Molecular Biology
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Module - 02
Basics of Biological system (Part 2)
Lecture-07 Cellular Metabolism (Part 2)

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 cellular metabolism and in this context in the previous lecture, we have discussed about the carbohydrate metabolism. So, we have discussed about the how the glucose is being phosphorylated within the glycolysis and that is how that particular glucose is going to be committed for the glycolysis and further you know further degradation into the crave cycle, so that it will be able to produce the energy and this energy what it is going to be produced is in the form of ATP or in the form of reducing equivalence and this energy is going to be utilized for many of the anabolic reactions. So, apart from the carbohydrate, we also have another molecule which is called lipids and these lipids are also been the major source of energy within the cell. So, in today's lecture, we are first going to discuss about the catabolic reactions of the lipid metabolic metabolisms and how it is actually generating the energy and subsequent to that we are also going to discuss about the anabolic reactions and at the end of this lecture, we are also going to discuss about the how the body is managing the different types of metabolic byproducts. So, as we have discussed in the past also in the previous lecture also that when you talk about the cellular metabolisms, you can have the two different types of metabolism, one is catabolism where you are actually going to have the energy producing reactions and within the catabolism, you are actually going to have the two different types of biomolecules, you can have the carbohydrate and or you can have the lipids.

Lipids are actually going to be processed within the glycolysis followed by the grape cycle whereas, the lipids are actually going to be processed under the beta oxidation and ultimately, both of these processes are going to produce large quantity of energy in the form of ATP slash NADH okay and this energy is actually going to be utilized into the anabolic reaction where you are going to have the biostatic pathway. So, within the anabolic reactions, we are going to discuss about the protein synthesis or amino acid synthesis and at the end, we are also going to discuss when you are going to do the catabolic reactions or the anabolic reactions, they both are actually going to produce the waste material right and this waste material also need to go through with some of the metabolic pathways so that it can be detoxifies. So, let us start with the beta oxidations. So beta oxidation as the name suggests is actually a metabolic pathway which is required for the lipids and you know the lipid is a chain, is a carbon, is made up of the fatty acids

plus glycerol right and this fatty acid part is actually going to be utilized into the beta oxidation to produce the energy and how we are going to get the fatty acids right.

So, when we consume the lipids into the food for example, if we take the food right for example, if we take the pizza right. So, pizza is actually going to have the lipids right and that lipid is actually going to be digested by the enzyme which is called lipase and that is how it is actually going to generate the fatty acid and then the fatty acid is going to be absorbed by the small intestine. And ultimately it is going to be transported to the liver and it is also going to be transported to the other body parts and it is actually going to be used for the beta oxidation to generate the energy. Now before we get into the beta oxidations, we have to first very briefly see how all these things are actually working. So what you are going to do is when you are going to take the fat into the food, fat will get into the stomach, so there is no digestion of the fat into the stomach right and then it will enter into the small intestine.

When it enter into the small intestine, the bile salt which is going to be released from the gallbladder is actually going to emulsify the fat. So what is mean by the emulsification is that it is actually going to make the fat molecules more polar in nature so that it will get dissolved into the aqueous environment and so that it will actually going to be have the proper action of the different enzymes. So in this process of the emulsification, it is actually going to form the micelles and the fatty acids and then it is actually going to present into the small intestine where it is actually going to be digested and that is how it is actually going to produce the fatty acids. These fatty acids are then going to be taken up into the blood and that is how it is actually going to form the chylomicrons. And then these chylomicrons are actually going to transfer to the capillaries of the blood to the different tissues.

So it is actually going to travel in the form of a chylomicrons and these chylomicrons are going to be targeted to the different organs depending upon the type of protein what is present onto the cell surface, onto the surface of these chylomicrons and that is how they are actually going to deliver the fat to the brain, muscles, livers and also on. And the fatty acids which are entered into the myocytes and adipocytes where they undergo the degradation or the beta-oxidations. And once it is going to go through the beta-oxidation, it is actually going to produce the carbon dioxide, it is actually going to produce the ATP and it is also going to produce the reducing chevalets. Now, why there is a need to have the beta-oxidations? So beta-oxidation is the sequential removal of the two carbon fragments from the carboxyl end of the fatty acids. During the process, the acetyl CoA is going to form as the bond between alpha and beta carbon atoms are broken.

It is named so because the beta carbon of the fatty acid is oxidized and the process occurs inside the mitochondria. So beta-oxidation occurs within the mitochondria and why it is called beta-oxidation? Because the bond between the alpha and beta chain is actually going to be broken. So this is actually the acid part and this is the alpha carbon, this is the beta carbon. So what has happened is that in a cyclic reactions, the bond between the alpha and beta is actually going to be broken down. And that is how this portion is actually going to be released and it is actually going to form the acetyl CoA.

And this portion is then going to be transported into the crepe cycle and it is going to be oxidized into the crepe cycle. Remember that the acetyl CoA is actually going to be combined within the crepe cycle and it is actually going to form the citric acid. And that is how it is actually going to enter into the crepe cycle. So beta-oxidation is actually the reaction which are going to lead to the breakdown of this particular fragment and in this process also it is actually going to generate some energy. So you can imagine that if you have a carbon of pentadeconoic acid, it is actually going to have this kind of breakage after every two carbons.

So it is actually going to have a breakage here, it is going to have a breakage here, it is going to have a breakage here like that. And all these two chain carbons are actually going to be get converted into the acetyl CoA and then these acetyl CoA will be transported or will be a part of the crepe cycle and that is how it is actually going to produce the energy. So beta-oxidation is that it is actually going to produce the acetyl CoA from the long chain fatty acids and then acetyl CoA will enter into the crepe cycle. So this process also requires the multiple steps. First of the step is that it actually requires the activation of the lipid molecules and then the transported of the lipid molecules within the mitochondria.

Remember that the beta-oxidation will occur inside the mitochondria compared to that the carbohydrate metabolism starts from the cytosol. So the fatty acids are activation and the transportation to the mitochondria. Enzymes for the beta-oxidations are located in the mitochondrial matrix which means the liquid part of the mitochondria. The fatty acids with chain length greater than 14 cannot cross the mitochondrial membrane as such. Therefore, they first undergo activation and then transportation aided by the three enzymatic reactions.

Once the fatty acid reach the target cell, their activation takes place in the cytosol. So fatty acid activation is a ATP dependent acetylation reaction in which the fatty acid is activated by the coenzyme A and ATP to form the fatty acyl CoA with the help of an enzyme which is called acyl CoA synthetase or it is also called acyl CoA ligase or acyl CoA thiophenase. Thus acyl CoA synthetase catalyzes the formation of a thioester

linkage between the carboxyl group of the fatty acid and the thiol group of the coenzyme A to yield the molecule which is called as fatty acid fatty acyl CoA. So this is the fatty acid and this group is going to be combined with this group and that is how it is actually going to form the fatty acyl CoA and in this reaction the ATP is actually going to be consumed because you know that it is forming a high energy bond. So this is actually going to be linked to the CoA and that is how it is going to form the fatty acyl CoA and the energy what is present in the ATP is actually going to be consumed.

Now once you have generated the fatty acyl CoA you are actually going to commit this particular lipid for beta oxidation which means you have already invested some energy or you have already invested some amount of energy into this so that you can be able to send this lipid for the beta oxidation inside the mitochondria and then it is actually going to be you know generate more amount of energy. Now the next step is the transportation into the mitochondria. So mitochondrial inner membrane is impermeable to almost all the fatty acid CoA and molecule which are transported to the mitochondrial matrix by the carnitine shuttle. So you can have a carnitine acyltransferase shuttle where you have a protein which is called as carnitine and this protein is actually going to bind the acyl coenzyme this and that is how it is actually going to help into the transportations. So you have the inner membrane, you have the outer membrane, this is the mitochondria and then how it is actually going to help is that each fatty acid coenzyme A is converted into the fatty acyl carnitine derivative in a reaction named transesterification by the enzyme carnitine acyltransferase A1 which is present in the outer membrane of the mitochondria.

So in the outer membrane of the mitochondria you have an enzyme which is called as carnitine acyltransferase 1 and it is actually going to join the carnitine to the incoming fatty acids. So the derivative is this derivative is located to the mitochondrial matrix by the acyl carnitine carnitine translocase which is present in the inner membrane of the mitochondria. This means once this is going to be formed it is actually going to be taken up into the inner membrane and then you are actually going to have the acyl carnitine translocase. This is actually going to allow the entry of this carnitine conjugated fatty acid molecules and once it enter into this then you are going to have the carnitine acyltransferase 2 which is actually going to remove. So once the fatty acid is regenerated via the carnitine acyltransferase 2 located onto the matrix side of the inner mitochondria, carnitine is transported.

So this carnitine protein is again transported back to the outer membrane and then it will be available for making a complex with the other molecule of the. So carnitine is transported back into the inner mitochondrial space via the acyl carnitine transporters which is then ready for the participation into the other reaction of the activating the fatty acids. So these are the this is the carnitine acyltransferase shuttle and it is actually going

to help in the transportation of these acetylated lipid molecules. Then we have the stages of the beta oxidation. So you can have the three stages.

Stage 1 you can have the beta oxidation, stage 2 oxidation of acetyl-CoA and stage 3 that is called as the oxidative phosphorylation. So in the stage 1 the long chain fatty acid is oxidized to yield the acetyl residue in the form of acetyl-CoA which is known as the beta oxidation. Then the stage 2 the oxidation the acetyl-CoA produced from the oxidation of the fatty acid is further oxidized to carbon dioxide via a cycle to yield the reducing balances. And then the stage 3 is that whatever the reducing equivalents are being generated they will be going to so electron derived from the oxidation of the stage 1 and 2 passes to the oxygen via the mitochondrial spectra chain for ATP synthesis by the oxidative phosphorylation. This means this is the stage 1 where the long chain fatty acid is actually going to be broken down after every 2 carbons.

And then it is actually going to generate the acetyl-CoA. So for example in this case it is actually a 16 membered carbon fatty acid. So it is actually going to generate the 8 acetyl-CoA. And then all these 8 acetyl-CoA is going to enter into the 30-grade cycle and it is actually going to generate the 16 carbon dioxide molecule and at the end it is actually going to generate the NADH and FADH2 along with that it is going to generate the ATP, GTP and all that. And then in the stage 3 NADH and FADH2 is actually going to enter into the oxidative phosphorylation and that is how it is actually going to generate the large quantity of ATP.

So let us talk about the stage 1 which is the beta-oxidations. So this is a stage 1, all the reactions of the stage 1. So once the fatty acid-CoA molecules are exported to the mitochondrial matrix, they are subjected to the repeated 4-step process. Each time the chain length reduces by the 2 carbon till the final product is the cycle itself. For example, if you start with the permeth oil, it is first going to break this bond and then it is actually going to break subsequent to that.

So there are multiple steps in the beta-oxidations. So first step is the oxidations. The first reaction is catalyzed by the 3 isozymes of acyl-CoA dehydrogenase. So it is a flavoprotein with FADH as the prosthetic group. The electrons extracted from the fatty acid-CoA are transferred to the FAD and a reduced form of dehydrogenase immediately imparts its electron to an electron carrier of the mitochondrial respiratory chain which is an electron transferring flavoprotein.

The reaction is analogous to the succeeded dehydrogenase reaction in the cystic acid cycle where FADH act as an electron receptor. So in the step 1, the acyl-CoA dehydrogenase is actually going to participate and it is going to oxidize the carbon.

Then in the step 2, there will be a hydrolysis. So in the second step of beta-oxidation cycle, the water is added to the double bond of the trans-enoyles-CoA to form the beta-hydroxyl acyl-CoA. The reaction is catalyzed by an enzyme which is called as the enoyl-CoA hydratease and which is similar to the reaction performed by the fumarate enzyme into the acetylated cycle.

And then the third step is the oxidation. In the third step, the beta-hydroxyl acyl-CoA undergoes dehydrogenation. So synthesize the beta-ketoacyl-CoA via the enzyme known as the beta-hydroxylacyl-CoA dehydrogenase. Here the NAD plus act as an electron acceptor. The NADH formed in the above reaction transferred its electron to the NADH dehydrogenase and electron carrier of the spectra chain.

So what will happen is that by the end of these beta-oxidations, it is actually going to produce the acetyl-CoA. Then we have the stage step 4 where you are going to have the thiolizes. So in the final reaction of the beta-oxidations cycle, the beta-ketoacyl-CoA is cleaved by the reaction with the thiol group of the coenzyme A to yield an acetyl-CoA molecule and a coenzyme A thioester of the fatty acid. Shortened by the two carbon atoms, the reaction is performed by the enzyme acyl-CoA-acyltransferase. So, for example, if we start with a fatty acid which is C16, the product is going to be undergo for the 8 oxidation, the product after 1 beta-oxidation will be C14.

So after 1 beta-oxidation, it is going to be C14. This means the 2 carbon which comes out is actually going to produce the acetyl-CoA. This is the acetyl-CoA which is going to be produced and the C14 carbon what is left is actually going to be go through these reactions again. This means it will go again, then there will be acetylation and all that. So this means it will continue till you are actually going to have the C2 on this side and you are going to have the acetyl-CoA.

So it is actually going to give you the acetyl-CoA at the end. This means if you start with the C16, what you are going to get is you are going to get 8 acetyl-CoA enzyme, acyl-CoA molecule which will enter into the phase cycle and on the top it is also going to produce the NADH and it is also going to produce the FADH and it is going to produce the ATP if required. So and all these 8 molecules will enter into the phase cycle. Now in the stage 2 of oxidation of acetyl-CoA, considering the permutoyl-CoA C16, 1 beta oxidation will give you the myristyl-CoA and an acetyl-CoA enzyme which undergoes 6 more rounds of beta oxidation to get the completely oxidized to yield the 7 more acetyl-CoA molecule. All the acetyl-CoA molecule produced into the beta oxidation of a single fatty acyl-CoA molecule get further oxidized in phase cycle to yield the NADH and FADH2.

This means the 1 molecule of acetyl-CoA produces 3 NADH molecule, 1 FADH2 molecule and 1 ATP or GTP. This means the 8 acetyl-CoA molecule is going to give you the 24 NADH molecule, 8 FADH2 molecule and 8 ATP. Overall reaction for a permutoyl-CoA can be represented as follows. Permitoyl-CoA plus 7 CoA plus 7 FAD plus 7 NADH plus 7 water molecule will give you the 8 acetyl-CoA plus 7 FADH2 plus 7 NADH plus 7 hydrogen molecule. This means if you started with the C16, it will actually going to leave 1 molecule of acetyl-CoA and actually going to small by the 2 atom.

Same is true by all these, right. And ultimately what will happen is that when the C14, it is actually going to produce the acetyl-CoA and it is also going to produce the remaining molecule is going to be the acetyl-CoA. This means the beta oxidation is actually going to generate a huge quantity of the liquid molecules are actually going to generate a huge quantity of energy, right. Remember that from the 1 acetyl-CoA, right, 1 acetyl-CoA you are actually going to generate 15 ATP molecule, right under the crate cycle. This means if I have 1 oxidation of 1 permethoyl-CoA, right, 1 permethoyl-CoA, it is actually going to generate the 8 ATP, 8 acetyl-CoA molecule. This means it is actually going to generate approximately 120 ATP molecules, right, from the beta oxidation.

Whereas it is also going to generate some or more amount of NADH and FADH2 even from the beta oxidation step as well. Now, how you are going to do a regulation of fatty acid biosynthesis and catabolisms. So fatty acid regulation biosynthesis and catabolism is completely been regulated by the location of the fatty acids. So in the liver the fatty acyl-CoA has 2 major pathways. It can either transported to the mitochondria via the carnitine shuttle to get oxidized or it can be converted into the thioacylglycerol and phospholipid via the cytosolic enzyme.

The carnitine shuttle which is a 3 step process is the rate limiting step for the fatty acid oxidation and therefore it is an important point of regulation. Once the fatty acids are transported to the mitochondrial matrix, they are destined, designated for the beta oxidation. So remember that if the carnitine shuttle is not going to be working or if it is not functional, then the lipid molecules or fatty acid will not enter into the mitochondria for beta oxidation. Instead they will go for the cytosolic enzyme and they will be utilized for the synthesis of the phospholipids and the tricyclic drops. And these are the storage molecules or sometimes the phospholipids are going to be a part of plasma membrane.

So mannoly-CoA, the first intermediate of the fatty acid biosynthesis via the acetyl-CoA also regulate the fatty acid oscillation. When there is an ample amount of glucose supplied to the liver, fatty acid synthesis begins from the acetyl-CoA which produces the

mannoly-CoA that inhibits the carnitine acyl transferase 1. So this means if you have enough amount of glucose, so that means the glucose is enough to give you the energy and in that case what will happen is that the acetyl-CoA is actually going to be withdrawn from the crepe cycle. So this means if you have enough quantity from the glucose oxidation, there will be an access of acetyl-CoA. And this acetyl-CoA then would be working as a precursor for the fatty acid biosynthesis.

And this acetyl-CoA, the first molecule what it is going to produce is the mannoly-CoA. And mannoly-CoA is actually an inhibitor of the carnitine acyl transferase, the first enzyme which is in the carnitine shuttle, right. And if the first enzyme in the carnitine shuttle is not working, it is not going to attach the carnitine to the fatty acids and as a result, there will be no transport of fatty acid from the cytosol to the mitochondria and as a result, it is not going to go through to the beta oxidation. Instead, it is actually going to be utilized for the fatty acid biosynthesis. This means it is going to be utilized for the synthesis of triacyclic role or the synthesis of the other phospholipids.

So when the NADH and NAD plus ratio is very high, this means the cell is sufficient enough with the energy, okay. So you can imagine like that, okay. If it is a very high ratio, this means you have more amount of NADH and you have less amount of NAD plus that means the cell has sufficient energy, then it is indicating the enough energy for the cell to perform vital activities. Beta-hydroxycoenzyme dehydrogenase is also been inhibited. High concentration of acetyl-CoA inhibits the thiolase, right.

So these are the enzyme or which are actually functional within the for during the beta oxidations. During the time of vigorous muscle contraction, the stimulus exercise or fasting the consumption of ATP is increased which reduces the concentration of ATP and increases AMP that activates the AMPK, the AMP activated protein kinase. And AMPK phosphorylate various other targets enzymes such as stile-CoA carboxylase which catalyzes the mineral-CoA synthesis. This phosphorylation and thereby inhibition of coagulate carboxylase bring down the concentration of mineral-CoA relieving the inhibition of fatty acid acylcarnitine transporters into the mitochondria and allowing the degradation of the stored fat to undergo oxidation to regain supply of ATP from the fats.

So these are the things, right. If you have the high glucose molecules, you are actually going to produce the insulin and insulin is actually going to participate into the fatty acid biosynthesis and regulation. So when the blood glucose level is high, the insulin dependent protein phosphatases dephosphorylate the acetyl-CoA carboxylase thereby activating it and ACC starts sizing the mineral-CoA which inhibits the carnitine acyl transferase 1 and thereby preventing the entry of fatty acid coenzyme, fatty acid CoA, fatty acyl CoA into the mitochondria. This means once you have the high blood glucose

level, it is actually going to induce the production of insulin and once there will be an induction of insulin, insulin will actually go and bind to the insulin receptor and that in turn is actually going to produce the large quantity of phosphatases. And once the large quantity of phosphatases is produced, it will actually going to dephosphorylate the acetyl CoA carboxylase. So acetyl CoA carboxylase is inactive when it is phosphorylated and it is active when it is dephosphorylated or native form.

So once the phosphatases are produced, they are actually going to have the active ACC and what is the job of the active ACC is that it is actually going to take up the acetyl-CoA from the crepe cycle and it is actually going to produce the manolil-Ka and manolil-CoA is actually going to form the fatty acid and manolil-CoA is actually a very, very potent inhibitor of the carnitine acyl transferase 1. So this means it is actually going to destroy the carnitine shuttle and once it is destroying the carnitine shuttle, it is actually going to destroy the transport of fatty acid into the mitochondria and if it is destroying the entry of the fatty acid into the mitochondria, it is actually going to abolish the beta oxidation of the fatty acids. And as a result, it is actually going to promote more the synthesis rather than the degradation of the fatty acids. So that is why it is always been recommended that if you want to reduce the amount of fat into your body, you always should ensure that there is no enough glucose present. This means what it means is that it is not the fat which actually increases the fat level, it is the glucose which actually increases the fat level because if you have a high quantity of glucose within the blood, it is actually going to promote the synthesis of fat rather than the fat burnout, right.

And that is why it is important that we should have the less amount of glucose into the blood. So when the blood glucose level drops, the glucagon release activates the pKa which phosphorylates and inactivate the ACC. The concentration of the melanin coate drops which leaves the inhibited entry of fatty acid into the mitochondria and replenishes the beta oxidation. So this is all about the catabolic reactions what we have just discussed, right. And what we have discussed, we have discussed about the catabolic reaction of the glucose and the lipids or the fatty acids and within the glucose, we have discussed about the glycolysis and we also discussed about the crepe cycle.

Whereas in the case of lipid molecules, we have discussed about beta oxidation and how the beta oxidation is producing the acetyl CoA and then if this acetyl CoA is entering into the crepe cycle and that it is now it is actually going to produce the large quantity of energy in the form of ATP. So now once you have generated the large quantity of ATP, this ATP is actually going to be utilized into the anabolic reactions. Anabolic reaction means the biosynthetic reactions and anabolic reactions are required for the growth of the organism or growth of the person, right. Because if you want to grow for example, if you want to grow from 1 mm to 1 centimeter, right. This means you actually require the

enough quantity of material, right.

So that you can actually be able to for example, if you want to increase the length, right. So you also have to synthesize the muscles, right. And muscles is nothing but made up of the different types of protein molecules, lipid molecules, right. So you also require the synthesis of protein and lipids and you also require the nucleic acid, right.

So if you want to do a synthesis, you also require the energy. So energy you have already produced, right. And this all energy is the endogenous energy, it is not the exogenous energy, right. And I am sure you all very much aware of what is mean by the endogenous energy, what is mean by the exogenous energy, right. For example, if you take a carbon molecule, if you take a carbon, right, and if you this, if you burn this carbon, it is actually going to give you the energy, right. This is exogenous energy, because it is always present outside, right.

That is how you do actually, you take the carbon, you burn it, and that is how you keep it into corner of your room and that actually keep the room warm actually. But this is not going to remain continuous, right. Whereas in these cases, you are actually producing the energy by running the different types of metabolic reactions within your body, right. So these are the endogenous energy. And that energy is actually going to be utilized for forming the bonds between the constituents.

For example, in this case, if you want to make the protein, you always have to make the bond between the amino acids. If you want the lipid synthesis, you always have to make the bond between the fatty acid and glycerol. Similarly, for the nucleic acid, you always have to make the bond between the nucleotides molecule. And that is how it is actually going to synthesize genome for the new cell, it is going to synthesize the plasma membrane for the new cell, it will also require the synthesis of the protein for the new cell. And once you have all these raw materials, the cell is actually going to enlarge in size and that is how it will actually going to help into the growth of the organism.

So let us discuss about the anabolic reactions. And what we are going to discuss, we are going to discuss about the biosynthesis of the amino acids, where all this energy is going to be utilized. So amino acid biosynthesis. Amino acids are categorized into the two different categories, essential and non-essential amino acid based on the biosynthesis. Thus, the amino acids which are actually you which you can be able to synthesize in your body by the raw material are called as the non-essential amino acids. Because these are the amino acids which you can be able to synthesize from the raw material.

Whereas the amino acids for which either you do not have the biosynthetic pathway or

you cannot synthesize from the raw material, because you do not have the requisite biosynthetic pathway, they are called as essential amino acids. So for the plant, plant can be able to synthesize all the amino acids. So it is actually all the amino acids are non-essential amino acids for the plant because plants can easily take the carbon dioxide, water and the other metabolites and it can be able to synthesize all amino acids. Because the plant has the biosynthetic pathway for all amino acids.

Whereas the animals are dependent on the plant to provide the amino acids. So these are the amino acids which are essential. So these are the amino acids for which there is no pathway present in the animals. This means these are the amino acids which it has to take from the plant. So it plant has to provide these and how the plant provide these? Plants are actually giving you different types of raw material, for example pulses. So if you take the pulse, pulse is actually going to be get digested into the digestive system and it is actually going to release the different types of amino acids.

For example, if you take the rice, rice is also going to produce some amount of amino acids which are funding into the essential amino acids. And then you have the non-essential amino acids where you actually have the biosynthetic pathway. So you have the pathway and you just require the raw material. So you actually require the ammonia, you require the carbon dioxide, you require all those kind of things and then you can be able to produce these amino acids or sometimes some of these amino acids are also being derived from the essential amino acids.

So that is also you can actually be able to have the biosynthetic pathway. So these are the 10 amino acids and these are also 10 amino acids. So biosynthesis of the amino acids. Principally, all amino acids are derived either from the glycolysis or citric acid cycle or pentose phosphate intermediates. These derivatives provide the carbon skeleton from the amino acids whereas amino group or the nitrogen in the same is provided either by the glutamine or the glutamate. Not all amino acids are synthesized by the organisms which they need from the outer environment either in the form of protein or from the dietary food.

These amino acids which they cannot synthesize by the organisms are called as essential amino acid and the rest are called as non-essential amino acid. The most important reaction that take part in almost all the biosynthetic pathway of different amino acids are reductive amination of the alpha-keto acids or the transaminations reactions or require a coenzyme PLP that is a pyrexyl phosphate. So this is an overview of the amino acid synthesis where you actually have the different types of amino acids derived from the carbohydrate metabolism. This is the glycolysis what you see here is from here to here right this is the glycolysis and then from the pyruvate this is the crepe cycle okay. And

what you see here is that from the first for example from the glucose you can actually be able to have the ribulosis phosphate and from that you can actually be able to have the synthesis of histidine.

Similarly from the 3-phosphoglycerate you can have the synthesis of serine and once you have synthesized the serine that serine can be converted into the glycine and the cysteine. Similarly 3-phosphoglycerate can enter into the pentose phosphate pathway and then pentose phosphate pathway is going to generate the Rheicose 4 phosphate and that along with the phosphoenolpyruvate can give you all the aromatic amino acid like tryptophan, phenylalanine and tyrosine and then we also have the other amino acids like aspartate, asparagine, methionine, theanine all that from the crepe cycle like the oxaloacids right. Similarly from the alpha-glutarH you can actually be able to produce the glutamate by the different types of metabolic reactions and once you produce the glutamate you can convert that into the glutamine, proline and arginine. Similarly from the pyruvate you can be able to produce the alanine, valine, leucine and isoleucine. So based on these kind of scheme the amino acid biosynthesis can be decided into the different families.

So you can have the glutamate family, you can have the pyruvate family, you can have aspartate family, serine family, aromatic amino acids and you can also have the histidine families. So when you talk about the glutamate family you only what you need is you require the synthesis of the glutamate. Once you synthesize the glutamate you can be able to synthesize the glutamate, glutamine, arginine and proline. Similarly once you have the pyruvate, from the pyruvate you can be able to generate the valine, alanine, leucine and isoleucine. From the aspartate you can be able to synthesize all these, from the serine you can be able to synthesize all these.

From the aromatic amino acids you can be able to have the tipto-phan, phenaniline and thiocine. So let us start first with the glutamate family. So biosynthesis of the glutamate and glutamine. So from the alpha-ketoglutarate which is present in the crepe cycle, you can be able to synthesize the glutamate and once you synthesize the glutamate you can be able to convert that glutamate into glutamine, proline or the arginine.

So biosynthesis of the glutamate and glutamine. So glutamine synthesis is an important mechanism of ammonia assimilation, transportation in different cells and secretion therefore after. So free ammonium ion, free ammonia is toxic for the cell which is converted into glutamine for the transportation. In bacteria and plant, the glutamate is derived from the glutamine catalyzes, from the glutamine catalyzes by enzyme known as GOGCAT or the glutamate oxo-glutarate aminocharsinase. Here the glutamine act as a nitrogen donor and alpha-ketoglutarate undergoes the reductive etiaminations. So what

you have is to have the alpha-ketoglutarate, glutamine, NADPH, ATP, remember this is NADPH not the NADPH and it is actually going to produce the two molecules of glutamate plus NADPH.

So you are actually going to utilize not only the ATP but also in the form of reducing equivalents. Animals do not have the glutamate synthesis, therefore they maintain the high level of glutamate by transamination of the alpha-glutarate while the amino catabolism. Glutamate can also be formed by the glutamate dehydrogenase in the single step reaction given below. The reaction takes place in the mitochondria, the reaction cannot distinguish between NADH and NADPH.

So alpha-ketoglutarate with ammonia, NADPH give you the glutamate and NAD+. Then we have the biosynthesis of the serine, glycine and cysteine. So from the 3-phosphoglycerate, so 3-phosphoglycerate you are going to get from the glycolysis and from the glycolysis then the 3-phosphoglycerate can be produced into the serine and serine can be converted into glycine and cysteine. So biosynthesis of serine, glycine and cysteine. So serine is derived from the oxidation of 3-phosphoglycerate by the phosphoglycerate dehydrogenase in the presence of NAD+, to produce the 3-phosphoglyce hydroxyl pyruvate and glutamine, since this transfer its amino group to the above synthesized product to yield the 3-phosphoserine followed by the hydrolysis of phosphate group by the enzyme called as phosphoserine phosphatase to yield the serine. The pathway for serine and glycine are almost the same except for the synthesis of glycine after the removal of carbon atoms from the serine by an enzyme called serine hydroxymethyl transferase or the SHMT.

In the above reactions, the beta carbon of the serine is accepted by the tetrahydrofolate in the presence of PLP. In plant and bacteria, cysteine is derived from the serine and for which the sulphur is obtained from the environmental sulphates. First, an acetyl group is attached to serine from the acetyl-OA to form the O-acetylserine. This reaction is performed by the enzyme serine acetyltransferase. The reduced sulphur is then incorporated into our product by enzyme called O-acetylserine thiolase to yield the cysteine.

In mammals, the process is quite different. The carbon skeleton and the sulphur for cysteine biosynthesis is given by the two different amino acid that is the serine and the methionine respectively. So, these are the reactions what is being shown here. You start with the 3-phosphoglycerate, it gets converted into 3-phosphohydroxypyruvate and then the glutamate is going to give you the amino group and that is how it is actually going to form the 3-phosphoglycerine and thioeposocerine is actually going to be hydrolyzed and it is actually going to give you the serine. And once the serine is being produced with the

help of the enzyme called serine hydroxymethyltransferase is going to be get converted into the glycine. And remember that tetahydrofolate or N-5-anten-metallentetahydrofolate is actually a shuttle between the nucleic acid and the protein molecules.

That is why this enzyme is actually can be shuttle the carbon pool between the protein metabolism as well as the nucleic acid metabolism. And then we have the biosynthesis of the aspartate family amino acids. So oxalacetate you have transaminations to form the aspartate and on the aspartate you can have the amidation to produce the arginine, asparagine from the aspartate you can have the methionine, thionine and lysine. Then we have the biosynthesis of the pyruvate family amino acids. So pyruvate family, pyruvate after the transamination can produce the alanine and the pyruvate can produce the valine, isolecine and leucine.

So and then we have the biosynthesis of the aspartate and alanine. So carbon skeleton for aspartate and alanine is derived from the oxalacetate and pyruvate respectively whereas amino group is provided by the mutamine for both the amino acids. In the above reaction, the alpha-kryton-lutarate is formed as the byproduct along with the alanine and aspartate as amino acid. This is an example of the transamination reaction and it is catalyzed by the amino transferase in the presence of coenzyme PLB. So you have this kind of transamination reactions where one side you have the oxaloacetate and glutamate and this side you are going to generate the aspartate and the alpha-kryton-lutarate.

So it can actually go in both the directions. So depending upon whether you require the aspartate or whether you require the glutamate, it can actually be able to convert the enzymes, convert the amino acid into each other. Same is true for the pyruvate and alanine also. And then we have the biosynthesis of the proline and the arginine. So these are the reactions what you are going to have for the biosynthesis of the proline and arginine.

So it starts with the glutamate. Glutamate is actually going to be having the energy of the ATP and it is actually going to form the gamma-glutamyl phosphate and there will be a phosphorylation reaction. So it is going to be catalyzed by an enzyme called glutamate kinase. And once you generate the gamma-glutamyl phosphate, then gamma-glutamyl phosphate is going to be reduced by an enzyme called gamma-glutamyl phosphate reductase and that is going to form the glutamate semi aldehyde. And then this semi aldehyde is actually going to be get converted into the parolin-5 carboxylase carboxylate and this 5-pharmacyl carboxylase is further going to be reduced by enzyme called parolin-carboxylase reductase and ultimately it is going to form the proline.

In animals, the arginine is produced from the glutamate in the urea cycle. Similarly arginine is derivative of the ornithine which can also be produced from the glutamate gamma semi aldehyde by transamination reaction. But cyclization of gamma semi aldehyde interdict the enough 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. So biosynthesis of the aromatic amino acids. So from the phosphoenolpyruvate, it is actually going to combine with the archaeosis phosphate from the pentose phosphate pathway and that is how it is actually going to form the tryptophan tyrosine and phenylalanine and tryptophan can further be converted into tyrosine if required.

So from the chorismate, it is actually going to form the anthraenoallene and then from here it is actually going to form the enolyl road carboxyphenyl amino carboxyribulose phosphate and from here it is actually going to form the indole-3-glycerol phosphate and ultimately it is going to be get converted into the tryptophan. So once it is going to form a tryptophan, it can be get converted into the tyrosine. So enzyme tryptophan synthase which performed the last reaction in the conversion from the chorismate to tryptophan has two subunit alpha 2 beta 2 that perform the two different parts of the whole reaction. Indole-3-glycerol phosphate alpha subunit is going to form the indole plus geseltii plus 3 phosphate and indole plus terrine is actually going to form the tryptophan and there will be a bowl of water. So the bowl formed in the first part of the reaction is moved to the channel from the alpha subunit, the beta subunit activate active site where it undergoes condensation with shift base intermediate such as the PLP and serine and in any one the tyrosine can be formed by the hydroxylation phenylalanine at C4 position by enzyme called phenyl hydroxylase.

So this is the tyrosine and when you have the phenyl hydroxylase, it is actually going to form the, so this is the phenylalanine actually and when it has the phenylalanine hydroxylase, there will be hydroxylation reaction. So it is going to have the hydroxylation on this side and it is actually going to form the tyrosine. Then we have the biosynthesis of phenylalanine and tyrosine in plant and bacteria. So in the plants and bacteria, the phenylalanine and tyrosine is derived from the chorismate where prefinite is a common intermediate and then the pathway diverges to the two branches, one forming the tyrosine from the 4-hydroxyl pyruvate and the other forming the phenylalanine from the phenyl pyruvate.

The final reaction is the transamination that involves the transfer of the amino group from the glutamine. So this is the pathway what is being shown from the chorismate, it is going to form the p-phenate and at this stage, it is going to bifurcate into the two pathway and one side it is going to form the 4-hydroxyl pyruvate, other side it is going to

form the phenyl pyruvate and then it is actually going to have the transamination reaction and that is how it is going on this side it is going to form the tyrosine whereas in this side it is actually going to form the phenylalanine. So regulation of the amino acid biosynthesis, so you can have the regulation of the different types of biosynthetic pathways and it all depends on the availability of the different types of metabolites and that is how they are actually going either going to upregulate or down regulate the different enzyme activities. For example, in this case the glutamine synthase, so amino acid biosynthesis is aerosterically regulated. The end product of the pathway generally regulate the enzyme that catalyze the initial step of the pathway.

Along with the acrylic modulation, feedback inhibition is also been seen to regulate the amino acid biosynthesis. The glutamine synthase is an important enzyme that participate in almost all the reaction with all of the amino acid biosynthetic reaction. Therefore, this enzyme is inhibited by the various other molecules such as AMP, CTP, glycine, allene, etc. The other mechanism seen are the sequential feedback mechanism which are more profound in the aromatic amino acid biosynthetic pathway. And this mechanism, the amino acid phenylalanine, tyrosine, tryptophan, sequentially inhibit the 3-isoline of the enzyme THV and that is how it is actually going to inhibit the synthesis of the aromatic amino acids. So this is all about the amino acid biosynthesis and what we have discussed, we have discussed about the catabolic reactions and we have also discussed about the anabolic reactions.

And so the purpose of the metabolic reaction is to produce the energy whereas the purpose of the anabolic reaction is to utilize that energy for the synthesis of the different biomolecules which they require for the synthesis of the different types of biomolecules such as proteins, lipids and the genome. And all this is required for the synthesis of the new cell so that they can be able to grow from the unicellular organisms to multicellular organisms or they can actually be able to produce the more number of cells so that they can be able to increase their number. So with this, I would like to conclude my lecture here. In our subsequent lecture, we are going to see more aspects of the biological system. Thank you.