Hello students, we are going to study peptidoglycan

synthesis from Unit 2 that is chemoheterotrophic

carbohydrate metabolism.

We are going to study structure of peptidoglycan and then

biosynthesis of peptidoglycan.

After studying this module, student will be able to

explain the structure of peptidoglycan and describe the

process of peptidoglycan synthesis.

First of all, let us understand what is peptidoglycan? It is a

major component of bacterial cell walls. It consists of

linear polysaccharide chains that are crosslinked by short

peptides. It is also known as murein, so this murein, or

peptidoglycan is made of alternating N- acetylmuramic

acid, abbreviated as NAM and N-acetylglucosamine

abbreviated as NAG residues. So these NAM and NAG residues are

joined through beta 1,4

glycosidic linkages. And tetrapeptide chains are

attached to the NAM groups. Now in this figure we can see

that the green circles which you see here represent N

acetyl glucosamine and blue circles represent N

acetyl muramic acid and the pink circles are the peptide chains.

Peptidoglycan serves a structural role in the

bacterial cell wall. It gives structural strength and it

counteracts the osmotic pressure of the cytoplasm.

In gram positive organisms peptidoglycan is 20-80 nanometer

thick outside the plasma membrane, whereas in case of gram

negative bacteria the cell wall is quite complex and

peptidoglycan is merely 2 to 7nanometer layer which is

surrounded by 7 to 8 nanometer thick outer membrane.

Now if you look at this diagram, it clearly shows the

difference in the thickness of peptidoglycan between Gram

positive organisms and Gram negative organisms. In case

of Gram positive organisms the peptidoglycan layer is

very thick, and in Gram negative organisms it is a

very thin layer.

There is another difference between the peptidoglycan of

most of the Gram positive and Gram negative organisms. Here we

can see example of peptidoglycan from *E. coli* wherein we see a

direct cross linking between the two chains of peptidoglycan. So

it is a direct cross link wherein the carboxy terminal of

D alanine is connected directly

to the terminal group of diaminopimelic acid, whereas in case of

S. aureus which is a gram positive organism, a peptide

inter bridge is present which consists of pentaglycine. So

this is another difference between Gram positive and Gram

negative organism peptidoglycan.

Now murein synthesis is different from synthesis of most

of the other biopolymers. There are two reasons: it is a 2

dimensional network rather than a straight chain, so repeating

units are bonded in two dimensions and the synthetic

reactions occurs both inside as well as outside the cell

membrane. Biosynthesis of Murein was elucidated by James.

Park and Jack Strominger in *Staphylococcus aureus*.

Coming to the major steps of peptidoglycan biosynthesis. In

stage one there is sequential assembly of repeating units of

murein within the cytoplasm while it is bound to UDP and

the product that is formed is called as parks nucleotide.

In stage two, there is, transfer of these incomplete murein

subunit from UDP to a lipid constituent of the cell membrane

that is bactoprenol phosphate. So this bactoprenol phosphate acts as a lipid carrier and here terminal

steps

in assembly take place.

And lastly, in stage three there is transfer of

completed murein subunit from the membrane to the growing

murein layer in the cell wall, where crosslinking of

peptide chains takes place. Now we're going to see these

steps in detail.

So in stage one there is conversion of UDP-N-acetyl glucosamine

to UDP-N-acetylmuramic acid followed

by sequential addition of amino acids to UDP-NAM to

form a pentapeptide side chains.

Now ATP is required for formation of each of these

peptide bond. And terminal 2 D-Alanines which are present are

added simultaneously as a

dipeptide. And the product that is formed is called as

Park’s nucleotide.

In stage two, the NAM pentapeptide is transferred from

UDP to a lipid carrier that is bactoprenol phosphate. If

you see this figure, this is the cell membrane. This is the

cytoplasm and this is the exterior of this cell.

In stage two, later on, UDP-NAG adds NAG to this to form the

peptidoglycan repeat unit.

And if a pentaglycine Interbridge is required, the five glycines are added using glycyl-tRNA molecules molecules at this stage.

Later, the bactoprenol is transporting the complete

subunit across the membrane to the outer surface. So bactoprenol pyrophosphate is acting as a carrier.

Now the peptidoglycan unit is attached to the growing end of

the peptidoglycan chain to lengthen it by one repeat unit.

And bactoprenol phosphate is released which travels back into

cytoplasm to carry on with the next round of this cycle.

So now the peptidoglycan unit has lengthened by 1

repeat unit.

Lastly, in stage three, crosslinking takes place between

the peptide side chains by the enzyme transpeptidase, so

transpeptidase brings about crosslinking between these

peptide side chains.

Another enzyme that is D-alanine carboxypeptidase, it

cuts off or clears off the terminal D-alanine from the

peptide chain. Because this terminal D-alanine does not take

part in the crosslinking.

The peptidoglycan biosynthesis is inhibited by the antibiotic

penicillin. Penicillin inhibits the enzyme catalysing the

transpiration reaction. This blocks the synthesis of a

complete, fully crosslinked peptidoglycan and leads to osmotic lysis. This is the reason why penicillin acts only

on growing bacteria and specifically Gram positive

bacteria that are synthesizing new peptidoglycan. So the

presence of penicillin inhibits the action of transpeptidase and

prevents cross linking between

the two peptide side chains. So in this module we have

studied differences between peptidoglycan of Gram positive

and Gram-negative organisms and we have seen the synthesis of

peptidoglycan in bacteria.

So these are the references for this module.

Thank you.