**Metabolic Engineering**
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**Lecture - 10**
**Review of Cellular Metabolism - Part E**

Review of cellular metabolism will be discussed in this lecture in terms of how the metabolic flux

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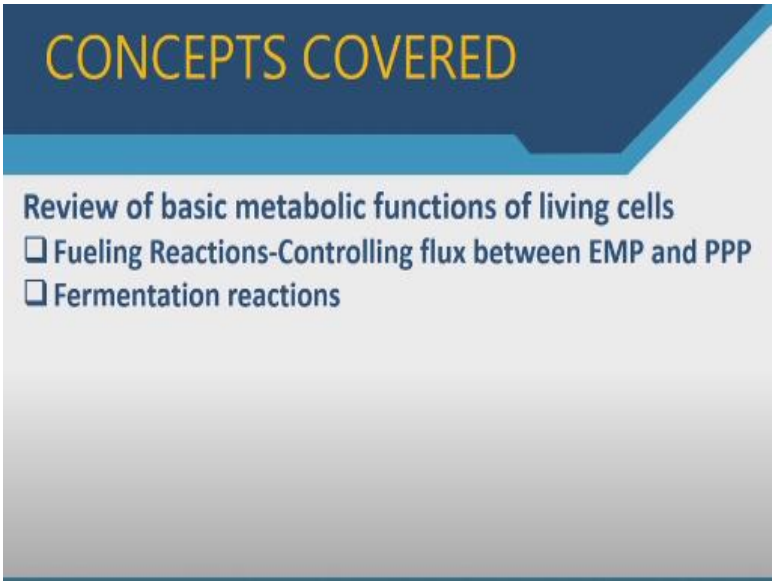


is controlled between the important glycolytic reactions like EMP pathway and pentose phosphate pathway. This will help us to understand the control of these important fueling reaction, which is representing the major part of the central carbon metabolism of any actively metabolizing cell. Fermentation reactions will also be discussed.

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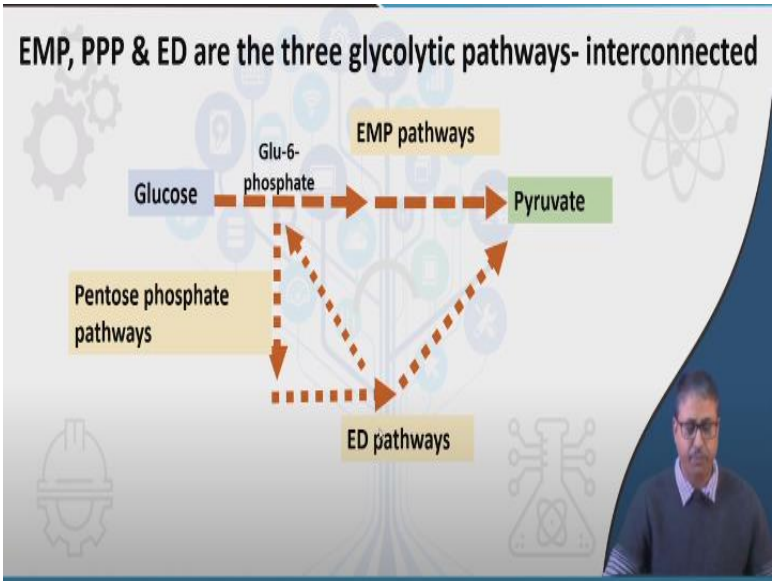


As it is discussed earlier, there are three major glycolytic pathways, which are responsible for representing the fueling reactions within cellular system. So within these three glycolytic pathways the glucose molecules or the representative other hexose sugar molecules are converted into the hexose monophosphate pool as we already discussed.

And then, if it is utilizing the EMP pathway as the major pathway then it will be converted to the pyruvic acid through the substrate level phosphorylation producing two moles of ATPs per molecule of glyceraldehyde 3-phosphate and also one mole of NADH H+ per mole of glyceraldehyde 3-phosphate. So together it will be four moles of ATP and two moles of NADH H+ per moles of glucose metabolized through EMP pathway.

The reactions which represent the pentose phosphate pathway and ED pathway also oxidize the glucose into pyruvate or different other intermediate metabolites and thereby allowing the cells to convert the hexose monophosphates into pyruvic acid.

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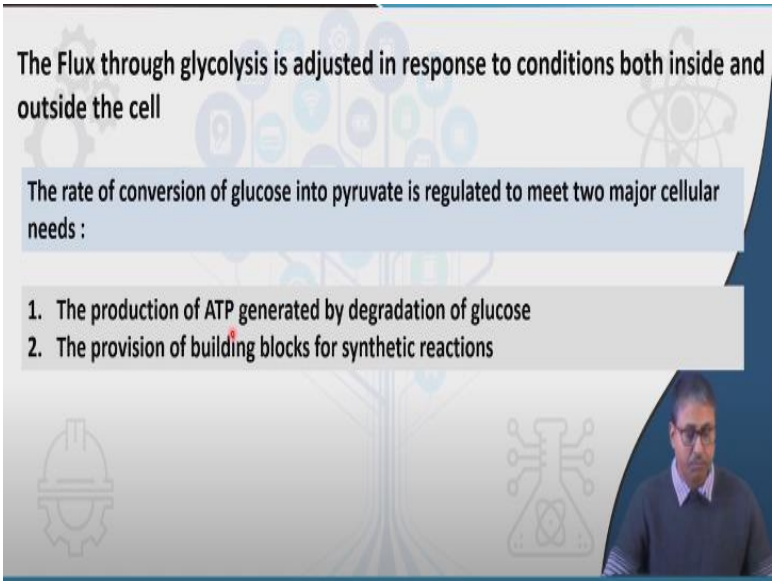


Now the flux through glycolysis is adjusted in response to conditions both inside and outside the cells. The rate of conversion of glucose into pyruvic acid is regulated to meet the two major cellular needs. So whatever amount of glucose is transported inside the cell is actively metabolized.

And this metabolism will be either through only EMP pathway or EMP pathway and pentose phosphate pathway or maybe majorly by pentose phosphate pathway or partly by ED pathway and partly by EMP and PP pathway. This all depends on what are the requirements of the cells. Now with respect to these requirements, there are two major needs of the cells.

The first one is the production of ATP, which is to be generated by the oxidation of the glucose. And the second one is the provision for building blocks for synthetic reactions. Now in actively growing cells would like to have lot of biosynthetic reactions going on to produce all the necessary macromolecules.

And those biosynthetic reactions would require a high amount of building blocks in order to facilitate those anabolic reactions or biosynthetic reactions. At the same time, the cellular activities including growth or non-growth related activities would define the ATP requirement of the cell. So cell generally implements a highly organized and structured regulation in order to cater to the needs of these ATP as well as the building blocks.

So both these needs are highly balanced and highly organized in order to control the glycolytic pathways.

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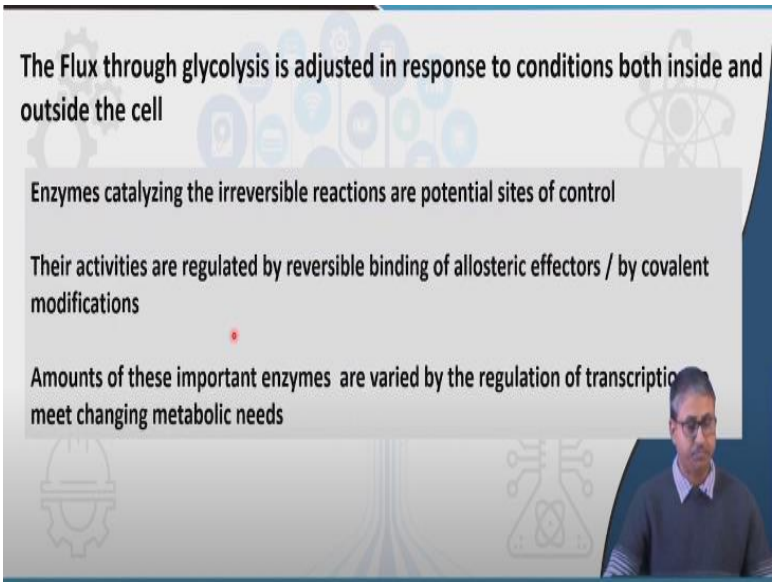


Now enzymes which are responsible for catalyzing these reactions are found to be either irreversible type or reversible type. So some of these reactions, some of these enzymes catalyzing the reactions are found to be involved in irreversible reactions. And these enzymes which are catalyzing the irreversible reactions are the potential sites of control, control of the flux within the particular path or between the two pathways.

Now the activities of these enzymes which are controlling the irreversible reactions are regulated by reversible binding of different allosteric regulators or allosteric effectors or by covalent modifications of the enzymes. Now amount of this enzyme, so the enzyme regulation could be by virtue of the allosteric mode of regulation or by covalent modifications in some cases.

However, the control is also executed in terms of the amount of enzymes which are present in any point of time within the cell. Now this amount of the important enzymes which are involved in the irreversible reactions are controlled in terms of regulating the transcription of the relevant enzyme coding genes.

So in accordance with the changed metabolic needs or the metabolic requirements, which are present within a cellular system, the cells can control the transcription or

the even the translation of those required enzyme genes and thereby controlling the amount of the enzymes which are to be present or which are actually to be present in a cellular system as well as their activities.

So both the activities and the amounts of these enzymes are controlled by different mechanisms.

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Now the major control points within the EMP pathway and PP pathways are discussed.

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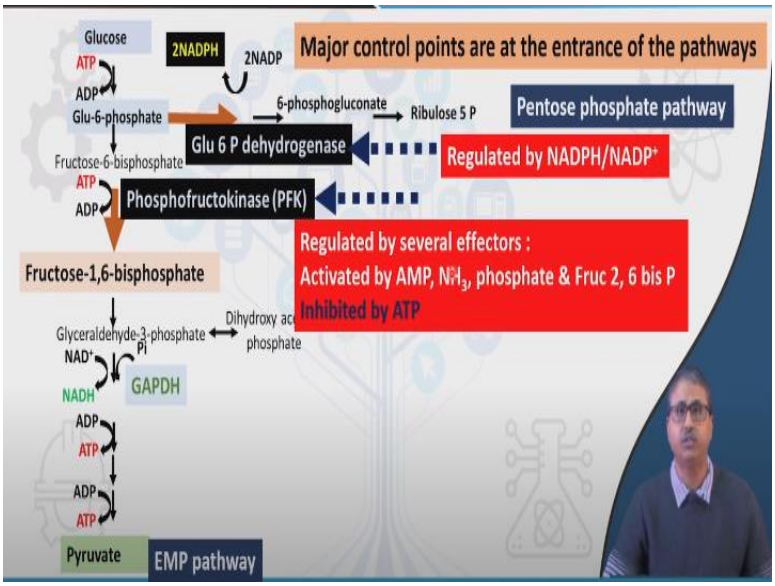


Now there are two major sites or reaction sites where these the flux between these pentose phosphate pathway and flux between the EMP pathways are controlled. As

we can see over in these two pathway schemes, that glucose is converted to the glucose monophosphate pool and this monophosphate pool is able to be utilized or providing the carbon backbone for both this pentose phosphate pathway as well as the EMP pathway.

In case of EMP pathway, it will be converting to fructose 1,6 bisphosphate and then by the substrate level phosphorylation and oxidation of these glyceraldehyde 3-phosphate would lead to the production of pyruvic acid. Whereas, in case of the pentose phosphate pathway, it will be oxidized to and decarboxylated. This oxidation will facilitate the synthesis of two moles of NADPH.

And then the pentose sugars, the pentose sugars eventually will convert into a number of intermediate sugars and some of the sugars will be used in the anabolic reactions representing the precursor molecules or some of the intermediates might convert into the fructose 6-phosphate or to the glyceraldehyde 3-phosphate thereby coming back to the main oxidative scheme of the glycolysis.

Now how do we control these? Because in these two pentose phosphate pathway and EMP pathways, the basic objectives or the basic deliverables of these two pathways are different. Although these two pathways are highly interconnected, the pentose phosphate pathway is responsible for producing the reducing power in the form of NADPH whereas, in case of EMP pathway, it is the NADH.

So there are differences between the use and how these reducing equivalents are further oxidized into different reactions. The other important difference between these two pathways are in terms of the deliverables are the intermediates which are produced.

The intermediates which are produced over the pentose phosphate pathway are mostly the pentose sugar, the erythrose 4-phosphate and other sugars molecules like sedoheptulose 7-phosphate, which are responsible for supporting distinct set of biosynthetic reactions. Whereas in case of EMP pathway, the intermediates like glyceraldehyde 3-phosphate and phosphoenolpyruvate etc., are responsible for a different set of biosynthetic reactions.

Now if we look into these two pathways, these both these pathways are starting from a common intermediate molecule which is the glucose 6-phosphate. So glucose 6-phosphate is converted to the phosphogluconate through the enzyme complex, which is glucose 6-phosphate dehydrogenase.

So this enzyme represents one of the very fundamental and irreversible reaction towards the pentose phosphate pathway. And the same type the phosphofructokinase or abbreviated as PFK is responsible for converting the fructose 6-phosphate to fructose 1,6 bisphosphate.

Now this glucose 6-phosphate dehydrogenase enzyme which is responsible for taking the flux of the carbon towards the pentose phosphate pathway is strongly regulated by the NADPH to NADP ratio. Whereas, the phosphofructokinase or PFK enzyme is allosterically regulated by several effectors where it is activated by adenosine monophosphate, ammonia, phosphate or fructose to 6-bisphosphate, it is inhibited by ATP.

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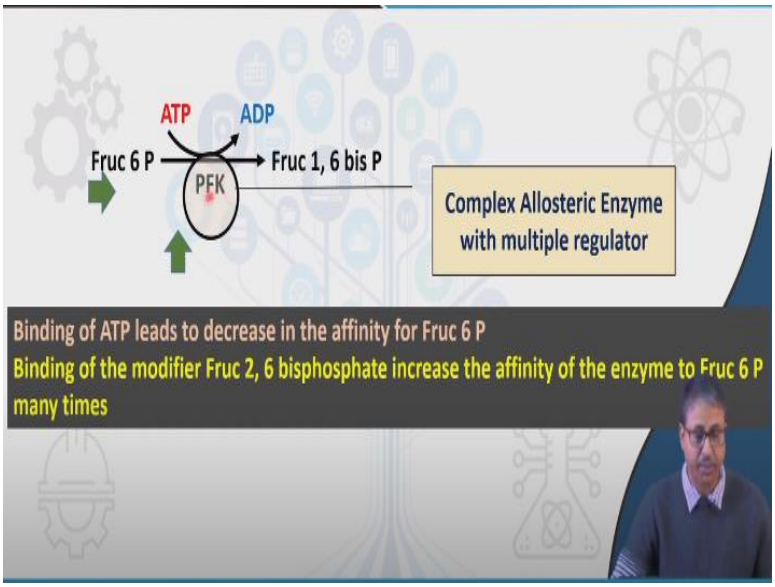


Now if we look at this conversion of fructose 6-phosphate to fructose 1,6 bisphosphate because this PFK which is controlling the flux towards the EMP pathway, this is one of the most well studied example, where we can see the how the metabolic flux between the two pathways are controlled very tightly. Now this

phosphofructokinase enzyme is a kind of a complex allosteric enzyme with multiple regulators.

So one of the regulators is the ATP. Now ATP binding to this PFK molecule is facilitated through a particular regulatory site. So ATP can bind to this PFK in a particular regulatory site not at the catalytic site and thereby it decreases the affinity towards fructose 6-phosphate.

That means, if the cellular system or the cell is having high concentration of ATP, the ATP will bind to the PFK in the regulatory site because PFK is having a different regulatory site for PFK and if ATP is in excess the PFK will be negatively affected and the enzymatic capability of the PFK towards converting the fructose 6-phosphate to fructose 1,6 bisphosphate will be declined as the affinity of those ATP bound PFK will be less than the non ATP bound PFK.

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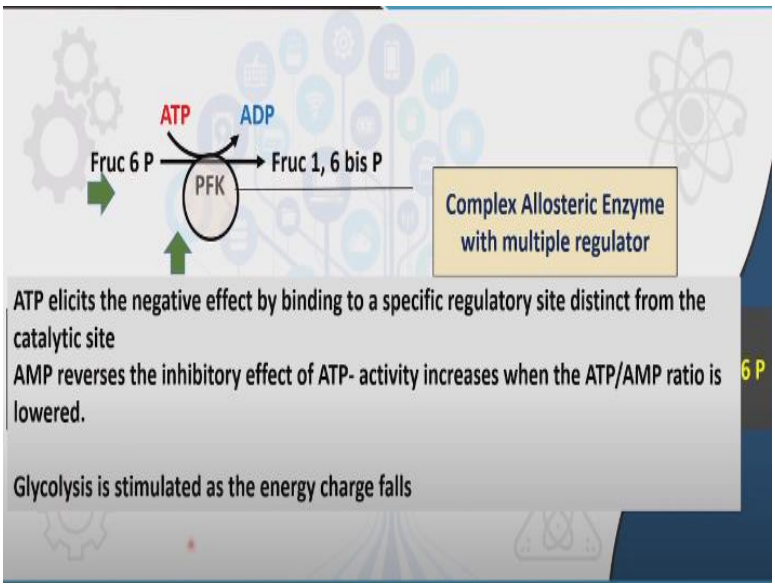


Now the ATP elicits the negative effect as we have discussed just now by binding to the specific regulatory site, which is distinct from the catalytic site. Now interestingly, the same enzyme PFK can be controlled positively. That means, its affinity towards fructose 6-phosphate or the negative effect of ATP can be reversed with binding of adenosine monophosphate into this enzyme.

Now AMP reverses the inhibitory effect of ATP thus increasing the activity particularly and this is increased when the ATP/AMP ratio is lowered. So cell they

represent the energy status in terms of the level of ATP or level of AMP, if there is a high concentration of AMP that represents that this cellular energy charge is low. So under this condition PFK will be activated.

And this activated PFK will be having a very high affinity towards fructose 6-phosphate thereby able to convert the fructose 6-phosphate to fructose 1,6 bisphosphate.

However, if the concentration of AMP is low, that means if the concentration of the ATP is high in the cellular system, then the PFK will be negatively controlled by the high ATP concentration in the way that the affinity of the PFK towards fructose 6-phosphate will be lowered and less amount of fructose 1,6 bisphosphate will be produced.

Now that means, the overall process of glycolysis through EMP pathway is stimulated as the energy charge falls. That means the concentration of ATP determines or the ATP/AMP ratio determines whether the fructose 6-phosphate will be actively converted to fructose 1,6 bisphosphate through this EMP pathway or not.

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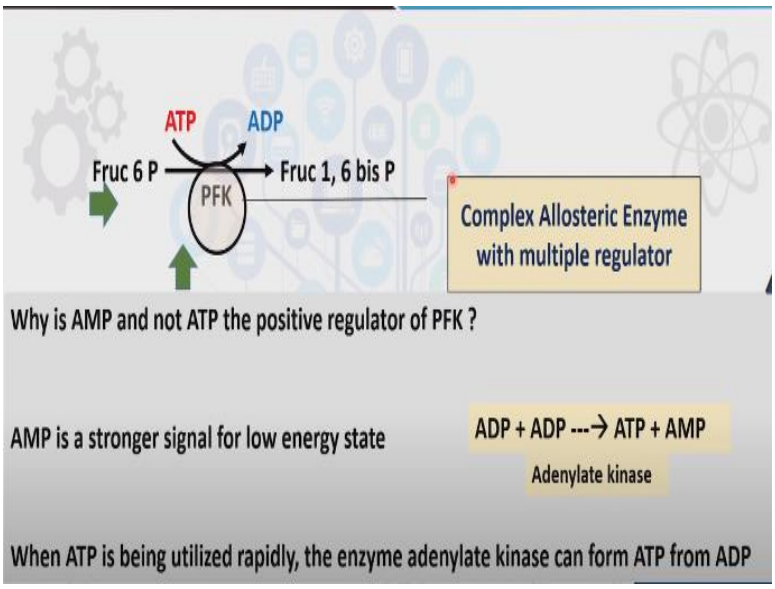


Now there is a question that why adenosine monophosphate and why not ATP is positive regulator of PFK. Now another component or intermediate of this ATP hydrolysis is adenosine diphosphate. So similarly why not ADP is the positive

regulator of PFK as well. Now it is found that AMP is a stronger signal for low energy state compared to ADP. Why so?

Because when ATP is being continuously utilized or rather utilized rapidly, there is an enzyme which is called adenylate kinase and these adenylate kinase can form ATP from two moles of ADP. Like two moles of ADP can react together and form ATP and adenosine monophosphate.

So the level of ATP is not actually so critical in terms of defining the cellular energy charge rather than it is the AMP which represent the cellular energy charge. So energy depleted cell would like to have or would have a high concentration of relatively higher concentration of adenosine monophosphate than that of adenosine diphosphate.

So the concentration of AMP as it rises the AMP gives a positive signal to the PFK binding to it and thereby lowering the negative effect of ATP or maybe ATP is not there in sufficient concentration. So the increasing the affinity of PFK towards fructose 6-phosphate and thereby allowing more flux towards fructose 1,6 bisphosphate and this fructose 1,6 bisphosphate can subsequently be oxidized and converted to pyruvic acid.

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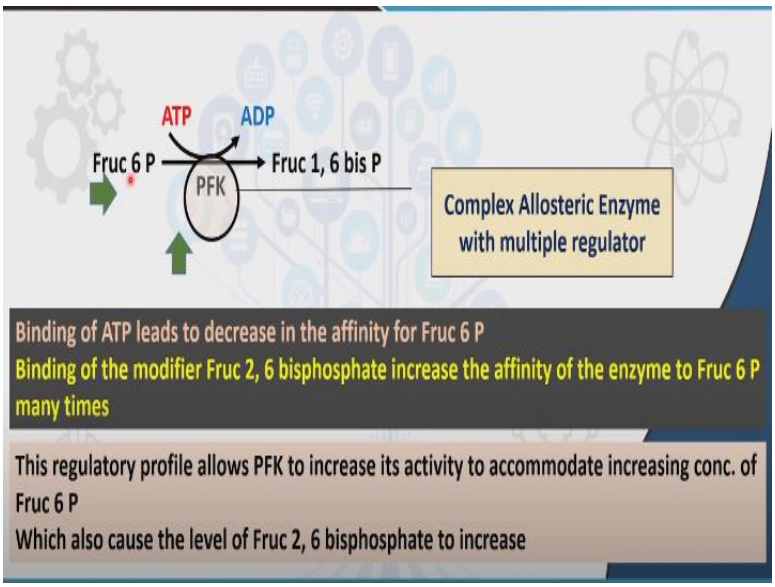


Now the second modifier of this PFK is fructose 2,6 bisphosphate, which is actually produced from fructose 6-phosphate or it is interconvertible. So fructose 2,6

bisphosphate binding of this fructose 2,6 bisphosphate to PFK increases the affinity of the enzyme to fructose 6-phosphate many times.

So that means, if a cell is having higher concentration of fructose 6-phosphate, then the fructose 6-phosphate can be converted, part of that fructose 6-phosphate can be converted to fructose 2,6 bisphosphate by another set of reactions. And those fructose 2,6 bisphosphate can bind to PFK and increase its affinity towards fructose 6-phosphate so that it can convert fructose 6-phosphate to fructose 1,6 bisphosphate.

And then fructose 1,6 bisphosphate will be metabolized through the EMP pathway successfully. Now this regulatory profile allows the PFK to increase its activity to accommodate increasing concentration of fructose 6-phosphate. Now what is the significance of this? The significance of this is as the carbon flux or the hexose flux within the cell or a particular cell increases the fructose 6-phosphate pool.

Or the concentration is also increased, because we know that this hexose sugar phosphates they are directly connected to the sugar sources which are, the sugar substrates, which are provided to the cellular system. So the higher concentration of fructose 6-phosphate is directly connected to a higher concentration of fructose 2,6 bisphosphate.

And higher concentration of fructose 2,6 bisphosphate activates the PFK positively thereby allowing more fructose 6-phosphate to be converted to fructose 1,6 bisphosphate which can cause the level of fructose 2,6 bisphosphate to increase.

So thereby this fructose 6-phosphate, fructose 2,6 bisphosphate and fructose 1,6 bisphosphate, all the three compounds are very tightly correlated in terms of activating the affinity of PFK particularly with respect to converting fructose 6-phosphate to fructose 1,6 bisphosphate.

However, fructose 6-phosphate to fructose 2,6 bisphosphate conversion is facilitated or catalyzed by entirely different set of reactions which are two enzymes reactions are responsible for that.

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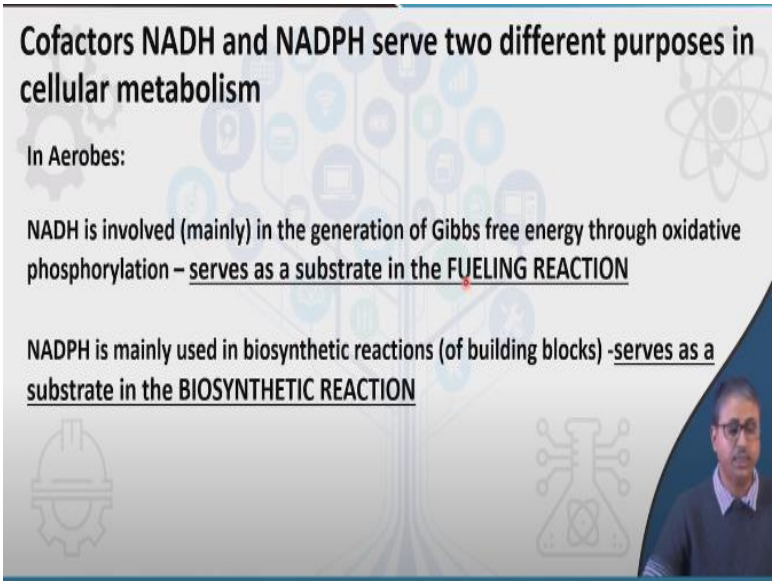


The second important criteria is the cofactors. The cofactors NADH and NADPH these two cofactors serve two different purposes in the cellular metabolism. As we have seen earlier the NADH is produced in the EMP pathway, whereas NADPH is produced in the pentose phosphate pathway. Now if we want to produce more NADPH, probably the pentose phosphate pathway would be the best one.

Whereas if we want more NADH, the EMP pathway would be the most appropriate one. Now in aerobic organisms, it is best exemplified that NADH, which is the product of the EMP pathway is involved in the generation of Gibbs free energy through oxidative phosphorylation. That is by serving as a substrate in the fueling reactions and thereby providing the electrons to the electron transport system.

Whereas the NADPH, which is the product of the pentose phosphate pathway is mainly used in the biosynthetic reactions, that is the anabolic reactions of producing the different building blocks thereby serving as a substrate in the biosynthetic reactions. Now this distinction is remarkable.

Like NADH is mainly responsible for the fueling reaction or generating the maximum amount of Gibbs free energy or sometimes the proton motive force through oxidative phosphorylation and the transferring the electrons to the electron transport system, whereas the NADPH is responsible for supporting the biosynthetic reactions.

So it is well demarcated within the cellular system that which one is for what function. Now depending upon the cellular requirement like if the cell is actively dividing, that means during the growth metabolism, the biosynthetic reactions will be prevalent and hence, the NADPH requirement will be higher.

Whereas, during the time of normal non-growth related metabolism, where the energy requirement would be high, maintenance related energy requirement will be high, then only the fueling reactions will be sufficient and relatively less flux may be expected through the pentose phosphate pathway.

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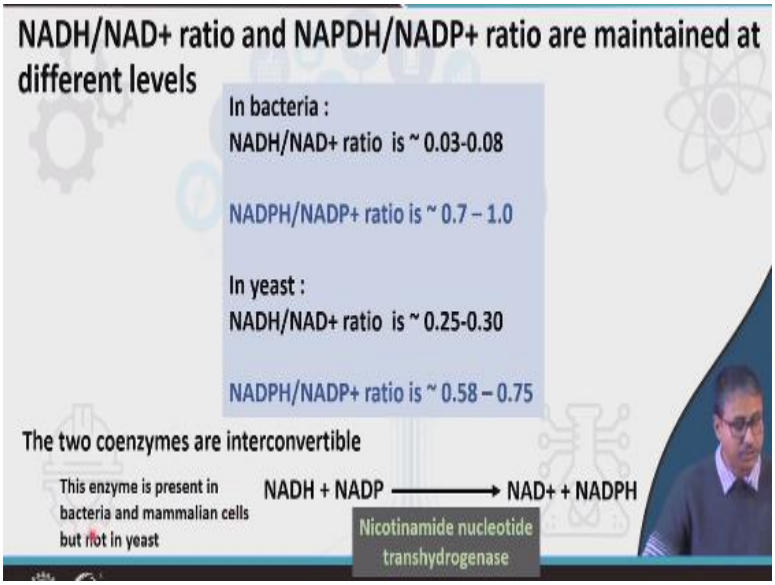


Now this ratio between the NADH and NAD+ and NADPH and NADP+ are maintained at different levels, but nearly constant level in case of bacteria, both in bacteria and in case of yeast. And as you can see it is NADH to NAD+ ratio is around 0.03 to 0.08 whereas NADPH to NADP+ ratio is around 0.7 to 1. In yeast also it is nearly equal except the case that in NADPH NADP ratio is slightly different, it is 0.58 to 0.75.

Now interestingly, these two coenzymes like NADH and NADPH are interconvertible. That means, in case of any exigency or any essential requirement, the cell would like to convert part of its NADH to NADPH through the enzyme nicotinamide nucleotide transhydrogenase. And this enzyme is present in many bacteria as well as in mammalian cells, but interestingly not in yeast.

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Next, we are going to discuss about the fermentative pathways. Now as the pyruvate which is produced as the end product of the three glycolytic pathways like EMP, PP and ED pathway, which will be further converted or further reacted or oxidized partly or sometimes reduced by several routes depending on the redox and energetic state of the cells.

Because pyruvate is only an intermediate of the glycolytic metabolism. So once the pyruvate is produced out of the glycolytic pathways, including either the EMP or the PPP or EMP and PPP together both as well as partly ED pathway, the pyruvate, which is produced by these pathways will be converted to different other products based on again the cellular condition or cellular requirement.

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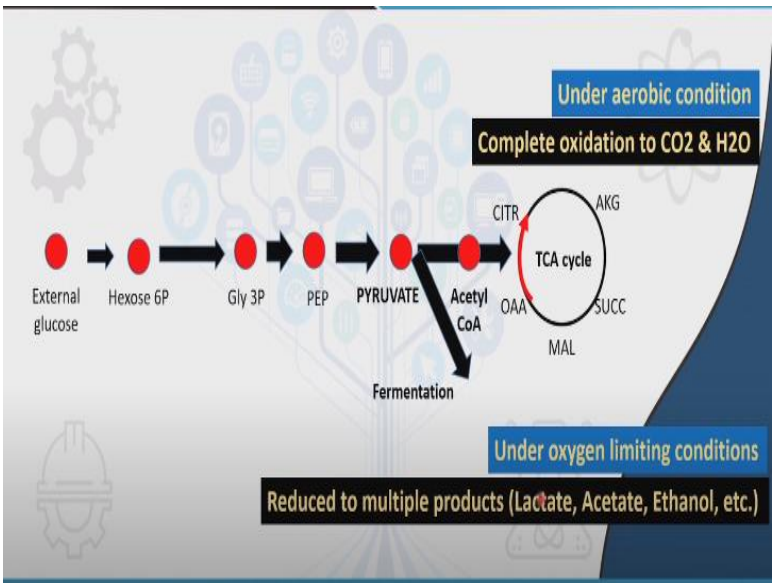

For example, during the aerobic growth of the organism or under aerobic condition, we can expect that the pyruvic acid or pyruvate will be converted to acetyl-CoA and this acetyl-CoA will be oxidized completely through the tricarboxylic acid cycle and this complete oxidation would lead to production of carbon dioxide and water and several molecules of NADH H+.

And these NADH H+ will be NADH will be donating the electrons to the electron transport system thereby facilitating the oxidative phosphorylation. This oxidative phosphorylation will lead to production of higher concentration of Gibbs free energy. So in essence under the aerobic condition, the pyruvic acid is going to convert into acetyl-CoA and this acetyl-CoA would like to or be will be oxidized completely leading to the formation of CO2, water and high amount of Gibbs free energy.

On the contrary, under oxygen limiting conditions generally under oxygen limiting conditions, because we will be seeing some exception in this regard. So under oxygen limiting conditions, however, the acetyl-CoA production will be reduced because the enzyme responsible for pyruvate to acetyl-CoA will not be activated in oxygen depleted condition.

Rather the other enzymes which will be responsible for taking the carbons of the pyruvic acid into other pathways like the fermentative pathways will be most prevalent. So during this fermentative pathway, the pyruvic acid is going to be reduced to multiple products like lactate, acetate, ethanol etc.

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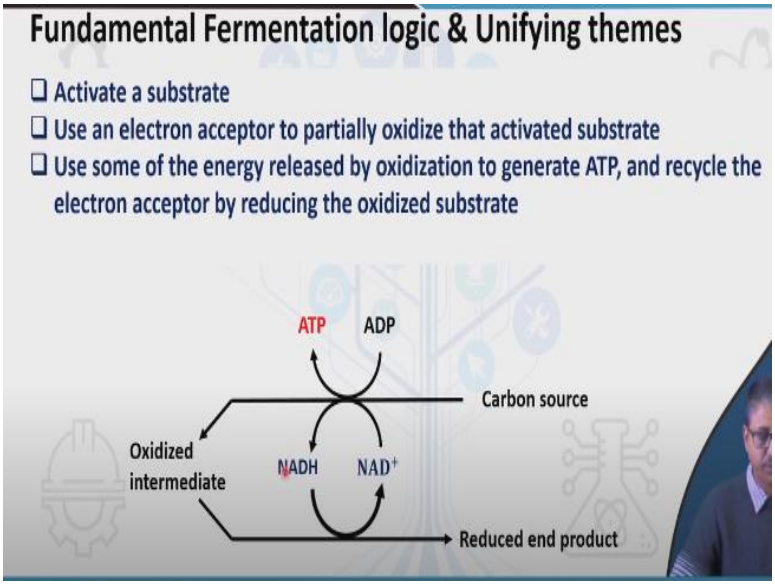


Fundamental fermentation logic and unifying themes. Now fermentation as we understand, it is going to be operated or it is operative within a cellular system under oxygen limiting condition. So fermentation uses basically the substrate level phosphorylation to synthesize the energy. How? Because it is the formation of the pyruvic acid from glucose which is included within the substrate level phosphorylation.

So those are the energy produced during this fermentation process within the subsequent conversion of pyruvic acid to other products of fermentation, the generation of ATP is very limited or almost not there. And it is actually facilitating only a partial oxidation of the organic compound.

Because the organic compound like hexose sugar which is oxidized till pyruvic acid will not be generally oxidized any further and this pyruvic acid rather would act as a electron acceptor in the subsequent reactions of the fermentation. However, to perform this partial oxidation in order to oxidize this carbon substrate and leading to the formation of the pyruvic acid.

And then the subsequent products of the fermentation, pathway intermediates acts as electron donors as well as as electron acceptors. Now unifying themes of this entire process is activated substrate. Use an electron acceptor to partially oxidize that activated substrate. And use some of the energy released by oxidation of generated ATP and recycle the electron acceptor by reducing the oxidized substrate.

For example, if we have the carbon source like the hexose sugar, the hexose sugar will be first activated, hexose monophosphates will be produced, then it will be further metabolized, and then the oxidized intermediates will be produced and those oxidized intermediates for example, the pyruvic acid, the production of these pyruvic acid from the carbon source would require some electron acceptor like the NAD+ will act as the electron acceptor and NADH will be produced.

Now some of these energy released by the oxidation will generate ATP. So substrate level phosphorylation will be there during the formation of for example, the glucose to pyruvic acid. Now how to recycle this NADH because it is not going to be going to be giving the electrons to the terminal electron acceptor or electron transport chain because it is not going to be aerobic or anaerobic respiration.

So in this case, some of this intermediates would act as electron acceptor and thereby allowing the oxidation of NADH to NAD+ and thereby finally producing the reduced end product. So the oxidized intermediates will eventually act as the electron acceptor accepting the electrons which are there with the NADH and thereby finally converting to different reduced product.

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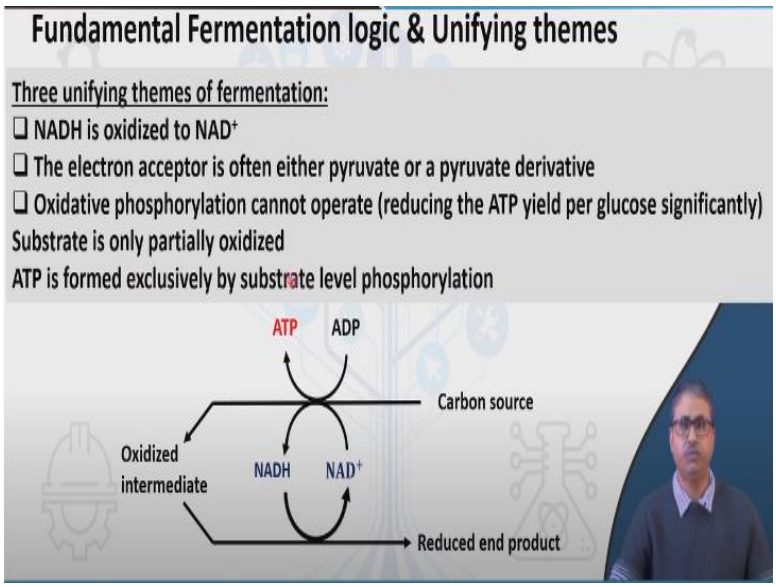


Now the unifying themes. First one is the NADH is oxidized to NAD+ through this process. Otherwise, there will be a lot of accumulation of NADH and the lack of NAD+ would eventually stop the glycolytic reactions. The electron acceptor is often

either the pyruvate or the pyruvate derivative. That means, a partially oxidized intermediate of the hexose sugar or the carbon substrate is acting as the electron acceptor.

Oxidative phosphorylation cannot operate. Oxidative phosphorylation which is involved when the organism is very sparing. And since, the NADH is not able to transfer the electrons to the membrane bound electron carriers which are involved in oxidative phosphorylation.

So thereby, during this fermentation process, oxidative phosphorylation is not operating and thus the ATP yield per glucose molecule is reduced significantly. Substrate is only partially oxidized because complete oxidation is not achieved because TCA cycle is not operating. And ATP is formed exclusively by the substrate level phosphorylation, oxidative phosphorylation is not operating.

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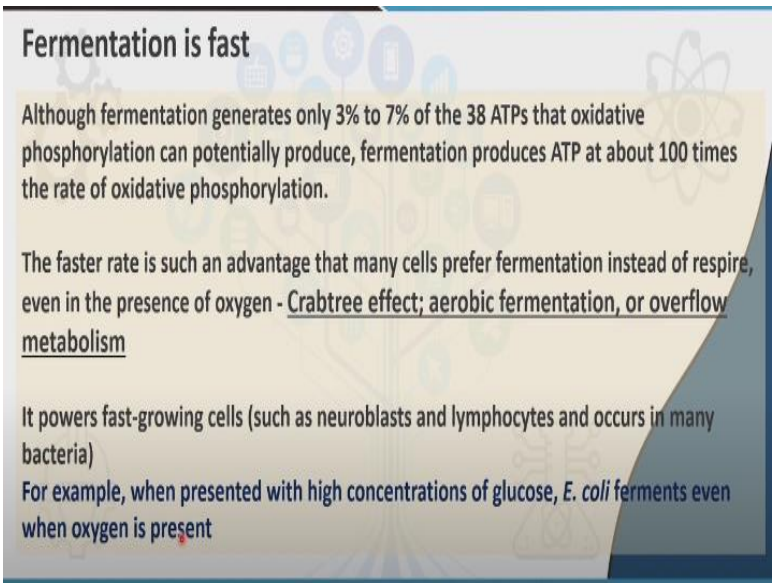


Now fermentation is a very fast process. Now although the fermentation process is generating only few ATP molecules compared to the oxidative phosphorylation based the aerobic metabolism of glucose completely through TCA cycle. This process the fermentation process produces ATP at about 100 times at the rate of oxidative phosphorylation.

Now we must highlight over here that this fermentation based production of ATP is basically the production of same 4 moles of ATP per mole of glucose, which are

already there in the EMP pathway. So those ATPs are only produced during the rest of the reactions generally, no more ATPs are produced. But there are few examples exceptions are there.

The faster rate because it is 100 times more faster the fermentation process rather than the oxidative phosphorylation and complete oxidation through TCA cycle, the faster rate is such an advantage that many cells prefer fermentation instead of respire, because it is a very fast process, even in the presence of oxygen.

So some cells, it has been noted that even in presence of oxygen, they prefer to run the metabolism through fermentation because the it is very fast and the accumulated sugar or accumulated glucose can be converted to some intermediates while producing a large number of ATP because it is 100 times faster than the TCA cycle and oxidative phosphorylation.

And this particular event is called Crabtree effect which is also referred as aerobic fermentation or overflow metabolism. Now particularly this Crabtree effect or overflow metabolism, that is the aerobic fermentation powers the fast growing cells, the cells which are growing very fast, such as the neuroblast, lymphocytes, and also occur in many other bacteria.

It has been discovered lately that in many other bacterial cells also this Crabtree effect is there and for example, when presented with high concentration of glucose E. coli ferments even more rapidly when oxygen is present. So that means in presence of oxygen, it is going to ferment even.

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Now one of the important strategy of fermentation is that what way to go because we will be seeing that there are multiple pathways of fermentation. Now these strategies for reducing the pyruvate because pyruvate is the intermediate of the glycolytic pathway or the product of the glycolytic pathway, which is further metabolized by the fermentative reactions.

So fermentative reactions they consider pyruvic acid as their starting molecule. Now the strategy of using or hot reactions will facilitate the further conversion of pyruvic acid into different fermentative products like lactic acid, acetic acid, ethanol etc., would determine that what are the requirements of the cell again, okay and accordingly the pathway names are there.

Now the choice for fermentation end product that what type of products are going to be formed determines the balance between the net ATP and net recycled electron acceptors. Because the number of ATP molecules are fixed that is the substrate level phosphorylation. That means per mole of puruvic acid produced, it is the two moles of ATP generated by substrate level phosphorylation from the glyceraldehyde 3-phosphate.

And one mole of NADH H+ per mole of pyruvic acid produced from EMP pathway. So those ATP and NADH are there and those are to be recycled because the cell needs ADP in order to produce ATP and also require the NAD+ in order to continue the EMP pathway.

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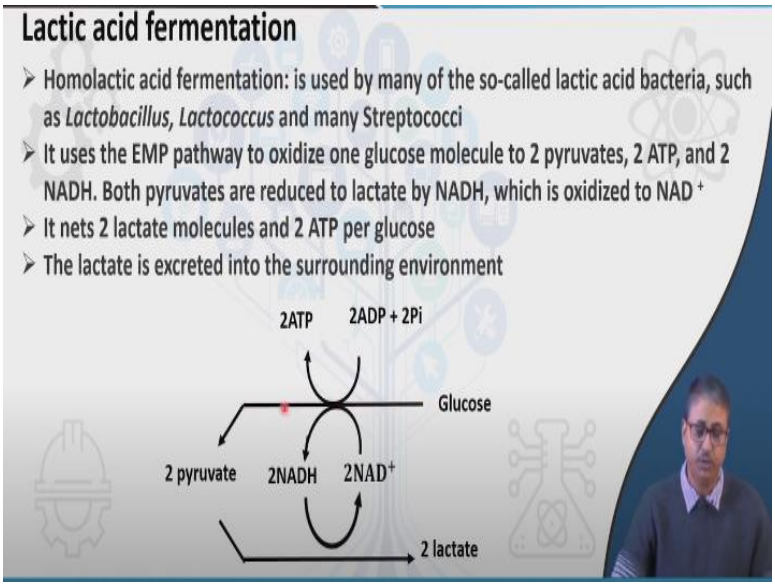


Now there are three general types of the fermentation mechanism. The first one is the lactic acid fermentation and the simplest one is the homolactic lactic fermentation, which is used or found in many bacteria which are called the lactic acid bacteria, although it is also a present in mammalian cells and other eukaryotic organisms as well.

So as you can see over here, the glucose is converted to pyruvic acid, one mole of glucose is metabolized to two moles of pyruvic acid. This is the intermediate or partially oxidized intermediate. Now this pyruvic acid can act as the electron acceptor. It accepts the electron from the NADH H+ and this the NADH is converted back to NAD+ so that this NAD+ can again participate in the upstream reaction where the glucose is converted to pyruvic acid.

So the net outcome of this reaction is the lactate molecules, two moles of lactate per mole of glucose, two moles of ATP which are produced in the substrate level phosphorylation and there will be NAD+ regenerated and this is important because this NAD+ is crucial, because it would only allow the other reactions of the glucose metabolism up to pyruvic acid because we must not forget that there are number of intermediates over here, which are being continuously produced.

And these intermediates are required for running a number of biosynthetic reactions.

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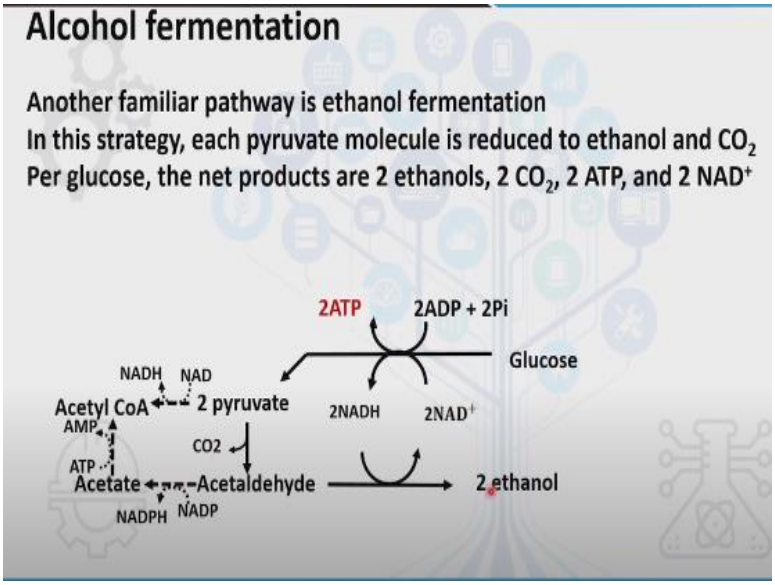


Next is the alcohol fermentation, which is also a very familiar pathway. And in this strategy the pyruvate molecule is reduced to ethanol and carbon dioxide. As you can see, the one of the simplest scheme is the glucose is converted to again to pyruvic acid and the pyruvates are converted to acetaldehyde and acetaldehyde to ethanol.

So it produces the two moles of ethanol, two moles of carbon dioxide because it is having a decarboxylation reaction and the two moles of ATP are generated and NAD+ is generated. Only difference between the lactic acid fermentation is that that it is a decarboxylation reaction and the products are of different type.

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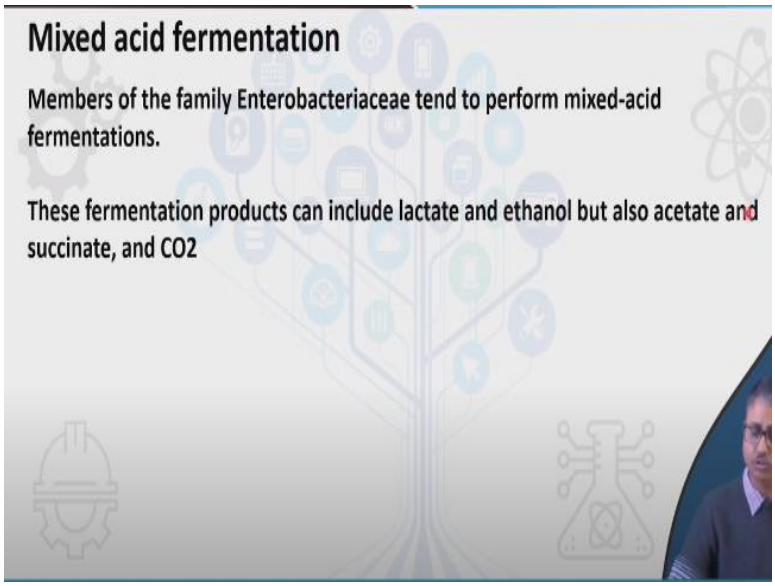


Now next is the mixed acid fermentation. Members of enterobacteriaceae and other organisms, prokaryotic organisms are also there, which tend to perform mixed acid

fermentations. Now this mixed acid fermentation products can include lactate and ethanol as well, but also acetate, succinate and carbon dioxide.

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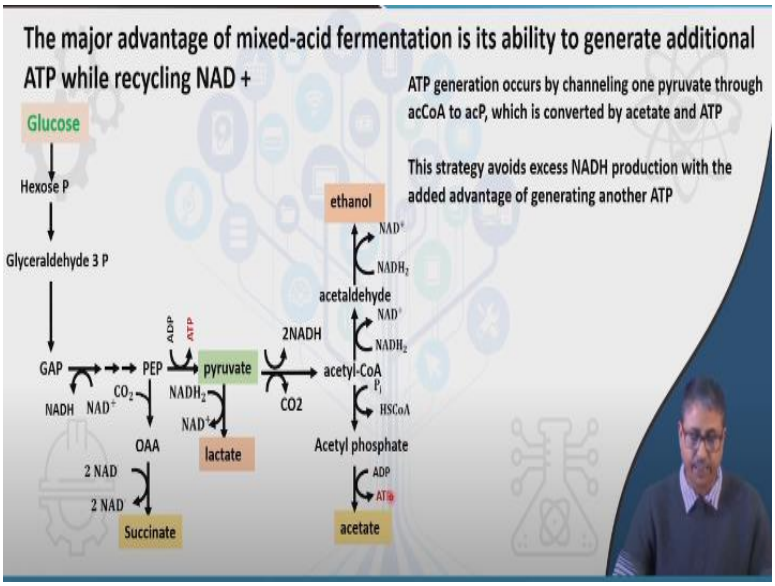


Now pyruvic acid which is produced or pyruvate, which is produced out of the EMP pathway from phosphoenolpyruvate to pyruvic acid can be converted to acetyl-CoA followed by that it can be will be converted to acetaldehyde to ethanol or it can be converted to acetate. It can also be reduced directly to lactate or even phosphoenolpyruvate, the major intermediate of the glycolytic or EMP pathway can be reduced further to produce the succinate or succinic acid.

Now in this scheme or the mixed acid fermentation, there is an interesting type of reaction which is the ATP generation, the scope for ATP generation through the conversion of pyruvic acid to acetate. Now ATP generation occurs by channeling one pyruvate through acetyl-CoA and then acetyl phosphate and this acetyl phosphate can produce one mole of ATP while it is converted to acetate.

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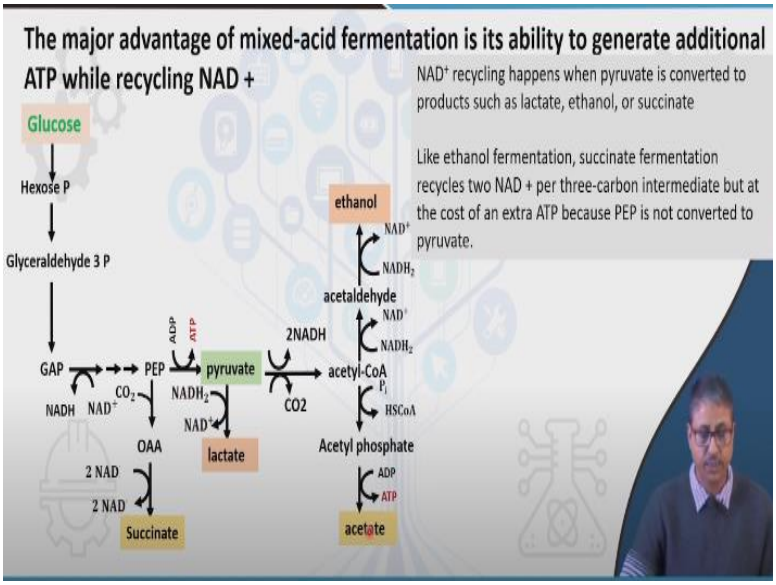


NAD+ recycling is almost a characteristic property of the all the reactions of the mixed acid fermentation also because the pyruvate is converted to either lactate, ethanol or succinate. We have a scope to regenerate NAD+ and this NAD+ is very critical to drive the oxidation of the glucose molecule. However, when only acetate is produced, this oxidation of NAD+ or the oxidation of NADH and generation of NAD+ is not achieved.

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So in this part of this review of metabolism, I have followed mainly the metabolic engineering textbook and the very interesting review article which is Glycolysis for Microbiome Generation.

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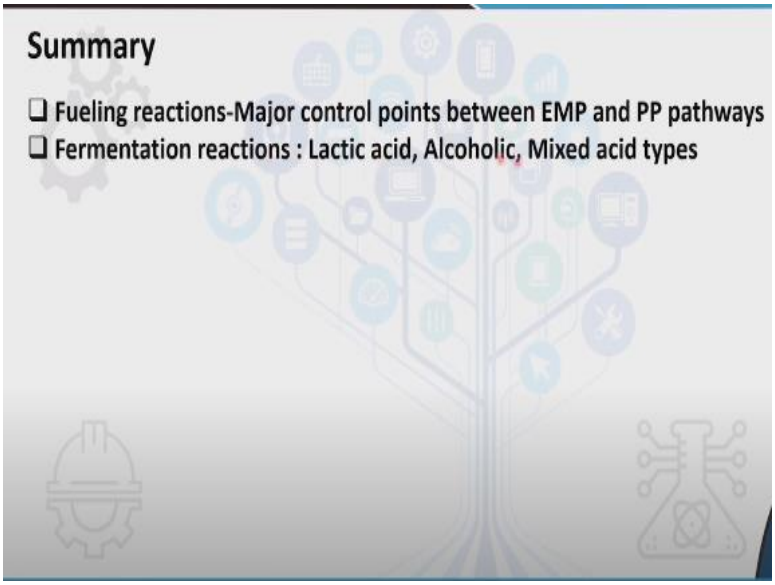


And to summarize, the fueling reactions are discussed, particularly the major control points between the EMP pathway and pentose phosphate pathway. And the basic architecture of the fermentation reactions like the lactic acid production, the alcoholic fermentation, and mixed acid type fermentations are briefly discussed. Thank you.