Basics of Biology
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Lecture 18
Carbohydrates (Part 3)

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 biomolecules and the understanding of the biomolecule is very important for us to realize the importance of these biomolecules in running several types of similar activities.

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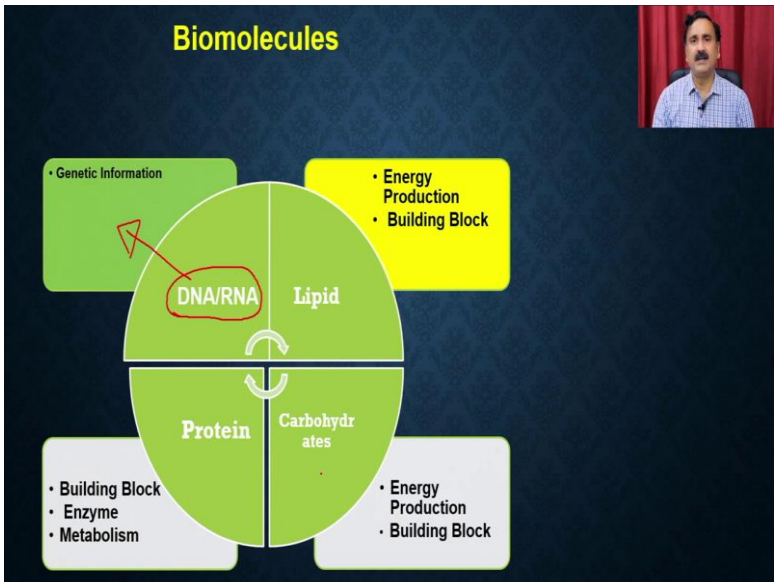

So, so far what we have discussed, we have discussed about the nucleic acids. So, in that we have discussed about the DNA and RNA, and these two molecules are important for the information to be stored in from the one generation to another generation, and that is how they are going to relay the information from one generation to the next generations. And subsequently that we were also discussing about the carbohydrates.

And carbohydrates are mainly been required for energy production and as well as in some cases, they are also been part of the building blocks, where they are modifying the some of the crucial similar factors and other things. So, if you recall in our previous lecture, we discuss about the different types of carbohydrates, we discuss about the monosaccharides, disaccharides and polysaccharides.

In addition, we have also discussed about the different types of structural as well as the biochemical details of these different types of carbohydrates and the carbohydrates are

present in the linear chain or to the cyclized form and they are also showing the different types of isobaric properties. So, with this brief discussion in the previous lecture, in today's lecture, we are going to discuss about the how the carbohydrates are participating into the energy productions.

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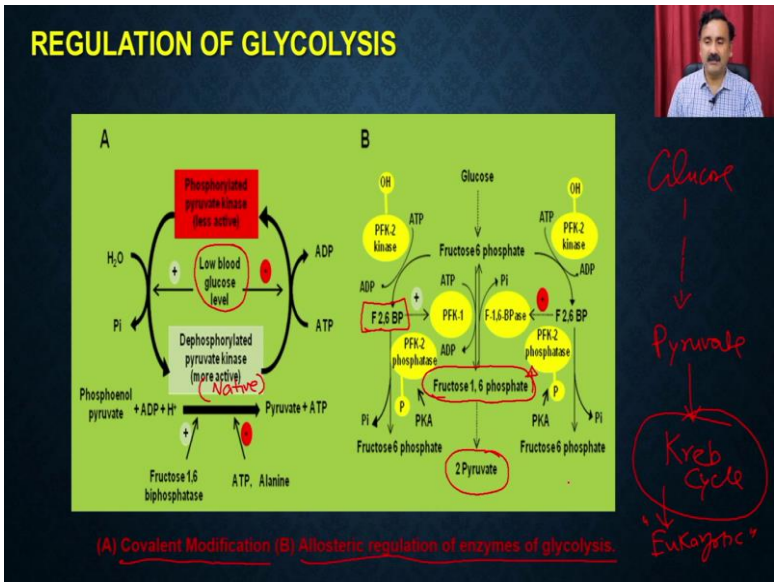

So, what we have discussed so far? We have discussed about the different steps of the metabolic reactions, what is happening into that glycolysis, what is the energy production within the glycolysis and under the different environmental conditions how the energy production is going to be modulated.

And in addition to that, we have also discussed about deregulation of the glycolysis by the different means, either it will be by the entry of the glucose into the cell by the mean of the insulin hormone or by the covalent as well as the allosteric regulation of the different enzyme what is present into the glycolysis.

After the glycolysis, so from the glucose once glucose is going to be utilized, and it is going to be produced the pyruvate, this pyruvate is going to enter into the Kreb cycle. And the Kreb cycle if only we present into the eukaryotic cell, it is not present in the prokaryotic cells. So, let us understand the next cycle which is called as the Kreb cycle.

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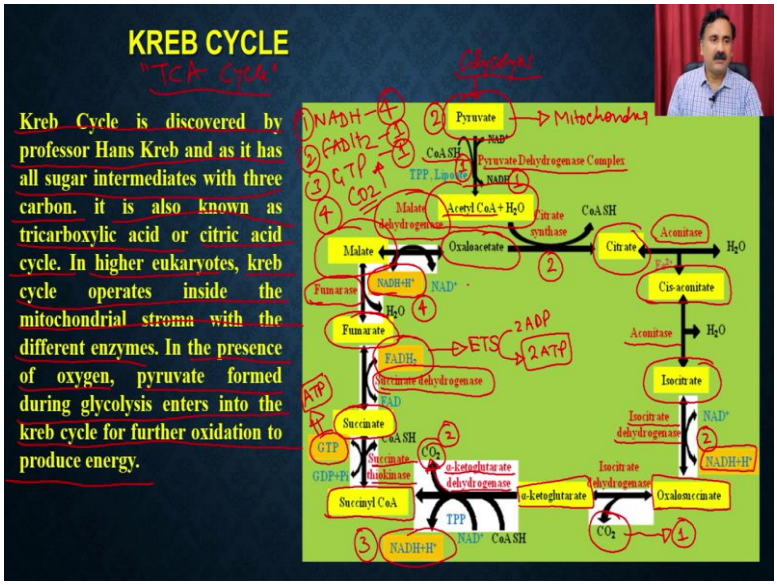

So, Kreb cycle, the Kreb cycle is named after these scientists who discovered the Kreb cycle. And Kreb cycle is discovered by the Professor Hans Kreb and it has all sugar intermediate with the three carbon that is why this is also called as the Tricarboxylic Acid Cycle or the TCA cycle. So, the Kreb cycle is also called as TCA cycle and it is been discovered by the scientists Hans Kreb. It is also known as the Tricarboxylic Acid Cycle or the Citric Acid Cycle.

In higher eukaryotes, the Kreb cycle operates inside the mitochondrial stroma with the different types of enzymes. In the presence of the oxygen, the pyruvate formed during the glycolysis inserts into the Kreb cycle further oxidation to produce the energy. So, what you see here is the different types of reactions what is happening into the Kreb cycle.

So, this pyruvate what you are going to see is it is going to be produced from after the glycolysis. So, once the pyruvate is going to be produced, it is going to be sent to the Kreb cycle, into the Kreb cycle. So, it will enter into the Kreb cycle by the pyruvate will enter, first the pyruvate will enter into the mitochondria and when it will enter into the mitochondria it is going to be get converted into the Acetyl CoA and the enzyme is pyruvate dehydrogenase complex.

So, pyruvate dehydrogenase complex is a multivariate protein enzyme complex where we have the different types of enzymes. And it is going to utilize the Co enzyme A to produce the Acetyl CoA and this is a dehydration reaction and what you see here is the first molecule of NADH is going to be produced in these reactions.

Well as soon as the Acetyl CoA is going to be produced, it is going to combine with the Oxaloacetate to produce the Citrate and the enzyme name is Citrate synthase. So, this is the first reaction and this is the second reactions. Now, once the Citrate synthase is going to produce the Citrate, the Citrate is going to be utilized by the Aconitate to produce the Cis-aconitate.

And the Cis-aconitate is going to be further modified into the Isocitrate. So, and the enzyme is Aconitate. So, in the second or third reactions, the Citrate is going to be get converted into the Isocitrate. Now, Isocitrate is going to be utilized by the enzyme which is called as the Isocitrate dehydrogenase and in this process again the another molecule of NADH is going to be produced.

So, this is the second NADH molecule which is going to be produced, the first NADH molecule is going to be produced when the pyruvate is getting converted into the Acetyl CoA. And the second molecule of NADH is going to be produced when the Isocitrate is getting converted into the Oxalosuccinate. Now, Oxalosuccinate is going to go for the decarboxylation reactions and that is how it is going to produce the Alpha-ketoglutarate by the enzyme which is called as the Isocitrate dehydrogenase.

Now, once the -- So, there will be a production of carbon dioxide in this process. And once the Alpha-ketoglutarate is being produced, it is going to be get converted into the Succinyl CoA and the Succinyl in this process again the NADH is going to be generated. So, this is the third NADH molecule what is going to be generated and the enzyme name is Alpha-ketoglutarate dehydrogenase and again another molecule of carbon dioxide is going to be produced.

So, this is the first molecule of carbon dioxide, this is the second molecule of carbon dioxide. Now, from this Succinyl CoA it is going to be utilized by the Succinate thiokinase and the Succinyl CoA is getting converted into the Succinate. And in this step the one molecule of GTP is going to be produced. So, instead of ATP it is going to produce the GTP.

GTP is having the similar or the identical amount of energy what is present into the ATP. Succinate is getting converted into the Fumarate, the enzyme is Succinate dehydrogenase and the one molecule of FADH2 is going to be produced. FADH2 is also going to be oxidized into the electron transport chain. But the only difference from the NADH is that FADH2 oxidation is only going to produce the two molecules of ATP from the two

molecule of ATP which means it is only going to produce that two molecule of ATP instead of the three molecules of ATP in the case of NADH.

And then the Fumarate is getting converted into the Malate, the enzyme name is Fumarase, and in this process again that one more molecule of NADH is going to be produced. And this is the fourth NADH molecule what has been produced with the glycolysis. And Malate is again getting converted into the Oxaloacetate and that is how with the help of the enzyme which is called as the Malate dehydrogenase.

Again, the Oxaloacetate is going to take the Acetyl CoA which is going to be produced from the pyruvate and that is how this cyclic reaction is going to be run for another round. So, what you see here is that we have the production of the NADH, we have the extensive production of NADH, we have the production of FADH2, we have the production of the GTP. And then there is a production of the carbon dioxide.

So, this carbon dioxide is going to be removed from the Kreb cycle. And how many molecules of NADH? You see that one molecule of NADH, second molecule, third molecule and fourth molecule, so we have the four molecules of NADH, we have the one molecule of FADH2, we have one molecule of GTP.

And if you see the pyruvate, so we are going to have the two molecules of pyruvate. So, that is how if you see all these molecules are going to be in the double the amount what is going to be produced. So, let us see what is the ATP balance sheet of the Kreb cycle, because ultimately that is what we are discussing here, how the ATP energy is being produced from the carbohydrates.

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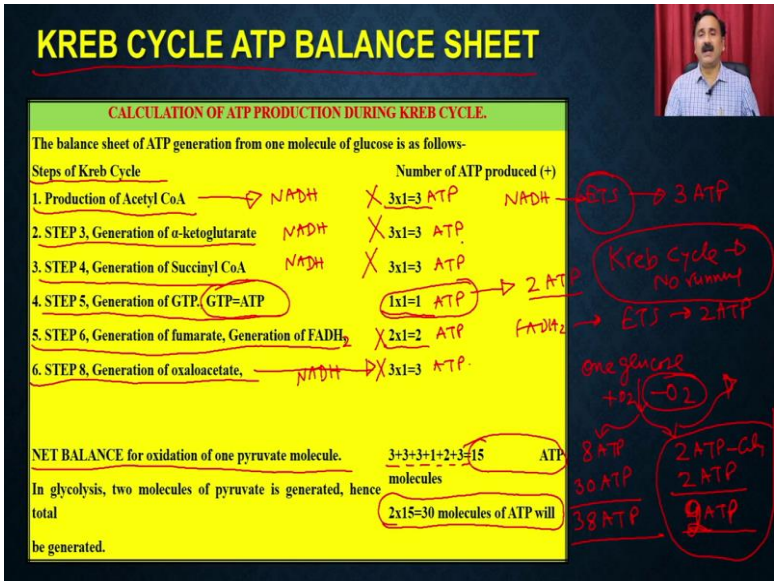

So, ATP balance sheet, what you see from the fifth cycle is very simple, there is no consumption of any type of energy, like you remember that in glycolysis, we are utilizing the two molecules of ATP and then only there is the production of eight molecules of, you know, a net production of eight molecules of ATP. Here, there is no such investment. So, what we see is a steps of Kerb cycle.

So, when there is a first step, when there will be a production of Acetyl CoA, it is going to give you the one molecule of NADH. And remember that if the NADH is going to be utilized into the electron transport chain, it is going to give you the three ATP molecule. And that is why we have put the 3 into 1 molecule. So, three ATP molecule is going to be produced in the production of Acetyl CoA.

Then step three, there will be a generation of alpha-ketoglutarate. And in that step, also, there will be a production of NADH, and that also is going to give you the three molecules of ATP. And then in the step four, there will be a generation of Succinyl CoA, and in this step, also, there will be a production of NADH, and that also is going to give you the three molecules of ATP.

Then the step five, there will be a generation of GTP. And as I said, GTP is going to have the same amount of energy what it has been found for the ATP, and that is one of the one molecule of ATP is being formed. Then in the step six, there will be a generation of fumarate and there will be a generation of FADH2. So, that is also going to give you that two molecules of ATP because FADH2, when it goes for the electron transport chain, it is going to give you the two molecules of ATP.

Then in the step eight, there will be a definition of oxaloacetate and that also is going to give you another molecule of NADH and that is how it is going to produce the three molecule of ATP. Now, what is the net balance for oxidation of the one molecule of pyruvate? So, there will be a net production of 3 3 3 1 2 3 and that is a 15 ATP molecule. But since the glycolysis is producing the two molecules of pyruvate, it is going to be the total production.

So, total production is going to be the 30 molecule of ATP molecule which will be generated. So, which means if you will start with the one glucose molecule, and if you consider that the there is a enormous amount of oxygen present, that it is going to give you the 8th ATP molecule into the glycolysis and it is going to give you the 30 ATP molecule into the Kreb cycle.

This means it is going to give you the 38 ATP molecule, the net 38 ATP molecule under the oxygen in the presence of oxygen, but if there is a no oxygen present, then it is going to give you the. So, what will be the energy production? If there is a no oxygen present, then it is going to give you that two ATP molecule into the glycolysis and it is going to sit here. If there is no oxygen present, then this is not going to work, this is not going to work, this is not going to work because there will be no electron transport chain which is going to be operational, this is not going to work also and this is not going to work.

So, in this case, it is going to produce only the one ATP molecule which means it is going to give you that two ATP molecule from the glycolysis as well. So, that is why if there is a no O2 present, then it is only going to give you the four ATP molecule. In fact, if the ATP, if the oxygen is not present, then that is going to make the Kreb cycle non-operational because there is no going to be, there will be no oxygen, so there will be no running of Kreb cycle.

And because of that, it is only going to utilize the glycolysis. So, there will be only two ATP what is going to be produced if there is no oxygen present. That is why the amount of oxygen is going to decide how the cells are going to modulate their metabolism. So, if there is be no oxygen present, then the pyruvate is what is been produced from the glucose molecule will not enter into the Kreb cycle, it will go and enter into the anaerobic oxidation, where the cells are going to produce the lactic acid and they are going to produce the other derivatives of lactic SS.

But apart from that, the Kreb cycle is extensively been involved into the energy production if the oxygen is present, and apart from that, the Kreb cycle is also been present in channelizing the different types of intermediates. So, let us see the significance or let us see the how we can be able to regulate the activities of the Kreb cycle so that it is not going to, so that it the all the reactions are under the proper control.

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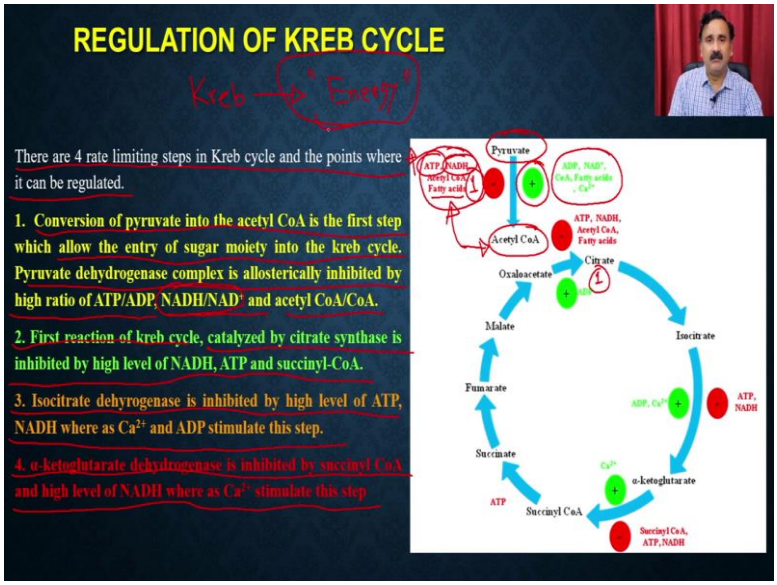

So, there are 4 rate limiting steps in the Kreb cycle and the point where it can be regulated. The step 1 is this, when there will be a conversion of pyruvate into the Acetyl CoA, and what you see here is that these are the molecule which are going to be negatively redecorate, which means if there is a enhance a very high amount of ATP, NADH, Acetyl CoA or fatty acid then that is going to inhibit this particular step.

Whereas, if there will be a very high quantity of ATP, NAD plus, Co enzyme A, fatty acid or the calcium it is going to amplify this particular reaction which is going to activate these particular reactions. So, the first reaction is the conversion of pyruvate into the Acetyl CoA is the first step which allows the entry of sugar moiety into the Kreb cycle. Pyruvate dehydrogenase complex is allosterically inhibited by the high ratio of the ADP to JDP or NADH to NAD plus and the Acetyl CoA and Succinyl CoA.

See, this is because of this only right because to require a very high ratio of this it is going to give you the inhibition of this, which means there is a very high quantity of energy what is already been present in the cell. So, if the energy is already present in the cell, why there is a need to run the Kreb cycle. So, because of these molecules like ATP is an energy molecule NADH is also a energy molecule, it is going to inhibit the Kreb cycle.

Then the second step is the first reaction of the Kreb cycle, which is catalysed by the citrate synthase and it is inhibited by the high level of NADH, ATP and Succinyl CoA. So, this is also the first step, this is the step also again, which is going to be synthesized by the citrate synthase. And that is also been very regulated or inhibited by the high level of these NADH, ATP and Succinyl CoA.

Then the third step is the isocitrate dehydrogenase which is inhibited by the high level of ATP, NADH whereas calcium and ADP stimulate this process. So, this is the third step where it is going to be again modified or can be modulated. Then the fourth step is the alpha-ketoglutarate which is inhibited by the Succinyl CoA and high level of NAD plus, whereas the calcium stimulates this process.

Now, the Kreb cycle, the Kreb cycle is not only for producing the energy. Kreb cycle is one of the central metabolic pathways, which are been responsible for, see the Kreb cycle is connected to the Acetyl CoA and Acetyl CoA is also connected to the fatty acids and all other kinds of pathway.

So, the intermediate what you see in the Kreb cycle are very much present in the many pathways what are present in the cell and that is why the Kreb cycle is not only for the production of energy, it is also been utilized for many other functions. So, let us see what are these functions and what is the significance of the Kreb cycle within the metabolism.

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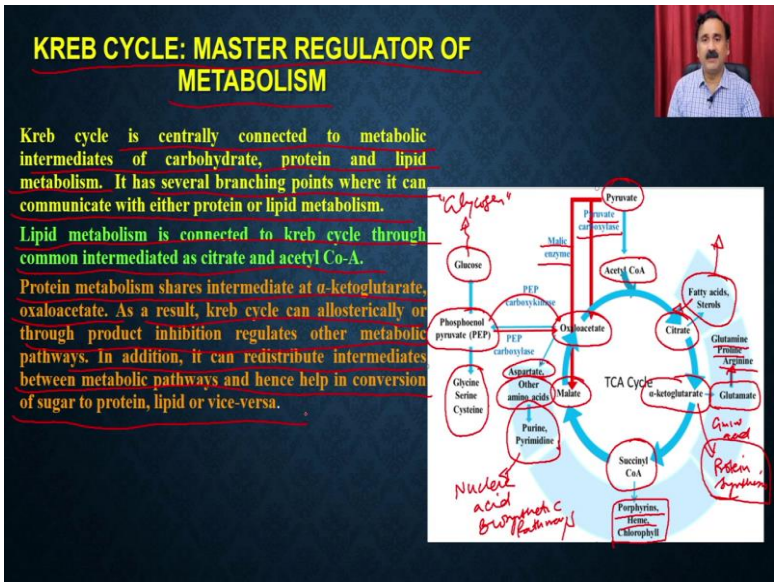

So, Kreb cycle is the master regulator of the metabolism. So, Kreb cycle is a centrally connected to the metabolic intermediates of the carbohydrate proteins and lipid metabolism,

it has several branching points where it can communicate with the other protein or the lipid metabolism. So, what you see here is that the protein, the Kreb cycle and it is being shown that how what are the different intermediates, which are been participating into the different types of other metabolic pathways.

So, what you see here is that the pyruvate it is been converted into the Acetyl CoA and then Acetyl CoA when it enters into the TCA cycle, it is producing the citrate. So, citrate is being connected to the fatty acid and stearoyl pathway. So, that is how it can be able to communicate. So, there will be a shuttling of the intermediate from the Kreb cycle to these pathways and exactly the same way the pathway, the intermediates could be shuttled back into the citric cycle also.

Then, once the citrate is getting converted into the Alpha-ketoglutarate, Alpha-ketoglutarate can directly be converted into the glutamate and the glutamate which is an amino acid is can be shuttled back and there are metabolic pathways, so that the glutamate can be converted into the arginine, proline and glutamine which means, at this stage it can easily be able to communicate with the protein synthesis machinery. So, you see the catabolic pathway is interacting with the anabolic pathways.

And then we have the Succinyl CoA. The Succinyl CoA is the precursor of the Porphyrins and the Heme as well as Chlorophyll synthesis. So, that is how it can shuttle the intermediate between the biosynthetic pathway of the Heme biosynthesis. And once the Succinyl CoA is getting converted into the Malate, the Malate is also getting shuttled with the pyruvate and the enzyme is the pyruvate carboxylase and as well as the malic enzyme.

Whereas the oxaloacetate what has been produced is can be converted into the Phosphoenolpyruvate or it is also can be converted into another amino acid which is called as the Aspartate or the other amino acids. And that is how, once it can be converted into the Aspartate or the other amino acid that also can enter into the Purine or the Pyrimidine pathway which means it also can enter into the nucleic acid biosynthetic pathway.

So, what you see here is that the Kreb cycle is a catabolic pathway, but it is participating with the different types of metabolic pathways. So, there it is the fatty acid biosynthetic pathway, protein synthesis pathway, Heme pathway or nucleic acid biosynthetic pathway or it is also can shuttle back to the phosphoenolpyruvate and phosphoenolpyruvate is a precursor for the glycine, serine and cysteine pathway.

So, that is why the -- And if there is a requirement, the Kreb cycle can also be able to produce glucose which can be stored in the form of the glycogen in the in the muscle cells. So, what you see here is that the Kreb cycle has the very, very huge role in terms of regulating the different types of metabolic pathways and the intermediates can go into the different types of metabolic pathways.

Like the lipid metabolism is connected to the Kreb cycle through the common intermediate such as the citrate and the Acetyl CoA. Similarly, the protein metabolism shares the intermediate as the Alpha-ketoglutarate, oxaloacetate. As a result, the Kreb cycle can allosterically or the through the product inhibition regulates other metabolic pathways.

In addition, it can redistribute the intermediates between the metallic pathway and health in the conversion of sugar to the protein lipid or vice versa. And because of the such a very high level of role in the metabolic pathways, the Kreb cycle is been taking place very high in terms of the evolutions.

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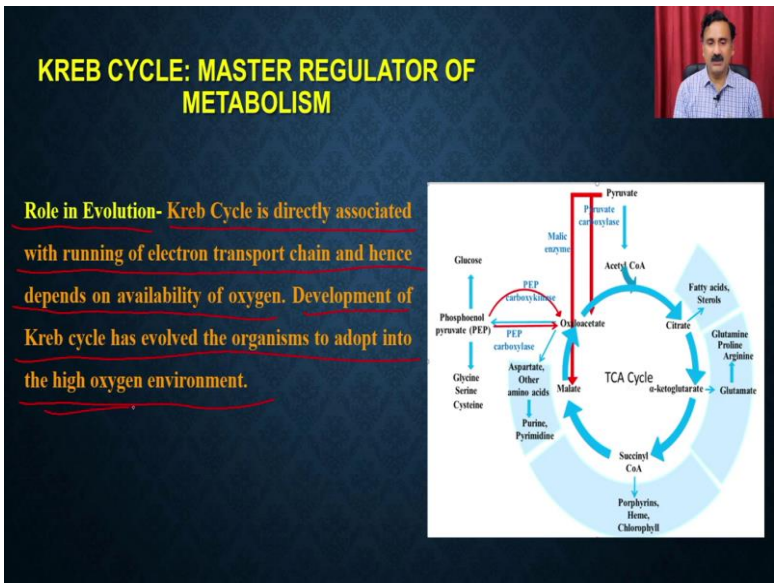

So, what is the role of the Kreb cycle in the evolution is that the Kreb cycle is directly associated with the running of electron transport chain, and hence depending on the availability of the oxygen. Deployment of the Kreb cycle has evolved the organism to adopot the high oxygen environment, which means earlier the people, like for example, the prokaryotic cells, they do not have the Kreb cycle.

Why they do not have the Kreb cycle? Because they are living in an environment where the oxygen availability is very low. That is why they are happy with the glycolysis pathway

and they are only producing the very low amount of energy by the glucose molecules. But with the with the development of the Kreb cycle and with the adaptation of the mitochondria into the eukaryotic system, the Kreb cycle has made it possible for the organism to adopt for the high energy environment.

Because in the high energy environment, the Kreb cycle can be operated and it can be able to help organism to produce the high high amount of energy. So, with this, we would like to conclude our lecture here. In our subsequent lecture, we are going to discuss more about the biomolecules. What we have discussed so far?

We have discussed about the carbohydrate structure and functions, and we have also discussed how the carbohydrates are being utilized into the different types of metabolic pathways to produce the energy. And we have discussed about the glycolysis, we have discussed about the regulation of the glycolysis and subsequent to that we have also discussed about the Kreb cycle and its regulations.

And lastly, we have also discussed about the significance of the Kreb cycle into the different types of metabolic pathways. So, with this, I would like to conclude my lecture here.

In our subsequent lecture, we are going to discuss about some more biomolecules. Thank you.