Enzyme Science and Technology
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Module - VI
Enzyme Catalyzed Biochemical Reactions
Lecture - 30
Amino acid Metabolism and Detoxification

Hello everyone, this is Dr. Vishal Trivedi from Department of Biosciences and Bioengineering IIT, Guwahati. And what we were discussing? We were discussing about the different properties of the enzyme in the course, Enzyme Science and Technology. So, in this context so far what we have discussed? We have discussed about the enzyme nomenclature, classifications and then in the previous module, we have also discussed about the enzyme structure.

So, we have discussed about the different types of methods to determine the primary structure, secondary structure, tertiary structure and as well as the quaternary structures. And if you recall in the previous module, we have discussed about how you can be able to produce the protein, the enzyme in a very very bulk quantities.

And in this context, we have discussed about how you can be able to isolate the gene of interest, how you can be able to clone that gene of interest into the vector of your interest and then how you can be able to utilize that recombinant DNA to over express the protein and purify the protein.

And once you purify the protein, you can actually be able to utilize that enzyme for you know studying the different types of properties of the enzyme. You can actually be able to use the enzyme for catalysing the different types of reactions or you can be able to use that enzyme for therapeutic applications.

So, in this context, in this particular module, we are discussing about the different types of enzyme different types of reactions, what the enzyme can actually be able to catalyse to drive the metabolic reactions.

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So, in this context, what we have discussed in the previous two lectures? We have discussed about catabolic reactions. So, when we were discussing about the catabolic reactions, the catabolic reactions are the reactions which are actually producing the energy. And we have discussed about the catabolic pathway of the two biomolecules.

We have discussed about the carbohydrate metabolisms and we have also discussed about the lipid metabolisms. And both of these metabolisms are interrelated to each other in many ways, so that the carbohydrate metabolism is cross talking to the lipid metabolism and vice versa.

So, both of these pathways are actually going to produce a large quantity of energy and this energy can be used for many applications. This energy can be used for the growth of the organisms. And when you want to grow; when you want to grow, you have to synthesize the new biomolecules. You have to synthesize the protein right, because you have to prepare the new cell, right.

So, you have to prepare the proteins, you have to prepare the lipids because you have to prepare the plasma membrane and then also you have to synthesize the nucleic acid. And all these synthesis part comes under the reactions collectively called as the anabolic reaction. So, anabolic reactions are the reactions which are actually mean, covering the biosynthetic pathways and here we can actually be able to discuss.

So, in this particular lecture we are discussing about the biosynthetic pathways which is related to the amino acids. So, here what we are discussing? We are discussing about the biosynthetic pathway of the amino acids. And so, we have the different types of amino acids. So, in this particular lecture we are discussing about the biosynthetic of the amino acids.

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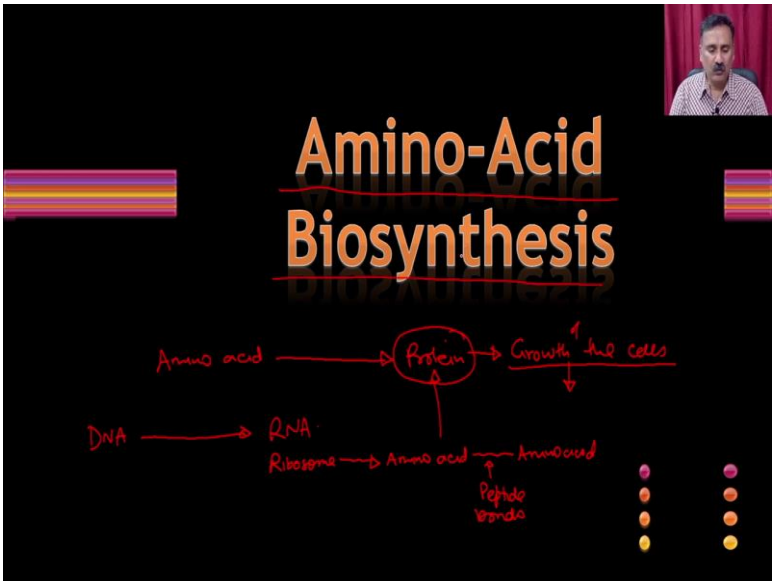

So, biosynthesis of the amino acids are very very important because when you synthesize the amino acids you are actually going to utilize these amino acids to synthesize the protein. If you recall in a prokaryotic system or in a eukaryotic system from the DNA you are actually going to produce the RNA.

And from the RNA, the RNA transcripts are actually going to be read by the ribosomes, right. And the ribosomes when it actually going to read the genetic code, it is actually going to utilize the amino acids corresponding to those genetic code and that is how they are actually going to use the different types of amino acids. And these amino acids are going to be coupled with the help of the peptide bond.

So, with the help of the peptide bond the two amino acids are actually going to be coupled and that is how it is actually going to give you ultimately the proteins, right. And the protein synthesis is actually or the enzyme synthesis is very very important for the meta running the metabolic reactions and also it is important for the growth of the cell.

Because the proteins are the integral part of the carbon membrane, proteins are the integral part of the cytosol and proteins are also playing a crucial role in catalysing the different types of reactions. Now, as far as the amino acid biosynthesis is concerned, the amino acids can be categorized into the two categories.

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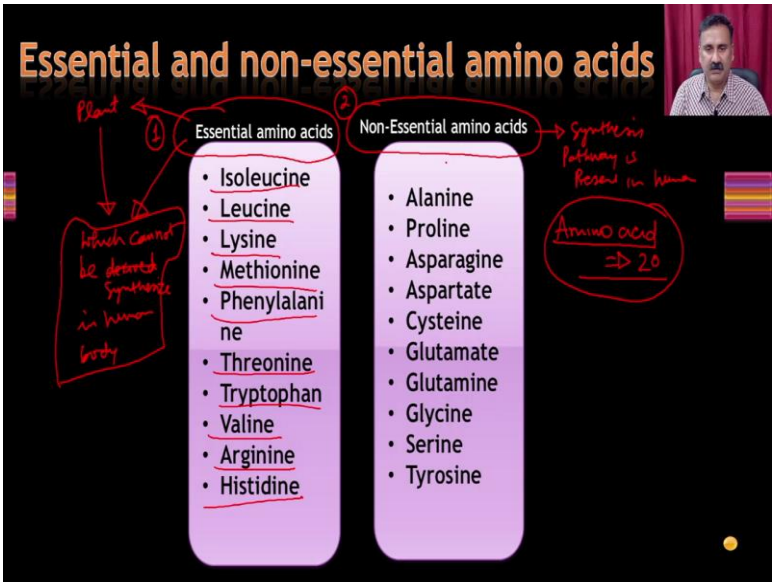

One is called as the essential amino acids and the other is called as the non-essential amino acids, right. So, you know that we have the 20 amino acids, 20 naturally occurring amino acids, right. You can actually have the more than 20 amino acids in the non-naturally non naturally occurring amino acid, but you have 20 amino acids as a naturally occurring amino acids.

And all these 20 naturally occurring amino acids can be categorized into the two category. One is called as the essential amino acid, the other one is called as a non-essential amino acid. So, the essential amino acids are like isoleucine, leucine, lysine, methionine, phenylalanine threonine, tryptophan, valine, arginine and histidine.

What is essential amino acids? Essential amino acids are the amino acids which cannot be synthesized in human body right or animal body. So, they are actually going to be synthesized in plant and from the plant you can actually be able to receive into the human.

And that is why these are called as essential amino acids because we do not have the amino acid synthesis pathways for these amino acids. Whereas, non-essential amino acids are the amino acids which for which the synthesis pathway is available, so synthesis pathway is present in human, right or they can be derived from the other metabolic intermediates, ok.

So, we can have the couple of examples from this, so that you will understand how the other metabolic intermediate could be able to use or could be able to utilize for the synthesis of the amino acids.

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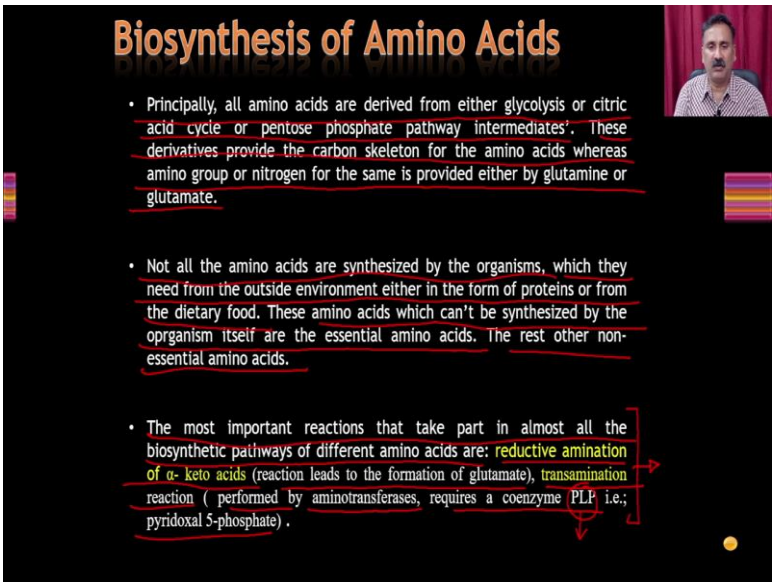

So, principally all amino acids are derived from the either glycolysis or the citric acid cycle or the pentose phosphate pathway intermediates. These derivatives provide the carbon skeleton for the amino acid whereas, the amino group or the nitrogen from the same is provided by the glutamine or the glutamate.

Not all the amino acids are synthesized by the organism which they need from the outer environment either in the form of protein or from the dietary food. These amino acids which cannot be synthesized by the organism itself are called as essential amino acid the rest other non-essential amino acids.

The most important reaction that take place in almost all the biosynthetic pathway of different amino acids are reductive amination of the alpha keto acid. The reaction which

is leading to the formation of glutamate and transamination reaction which is going to be performed by the enzyme which is called as amino transferase requires a coenzyme PLP where PLP is pyridoxal phosphate and pyridoxal phosphate is a vitamin ok.

And that is why sometime you might be deficient in the vitamin and that is why you cannot be able to synthesize some of these crucial amino acids. Now, as far as the amino acids synthesis is concerned amino acids can be synthesized either from the glycolysis or the TCA cycle or the pentose phosphate pathway.

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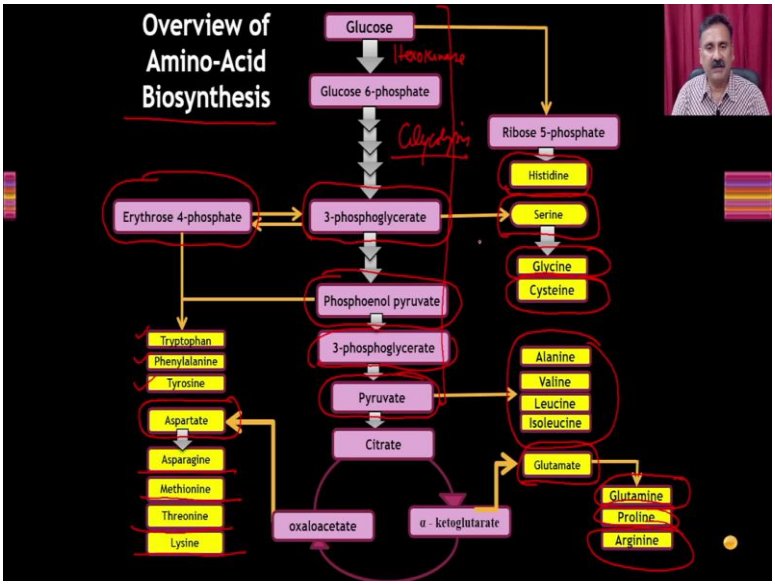

So, if you see an overview of the amino acid biosynthesis what you will see is that the glucose glucose 6 phosphate. So, this is actually what you see from here to here that is actually the glycolysis, right. And so, in the first step itself the glucose is getting converted into glucose 6 phosphate, right.

Where if you recall we can actually be able to use the hexokinase and the glucose also can be get converted into the ribulose triphosphate and the ribulose triphosphate can be then derived or can provide the biosynthesis of the histidine. Similarly, the glucose 6 phosphate with the help of different reactions can be converted into the 3 phosphoglycerate and the 3 phosphoglycerate can be channelized into a 2 different pathways.

One is called a erythrose 4 phosphate and the other one is called as a 3 glucophos 3 phosphoglycerate can be as the cursor for the serine biosynthesis. And once you have the serine biosynthesis, serine can also give rise to the glycine and as well as the cysteine. 3 phosphoglycerate can be converted into phosphoenol pyruvate and if you combine the erythrose four phosphate and the phosphoenol pyruvate that can be served as a precursor for the some of the aromatic amino acids such as tryptophan, phenylalanine and tyrosine.

Then the phosphoenol pyruvate is getting converted into the 3 phosphoglycerate and the 3 phosphoglycerate is getting converted into the pyruvate right and the pyruvate is entering into the TCA cycle right, so it is forming the citrate. So, pyruvate is a precursor for some of these amino acids like the alanine, valine, leucine and isoleucine.

Similarly, from the citric acid cycle you can have the amino acids like from the alpha keto-glutarate you can be able to have the precursors for the glutamate and from the glutamate you can be able to synthesize the glutamine, proline and arginine. On the other hand, the oxaloacetate can be a you know precursor for the synthesis of the aspartate and aspartate can be a precursor for the arginine, methan, asparagine, methionine, threonine and lysine.

So, this is just an overview to show that the importance of the carbohydrate metabolism in providing the different types of amino acids. So, you can see that from the each intermediates or almost all the intermediates are getting involved in the providing the precursor for the synthesis of some of the amino acids. Now, based on these amino acids can be derive can be classified into the different families.

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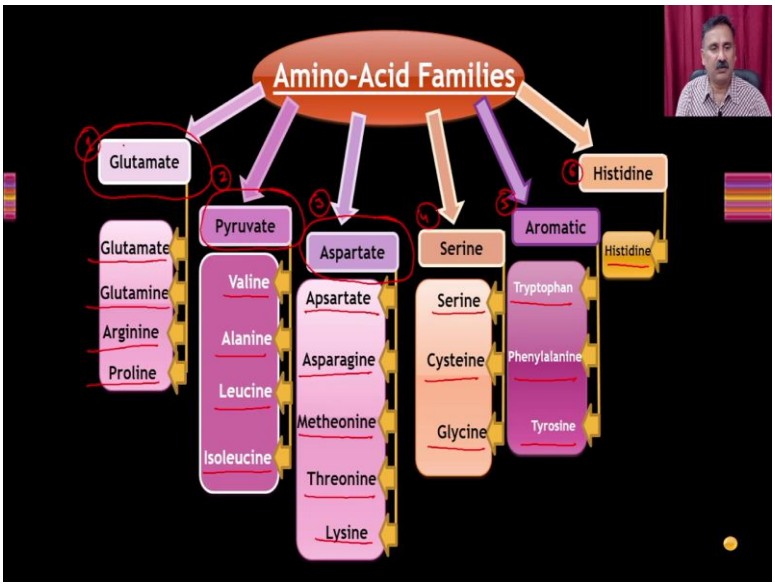

So, you can have the glutamate families. So, from the glutamate families you can have the synthesis of the glutamate, glutamine, arginine and proline. Similarly, from the pyruvate families the you can actually have the synthesis of valine, alanine, leucine and isoleucine.

From the aspartate you can actually you have seen that from the TCA cycle you can be able to synthesize the aspartate. And from the aspartate you can have the aspartate, arginine, asparagine, metheonine, threonine and lysine. Similarly, from the serine you can have the synthesis of serine, cysteine and glycine and from the aromatic amino acids you can have the tryptophan, phenylalanine and tyrosine.

And from the histidine you can have the synthesis of the histidine. So, these are the some of the families, amino acid families based on the biosynthesis. So, you can have the glutamate, you can have the pyruvate, you can have the aspartate, you can have the serine, you can have the aromatic amino acids and you can also have the histidine.

Now, let us see how you can be able to have the biosynthesis of some of the amino acids. So, we will start with the glutamate.

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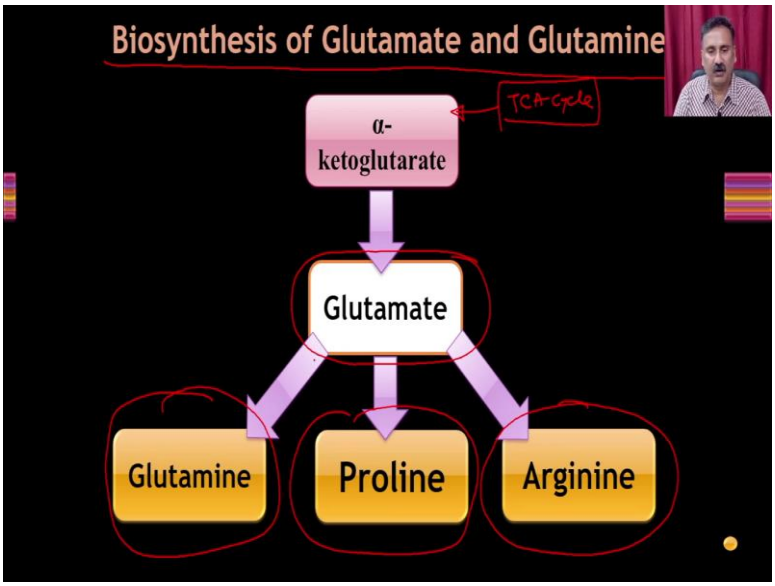

So, biosynthesis of the glutamate and the glutamate derivatives such as glutamine. So, alpha-ketoglutarate. So, you will you will get the alpha-ketoglutarate from the TCA cycle right. And once you prepare the alpha-ketoglutarate its actually going to be get converted into the glutamate by the help of the reactions which are going to be catalyzed. And the glutamate is then going to be get converted into glutamine, proline and arginine. So, how you can have the biosynthesis of all of these amino acids?

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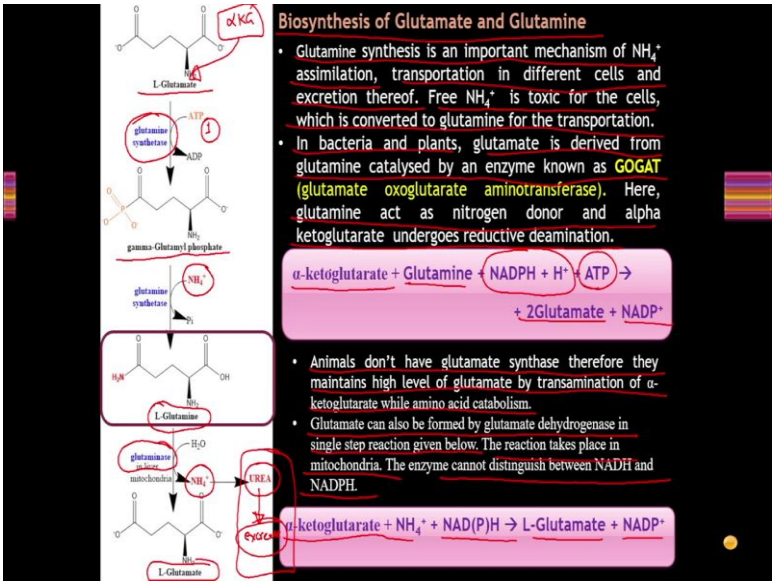

So, you can have the biosynthesis of the glutamate and glutamine. So, the glutamate is actually going to be synthesized from the alpha-ketoglutarate right. And from the alpha-ketoglutarate then the glutamine synthesis is an important mechanism of ammonium assimilations, transportation in different cells and excretion thereafter.

Free ammonium ion is toxic for the cell which is converted into glutamine for the transportations in bacteria and the plant, glutamate is derived from the glutamine of catalysed, glutamine catalysed by an enzyme and which is called as GOGAT like the glutamate oxoglutarate amino transferase. Glutamine act as a nitrogen donor and alpha-ketoglutarate undergoes reductive deaminations.

So, the action what you are going to get is alpha-ketoglutarate plus glutamine gives the glutamate plus NAD plus and you will see that it is actually going to be used reducing equivalent and as well as the energy in terms of ATP. So, this is what it is going to form, right. From the glutamate you are going to have the these reactions and that is how it is actually going to synthase the from the glutamine to glutamate.

Animals do not have the glutamate synthase therefore, they maintain the high level of glutamate by the transamination of the alpha-ketoglutarate while the while amino acid catabolism.glutamate can also be formed by the glutamate dehydrogenase in a single step reaction in below. The reaction take place in the mitochondria.

The enzyme cannot distinguish between NADH and NADPH. So, alpha-ketoglutarate with ammonia and NADPH will give you the glutamate and NAD plus. So, what you see here is that the from the glutamate it is actually going to first get the you know consumption of one amount of ATP and as a result it is actually going to form the gamma glutamyl phosphate.

The enzyme what is going to catalyse this reaction is called as glutamine synthesis and then from the glutamine synthesis is again going to catalyse another round of reaction where it is actually going to take the ammonia from the cell, right. And it is actually going to assimilate that ammonia to synthesize the L-glutamine and L-glutamine is actually going to be, you know, if it is, if there is a requirement of production of L-glutamate, the L-glutamine is actually going to be, you know, get cleaved.

The ammonia is going to be cleaved by the enzyme which is called as glutaminase and that is how the ammonia is going to be released. And this ammonia is going to be a toxic by product. As I said, you know, ammonia is very toxic. So, this ammonia is going to be assimilate in the form of urea and the urea is actually going to excrete out from the body. This anyway we are going to discuss in detail later on. And by doing so, the glutamine is going to be get converted into the glutamate.

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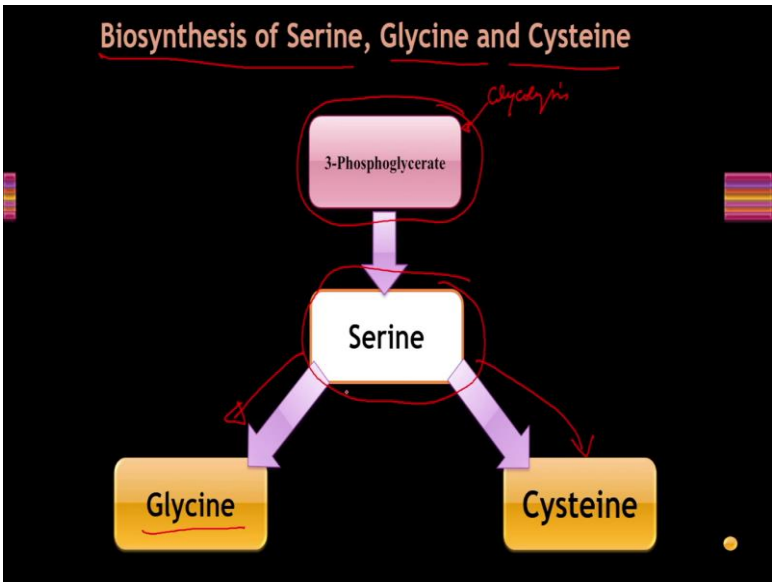

Then the second pathway is the biosynthesis of the serine glycine and the cysteine. So, 3 phosphoglycerate, the 3 phosphoglycerate is going to be synthesized during the glycolysis and that is actually going to give you the serine. And that serine is going to be a precursor for the two enzyme two amino acids; one is called as the glycine and the cysteine right.

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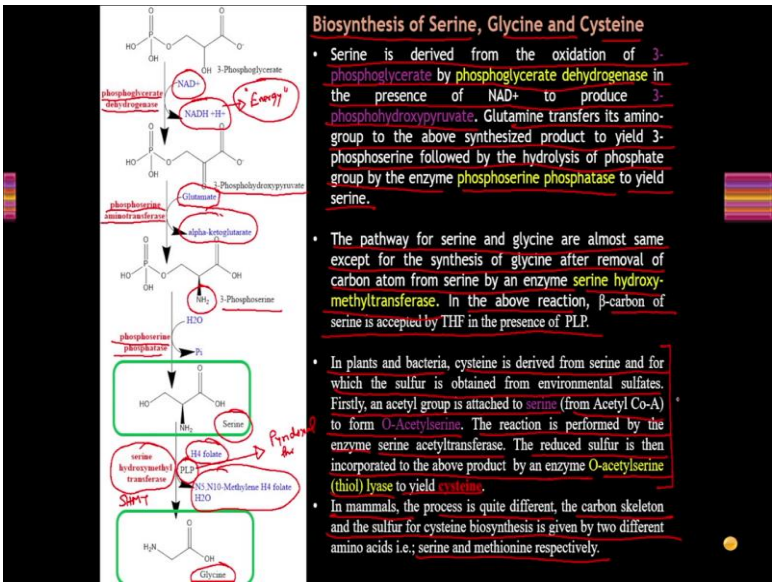

So, how we are going to have the biosynthesis of serine glycine and cysteine? Serine is derived from the oxidation of three phosphoglycerate by an enzyme which is called as phosphoglycerate dehydrogenase in the presence of NAD plus to produce the 3 phospho hydroxypyruvate.

So, this is what 3 phosphoglycerate, it is actually going to be get the reduction and as a result of this the it is actually going to form the 3 phospho hydroxypyruvate and the enzyme what you are going to get like this reaction is called as phosphoglycerate dehydrogenase. And one molecule of NAD plus is going to be get converted into NADH which means it will actually going to produce some amount of energy.

So, instead of consuming the energy it is actually going to you know produce energy. And then in the second step the glutamine transfer its amino group to the above-synthesized product to yield the 3 phosphoserine followed by the hydrolysis of phosphate group by the enzyme phosphoserine phosphatase to yield the serine. So, in the second step since you do not have the ammonia into this molecule the glutamate is going to contribute the into the ammonia right.

So, glutamate is going to get converted into alpha-ketoglutarate and it is actually going to transfer the ammonia to the molecule and as a result it is actually going to form the 3 phosphoserine and this reaction is going to be catalysed by an enzyme which is called as phosphoserine amino transferase.

And once if the phosphoserine is going to be formed, then there will be a dephosphorylation reactions which is going to be catalysed by the phosphoserine phosphatase and as a result it is actually going to synthesize the glycine. And as a result, it is going to synthesize the serine.

Once the serine is formed it is actually going to be act by the enzyme which is called as serine hydroxy methyl transferase or SHMT and by the help of this the serine the serine is going to be get converted into the glycine the tetra hydro folate is going to be get converted into N5 and 10 methylene tetra hydro folate.

And the serine hydroxy methyl transferase the SHMT is always utilizing the PLP or the paradoxyl phosphate as a cofactor for catalysing these reactions. So, the pathway for the serine and glycine are almost the same except for the synthesis of glycine after the removal of carbon atom from the serine by an enzyme which is called as serine hydroxy methyl transferase.

In the above reaction the beta carbon of the serine is accepted by the tetra hydro folate in the results of PLP. In plants and bacteria cysteine is derived from the serine and for which the sulfur is obtained from the environmental sulfates. Firstly, and acetyl group is attached to the serine from the acetyl CO A to form the O acetyl serine. This reaction is performed by the enzyme which is called as serine acetyl transferase.

The reduced sulfur is then incorporated into the above product by an enzyme which is called as O acetyl serine lyase to yield the cysteine. In mammals the process is quite different the carbon skeleton and the sulfur for cysthene biosynthesis is given by the two different amino acid that is the serine and the methionine respectively. So, in the cysteine synthesis is different in the plant versus the animals.

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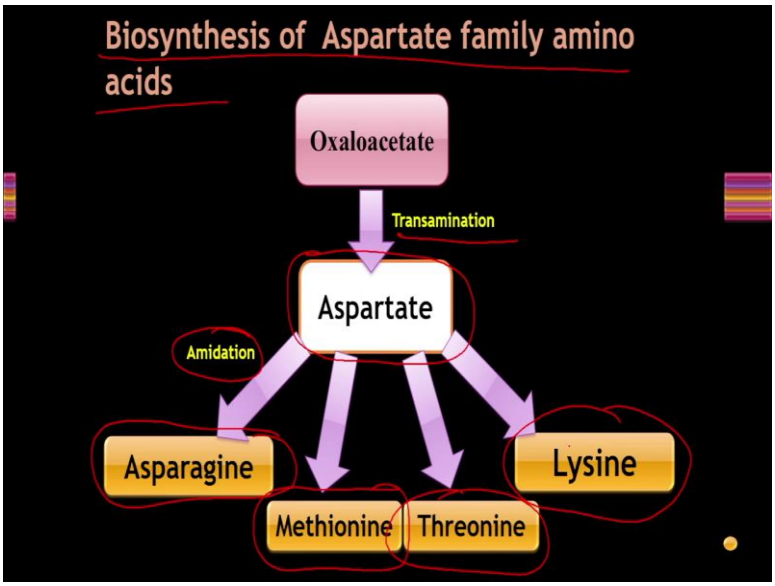

Then we have the another biosynthesis of the aspartate family amino acids. So, from the oxalo acetate you are going to have the trans-amination reaction and that is going to synthesize the aspartate.

And from the aspartate it is actually going to give you the asparagine if there will be amidations, then it is actually going to form the asparagine whereas, from the aspartate you can be able to synthesize the amino acids, threonine and lysine. So, from the aspartate you can be able to synthesize the methionine, threonine and lysine.

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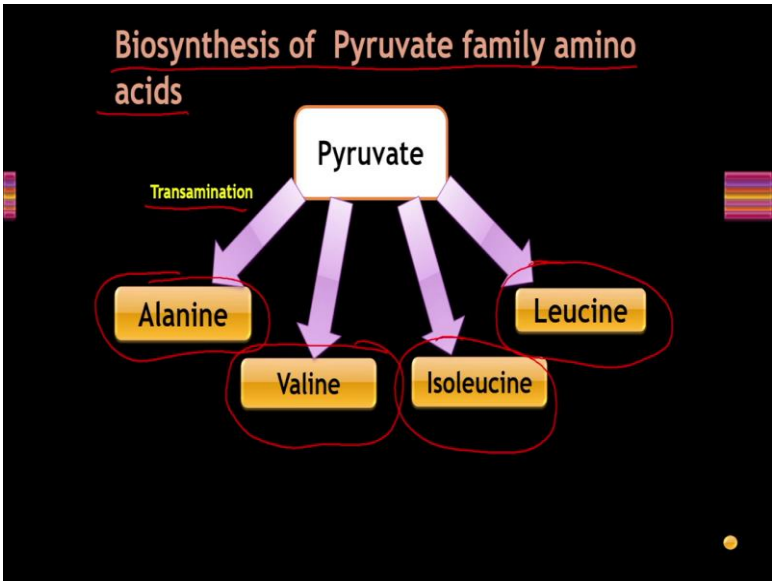

Then we have the biosynthesis of the pyruvate family amino acids. So, from the pyruvates you can actually have the trans-amination that is going to give you the alanine. From the pyruvate you can actually have the is a precursor for the valine, isoleucine and as well as the leucine biosynthesis. So, let us see how you can actually have the biosynthesis of the aspartate family groups.

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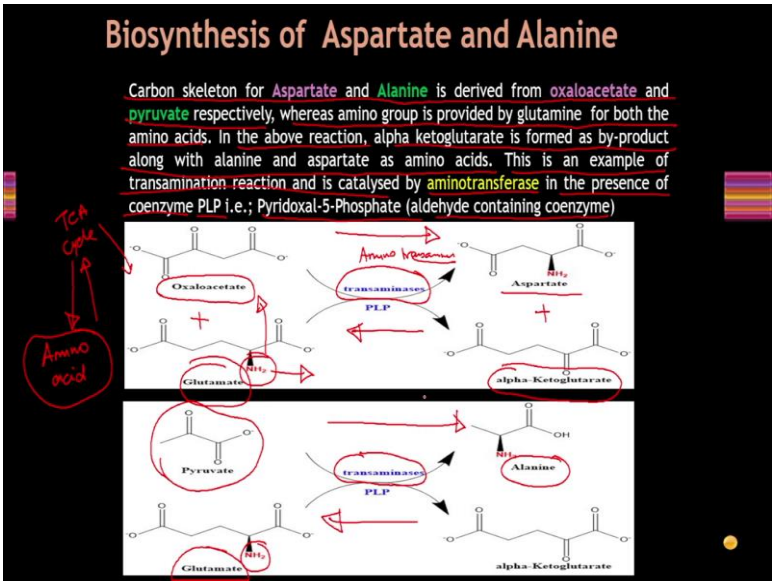

So, the carbon skeleton for the aspartate and alanine is derived from the oxaloacetate and the pyruvate itself respectively whereas, the amino group is provided by the glutamine for both the amino acids. In the above reactions, alpha-ketoglutarate is formed as by a byproduct along with the alanine and aspartate as amino acid. This is an example of the trans-amination reaction and it is catalysed by the amino transferases in the presence of the coenzyme that is the PLP.

So, pyridoxyl 5 phosphate or the aldehyde containing the coenzyme. So, what you have is you are actually going to have the oxaloacetate. So, oxaloacetate you are going to get from the TCA cycle right. And this oxaloacetate is going to react with the glutamate and then there will be a trans-amination reaction.

So, this amino group is actually going to be transferred on to the oxaloacetate and as a result it is actually going to form the aspartate. On the other hand, the glutamate is going to get converted into the alpha- ketoglutarate and this type of reactions are called as the

trans-aminations and these reactions are going to be catalysed by the enzyme which is called as the trans-aminases or the amino trans-aminases ok.

So, in this reaction what it is happening is that it is actually you know taking the amino group from the one enzyme and one amino acid and it is converting putting it on to the second molecule. So, there is a transfer of amino group from the one molecule to other molecule and that is how it is actually going to set aside the one amino acids. These reactions are reversible.

So, you can actually have if there will be aspartate and alpha- ketoglutarate it is actually going to run in this direction and it is actually going to synthesize the oxaloacetate glutamate. And that is how the TCA cycle is can very easily be able to communicate with the amino acid biosynthesis right.

So, you can imagine that if there will be a deficiency of amino acid, the TCA cycle will pull the intermediate towards amino acid biosynthesis and the reaction will runs in this direction and that is how you are going to have this synthesis of aspartate. But if there will be access of aspartate.

Then the reactions are going to run in this direction and that is how it is actually going to run the TCA cycle as a faster rate and you are going to have the very high quality of synthesis of oxaloacetate and that oxaloacetate will enter into the 5th cycle for energy production.

And as a byproduct, it will also going to synthesize the glutamate and that glutamate is actually going to use for the protein synthesis. Similarly, the similar kind of transamination reaction can also occur with the pyruvate. So, in the in this case, you have the pyruvate and the glutamate and you can have the amino group which is going to be transferred onto the pyruvate and it is actually going to synthesize the alanine and the alpha ketoglutarate.

This reaction is also going to be catalysed by the transaminases and this also has the same same kind of significance. When you have the shortage of the sugar, right there will be this reaction is going to run in this direction or if there will be a shortage of glutamate, its going to run in this direction, but if there is a requirement of alanine, they are going to run in this direction.

So, this is actually, these are the reactions which are actually going to connect the carbohydrate metabolism as well as the protein metabolism and that is how they are actually going to keep a fine balance on the you know on the biosynthetic pathway and as well as the catabolic pathways.

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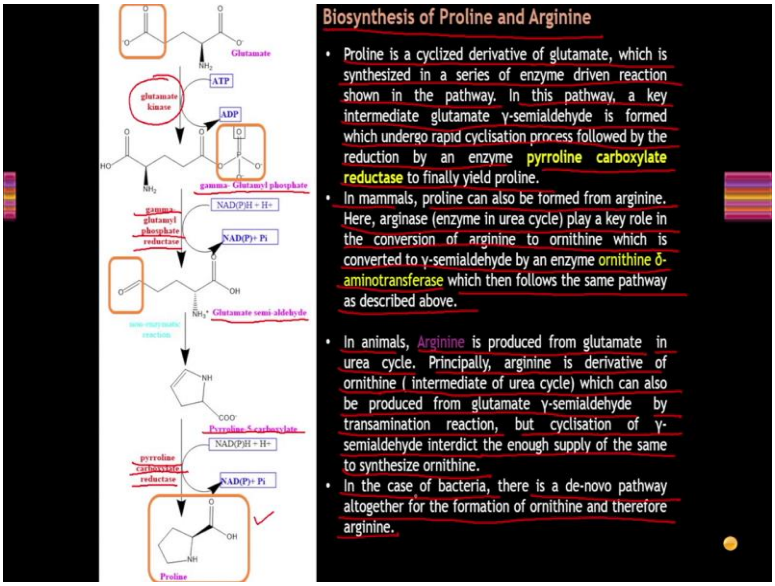

Then we have the biosynthesis of proline and arginine. So, proline is a cyclized derivative of glutamate which is synthesized in a series of enzyme derived reaction shown in the pathway, this is the pathway for the proline synthesis. In this pathway, a key intermediate, glutamate, gamma, semi-aldehyde is formed which undergoes rapid cyclization process followed by the reduction by an enzyme which is called as pyroline carboxylate reductase to finally, yield the proline.

In mammals, the proline can only be formed from the arginine. Here the arginine play key role in the conversion of the arginine to ornithine which is converted to the gamma semi-aldehyde by an enzyme ornithine alpha amino transferase which then follows the same pathway as described above. In animals, the arginine is produced.

So, this is what you have the synthesis of the proline. So, from the glutamate you have the phosphorylation by the enzyme which is called as glutamate kinase and it is actually going to synthesis going to form the gamma glutamine phosphatase. Phosphate, gamma glutamine phosphate and gamma glutamine phosphate is going to be oxidized to by the

enzyme by the called as gamma glutamine phosphate phosphate reductase. So, it is actually going to be reduced.

And that is how it is actually going to form the glutamate semi-aldehyde and glutamate as soon as the gami glutamate semi-aldehyde is going to be formed it is actually going to get cyclized to give you the parolin 5 carboxylate and parolin 5-carboxylate is going to be go for the another round of reduction by the enzyme which is called as parolin carboxalate reductase and as a result it is actually going to form the proline.

And whereas, in the case of in animals, the arginine is produced from the glutamate in urea cycle. Principally arginine is derived of is a derivative of the ornithine which can also be produced from the glutamate gamma semi-aldehyde by the trans-amination reaction.

But the cyclization of gamma semi-aldehyde interdict the inner supply of the same to synthesize the ornithine. In the case of bacteria there is a de-novo pathway altogether for the formation of ornithine and therefore, arginine also.

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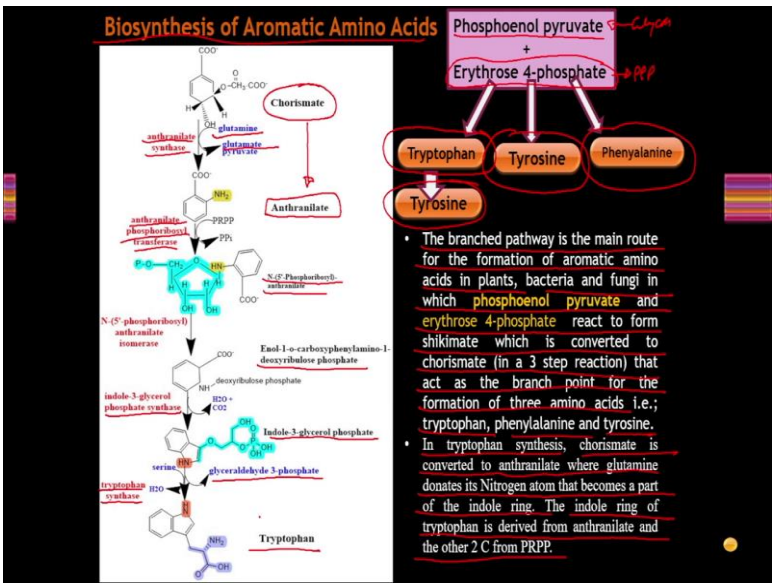

So, these are the another pathway of the aromatic amino acids. So, in the aromatic amino acids you can actually be able to use the phosphoenol pyruvate which is going to be formed from the glycolysis and the erythrose four phosphate which is from the pentose phosphate pathway and when they come together they are going to serve as a precursor

for all the aromatic amino acids such as tyrosine, tryptophan, phenylalanine and the tyrosine.

So, tryptophan what is going to be formed can be converted into tyrosine. The branched pathway is being root for the formation of aromatic amino acid in the plant bacteria in fungi in which the phosphoenol pyruvate and the erythrose 4 phosphate react to form the shikimate which is converted into the chorismate and that acts as a branch point for the formation of three amino acids that is the tryptophan, phenylalanine and tyrosine.

In tryptophan synthesis the chorismate is converted into anthranilate where the glutamine donates donates its nitrogen atom that becomes a part of the indole ring. The indole ring of the tryptophan is derived from the anthranilate and the other 2 carbon from the PRPP which is phosphoenol pyruvate.

So, in the first step you are going to have the synthesis of the chorismate with the by the interaction of the phosphoenol pyruvate and erythrose 4 phosphate which is going to form the shikimate and then shikimate is going to be converted into the chorismate. So, once the chorismate is going to be formed it is actually going to get the amino group from the glutamine and the enzyme what is going to catalyse.

And it is going to get converted into the glutamate and the enzyme what is going to synthesize this reaction is called as the anthranilate synthase and as a result it is actually going to form the anthranilate right. So, from the chorismate you are synthesizing the anthranilate and from the anthranilate it is actually going to get the pyrophorus phosphate.

So, anthranilate phosphoribosyl transferase is going to catalyse the addition of these ribose sugars and that is is how it is actually going to form the 5 phosphoribosyl anthranilate and then anthranilate is getting converted into the indole 3 glycerol phosphates synthase.

With the help of this it is actually going to form the indole 3 carboxyphenyl amino deoxyribulose phosphate and that get converted into indole 3 phosphoglycerate and that is going to get the conversion of this into the tryptophan with the help of the enzyme which is called as tryptophan synthase and the serine is actually going to get converted

into glyceraldehyde 3 phosphate and that is how you are going to have the synthesis of tryptophan.

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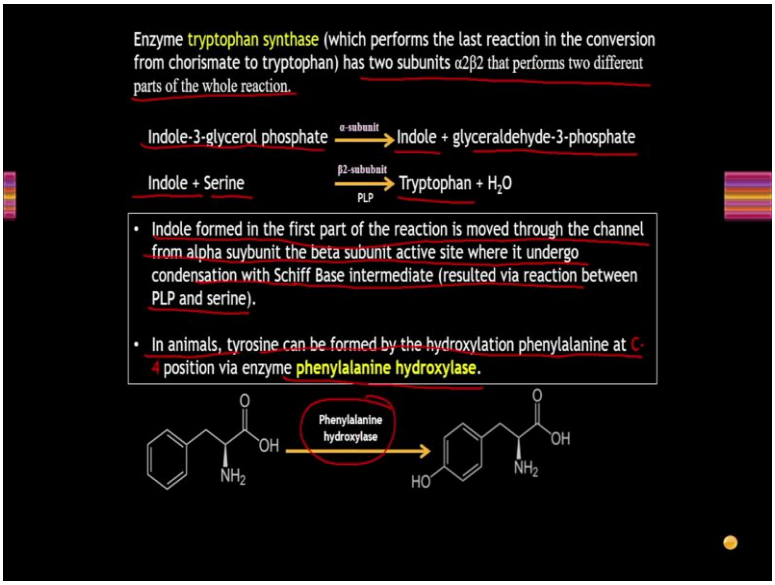

From the tryptophan the enzyme synthase which form the last reaction in the conversion has two subunits right and the two part of the whole reaction. So, indole 3 glycerol indole 3 glycerol phosphate is going to first get converted into indole and the glyceraldehyde three phosphate and the indole is going to react with serine and it is actually going to form the tryptophan.

So, indole form in the first part of the reaction is moved through the channel from the alpha subunit the beta subunit activate where it undergoes condensation which Schiff base intermediates and results in the reaction between the PLP and serine. In animals the tyrosine can be formed by the hydroxylation phenylalanine and the C4 position by the enzyme which is called as acetylene hydroxylase.

So, the tyrosine what is going to be formed when it is going to get the hydroxylation it is going to form the phenylalanine and the enzyme what is going to catalyse is called as the phenylalanine hydroxylase.

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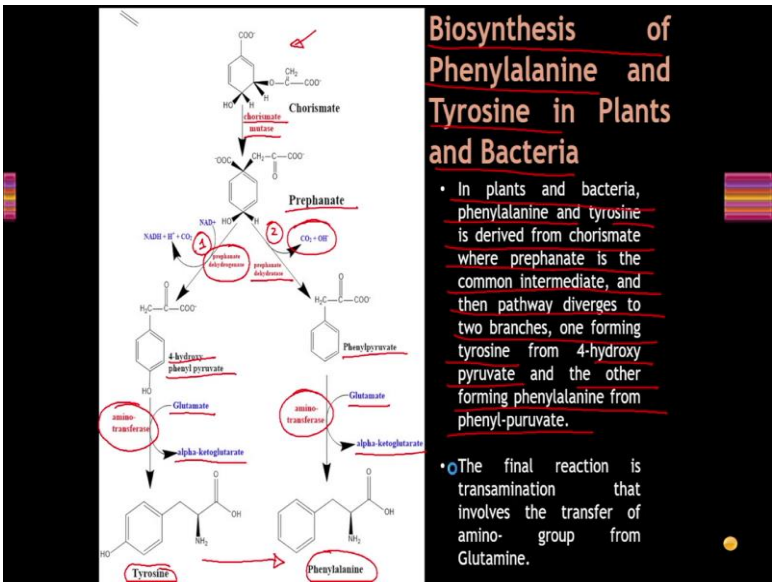

Then we have the biosynthesis of the phenylalanine and tyrosine in the plants and bacteria. So, in the plants and bacteria phenylalanine and tyrosine is derived from the chorismate whereas, prephanate is the common intermediate and then pathway diverges to the two branch one forming the tyrosine and from the 4 hydroxyl pyruvate and the other is forming the phenylalanine from the phenyl pyruvate.

So, this is what you have first you have synthesized the chorismate right. So, chorismate is going to be synthesized you might have you might have seen how the chorismate is formed when we were discussed when we the the phosphoenol pyruvate and the erythrose 4 phosphate is reacting with each other and forming the chorismate and the chorismate is actually getting converted into the prephanate by the enzyme which is called as chorismate mutase and the prephanate is getting diverged into the two pathway.

One is with you know giving rise to the synthesis of the tyrosine the other is going to give rise to the synthesis of phenylalanine. So, in the first step of the tyrosine synthesis the prephanate is getting you know oxidized to give rise to the 4 hydroxyl phenyl pyruvate and the enzyme what it catalyses the reaction is called as prephanate dehydrogenase and then for 4 hydroxyl phenyl pyruvate there will be amino transferase reaction and that is how the glutamate is getting converted into alpha ketoglutarate.

And that is how the 4 hydroxyl phenyl pyruvate; pyruvate is getting converted into the tyrosine. Similarly, the in the 2nd pathway, so this is the 1st pathway, the 2nd pathway

you the prephanate can also form the phenyl pyruvate with the help of the enzyme which is called as prephanate dehydrogenase and there will be a decarboxylation reactions and then this actually going to get the amino transferase and that is how it is actually going to form the alpha ketoglutarate.

And it is going to form the phenylalanine and you might have seen that the tyrosine also can get converted into the phenylalanine with the help of the enzyme which is called as the phenyl hydroxylase. So, the final reaction of transamination involved the transfer of amino group from the glutamine.

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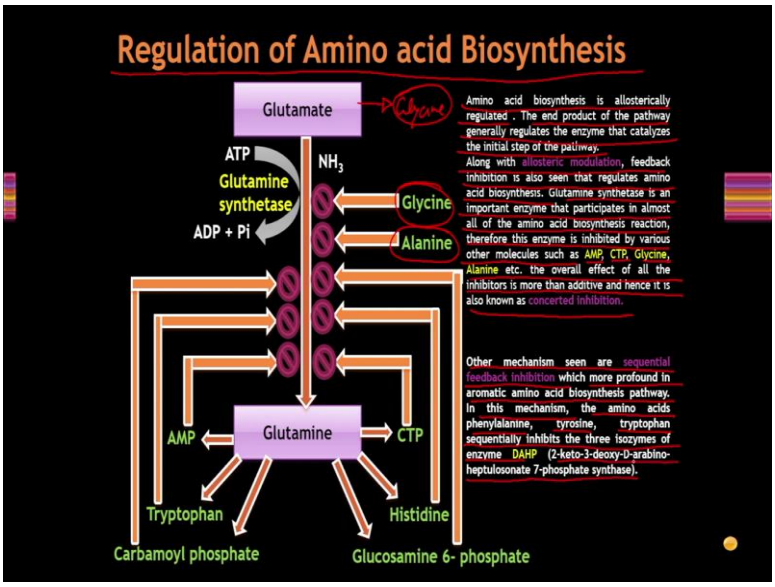

Then we have how we can actually have the regulation of the amino acid biosynthesis right. So, from the glutamate you can have the synthesis of glutamine the enzyme what it catalysis is reaction is called as glutamine synthesis and there are many amino acids which are actually going to block this activity.

So, amino acid biosynthesis is allosterically regulated and the product of the pathway generally regulate the enzyme that catalyses the initial step of the pathway. Along with the allosteric modulations feedback inhibition is also seen that regulate the amino acid biosynthesis. Glutamine synthesis is an important enzyme that participates in almost all the biosynthesis pathway reaction therefore, this enzyme is inhibited by various other molecules such as AMP, CTP, glycine, alanine.

The overall effect of all the inhibitor is that the more additive and it is hence it is known as the concerted inhibitions. So, since the glutamate can also be you know formed the glutamine and then from the glutamate you can also have the synthesis of many other molecules like the glycine and cysteine and all that glycine is actually going to you know inhibit this activity of glutamine synthesis. Alanine is also going to inhibit this activity.

So, other mechanisms seen are sequential feedback mechanism which are more profound in the aromatic amino acid biosynthesis pathway. In this mechanism the amino acids phenylalanine, tyrosine, tryptophan sequentially inhibit the 3 isozyme of the enzyme which is called as DAHP or 2-keto 3-deoxy arabino heptulosonate seven phosphate pathway.

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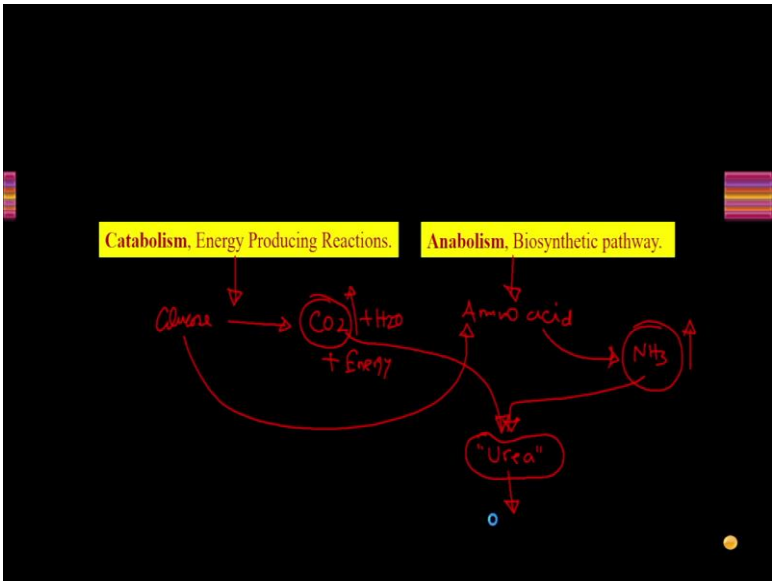

So, this is all about the catabolic reactions what we have discussed and the anabolic reactions, but whether you catalyse the catabolic reactions where you are going to convert the glucose into the carbon dioxide plus water right and that is how you are actually going to produce some energy or whether you are going to run the anabolic reactions.

So, that the some of these glucose derivatives are going to be get converted into amino acids and in this pathway also there will be a production of ammonia. So, whether you are forming the carbo you know forming the carbon dioxide or whether you are releasing the ammonia into the reactions both of these you know intermediate or both of these

molecules are you know toxic to the cell and that is how you can actually be able to have the pathway.

So, that you can actually combine these two and form the one of the very very less toxic byproduct and that is called as the urea. So, urea is actually going to be a natural non-relatively less toxic by product which can be synthesized with the help of the ammonia and the carbon dioxide to form the and that actually is going to be you know released out in the excrete.

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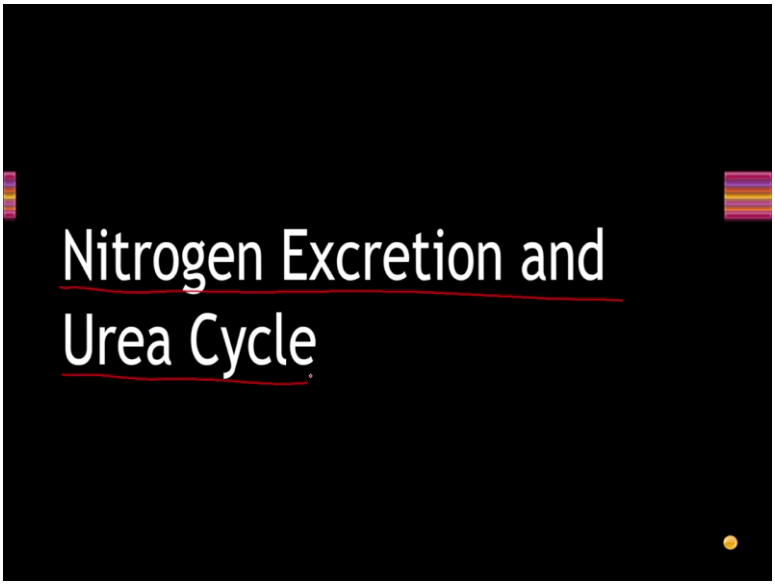

So, how the urea excretion or the nitrogen excretion is going to take place. So, nitrogen excretion and the urea cycle.

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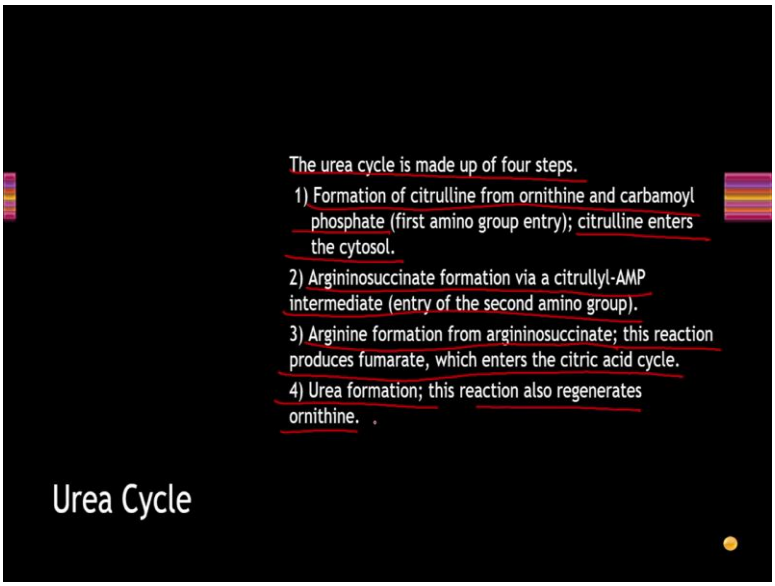

So, the urea cycle is made up of a four step; the formation of citrulline from the ornithine and carbonyl phosphate, citrulline enters the cytosol. Then we have the argininosuccinate formation via citrulline AMP intermediates and the arginine formation from the argininosuccinate this reaction produces the fumarate which enters the citric acid cycle and the urea formation this reaction also regenerates the ornithine.

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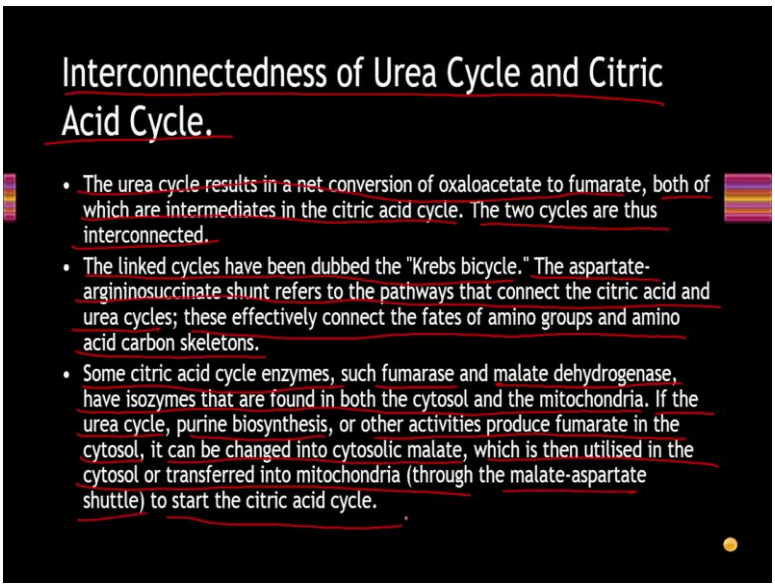

Interconnection of urea cycle and the citric acid cycle. The urea cycle results in the net conversion of oxaloacetate to fumarate both of which are intermediate in the citric acid

cycle, the two cycles are then interconnected. The linked cycles have been dubbed the krebs bicycle. The aspartate argininosuccinate shunt refers to the pathway that connects the citric acid cycle and the urea cycle; these effectively connect the fades of the amino groups and the amino acid carbon skeleton.

Some citric acid enzymes such as fumarase and the malate dehydrogenase have the isozymes that are found in both the cytosol and the mitochondria. If the urea cycle the purine biosynthesis or other activities produce fumarate in the cytosol it can be changed into the cytosolic malate, which is then utilized in the cytosol or transferred into the mitochondria to the malate aspartate shuttle shuttle to start the citric acid cycle.

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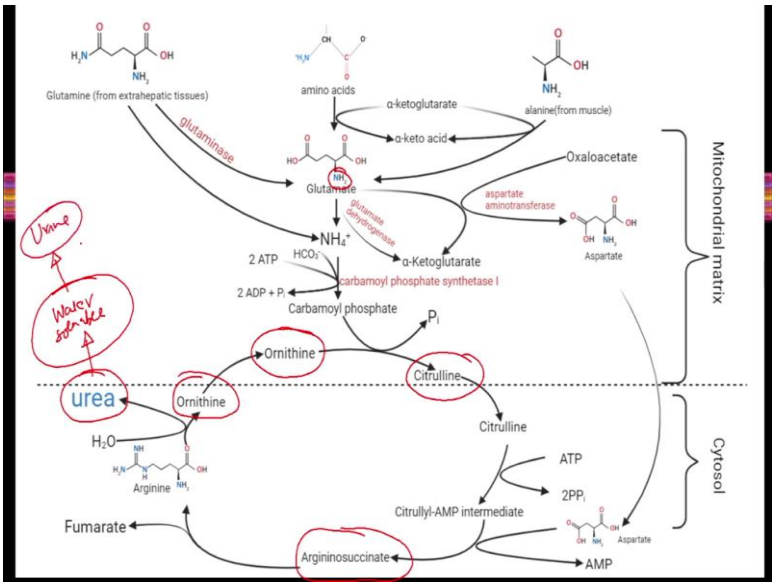

So, this is what it is actually. So, you have the glutamine and from the glutamine you are going to have the production of glutamate and ammonia, then from the ammonia can be shuttled between the different amino acids with the help of the amino acid transaminase and all that and as a result you are going to have the synthesis of the ornithine and ornithine is getting converted into citrulline.

And citrulline is getting converted into the argininosuccinate and then argininosuccinate is reproducing the ornithine and with the help of that it is actually going to form the urea. So, it is actually going to take up the nitrogen toxic products from the mitochondria. So, in these are the reactions what are going to catalyse the mitochondria and these are the

reactions what are going to synthesize the cytosol and ultimately it is actually going to produce a urea and urea is a water soluble product.

So, its actually going to be solubilized in water and that is how it is actually going to be excreted out in the phase of urine.

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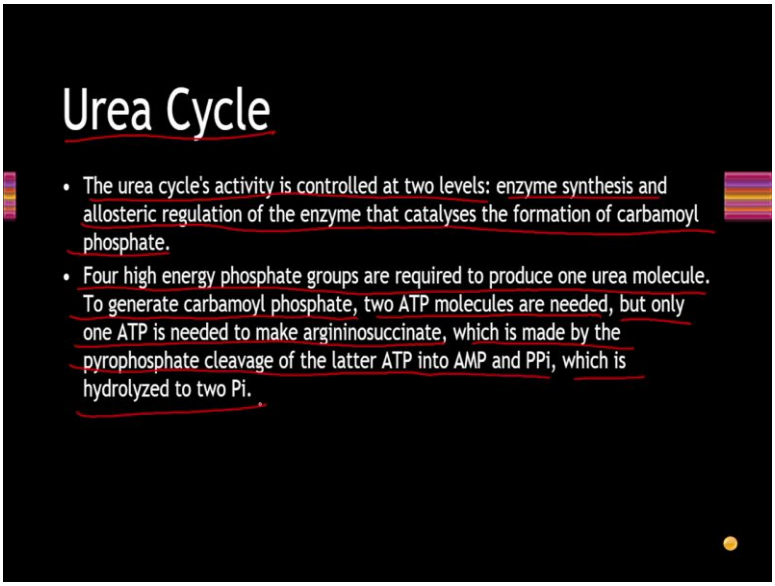

So, the urea cycle the urea cycles activity is controlled at two levels; enzyme synthesis and the allosteric regulation of the enzyme that catalyses the formation of carbamoyl phosphate. Four high energy phosphate groups are required to produce one urea molecule to generate the carbamoyl phosphate to ATP molecules are needed.

But only one ATP is needed to make the argininosuccinate which is made by the pyrophosphate cleavage of the latter ATP into AMP and PPi which is hydrolyzed to give the two Pi.

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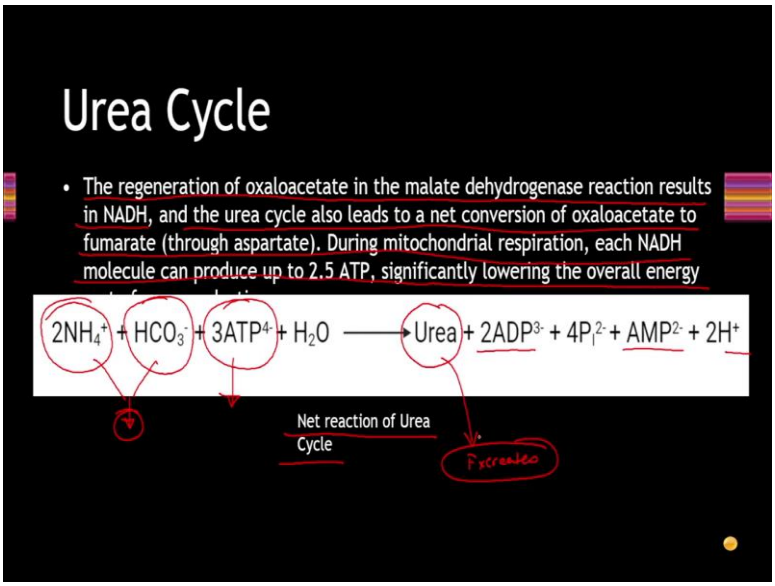

So, the urea cycle the regeneration of the oxaloacetate in the malate dehydrogenase reaction results in NADH and the urea cycle also need to be the net conversion of oxaloacetate to fumarate. During the mitochondrial reaction respiration each NADH molecule can produce up to significantly lowering the overall reactions.

So, you can have the two molecules of ammonia you can have the bicarbonates you can have the ATP and that is how it is actually going to form the urea with 2 ADP and AMP and water. So, the net reaction of the urea cycle is that you are going to consume a large quantity of energy that the 3 ATP and it is actually going to fix the ammonia and as well as the carbon dioxide from the bi products and that is how it is actually going to form the urea and urea is going to be excreted out from the body by the urine ok.

So, this is all about the catabolic and anabolic reactions where the enzymes are playing very crucial role. So, what we have discussed? We have discussed about the catabolic reactions which are responsible for energy productions and in that context, we have discussed about the carbohydrate metabolisms and as well as the lipid metabolisms and within the carbohydrate metabolism we have discussed about the we have discussed about the glycolysis.

And as well as the grape cycle and we have you know discussed how the grape dichroisms and grape cycles are important for the energy production and how these inter how these you know pathways are connected to the other pathways for the for making a

fine balance. So, that you can be able to control the different intermediates from the different pathways and that is how the grape cycle is called as the central pathway.

And then we also discuss about the lipid oxidation. So, we have discussed about the beta oxidation different steps in the beta oxidation and how the beta oxidation is producing the large quantity of energy because every beta oxidation cycle is producing the one molecule of acetyl CO A and that one molecule acetyl CO A is entering into the grape cycle and that is how it is also running the you know it is also producing the large quantity of energy through the utilization of the grape cycle.

And at the end we have also discussed about the anabolic pathways. So, anabolic pathways are responsible for the biosynthesis of the different types of biomolecules such as the lipid molecules, the protein molecules and as well as the the amino acids. And in this particular context we have discussed about the biosynthesis of the different types of amino acids. So, we discussed about the essential amino acid and as well as the non-essential amino acids.

And what we understood from the biosynthetic pathway is that the biosynthetic pathway utilizes the energy what is being produced during the catabolism to run the this condensation reactions and all other kinds of reactions to synthesize the new molecules. And what we have also seen that anabolic reaction and as well as the catabolic reactions are communicating with each other through the some of the crucial intermediates.

And the enzymes play a very crucial role in all of these pathways and as well as the crucial steps and that is how you might have seen that many of the reaction intermediates are allosterically or feedback mechanism where is modulating the activity of these environments that is how it is controlling the reaction intermediates.

So, with this I would like to conclude my lecture here in our subsequent lecture we are going to discuss some more interesting aspects related to enzyme.

Thank you.