I'm Dr. Deeparani Prabhu from PES'sSRSN College of Arts and Science. Today I'll be discussing with you all a part of ZOC 106 Biochemistry and Metabolic Processes.

We're going to have a look at the third Unit Carbohydrate Metabolism, in which we're going to look at the sequence of reactions and regulation of Pentose Phosphate Pathway. This is the Module number 23 that I'm discussing.

In this we are going to have a look at Pentose Phosphate pathway or Hexose Monophosphate Shunt as an alternate pathway to glycolysis.

Also we will have a look at the location of the pathway.

The sequence of reactions of Pentose Phosphate Pathway, the Oxidative phase followed by the Non-oxidative phase and all the enzymes that are involved in each of the reactions.

At the end of this module you will be able to know the importance of Pentose Phosphate Pathway and the sequence of reactions of Hexose Monophosphate Shunt. Also the various reactions, detailed aspect of the oxidative and nonoxidative phases of PPP.

To begin with, Pentose Phosphate Pathway PPP or Hexose Monophosphate Shunt. It is an alternate pathway for the breakdown of glucose, glycolysis being the predominant pathway for glucose breakdown.

It is a primary pathway for synthesis of Pentose Phosphates, the precursors for synthesis of nucleotides, hence designated as Pentose Phosphate Pathway or PPP.

It branches from glycolysis at the level of Glucose 6-phosphate, so it is also called as Hexose monophosphate pathway. Sometimes described as Hexose Monophosphate Shunt as the pentose phosphate pathway intermediates when not being utilized for RNA or DNA synthesis are recycled into the main glycolytic pathway by the formation of Fructose 6 Phosphate and Glyceraldehyde 3 Phosphate. It's basically a multi functional pathway.

Very important in non dividing cells like RBC’S where there is a limited need for DNA and RNA synthesis. It's also called after one of the intermediates as the Phosphogluconate Pathway.

Where exactly PPP occurs?

In the animal cells it is occurring in the cytoplasm.

The role of the pathway is mainly anabolic rather than catabolic. In humans, the level of expression of the enzymes of the pathway varies widely in different issues. High levels are seen in liver, adrenal cortex, testicles, ovaries,

thyroid, mammary glands during lactation, and in red blood

cells. These other tissues which are requiring constant supply of

energy, pH to support reductive biosynthesis and/or to counter

the damaging effects of oxygen radicals. Let us have a look at the

sequence of reactions of the Pentose phosphate pathway. There are two distinct

phases in the pentose phosphate pathway.

The first is the Oxidative phase in which NADPH is generated.

Second is the non oxidative synthesis of five carbon sugars.

This flow chart depicts the overview of Pentose phosphate

pathway or Hexose monophosphate shunt. If you have a look at it,

you will see we are having three reactions in the oxidative

phase and four reactions in the non oxidative

phase. So totally we're having around 7 steps which will

complete the hexose monophosphate shunt. The shunt when we are going to study,

We have to start from the Glucose 6 phosphate step. Let us look at the individual steps in detail.

To start with, the oxidative phase. Basically it is comprising of three reactions.

Two are irreversible oxidation, which are the 1st

and the 3rd reaction and one more is a hydrolysis.

Let us look at step one.

The oxidation of Glucose 6-phosphate to 6-phosphoglucono-δ-lactone an intermolecular ester takes place. This is a reaction catalyzed by glucose 6 phosphate dehydrogenase, which is unique to the pathway. It's an irreversible step.

The enzyme is the major control point for the flow of metabolites through the pathway.

What happens is a hydride ion from carbon, one of glucose 6 phosphate is transferred to NADP+ that acts as an oxidizing agent. This reaction is important giving the first molecule of NADPH of the pentose phosphate pathway.

Second step involves hydrolysis of 6 Phosphogluconolactone to 6 phosphogluconate. It's catalyzed by Gluconolactonase.

Third step again is oxidation of 6-Phosphogluconate followed by decarboxylation, to form ribulose 5 phosphate which is again a very important intermediate. Here carbon dioxide is released and the second NADPH is generated. Also hydrogen H+ is generated from NADP+.

The enzyme involved is Phosphogluconate dehydrogenase. Let us have a look at the Nonoxidative phase. We start with the Ribulose 5-phosphate which has been formed in the earlier step and we can see Ribulose 5-Phosphate has two options, Isomerisation if keto isomerase is available then it will get converted to Ribose 5- phosphate, epimerase is generated that is depending on the requirement of the cell Ribulose 5- phosphate will either go and form Ribose 5-phosphate or

Xylulose 5-phosphate.

Let us have a look at the 4th step which is the first step of the non oxidative phase? Here

Ribulose 5-phosphate isomerized to Ribose 5-phosphate

by the enzyme 5-Phosphate ketoisomerase or it might be

epimerized to xylulose 5-phosphate by the enzyme Epimerase.

The Step 5 involves the transfer of two carbon moiety from Xylulose 5-phosphate to Ribose 5-Phosphate

in the presence of the enzyme transketolase, which finally

forms 7 carbon moieties. Sedoheptulose 7- phosphate and the

three carbon compound, Glyceraldehyde 3-phosphate.

The transketolase enzyme is again a very important enzyme

which is requiring the coenzyme Thiamine Pyrophosphate, TPP and magnesium ions.

The step 6 is in the presence of the enzyme transaldolase, a

three carbon fragment is transferred from Sedoheptulose 7-phosphate to

Glyceraldehyde 3-phosphate, to give Fructose 6- phosphate and Erythrose 4-phosphate.

7th step involves again Transketolase, which comes into picture for the second time. The

enzyme transketolase, which carries out the transfer of two

carbon fragment from xylulose 5phosphate to Erythrose 4-phosphate,

to give Fructose 6-phosphate and Glyceraldehyde 3-phosphate.

Transketolase requires Thiamine Pyrophosphate it is the one which transfers 2 carbon units

whereas transaldolase transfers 3 carbon units.

Ribose 5-phosphate and Xylulose 5-phosphate undergo reactions catalyzed by them.

That is what we have seen when we have started with the nonoxidative phase and it is catalyzed by Transketolase and transaldolase that transfer carbon units, ultimately forming Fructose 6- phosphate and Glyceraldehyde 3-phosphate.

Let us have a look at the overall reaction of the Pentose phosphate pathway.

We start with Glucose 6- Phosphate which interacts with NADP+ to yield Ribulose 5-phosphate, it gives carbon dioxide and gives a very important intermediate that is NADPH.

Ribulose 5-phosphate is then depending on which enzyme is available, it will yield either xylulose, so it's going to give us Xylulose 5-phosphate and Ribose 5-phosphate. These two interact to finally give Fructose 6-phosphate and Glyceraldehyde 3-phosphate.

Now, if there is no requirement, if RNA or DNA synthesis is not taking place, then these intermediates, that is Fructose 6-Phosphate and Glyceraldehyde 3-Phosphate, will be shunted back to the glycolytic pathway at different steps. So that's all in this module. I would also request you all to go through the 2nd subsequent module, Module number 24, which I'm going to discuss with regards to the Regulation and the significance of the same pathway. These are the references you all can refer these three books as well as there are a number of references on the web also, this will help you in understanding this particular topic in a very detailed manner. Thank you.