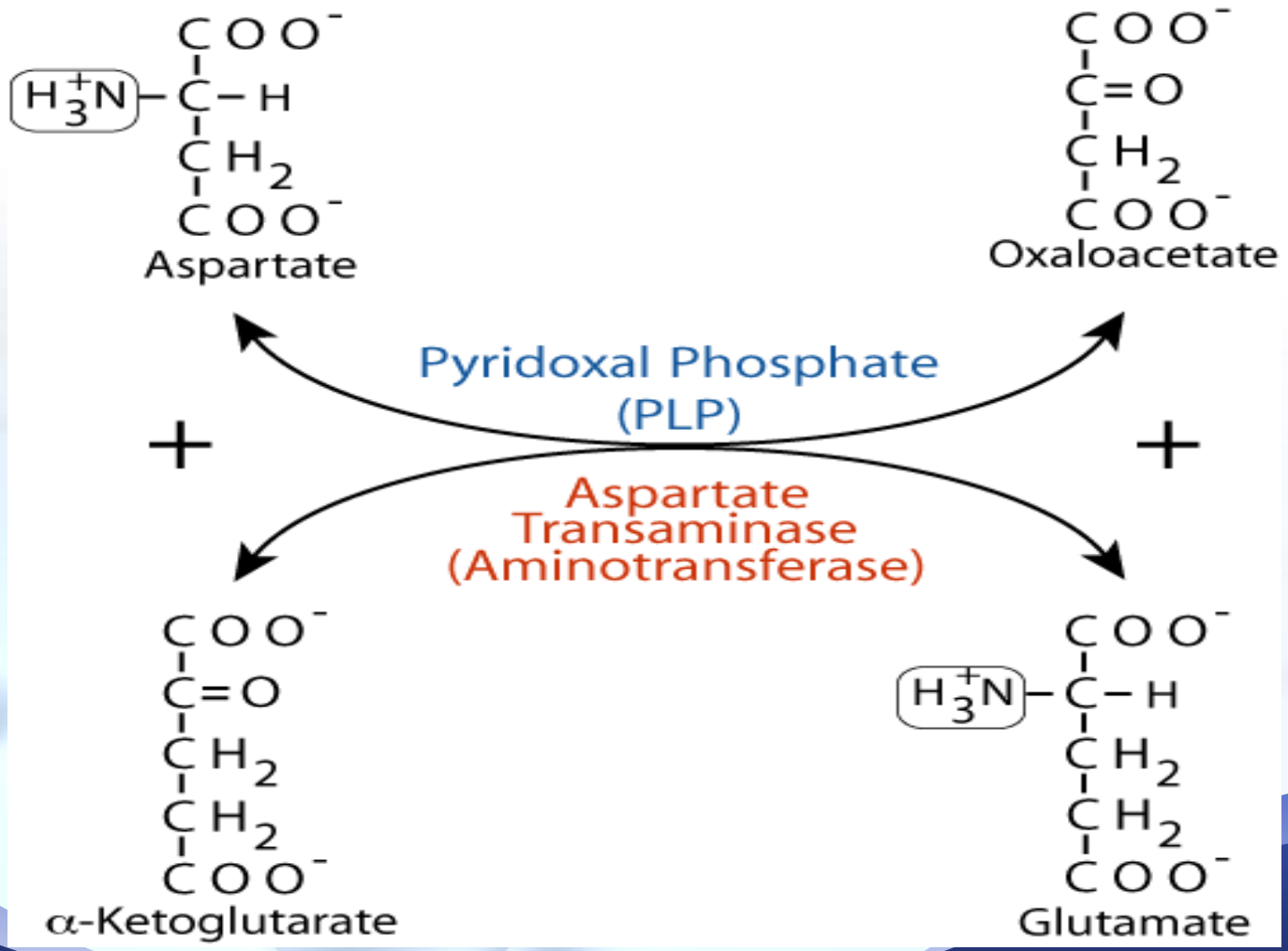
Transamination and Deamination



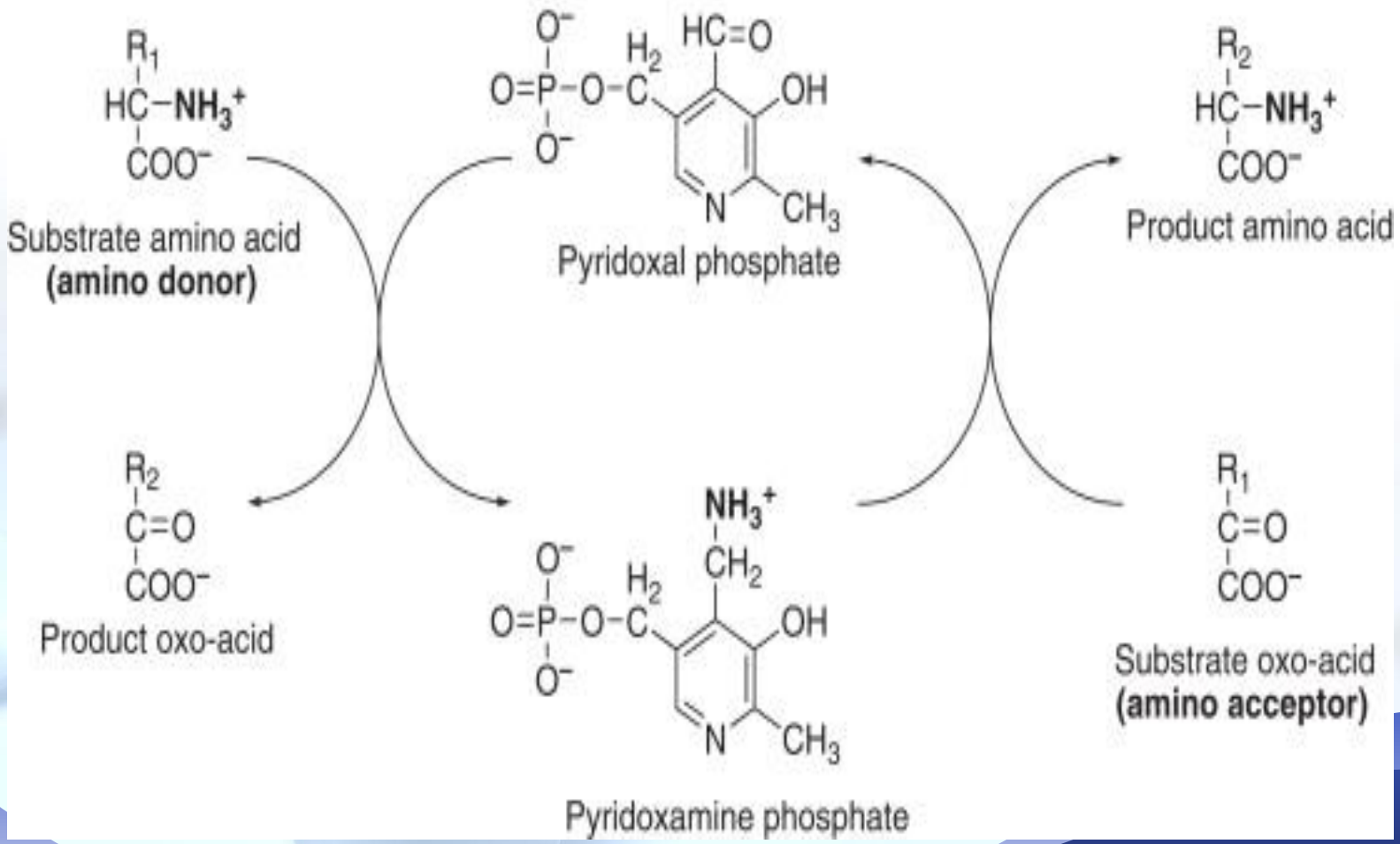
Protein-a.a-urea cycle



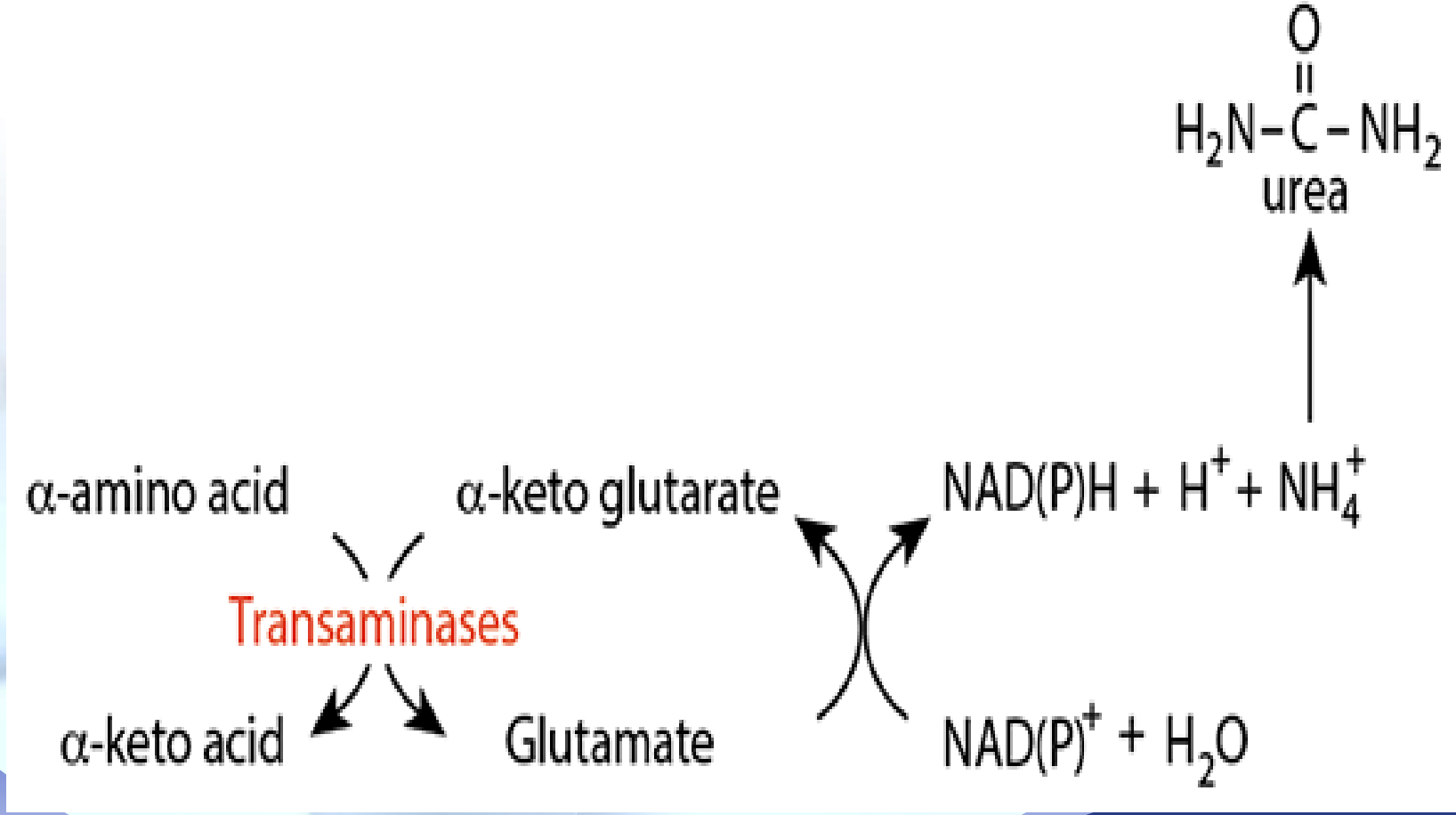
Transaminase



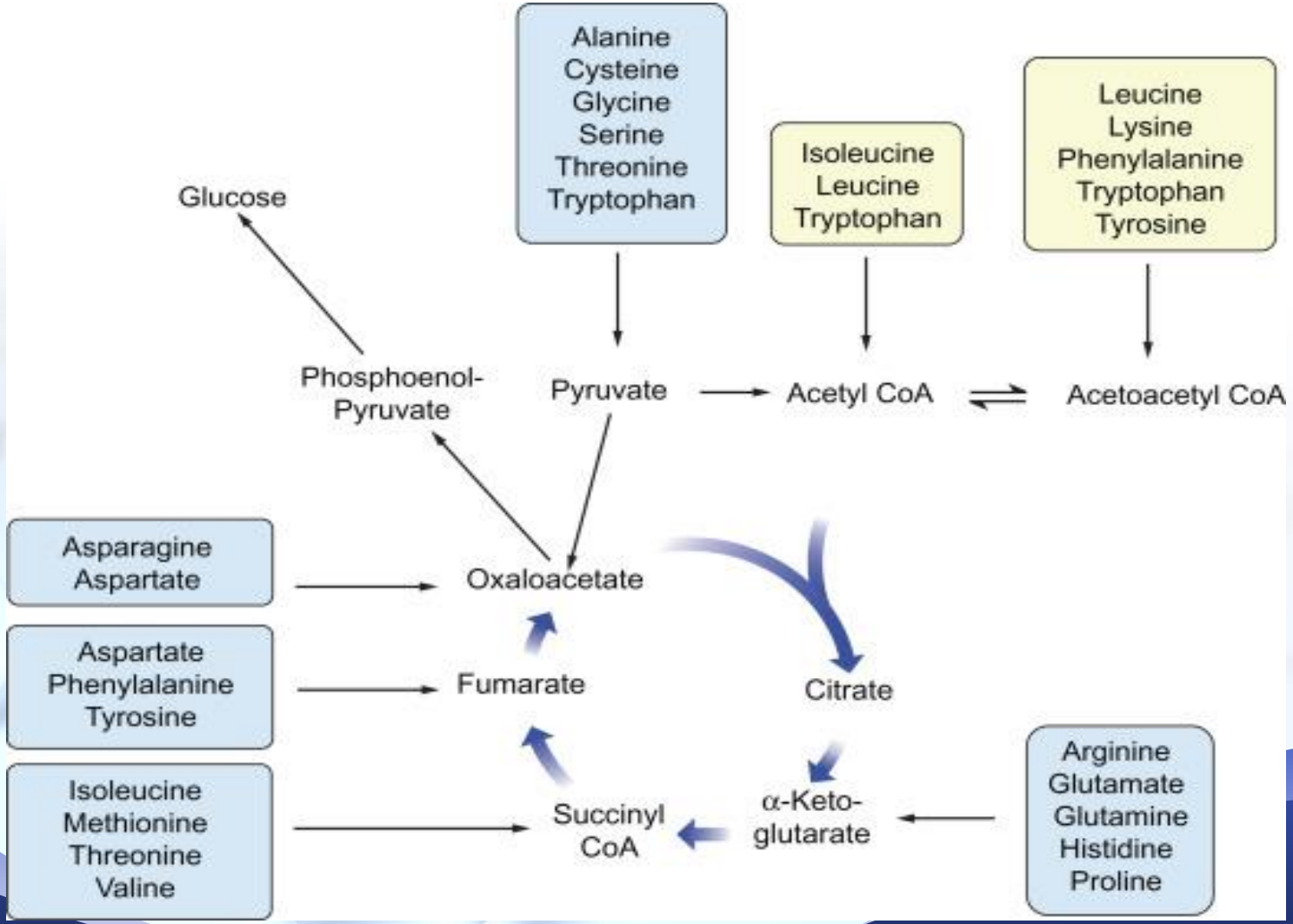
Pyridoxal phosphate (Vitamin B6)



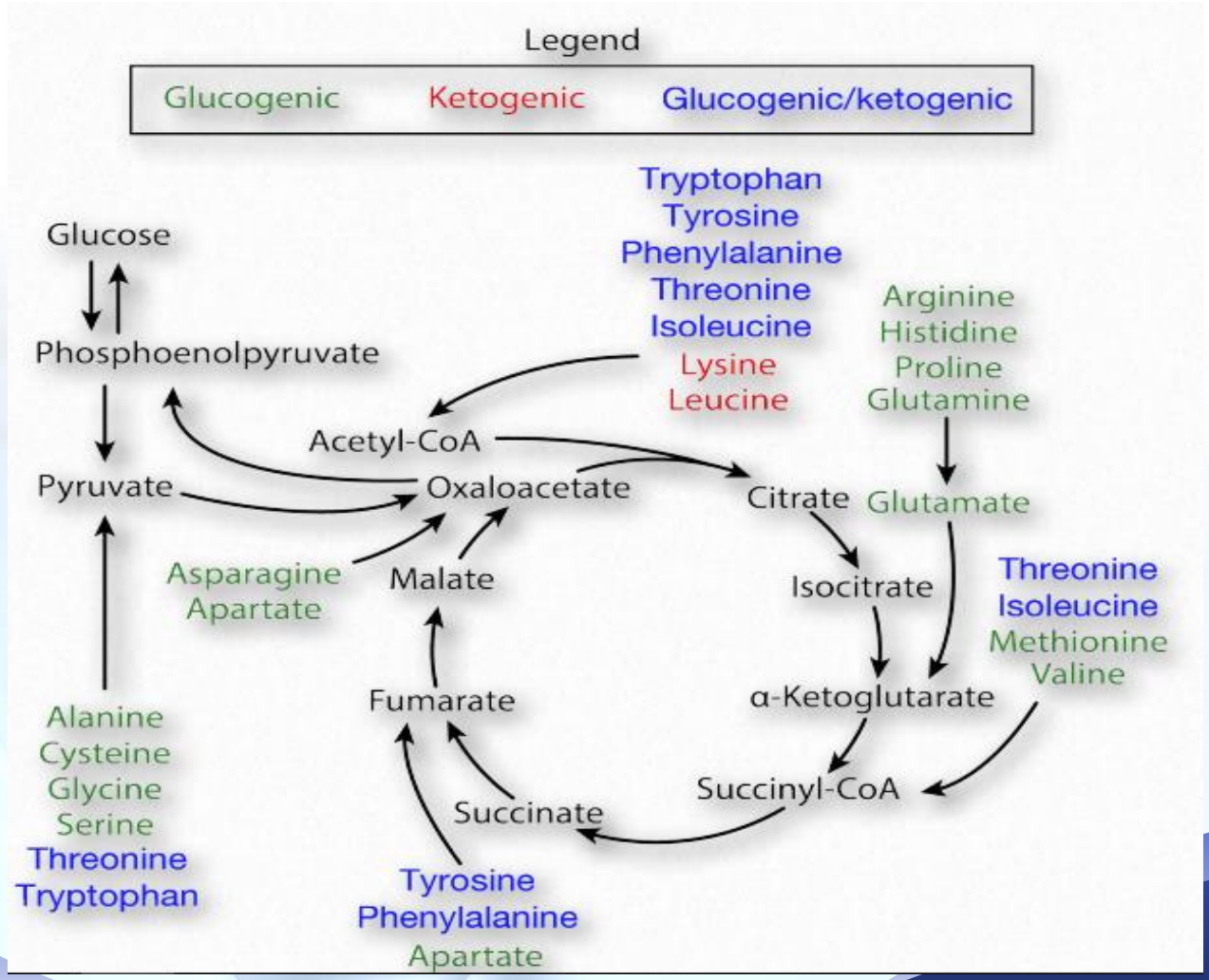
Transamination



Glucogenic/Ketogenic amino acids



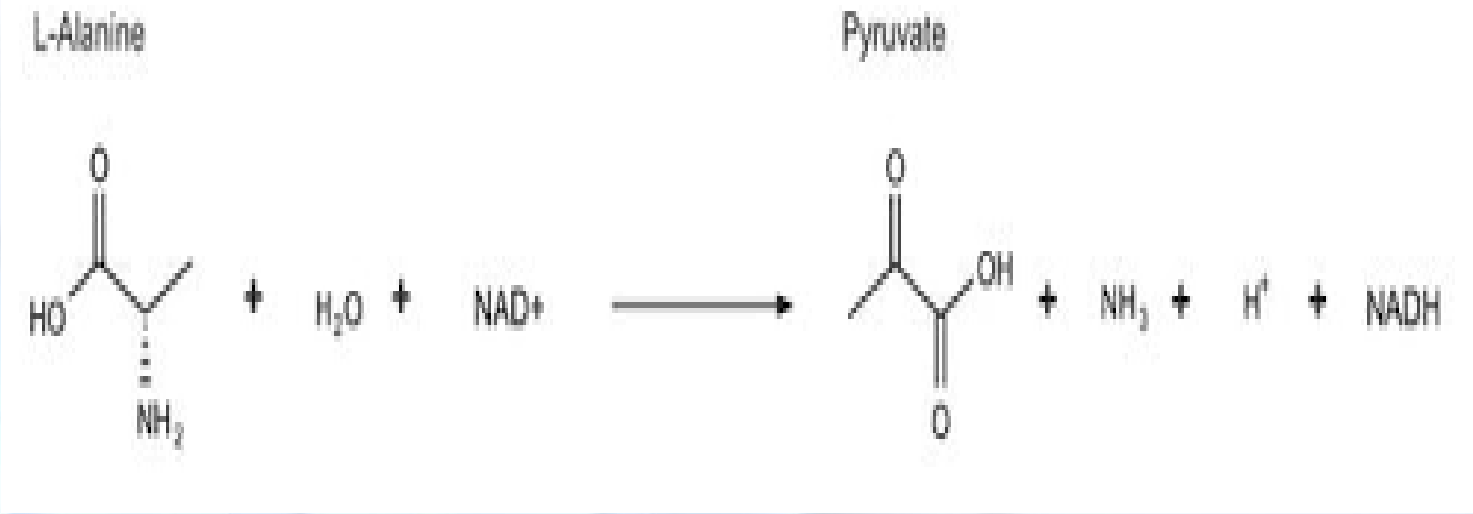
Catabolism of amino acids



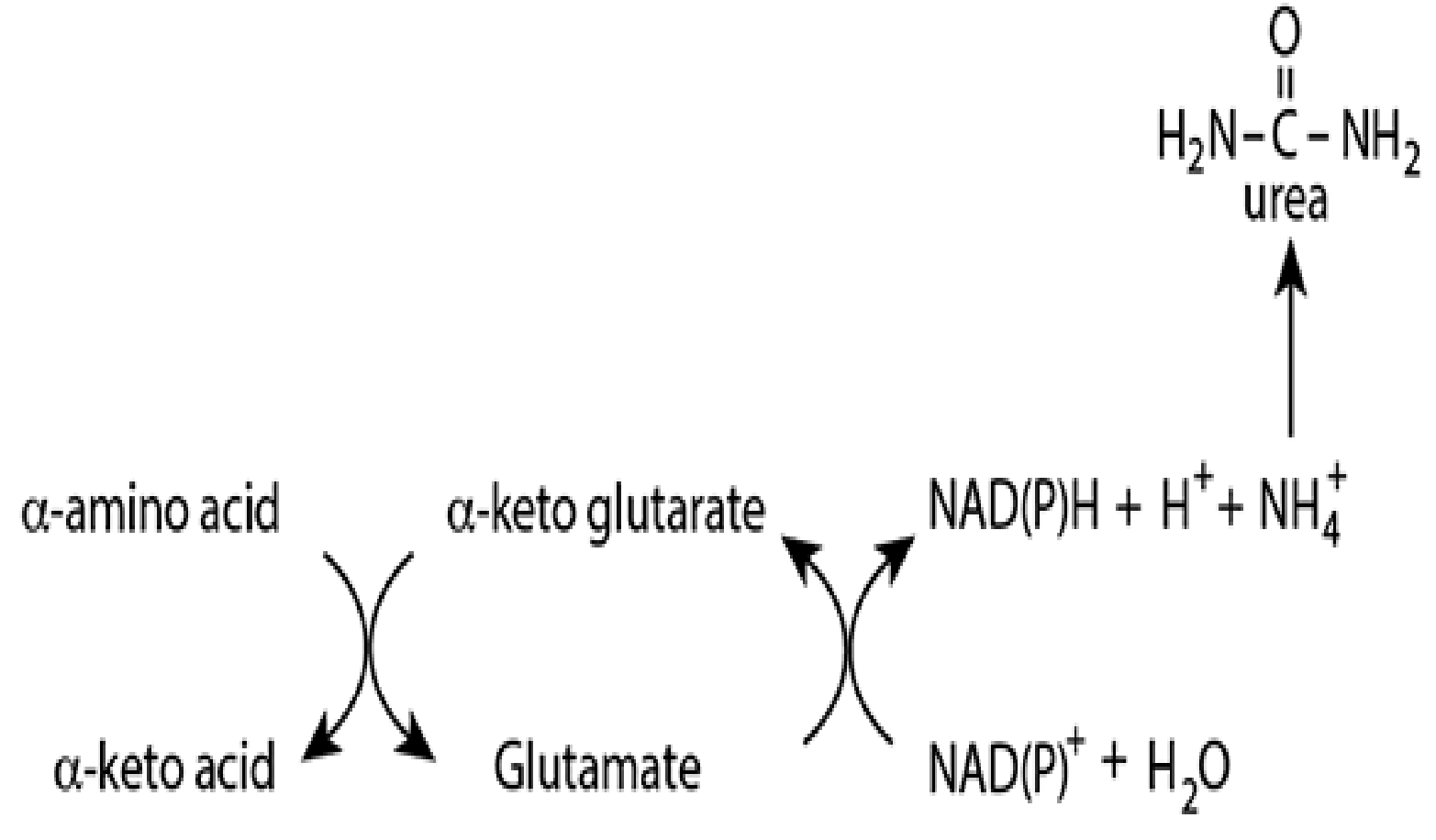
Glucogenic/Ketogenic amino-acids

Glucogenic amino acids	Glucogenic and ketogenic	Ketogenic amino acids
Alanine, Arginine, Asparagine, Aspartate Asparagine, Cysteine, Methionine Glutamate, Glutamine, Glycine, Histidine Proline, Serine, Threonine,Valine	Tyrosine Isoleucine Phenylalanine Tryptophan	Leucine Lysine

Alanine dehydrogenase



Transaminases-Glutamate dehydrogenase



Glutamate Dehydrogenase

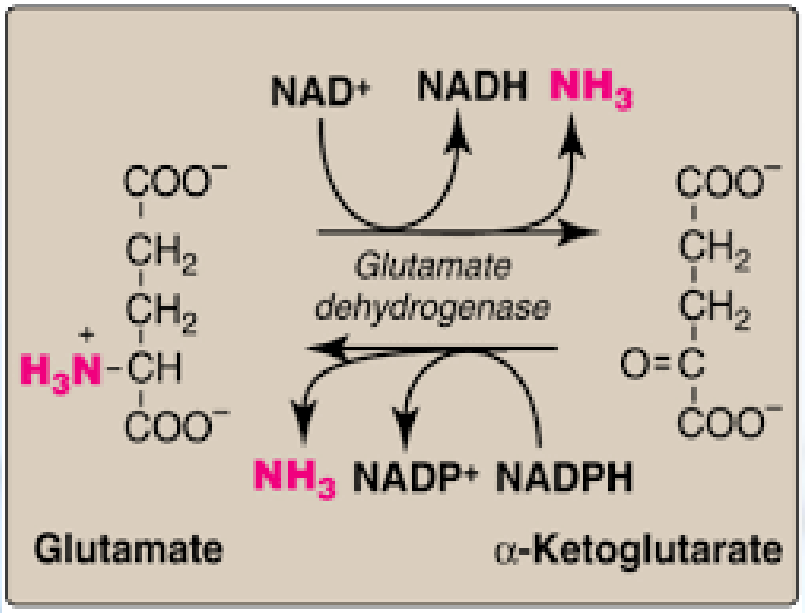
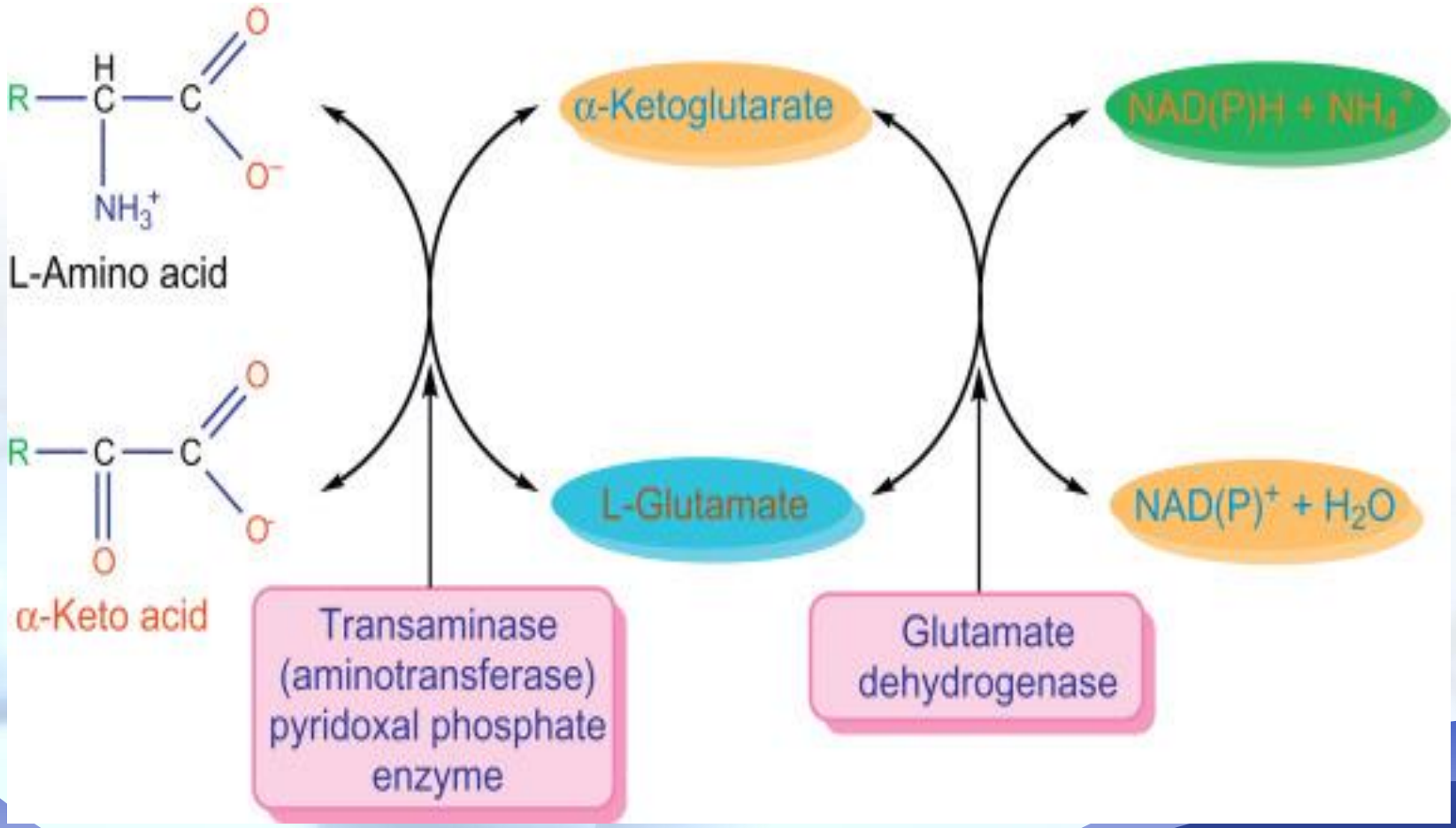
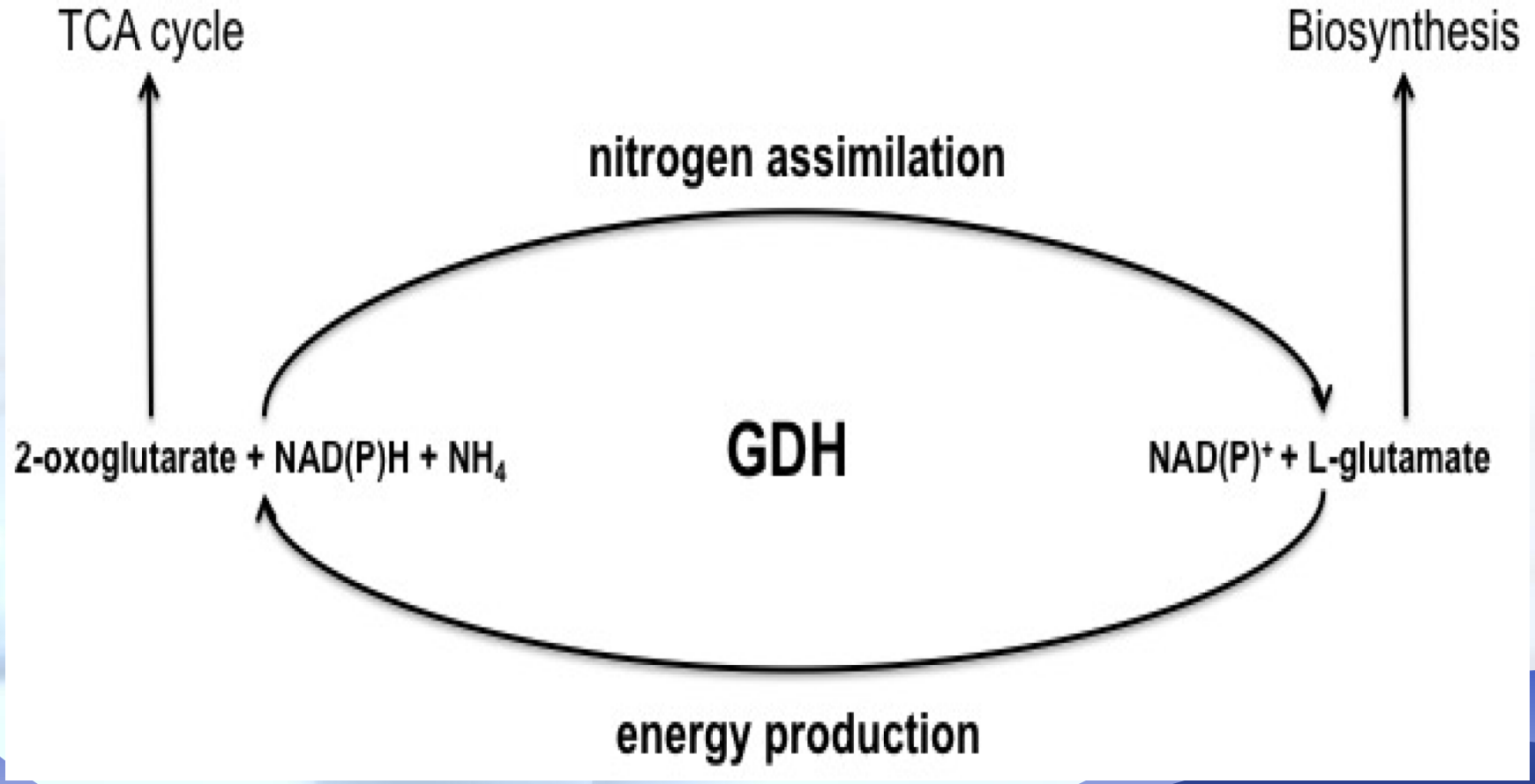


Figure 19.11
Oxidative deamination by glutamate dehydrogenase.

Glutamate Dehydrogenase



Glutamate Dehydrogenase



Regulation of GDH

1. Allosteric Regulation

ADP/AMP/NAD+ (activators): GDH is activated by low-energy signals such as ADP and AMP.

GTP/ATP/NADH (inhibitors): High-energy molecules like GTP and ATP inhibit GDH activity.

2. Hormonal Regulation

Insulin: In the fed state, insulin decreases GDH activity, which inhibits the catabolism of amino acid.

Glucagon and Cortisol: During fasting or stress, these hormones promote GDH activity to increase amino acid catabolism-glucose

4. Post-translational Modifications

ADP-ribosylation: inhibits

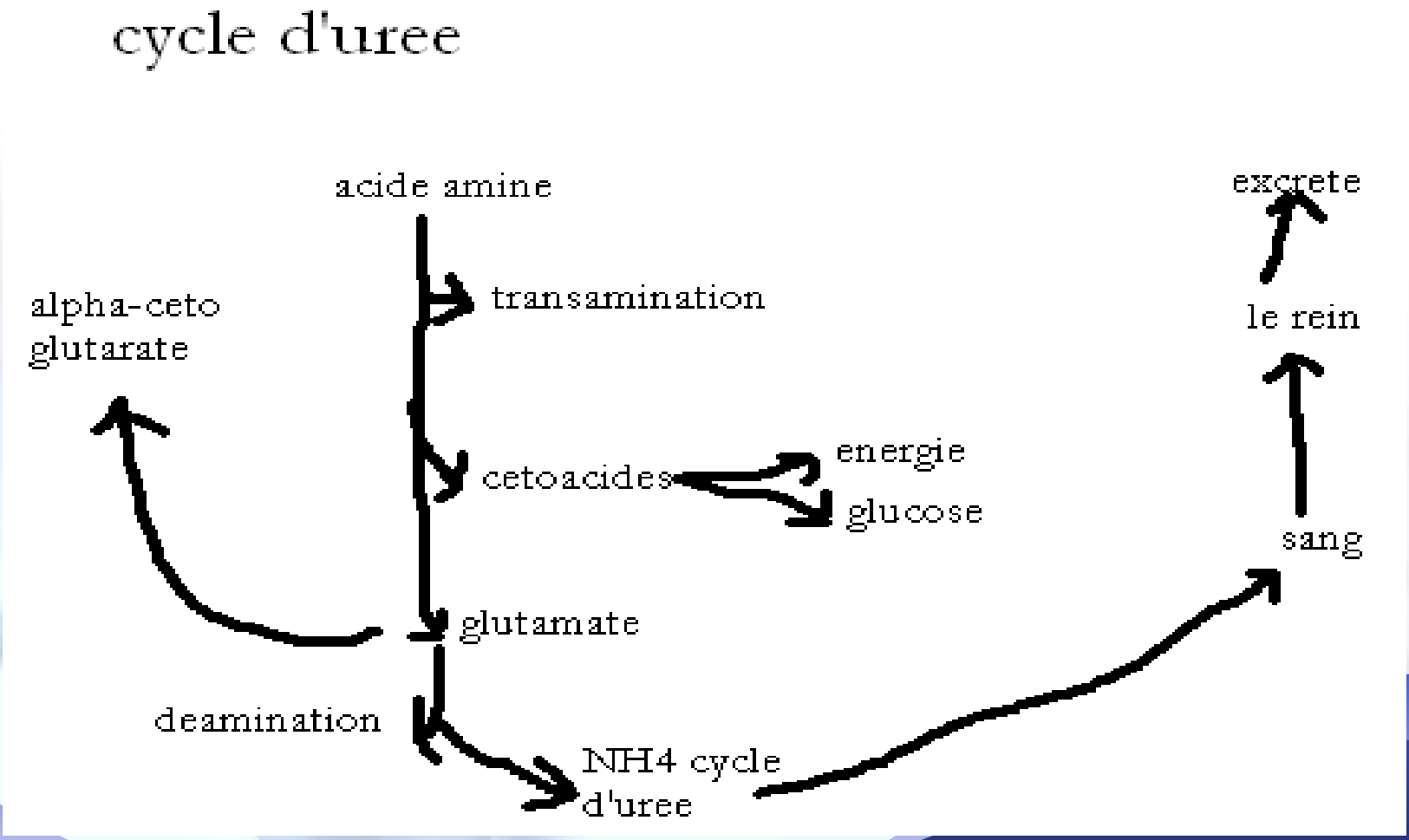
Acetylation: inhibits

5. Tissue-Specific Regulation

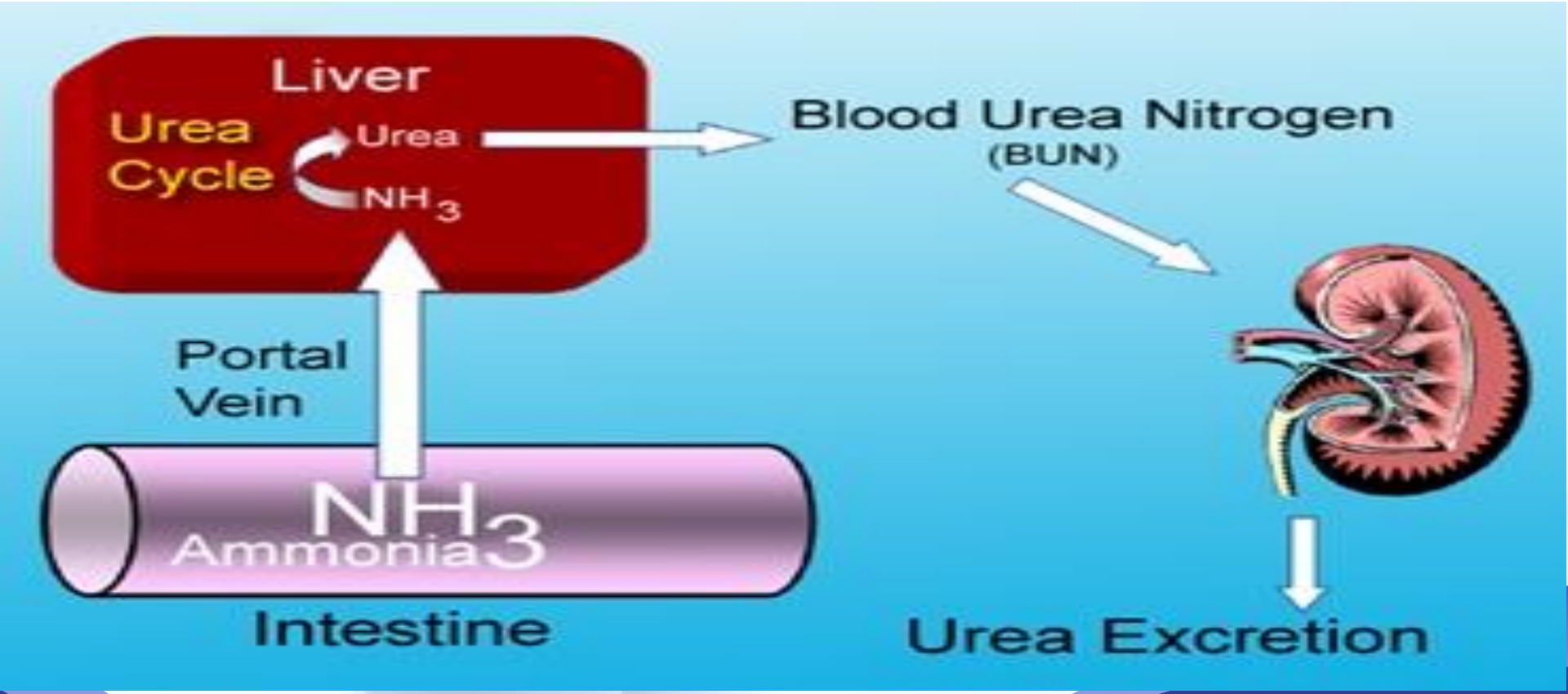
In the **liver**, GDH plays a significant role in amino acid degradation for gluconeogenesis, especially during fasting.

In the **brain**, GDH regulation is crucial for controlling neurotransmitter levels,

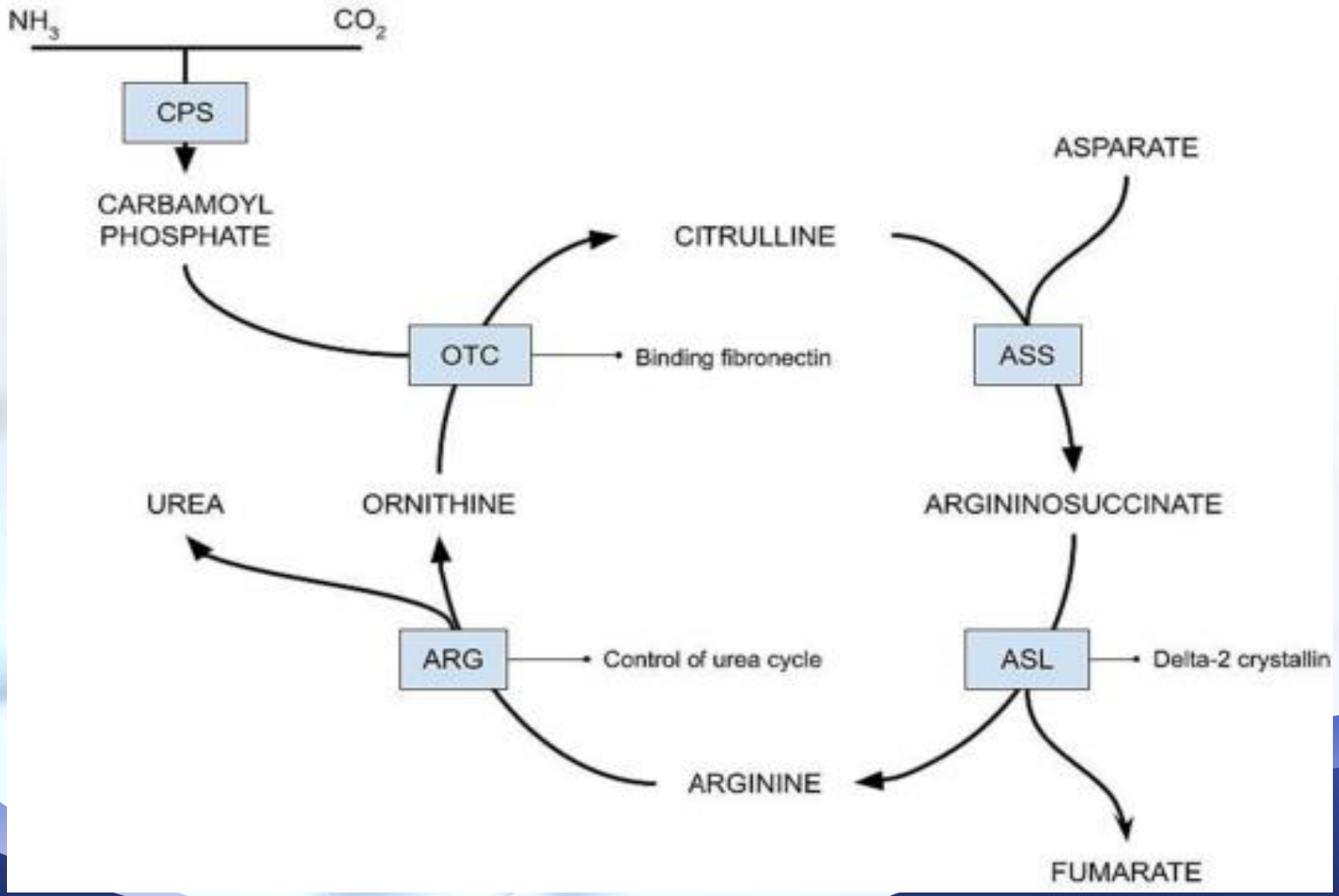
Cycle d'uree


cycle d'uree
acide amine
transamination
alpha-ceto
glutarate
cetoacides
energie
glucose
glutamate
deamination
NH4 cycle
d'uree
excrete
le rein
sang

Urea Cycle


Liver
Urea Cycle
Urea
NH_3
Blood Urea Nitrogen
(BUN)
Portal Vein
NH_3
Ammonia
Intestine
Urea Excretion

Urea Cycle


NH_3
CO_2
CPS
CARBAMOYL PHOSPHATE
CITRULLINE
ASPARATE
OTC
Binding fibronectin
ASS
UREA
ORNITHINE
ARGININOSUCCINATE
ARG
Control of urea cycle
ASL
Delta-2 crystallin
ARGININE
FUMARATE

Urea cycle enzymes

Carbamyl phosphate synthetase I (CPS-I),

Ornithine transcarbamylase (OTC),

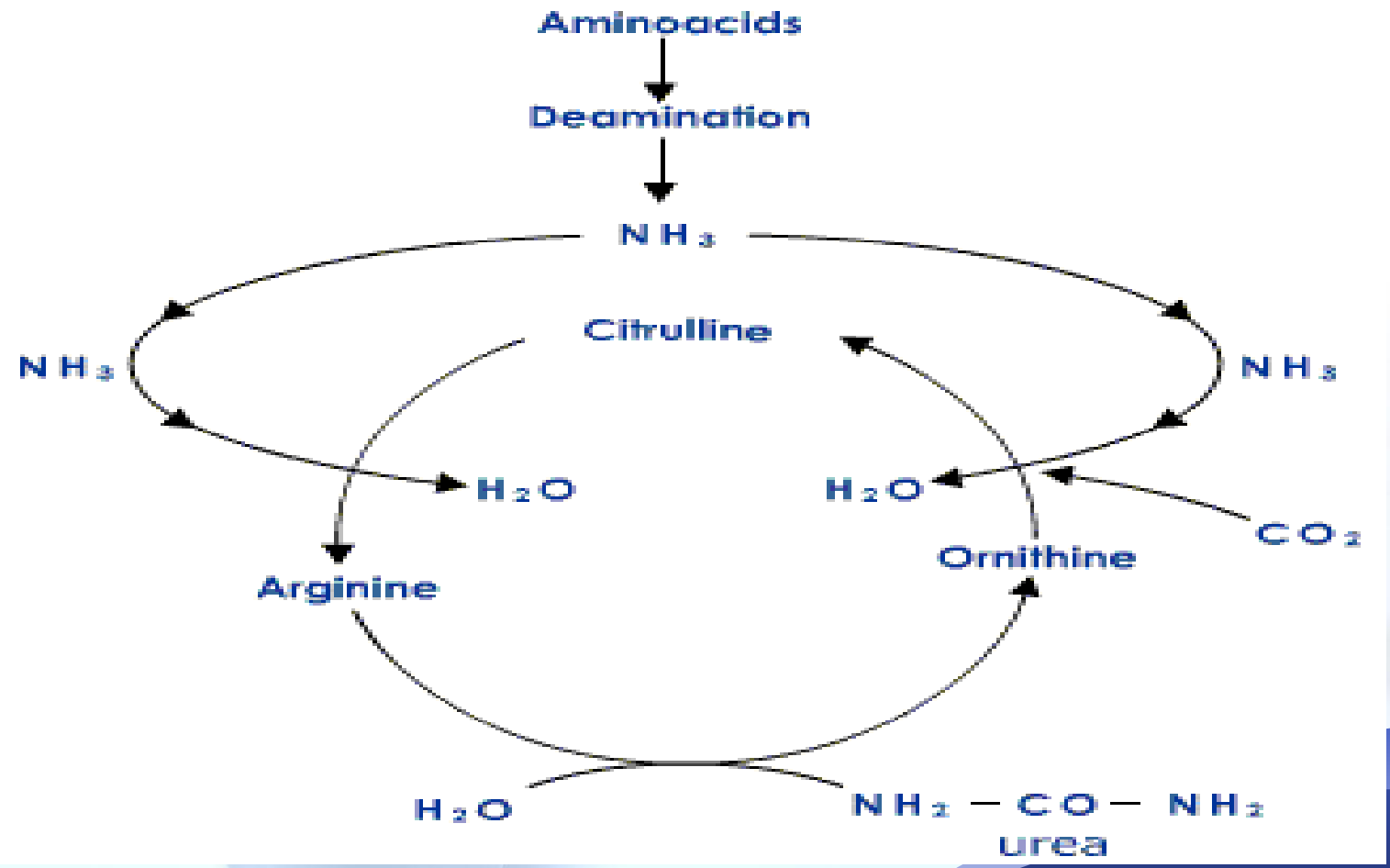
Argininosuccinate synthetase (AS),

Argininosuccinate lyase (AL),

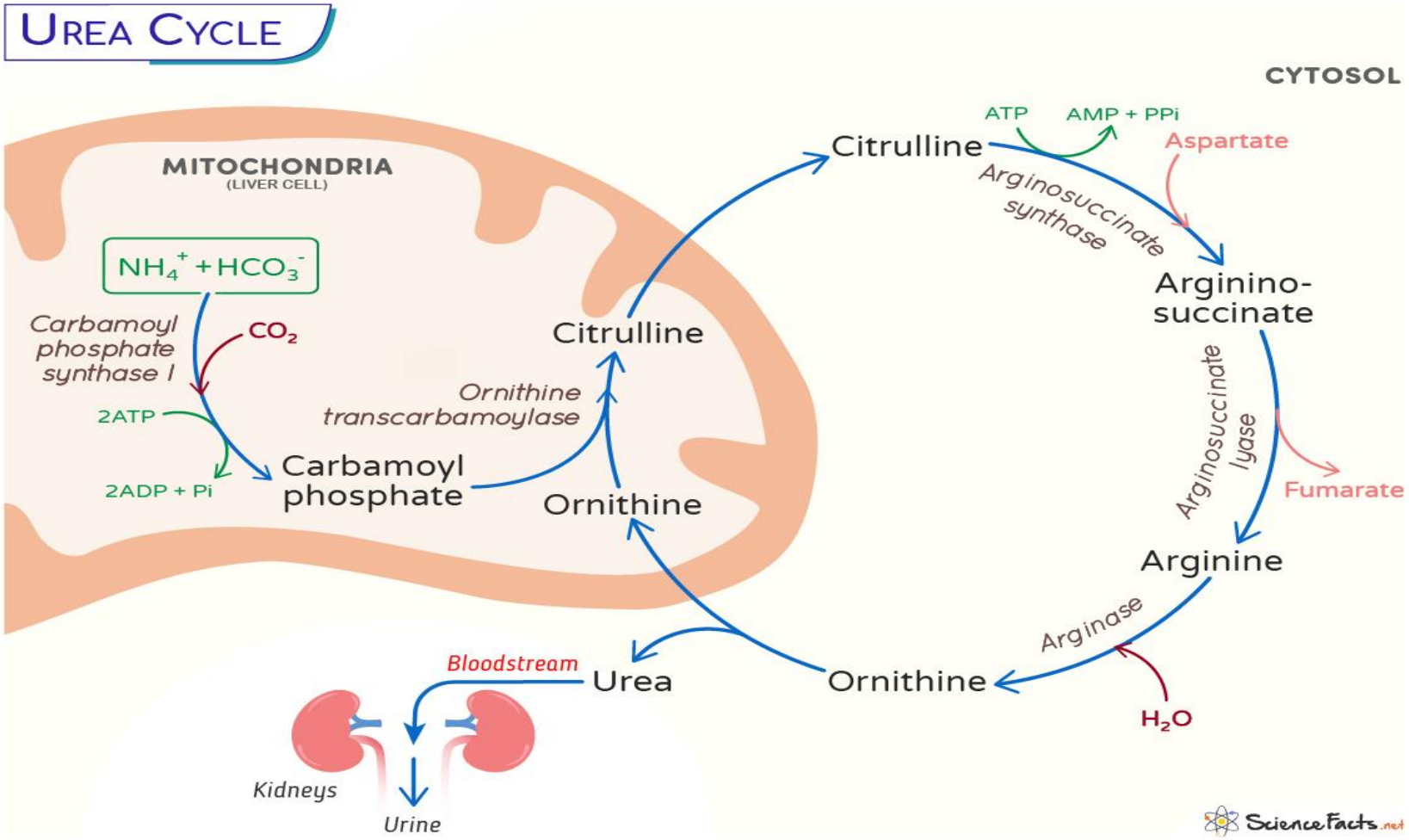
Arginase (ARG),

Acetylglutamate synthase (NAGS)

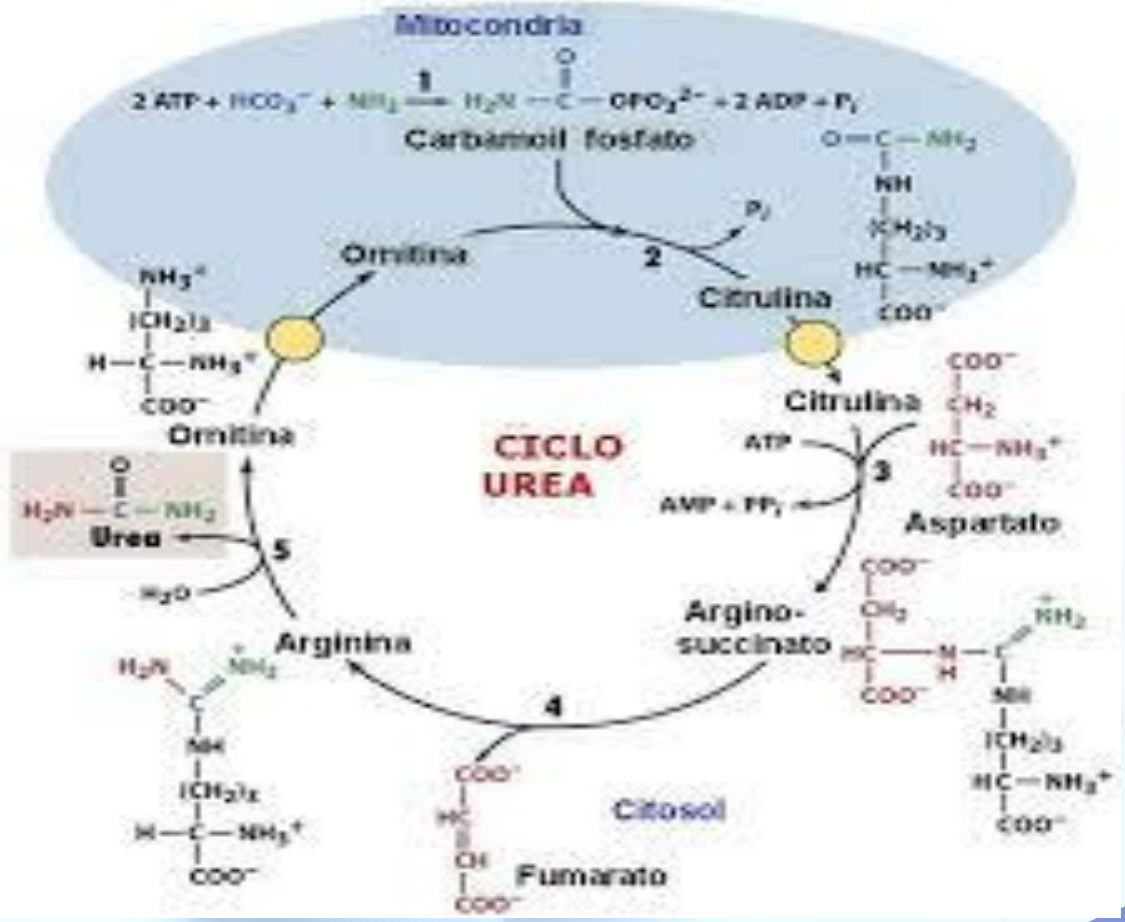
UREA CYCLE


Aminoacids
Deamination
NH3
NH3
NH3
Citrulline
H2O
H2O
CO2
Ornithine
Arginine
H2O
NH2 — CO — NH2
urea

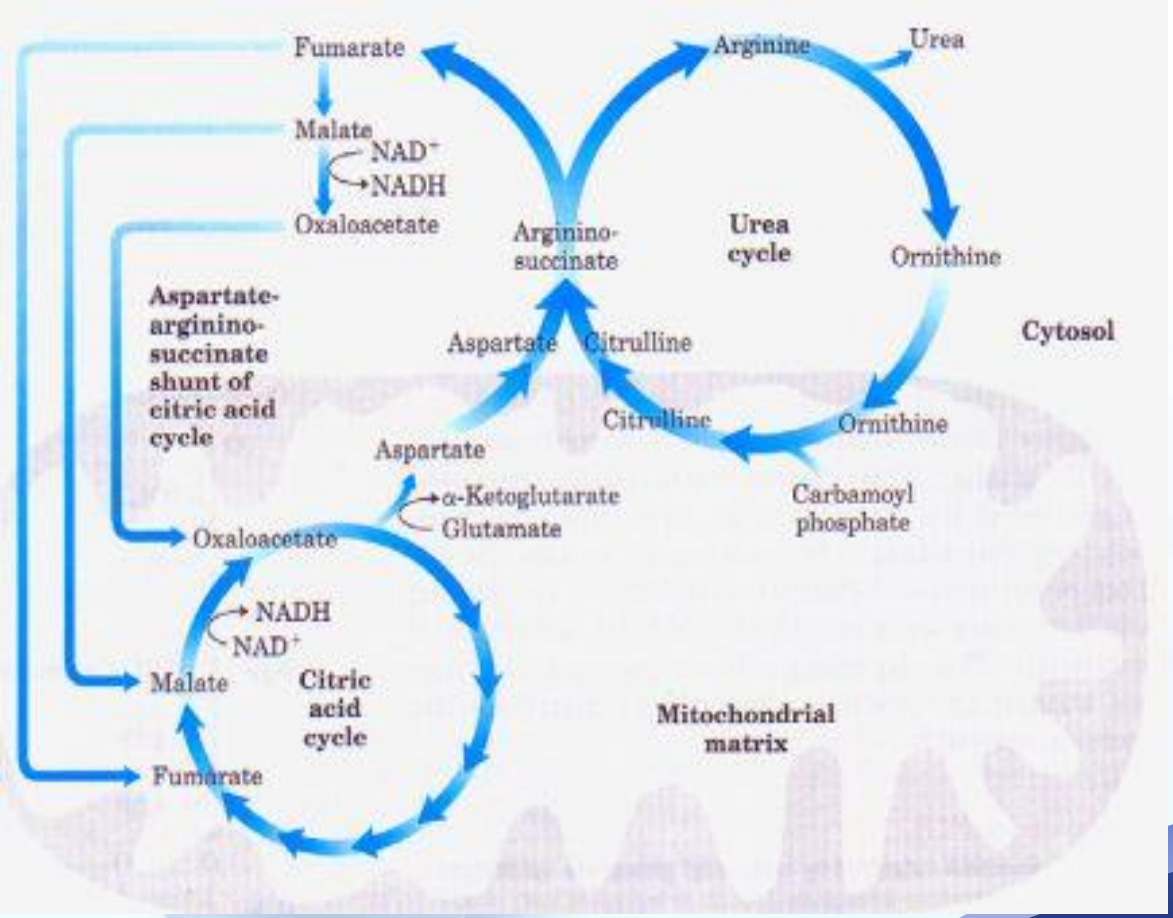
Urea Cycle


UREA CYCLE
CYTOSOL
MITOCHONDRIA
(LIVER CELL)
$NH_4^+ + HCO_3^-$
Carbamoyl phosphate synthase I
CO_2
2ATP
2ADP + Pi
Carbamoyl phosphate
Ornithine transcarbamoylase
Citrulline
Ornithine
ATP
AMP + PPi
Aspartate
Citrulline
Arginosuccinate synthase
Arginino-succinate
Arginosuccinate lyase
Fumarate
Arginine
Arginase
H_2O
Ornithine
Urea
Bloodstream
Kidneys
Urine
ScienceFacts.net

Urea Cycle


Mitocondria
2 ATP + HCO3- + NH3
1
H2N — C — OPO3 2- + 2 ADP + Pi
Carbamoil fosfato
Ornitina
2
Pi
Citrulina
Ornitina
CICLO UREA
Citrulina
ATP
AMP + PPi
3
Aspartato
Urea
5
H2O
Argino-succinato
Arginina
4
Citosol
Fumarato

TCA –Urea Cycle



N-Acetyl glutamate-Regulator of Urea cycle

1. Activator of Carbamoyl Phosphate Synthetase I (CPS I)

NAG's primary role in nitrogen metabolism is as an allosteric activator of **carbamoyl phosphate synthetase I (CPS I)**

.

2. Synthesis of N-Acetylglutamate

NAG is synthesized from glutamate and acetyl-CoA by the enzyme **N-acetylglutamate synthase (NAGS)**. The synthesis of NAG is regulated by:

Glutamate levels: Glutamate serves as a precursor for NAG production, linking amino acid metabolism to nitrogen regulation.

Arginine levels: Arginine acts as an allosteric activator of NAGS, promoting NAG synthesis.

3. Regulation of the Urea Cycle

NAG is essential for maintaining urea cycle activity, especially under conditions of **high protein intake** or **amino acid catabolism**,

4. Ammonia Detoxification

Ammonia is a highly toxic byproduct of amino acid metabolism.

5. Connection to Amino Acid Metabolism

NAG links nitrogen metabolism with the availability of amino acids, particularly glutamate and arginine. High levels of these amino acids, which occur when there is active protein breakdown or amino acid catabolism, signal the need for increased urea cycle activity.

Ammonia Elimination in Different Organisms:

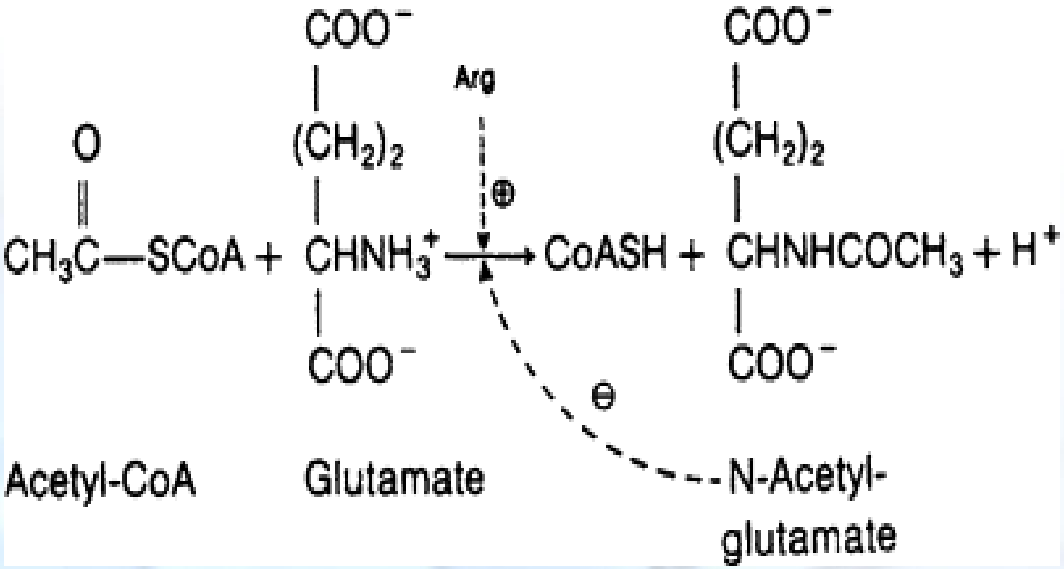
Ammonotelic organisms (e.g., fish, amphibians) excrete ammonia directly, usually in aquatic environments.

Ureotelic organisms (e.g., mammals, amphibians) convert ammonia into urea via the urea cycle for excretion in urine.

Uricotelic organisms (e.g., birds, reptiles) convert ammonia into uric acid, which is excreted as a solid or semi-solid with minimal water loss.

Some **organisms, like sharks**, retain urea for osmotic regulation, while **amphibians** and other animals can switch between excretory methods based on environmental conditions

N-acetylglutamate synthase



Urea Cycle Regulation:

Allosteric activation of CPS I by **N-acetylglutamate (NAG)**, which is synthesized in response to arginine levels.

Substrate availability (ammonia and aspartate) influences the activity of enzymes in the urea cycle.

Induction of urea cycle enzymes occurs in response to increased dietary protein or prolonged fasting, which increases nitrogen load.

Hormonal control: Glucagon and glucocorticoids increase urea cycle enzyme expression, while insulin decreases it.