

Lecture: 28

TRANSAMINATION, DEAMINATION AND DECARBOXYLATION

- Protein metabolism is a key physiological process in all forms of life.
- Proteins are converted to amino acids and then catabolised.
- The complete hydrolysis of a polypeptide requires mixture of peptidases because individual peptidases do not cleave all peptide bonds.
- Both **exopeptidases and endopeptidases** are required for complete conversion of protein to amino acids.

Amino acid metabolism

- The amino acids not only function as **energy metabolites** but also used as **precursors** of many physiologically important compounds such as **heme, bioactive amines, small peptides, nucleotides and nucleotide coenzymes**.
- In normal human beings about 90% of the energy requirement is met by oxidation of carbohydrates and fats. The remaining 10% comes from oxidation of the carbon skeleton of amino acids.
- Since the 20 common protein amino acids are distinctive in terms of their carbon skeletons, amino acids require unique degradative pathway.
- The degradation of the carbon skeletons of 20 amino acids converges to just **seven metabolic intermediates** namely.

i. Pyruvate

ii. Acetyl CoA

iii. Acetoacetyl CoA

iv. α -Ketoglutarate

v. Succinyl CoA

vi. Fumarate

vii. Oxaloacetate

- Pyruvate, α -ketoglutarate, succinyl CoA, fumarate and oxaloacetate can serve as **precursors for glucose synthesis** through gluconeogenesis. Amino acids giving rise to these intermediates are termed as **glucogenic**.
- Those amino acids degraded to yield **acetyl CoA** or acetoacetate are termed **ketogenic** since these compounds are used to synthesize ketone bodies.
- Some amino acids are **both glucogenic and ketogenic** (For example, phenylalanine, tyrosine, tryptophan and threonine).

Catabolism of amino acids

The **important reaction** commonly employed in the breakdown of an amino acid is always the **removal of its α -amino group**. The product **ammonia** is excreted after conversion to **urea** or other products and the carbon skeleton is degraded to CO_2 releasing energy. The important reaction involved in the deamination of amino acids is

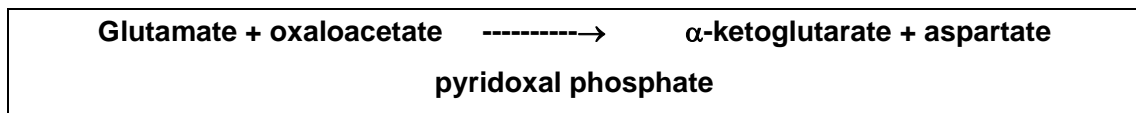
i. Transamination

ii. Oxidative deamination

iii. Non oxidative deamination

Transamination

- Most amino acids are deaminated by transamination reaction catalysed by **aminotransferases or transaminases**.
- The **α -amino group** present in an amino acid is transferred to an α -keto acid to yield a new amino acid and the α -keto acid of the original amino acid.
- The predominant amino group acceptor is **α -keto glutarate**. Glutamate's amino group is then transferred to oxaloacetate in a second transamination reaction yielding aspartate.



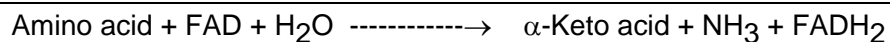
- **Pyridoxal phosphate**, the coenzyme of pyridoxine (vitamin B6) plays an important role in these reactions.
- Amino transferase reactions occur in two stages.
 - Pyridoxal phosphate is covalently attached to the amino transferases via a **Schiff's base linkage** formed between the aldehyde group of pyridoxal phosphate and the **epsilon amino group of lysine** residue of the enzyme. Pyridoxal phosphate is converted to pyridoxamine phosphate.
 - In the second stage, the amino group attached to pyridoxamine phosphate is transferred to a different keto acid to yield a new amino acid and releases pyridoxal phosphate

Oxidative deamination

- Transamination does not result in net deamination, since one amino acid is replaced by another amino acid.

- The **function of transamination is to funnel the amino nitrogen** into one or a few amino acids.
- For glutamate to play a role in the net conversion of amino groups to ammonia, a mechanism for glutamate deamination is needed so that α -ketoglutarate can be regenerated for further transamination.
- The generation is accomplished by the oxidative deamination of glutamate by glutamate dehydrogenase.
- Glutamate is oxidatively deaminated in the mitochondrion by glutamate dehydrogenase. **NAD⁺ or NADP⁺** functions as the coenzyme.
- Oxidation is thought to occur with the transfer of a hydride ion from glutamate's α carbon to NAD(P)⁺ to form α -iminoglutarate, which is then hydrolysed to α -ketoglutarate and ammonia.
- The ammonia produced is then converted to urea in mammals

Two non-specific amino acid oxidases namely, **L-amino acid and D-amino acid oxidases** catalyse the oxidation of L and D-amino acids utilizing **FAD as their coenzymes**.



Non-oxidative deamination

- Amino acids such as serine and histidine are deaminated non-oxidatively
- The other reactions involved in the catabolism of amino acids are decarboxylation, transulfuration, desulfuration, dehydration etc.

Decarboxylation

- The decarboxylation process is important since the products of decarboxylation reactions give rise to physiologically active amines.
- The enzymes, **amino acid decarboxylases** are **pyridoxal phosphate-dependent enzymes**.
- Pyridoxal phosphate forms a Schiff's base with the amino acid so as to stabilise the α -carbanion formed by the cleavage of bond between carboxyl and α -carbon atom.

➤ The physiologically active amines epinephrine, **nor-epinephrine**, **dopamine**, **serotonin**, **γ-amino butyrate** and **histamine** are formed through decarboxylation of the corresponding precursor amino acids.