Molecular Biology
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Module - 02
Basics of Biological system (Part 2)
Lecture-06 Cellular Metabolism (Part 1)

Hello everyone, this is Dr. Vishal Trivedi from department of bioscience and bioengineering IIT Guwahati and what we were discussing, we were discussing about the molecular biology and so far what we have discussed, we have discussed about the basics of the biological system. So, if you recall in the previous module, we have discussed about the cellular structures, we have discussed about the prokaryotic cells, eukaryotic cells and then we also discuss about the different types of organelles, what are present in the prokaryotic cell. And in today's lecture, we are going to extend our discussion about the basics of the biological system and in this context, we are going to discuss about how the cells are actually going to acquire the energy. So, in today's lecture, we are going to discuss about the cellular metabolisms and how the cells are performing the different types of metabolic reactions to acquire the energy and how it can actually be able to utilise that energy to synthesise the different types of biomolecules.

Now, the first question comes, why the cell is actually requiring the energy, whether it is a prokaryotic cell or whether it is a eukaryotic cell such as the animal cell, plant cell, fungi, it requires the energy, it requires to run the cellular metabolisms to acquire the energy, right. Because whether it is a prokaryotic cell and prokaryotic cell actually require the energy to grow, replicate and produce and you will see in the later on in this particular course that there are so many different types of cellular activities which are operating within the cell and that they are very, very crucial for maintaining the cell. For example, one of the crucial factor is the DNA replications and DNA replication is very important because it is actually required not only for synthesis of the new DNA strand, but it also requires for the repairing of the damaged DNA and repairing of the damaged DNA is important because it is actually going to protect the organisms for going for the death pathway. So, energy can be acquired from running the cellular metabolisms.

And as far as the cellular metabolism is concerned, we have two different types of cellular metabolisms. We have either the catabolic reactions or the anabolic reactions. Catabolic reactions are as I said, you know, they are the energy producing reactions. So, these are the reactions which are actually going to produce the energy. So, in this you are actually going to use the biomolecule which is responsible for producing the energy such as the carbohydrate and mostly the lipids.

These are the two major biomolecules which are being used for producing the energy. Under a very, very strong and very, very starvation conditions, the organisms can also utilize the proteins for the energy production. So, in those cases, the protein is going to be get converted into the carbohydrate and lipids and then it is actually going to run the catabolic reactions to produce energy. But that is very rare and it happens only under those conditions when you are going through starvation reactions. So, and then once you are actually going to do the catabolic reactions for the carbohydrate or lipid, you are actually going to produce the energy and that energy would be in the form of the ATP.

And this energy is actually going to be utilized for the anabolic reactions. So, this energy is actually going to utilize to drive the reaction so that you are actually going to have the synthesis of the new biomolecules. For example, if I want to synthesize a protein and you will see this when we are going to discuss about the biomolecule into the later part of this particular course that a formation of a bond is required. So, protein is made up of the amino acids. And these amino acids for example, the amino acid 1 and it is actually going to be converted going to be attached to the amino acid 2 by a bond which is called as the peptide bond.

And you know that the bond formation is always required that you are actually going to spend some amount of energy. So, when you spend the energy, you are actually going to activate the functional group what is present onto the amino acid number 1 and to amino acid 2 and that is how they are actually going to combine together and they are actually going to form a protein or peptide for example, where they are actually going to be linked by a peptide bond. So, basically what your cellular metabolism is a submission of all the reactions whether it is the catabolic reaction or the anabolic reactions. So, the anabolic reactions are required for the production of energy, whereas the anabolic reactions are required to utilize this energy for the biosynthesis because once the synthesis is done, it is actually going to contribute in terms of the growth of the organisms or the other kinds of functions. For example, it is actually going to help to produce the gametes, it is going to help the produce to give the nutrition to the daughter cells and so on.

So, these two reactions are always been under the coordination to each other and as a result, they are actually going to be responsible for the cellular health of the particular cell. So, let us start first with the catabolic reactions and we are going to start with the carbohydrate metabolisms. So, very briefly we are going to discuss about the carbohydrate metabolisms, then we will discuss about the lipid metabolisms and mostly we are going to discuss about the catabolic reactions. And then we are going to discuss about the anabolic reactions and at the end, we are also going to discuss how the you

know the cellular metabolism is taking care of the toxic products being produced during the catabolic reaction or to the anabolic reactions. So, when we talk about the carbohydrate metabolism, carbohydrate metabolism and you know that the carbohydrate metabolism is going to start once you have any food.

So, for example, if I have a food for example, if I have the rice right. So, if I have a rice in the lunch, what will happen is the rice will enter into my stomach right and then followed by the stomach, it is actually going to enter into the small intestine and from its small intestine, it is actually going to enter into the large intestine and afterwards it is actually going to be the undigested product is going to be removed from the anus right. So, food whether it is a rice right, rice is a good source of carbohydrate right, but this carbohydrate is a polymeric carbohydrate right. So, it is actually going to have the starch. Now starch you cannot put it into the catabolic reactions.

The starch has to be converted into the simple sugar such as glucose and fructose and they will enter into the catabolic reactions. So first you are going to take the rice, you are put it into the stomach, in the stomach it will actually going to start digesting right and from the small intestine, the starch is completely going to be get converted into glucose right and glucose is a monomeric sugar which is going to be ready to be get into the catabolic reactions and then this glucose is going to be absorbed by the willy and the micro-willy what is present onto the small intestine cell surface and they are actually going to be present into the blood right. So, once they are absorbed, they are going to put into the blood and from the blood, it will enter into the different organs. So, it is actually going to enter into the liver, it is actually going to enter into the muscles and so on. So brain, spleen and all that okay.

So all the organs, it is actually going to be get distributed and within the liver, muscles, spleen, brain, nervous tissues and all other, all these places, these glucose is actually going to be utilized for running the catabolic reactions and they at the end, they are going to produce the energy right. And when you have the excess amount of glucose, that glucose is going to be stored in the form of the glycogen within the different types of tissues. So that when you are going to do the starvation, that glycogen is getting converted into the glucose and that is how actually it is actually going to provide you the running force for the moment when you are not taking the nutrition from outside. So for example, when you sleep in the night, you are going to take the dinner right. But that dinner is actually going to serve the food for few hours.

After that, it is actually going to start utilizing the stored material what is present in your liver, muscles, spleen and brain. So these are the catabolic reactions what is going to be utilized right. And they will be utilized to produce the energy and that energy is

actually going to utilized for running the normal reactions what is going to be performed by the different organs or they are actually going to be utilized for bio-acetic pathway. Now as far as a carbohydrate is concerned, it is actually going to be the central pathway for catabolism. So that is why it is actually very important that we should understand the carbohydrate metabolism.

So carbohydrate metabolism is in the central right as far as the catabolic reaction is concerned and majority of the pathways are actually getting diverged from the carbohydrate metabolism. Now, once the glucose is produced, it will enter into the different types of organs and within the different types of organs, it is actually going to first into a series of reactions which is called as the glycolysis and at the end of the glycolysis, it is actually going to produce the pyruvic acid and that pyruvic acid will enter into another cyclic reaction which is called as the Krebs cycle. So in today's lecture, we will discuss about the catabolic reactions such as the glycolysis and the Krebs cycle. So glycolysis, glycolysis is a central pathway to the carbohydrate metabolism and it is the universal pathway which is found in the prokaryote or the eukaryotic cell. It is a breakdown of a six-membered glucose into the two three-membered carbon sugar to feed the carbon to Krebs cycle in the presence of oxygen.

So you can have the two different scenarios when you have the oxygen present such as the organisms like us and it can be also be functional even if you do not have the oxygen, right. So if it is present in the presence of oxygen, the glucose is getting converted into a two three-membered carbon sugar and that is going into the Krebs cycle or it is actually going to send for the anaerobic oxidation in the absence of oxygen. So in the different types of pathogenic organisms like bacteria and other kinds of organisms, when the oxygen is limiting, it will not going to be get converted into the pyruvic acid. Instead of that, it is actually going to be get converted into the anaerobic products and that is how they will, these organisms are also going to survive. So hence, it is play a pretty crucial role for the adaptation of a living organism under the different types of stress conditions.

The glycolysis is a 10-step chemical reaction to enable the glucose for its optimal oxidations. So glycolysis is a 10-step reaction, right and these are the 10 steps, right. You have the step number 1, 2, 3, 4, 5 and in the 10th step, you are going to generate the pyruvate. So this is the step number 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10, okay. So in the step number 1, you are actually going to do the activation of the glucose molecule.

Okay, because you have to invest some energy so that the glucose will be destabilized because once you add the phosphorylated group to the glucose molecule, it is actually going to contain the very high energy and when it contains the high energy, the high energy is always making the system unstable. So phosphorylation of the glucose, so the

glucose produced after the glycogen breakdown is phosphorylated by the enzyme which is called as the glucokinase. Remember that glucokinase is only present in the liver whereas the hexokinase is present in the all other tissues especially in the muscles. So in most of the organs such as brain, spleen, muscles, it is hexokinase which is the major enzyme which is going to catalyze the reaction number 1 but in the case of liver, it is actually going to be the glucokinase. So in the phosphorylation reactions, in the phosphorylation reaction, the phosphate that is the gamma phosphate group of ATP is transferred to the glucose to form the glucose 6-phosphate.

The phosphorylation reaction of glucose to produce the glucose 6-phosphate mark the molecule for the glycolysis and in this process, the one molecule of ATP is utilized in the step. So once the glucose which is unphosphorylated, so this glucose is actually going to be produced from the glycogen. Remember that I talked about the stored glycogen. So once you require the energy, that glycogen is going to be broken down and it is actually going to form the glucose. This glucose can participate in the different types of reactions.

So to commit this glucose for the carbohydrate metabolism or the catabolic reactions, what you are going to do is you are going to take the carboglucose and with the help of the hexokinase or the glucokinase, it is going to be get converted into glucose 6-phosphate. Once you generate the glucose 6-phosphate, there is a big difference. This is the neutral molecule. There is no charge on the glucose molecule. Whereas once you generate the glucose 6-phosphate, this is actually going to be the negatively charged molecule.

And once you generate a negatively charged molecule, you are actually going to trap the molecule within the cell. Because a charged molecule cannot be freely available to go out of the cell, because the charged molecule, the movement of a charged molecule from the cell requires the energy. This means and glucose 6-phosphate is going to be entrapped within the cell and then it is actually going to be committed for no other reaction, but that glycolysis and then it will actually going to do the reaction number 2. Now, in the step number 2, there will be a conversion of glucose 6-phosphate to the fructose 6-phosphate because you are going to have the isomerization reaction. So, in the step number 2, the glucose 6-phosphate what you have generated from the glucose is going to be get converted into fructose 6-phosphate and the enzyme what is going to catalyze this is called as a phosphor-freto isomerase.

Now, in the step number 3, another series of oxidation is or another series of phosphorylation is going to be take place in the step number 3. So, in the step number 3, you are going to have the phosphor-freto kinase catalyzing the another round of phosphorylation. So, you have first phosphorylation here and you have the second

phosphorylation here and as a result, you are going to generate a molecule which is called as fructose 1, 6 bisphosphate and this molecule is a very high energy molecule and very unstable molecule. So, in the step number 3, the sugar is further phosphorylated at the carbon number 1 to produce the fructose 1, 6 bisphosphate by the action of an enzyme which is called as phosphofructo kinase. In the phosphorylation reactions, the phosphate that is a gamma phosphate group of ATP is transferred to the phosphorylated sugar to form the fructose 1, 6 bisphosphate.

One molecule of ATP is utilized in this step. So, remember that we have utilized one ATP here and one ATP in the reaction number 3. Now once the fructose 1, 6 bisphosphate is generated, which is actually we have very, very, very unstable molecule, it is actually going to be act by the aldolase in the reaction number 4. So, in the reaction number 4, the aldolase is actually going to break or it is actually going to break the molecule into the two different molecules, the glyceraldehyde 3 phosphate or the dihydroxyacetone phosphate. So, in the step number 4, there will be a cleavage of fructose 1, 6 bisphosphate and this step is catalyzed by an enzyme which is called as the aldolase or fructose 1, 6 bisphosphate and aldolase to generate the glyceraldehyde 3 phosphate which is called the aldose and the dihydroxyacetone phosphate which is called as the ketose.

So, there will be a cleavage of this high energy bond. Remember that until this, you have the 6 membered carbon, 6 membered ring. Now at this stage, it is actually going to be get converted into the 3 membered rings and that is a cleavage of the sugar molecule. Now in the step 5, this is the step number 4, you are going to have the isomerization reactions and the conversion of the dihydroxyacetone phosphate to the glyceraldehyde 3 phosphate. So, interconversion of the triose phosphates, so 3 carbon sugar formed in the step 4 undergoes the internal convergence as the glyceraldehyde 3 phosphate can readily be entered into the next step.

The ketose generated in the step 4 is reversibly converted into the glyceraldehyde 3 phosphate by the triose 3 phosphate isomerase. So this is also a very, very important enzyme because it is actually going to convert the dihydroxyacetone phosphate into the glyceraldehyde 3 phosphate. And now afterwards, so it is actually going to generate the 2 molecules of glyceraldehyde 3 phosphate. Remember that from fructose 1, 6 base phosphate, aldolase is actually going to break this into the glyceraldehyde 3 phosphate and the dihydroxyacetone phosphate. So it is actually going to generate the 1 molecule of this and 1 molecule of this, but with the action of phosphotriose isomerase, this molecule is getting converted into this and as a result of this, the 2 molecule of glyceraldehyde 3 phosphate is going to be generated from the fructose 1, 6 base phosphate.

Now in the step number 6, this is the first time when you are actually going to see a generation of the ATP. So you are going to see the generation of the reducing equivalence and this reducing equivalence are actually going to produce the ATP. So in the step 6, what you are going to do, so this is the step number 6, what we are going to do is you are going to see the dehydrogenase reactions and there will be a generation of the reducing equivalence. So in the step 6, the glyceraldehyde 3 phosphate, the glyceraldehyde 3 phosphate is going to be get converted into the 1, 3 base phospho-desirate and in this step, the 1 molecule of NADH is produced after the oxidation of the aldehyde group of the glyceraldehyde 3 phosphate with the help of the enzyme glyceraldehyde 3 phosphate dehydrogenase. This enzyme is very important for the many types of the therapeutic applications such as generation of the different types of drugs and other kinds of thing because this is the enzyme which is actually going to be first time going to produce the reducing equivalent and these reducing equivalence when they will put into the electron transport chain, they are actually going to produce the ATP.

So that is why if you mutate or if you inhibit this particular enzyme, you are actually going to destroy the glycolysis and you are also going to block the production of the energy. Even in those organism where the oxygen in the absence of oxygen, the glycolysis is going to be keep running and keep giving them the enough energy so that they can be able to survive under the stress conditions. Now once you generated the 1, 3 base phospho-glycerate from the glyceraldehyde 3 phosphate, it will be converted into the next reaction and the next reaction is the seventh reaction. So in the step 7, in this step, the phosphate group from the 1, 3 base phospho-glycerate is removed by the phosphoglycerate kinase with an acyl group transferred to the ADP to generate the ATP molecule. So in this is the first step where you are directly going to see a generation of the ATP molecule and this is the enzyme which is actually responsible for generation of the first ATP molecule.

And 1, 3 base phosphoglycerate is going to be get converted into 3 phosphoglycerate and the phosphate what is present on the carbon 1 is actually going to be taken up by the ADP molecule and as a result, it is actually going to generate the ADP molecule. So this is the step number 7 which is actually the step which is going to generate the energy first time. Remember that in the step number 6 also you have generated the energy but that is indirect energy. It is actually going to get into the electron transport chain and then it is actually going to produce the ATP. But here directly you are going to get the ATP molecules.

Now from the 3 phosphoglycerate, there will be isomerization reactions and it is actually going to get converted into the 2 phosphoglycerate. So in the step number 8, you are going to have the conversion of the 3 phosphoglycerate to the 2

phosphoglycerate which means there will be a change of the position of the phosphate group within the molecule and this reaction is going to be catalyzed by an enzyme which is called as a phosphoglycerate mutase and it is actually going to form the 2 phosphoglycerate. Now in the step number 9, there will be a dehydration of the 2 phosphoglycerate to phosphoenol pyruvate. The enzyme enolase catalyzes the dehydration reaction to produce the phosphoenol pyruvate, a compound with a high phosphoryl group transfer potential. So now from the 2 phosphoglycerate, the enolase is actually going to remove the one molecule of the water and as a result, it is actually going to form the phosphoenol pyruvate.

And from the step number 10, which is the last step of the reaction, so this is the step number 9, which is the step number 10, the phosphoenol pyruvate is actually going to give up another phosphate and as a result, it is actually going to generate the pyruvate and the enzyme phosphoryl pyruvate kinase and here again, you are actually going to produce the direct energy which means it is actually going to produce the instant energy and it is actually going to produce the ATC. So the first time, you have produced the energy here and the second time, you are going to produce the energy here. And in the step number 10, the phosphate group from the phosphoenol pyruvate is transferred by the pyruvate kinase with an acyl group, phosphate group transferred to the ATP to generate the ATP molecule. Now this is the glycolysis ATP balance sheet and what you see here is that I have given you that how much amount of investment and what will be the production. So in the investment, remember that in the step number 1 to 4, there is an investment of two ATP molecule because you are utilizing the ATP molecule in the step number 1 and in the step number 3.

Now, once you have invested the two ATP molecule because you have activated with the step number 1, you have activated the molecule and you have phosphorylated the glucose so that it will be committed for the glycolysis and in the step number 2, you have phosphorylated fructose 6 phosphate so that it will be going to produce the fructose 1, 6 bisphosphate and it is actually going to be ready for the cleavage reactions. And fructose 1, 6 bisphosphate is a very, very high energy unstable molecule. So once you generated the unstable molecule, it will actually going to go into the downstream reaction. So in the step number 6, the ATP is actually going to be produced, NADH is actually going to be produced and that NADH when it goes into the electron transport chain, it is actually going to give you the ATP molecule. Then in the step number 7, there will be a generation of ATP when you are leaving the one ATP molecule to the one phosphate groups to the ADP and in the step number 10, which is the final step phosphoenol pyruvate is also giving one phosphate molecules to the ADP and that is how you are actually going to have the two different types of ADP molecule.

And remember that after the step number 5, you have the cleavage of fructose 1, 6 bisphosphate to the glyceraldehydes 3 phosphate and dihydrogenes phosphate. So you are actually going to have two molecules of the glyceraldehydes 3 phosphate. So the one molecule when going to process, it is going to produce the one molecule of NADH, one molecule of ATP and one molecule of ATP in this. But since you have two molecules of NADH, two molecules of the d33 phosphate, it is actually going to produce the two molecules of NADH and when the two molecules of NADH is going to process, it is going to generate the six molecules of ATP. And in the step number 7 and 10, it is also going to generate the two molecules.

So total T, what you are going to see here is that this is the final balance sheet. So 6 is from the NADH, 2 is from the reaction number 6 and 2 is from the reaction number 10 and these are the two reactions, two ATP what you have actually invested. So at the end, you are actually going to have the 8 ATP molecules. So at the end of the glycolysis, if you have the oxygen present, one molecule of glucose is actually going to give you the 8 ATP molecules. Now, if it is a reaction, it is actually going to be regulated by many methods.

So one of the major method is that you are actually going to regulate the level of glucose and that is always being done by the different types of hormones. You know that the different types of hormones are regulating the concentration of the glucose within the blood and outside within the cell also. And one of the such hormones is called as insulin hormone. And insulin actually binds to a septum which is called as the insulin septum and these are the protein tyrosine based receptors and they will actually going to you know drive the reaction inside the cell in such a way that it is actually going to down regulate the glucose. So it will actually going to enhance the uptake of the glucose.

So what happened is that when you have the insulin binding to the insulin receptor, it is actually triggering the opening of the glucose transporters. So you have a glucose transporter and they are actually going to increase the entry of the glucose inside the cell and once they are actually going to enter inside the cell, so they will be going to take up the glucose, they will be going to take inside and then they will recycle and go back. So in the step number one, the insulin will bind to the receptor into the cell membrane and activated receptor promote the recruitment of glucose transporter from the intracellular pool to the cell membrane. So once that happens, you are actually going to have a very high concentration of the glucose transporters such as GLUT3 and GLUT4 and they will actually going to enhance the uptake of glucose from the bloodstream. And once it enters and suppose the glucose is less, then what will happen is that these transporters are actually going to be taken up into the intracellular vesicles.

And by doing this, it is actually going to regulate the level of glucose into the blood. Apart from this, the glycolysis can also be regulated at the level of the feedback mechanism and as well as the covalent modifications. So this is the example of the covalent modification and this is the example of the allosteric regulations. And I am not going to discuss in detail about this because this course is more about the molecular biology, but what will happen is that in the case of the covalent modifications, the pyruvate kinase, which is actually the enzyme that is catalyzing the 10th reactions can be present in two different forms. It can be a phosphorylated form or it can be a dephosphorylated form.

The dephosphorylated or I will say the native enzyme is actually very active, but when it gets phosphorylated, it becomes less active. So because of this, it can actually be able to get modulated by the different types of parameters. For example, if there will be a low blood glucose, it is actually going to drive the reaction in such a way that it is actually going to convert the dephosphorylated pyruvate kinase to the phosphorylated pyruvate kinase and so on. Apart from that, you are also going to have the modulations either by the fructose monstic bisphosphate, the level of phosphor and the ATP and alanine. So ATP if there is a sufficient quantity of ATP what is present inside the cell, it is actually going to down regulate the activity of these enzymes.

Whereas if the level of fructose monstic bisphosphate is very high, it is actually going to increase the activity of this particular enzyme. Same is true when you are talking about the allosteric regulation. So here also you have the many types of allosteric regulators. So phosphor-fructokinase is actually an enzyme which is going to be allosterically be regulated by the fructose 2, 6 bisphosphate. So what is mean by the allosteric regulation is that the molecule will not going to bind to the active site, but it will bind to a allosteric site and because of that either it will increase the activity of that particular enzyme or it will actually going to decrease the activity of that enzyme.

And either of these ways you are actually going to see or you are going to be able to regulate the enzyme activity and at the end you are going to regulate the glycolysis. Now from the glycolysis the glucose is going to be get converted into the pyruvate. Now this pyruvate will enter into another chain, another reaction which is called as the Krebs cycle and Krebs cycle is a chain reaction cycle. So the Krebs cycle as the name suggests the Krebs is a name of the scientist and the Krebs cycle is discovered by Professor Hans Kep and it has all sugar intermediate with the 3 carbons. Remember that in the glycolysis we have started with the 6 carbon and then it will enter into the 3 carbon whereas in this case all the carbohydrates are of 3 carbon sugar.

It is also known as the tricharmoxic acid or the citric acid cycle. In higher eukaryotes

the Krebs cycle operates inside the mitopondyl stroma with the different enzyme. In the presence of oxygen the pyruvate formed during glycolysis enter into the Krebs cycle for further oxidation to produce the energy. So what we have is we have the pyruvate right. So this pyruvate is coming from the glucose from the glycolysis right.

Now this pyruvate is going to be entered into the Krebs cycle. So it will get converted into the acetyl CoA and pyruvate is actually going to converted into acetyl CoA with the enzyme which is called as pyruvate dehydrogenase complex. This is a multi-manic enzyme complex and it requires the different types of cofactors like TPP, lipoate and in this process one molecule of NADH is actually going to be produced. Now acetyl CoA is actually going to enter into the Krebs cycle. So this is actually the Krebs cycle right and the acetyl CoA is going to be combined with the water and it is actually going to form the citrate and the enzyme is citrate synthase.

So this is the reaction number 1 okay. Now from the citrate you are going to have the two reactions of the dehydration reactions. So in the first step of dehydration when the first molecule of water is going to be removed by the enzyme aconitase it is actually going to form the cis aconitase and from the cis aconitase when there will be another round of removal of water it is actually going to form the isocitrate okay. So this is the reaction number 2, this is the reaction number 3 and now in the reaction number 4 the isocitrate is going to be get converted into oxalosuccinate and the one molecule of NADH is actually going to be reduced and the enzyme which is going to catalyze this reaction is called as the isocitrate dehydrogenase. Now from the oxalosuccinate it is going to be there will be a decorpoxylation reactions and as a result there will be a removal of carbon dioxide and that is how it is actually going to form the alpha-ketoglutarate and the enzyme is isofetrate dehydrogenase. And from the alpha-ketoglutarate there will be a generation of the NADH molecule and there will be removal of the decarboxylation reaction.

So it is going to produce the one molecule of carbon dioxide and there will be a generation of NADH molecule and the enzyme which is going to catalyze the conversion of the alpha-ketoglutarate to succinyl CoA is the alpha-ketoglutarate dehydrogenase. Now from the succinyl CoA you are actually going to generate the succinate and in this process it is actually going to produce the one molecule of GTP. Remember that the GTP is of the same energy as the ATP okay. And then this enzyme this reaction is going to be catalyzed by an enzyme which is called as succinate thiokinase. Now from succinate it is actually going to form the fumarate and the enzyme is succinate dehydrogenase and in this process the one molecule of FADH2 is going to be produced.

And from the fumarate it is actually going to form the malate and the enzyme is called

as a fumarate and then will be a removal of water right from the malate to generate the fumarate. So there will be hydrogen reactions and from the malate it is actually going to form the oxaloacetate and in this process also there will be a generation of the NADH molecule and the enzyme which is going to catalyze this reaction is called as malate dehydrogenase and again the oxaloacetate is going to combine with the acetyl CoA from the pyruvate to form the citrate and that is how it is actually going to complete the reactions. So this is the step number 4, this is step number 5, this is the step number 6, this is step number 7, 8, 9 and this is the step number 10 okay. So by doing this cyclic reactions you are actually going to be utilized the one glucose molecule completely and you are going to oxidize that into the form of the ATP and NADH and as a result you are going to produce a very high quantity of energy especially when you are actually going to have the enormous amount of oxygen present so that you can be able to run the electron transfer chain optimally.

So let us see how much energy you are going to produce. So there is no investment as far as the phase cycle is concerned right because you are not going to invest any ATP molecule. You have already invested ATP molecule if you are talking about the glycolysis but once you activated the glucose molecule for the carbohydrate catabolic reactions then it is fine. So in the step number 1 there will be a production of a style CoA right when the pyruvate is getting converted into a style CoA and that is how it is actually going. So there is a one generation of NADH molecule and the NADH molecule is going to give you the 3 ATP molecule. Then in the step number 3 there will be a generation of the alpha-thryl-thryl-butyrate and then also you are going to have G1 molecule of NADH.

So here you have one molecule of NADH, here also you have one molecule of NADH. Then in the step number 4 there will be a generation of succinyl CoA, there also you are going to have the NADH molecule right. Then you also have the generation of GTP. So GTP is also having the same energy as the ATP so there will be one ATP molecule which is going to be produced and then in the step number 6 there will be a generation of slumarate. So there will be a generation of FADH2 rather than NADH and it is actually going to give you the 2 molecules. So here you are going to have the FADH and the step number then 8 there will be a generation of oxaloacetate.

So that also is going to give you the one molecule of NADH okay. So at the end what you see here is this is the net balance of the oxidation of one pyruvate molecule and it is actually going to give you the 15 ATP molecule. And since from one glucose molecule you are producing the 2 pyruvate molecule so it is actually going to generate the 30 ATP molecule right. Now because so at the end if you talk about the glucose and if there is a ample amount of oxygen present what will happen is that with the help of the glycolysis

it is actually going to produce 8 ATP molecule and with the help of the grape cycle it is actually going to produce the 30 ATP molecule. And at the end from the one glucose molecule you are going to produce the 38 ATP molecule that only when you are actually having the oxygen present. If there is a no oxygen present then the production of ATP from the glycolysis and as well as the production of ATP from the grape cycle is actually going to be reduced.

Because majority of these NADH molecule or the FADH molecule will not going to enter into the grape cycle for the oxidation and as a result they will not going to produce any energy if the oxygen is not produced and same is true for the glycolysis. So, here there is a question comes what would be the oxygen what would be the amount of ATP produced when you do not have the oxygen that you are actually going to figure out and you can have to tell me. Now how you are going to regulate the grape cycle so regulation of the grape cycle can be done at the four level. One is you can actually have the conversion of pyruvate into acetyl-CoA is the first step which allows the entry of sugar moiety into the grape cycle and the pyruvate dehydrogenate complex is aerosterically inhibited by the high ratio of ATP to ADP, NADH and acetyl-CoA which means if you have high quantity of energy whether in the form of the ATP or whether in the form of the reducing equivalent then you are actually going to elosterically going to reduce the activity of the pyruvate dehydrogenate complex. So if you have the ATP you have NADH you have acetyl-CoA or if you have enough quantity of fatty acids then you are not going to run the carbohydrate metabolism then you are actually going to take the fatty acid and directly enter into the grape cycle and run it.

On the other hand if you have the very high quantity of NADH, FAD plus, acetyl-CoA or calcium then you are actually going to increase the activity of this activity and the more of the pyruvate is getting converted into the styrofoam because it is actually elosterically going to enhance the activity of the pyruvate dehydrogenate complex. Then the first reaction of the phase cycle is catalyzed by the citrate synthase is inhibited by the high level of NADH, ATP and acetyl-CoA. So the first reaction is also going to be modulated by the presence of the ATP, NADH, styrofoam or fatty acids. The same logic if you have a high quantity of energy then you would not like to run the crepe cycle. Then we have the isolated dehydrogenase which is also going to be regulated by the ATP and NADH whereas in the case of ADP and calcium which is actually going to increase the activity.

And then we have the alpha-2-protarate which is actually going to be inhibited by the succinyl-CoA and the high level NADH whereas the calcium is stimulating the system. So this is what is given here. Now crepe cycle is a central metabolic pathway. As I said carbohydrate metabolism is a central metabolic pathway. And that is why it

communicates with the many types of metabolic pathways so that they can be able to make the good coordination.

For example you should not, you do not want that there will be enhanced production of the isocitrate. And on the other hand if one reaction requires the isocitrate for its own, you know for as a reactant right then you should take the isocitrate from here and put it into that. So that is why the crepe cycle is a central metabolic pathway and it actually requires the metabolites for the different types of the other metabolic pathway as well. And that is why what you see here is that the TCA cycle or the tricarbic acid cycle is having the different types of intermediate. For example it has citrate, it has the alpha-2-protarate, succinyl-CoA, malate and the oxaloacetate.

And what you see here is that if the citrate, citrate is actually communicating with the fatty acid and steroid because citrate can be used in that particular biosynthetic pathway. Same is true for the alpha-glutobutarate, it can actually be able to communicate with the synthesis of the amino acids like glutamate and once the glutamate is formed it can actually be able to generate the glutamine, prolineal, arginine. All these you are actually going to see when we are going to discuss about the anaerobic oscillations, when we are going to discuss about the anabolic reactions. Same is true from here also how the oxaloacetate is communicating with the phosphoenol parvate, glycine, serine and all that. And carbohydrate and fat metabolism is also very actively interacting with the different types of intermediate photo present in the TCS cycle.

And the Krebs cycle because it is a central metabolic pathway, it is a master regulator of metabolism because it can regulate not only the carbohydrate metabolism, but also the metabolism of the other metabolic pathways such as fatty acid biosynthesis pathway, fatty acid oxidations, protein synthesis and the nucleotide synthesis. So, this is all about the catabolic reactions of the carbohydrate metabolism. In our subsequent lectures, we are going to discuss about the catabolic reactions of the fatty acids and then we are going to move on to discuss about the anabolic reactions and how the energy what you are going to generate into the catabolic reaction is going to be utilized into the anabolic reaction for the synthesis of the biomolecules. So, with this, I would like to conclude my lecture here. In our subsequent lecture, we are going to discuss more about the catabolic reactions of the lipids and as well as the anabolic reactions of the other biomolecules. Thank you.