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.

Glutamate + oxaloacetate ----------→ α-ketoglutarate + aspartate

pyridoxal phosphate

- **Pyridoxal phosphate**, the coenzyme of pyridoxine (vitamin B6) plays an important role in these reactions.
- Amino transferase reactions occur in two stages.

o 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.

o 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.**

$$\text{Amino acid} + FAD + H_2O \dashrightarrow \alpha\text{-Keto acid} + NH_3 + FADH_2$$

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.