Basics of Biology
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Module V: Molecules of the Life (Part-II)
Lecture - 22
Proteins (Part-III)

Hello everyone, this is Doctor Vishal Trivedi from Department of Biosciences and Bioengineering IIT, Guwahati and what we were discussing, we were discussing about the living organisms. And in this context, so, far what we have discussed? We have discussed about the classifications in the first module, then we have discussed about the evolutions and then we also discuss about the different types of cells.

So, we have discussed about the prokaryotic cell and as well as the eukaryotic cell, and while we were discussing about the cell, we have discussed about the different types of molecules, which are actually participating into the different types of reactions, what is been happening into these organelles, such as we are discussing about the mitochondria or the chloroplast and we are discussing events.

So, when we were discussing about the electron transport chain or the for the photosynthesis, we discuss about the different types of molecules which are participating into these reactions. So, in the subsequent module, we have also discussed about the different types of biomolecules. In the previous module we have discussed about the duplicated we have so, we have discussed about the DNA and RNA which are actually going to serve as the molecule to carry the genetic information from one generation to the next generations.

In most of the organisms the DNA is the genetic material, but RNA is also been present as the genetic material in some of the organisms. Subsequent to that, we have also discussed about the carbohydrates and its structure and functions. And we have also discussed about the different types of metabolic reactions where the carbohydrates are being utilized and they are actually being oxidized to produce the energy.

So, we have discussed about the glycolysis or the crop cycles and subsequent to that, we have also discussed about the structure classification as well as the function of the lipid molecules. Now, in the previous lecture, we have discussed about the protein structures. So, we have discussed about the primary structures, we have discussed about the secondary structures, we discuss about the tertiary and as well as the quaternary structures.

In addition to discussing the structures, we have also discussed about the different types of method what you can use to determine the primary secondary, tertiary or the quaternary structures, we have discussed about the Sangers method or the Edman degradation method to sequence the particular protein so, that you will be able to know what is the amino acid sequence present in that particular protein. And then subsequent to that, we have also discuss about the some of the experimental methods such as the X-ray crystallography or to the NMR spectroscopy.

We have not done very extensive discussion about these techniques, but there are a couple of good MOOC courses which are already been available for study these courses, these aspects of the structure solution by the spectrography or to the NMR spectroscopy. Subsequent to that, we have also discussed about the homology modeling and how we can be able to use the homology modeling as a computational tool to solve the 3-dimensional structure of a particular protein.

So, that also we have not discussed in detail because there are a couple of courses available and there are very good resources are available in case you are interested to study or you want to know more about those particular aspects. So, in today's lecture, we are going to discuss about the function of the proteins and we also going to discuss about how you can be able to detect the proteins in a given biological fluid. So, let us start today's lecture. So, in today's lecture, we are going to discuss about the protein functions.

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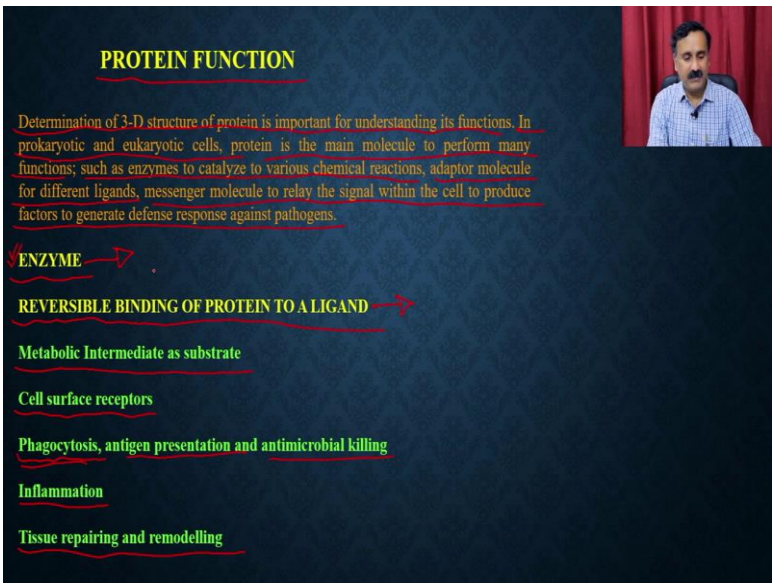

So, when we talk about the protein functions, we are actually going to discuss first about the different types of functions what the protein can actually be able to perform. So, the protein functions when we talk about protein functions, the determination of a 3-dimensional structure of a protein is important for understanding its functions.

As we can recall that the 3-dimensional structure of a protein is actually going to tell a body, it is going to be function. And that is why, people are actually going with the extensive solutions like extensive 3-D structure solution of the different types of protein so that you can be able to know what is the function of that particular protein.

I am sure you might have heard about the different types of structural genomics projects, what is running in different parts of the world and different scientists are involved in that particular activity so that they can be able to solve the structures of all the protein what is present in a particular genome of an organism.

And that is how you can be able to know what function this particular protein is actually going to perform. And depending on this information, you can be able to utilize that information to either the, develop the drugs, so, because if that particular function is be is crucial for that particular organism, then you can be able to disrupt that interaction.

And that is why the people are doing like, for example, you can have the mycobacterium is structural genomics, or malaria structural genomics and so on. So, the purpose of this structural genomics project for the particular pathogenic organism is that we want to know, the function the 3-dimensional structure of the particular protein, so that it, we are also going to deduce the function of that particular protein and if the function is very crucial, then we can be able to disrupt the function by developing the different types of drugs out the molecules, and that is how we can be able to design the new drugs.

So, that is like the 3-D structure of a protein is important for understanding its functions. In prokaryotic, as well as the eukaryotic cell, the protein is the main molecule to perform many functions such as the enzyme to catalyze the various chemical reactions, did I was working as an adapter molecule for the different types of ligands, then it is a messenger molecule to really the signal within the cell to produce the factor to generate the different response against the pathogenic organisms.

So, it has the different types of roles the it could be a role in catalyzing different types of chemical reactions, it could be adapter molecule for the different types of ligands and that is

how it is actually going to participate into the different types of biological responses, and then it also can relay the information from the one part of the cell to another part of the cell or it actually can work as a messenger. So, that it can actually go from the one cell to another part of another cell and therefore, it actually can convey the message.

So, categorically we have going today in today's lecture, we are going to discuss about the protein as an enzyme. And then we also going to discuss about the function of a protein as the reversible binding of the protein to a ligand. In this particular category, when the you are actually going to see the function of a protein as adaptor molecule, it is actually going to participate into different types of functions, like for example, it going to work as a metabolic intermediate as a substrate.

So, that is going to be a ligand for that protein molecules, then it also can function as a cell surface receptor so that it can actually can receive the ligand from the different sources and that is how it actually can relay the signal from the one cell to another cell. Then it also can function as an adapter molecule to catalyze the different types of immunological responses, whether it is the phagocytosis, antigen presentation, anti-microbial killing or to the inflammations. In addition to that, the proteins are also been known to catalyze the tissue repair and as well as the remodeling. So, let us start first with the protein function as an enzyme.

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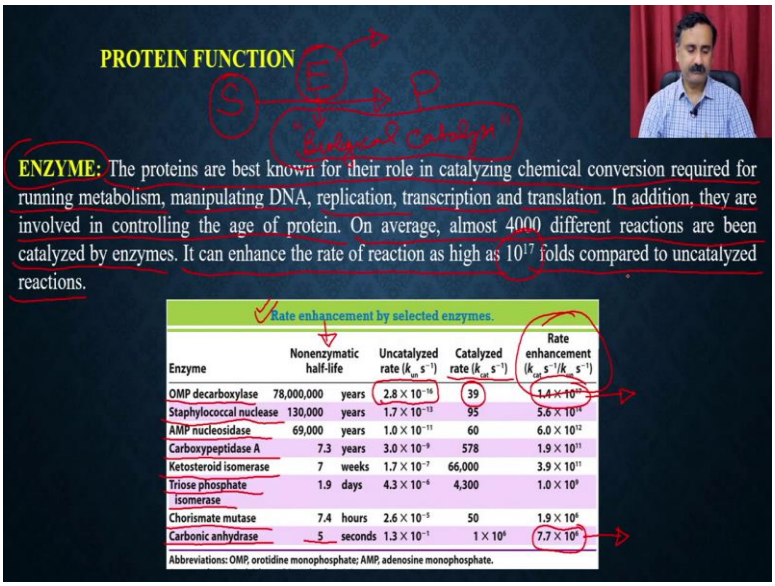

So, the enzyme, the proteins are best known for their role in catalyzing the chemical conversion required for running the metabolism, manipulating the DNA, replication,

transcription and translations. So, in addition, they are involved in controlling the age of your protein. So, what is that, proteins are working as an enzyme and a function of the enzyme is that it is actually going to facilitate the conversion of the substrate into the product. If you see the non-catalyze reactions, the non-catalyzed reactions are going to be very slow compared to the enzyme catalyzed reaction.

So, enzyme is actually not only facilitating the conversion of the substrate into the product, but it also facilitating it at a very, very high rate. And that is why the enzymes are also called as the biological catalysts. What that means is that it is actually going to enhance the conversion rate and it since it is our enzyme you might have seen that we have when we were discussing about the carbohydrate metabolism whether it is a reaction which are involved into the glycolysis or the Krebs cycle there are so many different types of enzyme which are participating into the different types of reactions, whether it is a hexokinase or Glucokinase or some other enzymes, all these enzymes are catalyzing the different types of reactions.

Apart from that when we are going to discuss about some more aspects of the enzyme like where we are actually going to discuss about manipulating the DNA. So, enzymes are also involved in DNA repair and damages. The enzymes are also involved in DNA and applications where the enzymes are actually going to, make the 2 copies of a particular DNA molecule or they are also been involved in transcribing the information that is given onto the DNA sequence. And that is how they are actually going to produce the messenger RNA and then the messenger RNA is also going to be translated by the ribosomal machinery.

So, ribosomes are also been made up off of the protein and then they are also there are so many enzymes which are participating into the events. So, what you see here is that the enzymes are catalyzing the various types of reactions. So, on average, what you see here is that on average, almost 4000 different reactions are being catalyzed by the enzyme. And one of the best part is that it can enhance the rate of reaction as for as big as 10 to power 17 folds compared to the uncatalyzed reactions.

So, I have given you a table where we are showing the different types of enzyme and its different types of properties. So, what I am showing is the enzyme like the OMP decarboxylase, Staphylococcal nuclease, AMP nucleosidase, carboxypeptidase A, ketosteroid isomerase, Triose phosphate isomerase, Chorismate and carbonic anhydrase. And what I am showing is the different types of properties like the half-life, so half-life is very high in terms

of the OMP decarboxylase compared to that, it is very small in the case of carbonic anhydrase and then we also have the what will be the uncatalyzed rate reaction.

So, what you see here is the uncatalyzed rate reactions are pretty slow. So, they are 10 to the power minus 16 compared to that, we are actually having the catalyzer rate. So, catalyzed rates are 39. So, if you see the rate enhancement rate, enhancements are 10 to power 17 in the case of mpg carboxylase. Similarly, the rate of the rate enhancements are pretty high even if it is very low, it will be low as like 10 to power 6, which is in the case of the carbonium anhydrase.

So, the purpose of an enzyme is not only to catalyze the enhanced reaction, it also are providing the specificity because the enzymes are only recognizing their cognate substrate and that is how they are also bringing the specificity into the system. And you might have seen when we were talking about the glycolysis, the enzyme or actually its activity can be modulated by the different types of modifications. For example, we can modify the enzyme activity by covalent modification or the allosteric modifications.

So, these are the things which are possible in with the enzyme because enzymes are made up of the protein and the protein structure can be modulated by the subtle changes in the either the amino acid sequences or the subtle changes in the interaction that are involved into the folding the particular protein.

For example, if you do a phosphorylation of a particular protein, then you are actually going to compromise the some of the interactions or you are actually going to facilitate some of the reaction because that depends whether you are actually going to enhance the reactions after the phosphorylation or you are actually going to reduce the reactions.

Because in some cases, the phosphorylation is enhancing the reactions and so in some cases, the phosphorylation is reducing the reactions. If you remember, when we were talking about the glycolysis we said that pyruvate kinase when it is phosphorylated is less active and when the pyruvate kinase is non- phosphorylated it is more active. So, that kind of modulation is also possible with the enzyme because they are made up of a protein and the protein structure can be modulated by simply disrupting some of the interactions.

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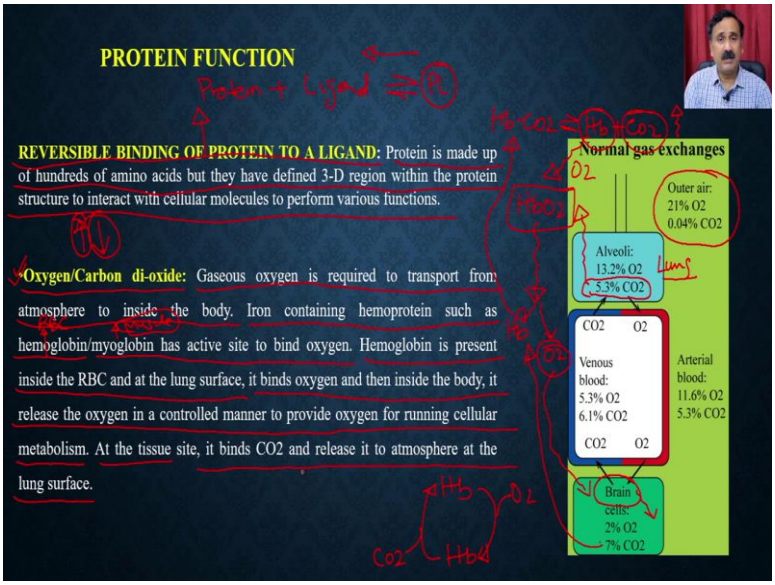

Now, let us move on to the next function. And the next function is reversible binding of a protein to a ligand. So, one of the main features of a protein is that protein is actually can bind to its ligand and that ligand binding is not covalent it is actually reversible, which means the protein is actually going to form the protein ligand complex and depending on the concentration of these pairs like if the consolidation of the PL will go up, then it actually can dissociate and give you the protein and ligand. So, that is why these kinds of events are actually reversible and that is why you can actually be used this for many types of applications.

So, protein is made up of the hundreds of amino acids, but they have a defined 3-D region where the protein is structured to interact with the cellular molecule to perform the different types of functions, what are the functions? One other function is gaseous exchange. So, we can actually have the gaseous exchange possible simply because the different types of ligands have the binding efficiency to the protein differential under different environments. One of the classical examples is the export and import of the oxygen as well as the carbon dioxide.

So, that when we are running the metabolism, for example, when we were talking about the Krebs cycle, the protein is utilizing the glucose molecules and then it is producing the large quantity of carbon dioxide. So, 2 molecules of carbon dioxide are being produced, when we are actually running the Krebs cycle and these carbon dioxide molecules are not good for the body. They have to be removed from the from the cell and how you are going to do that is

you are actually going to throw that carbon dioxide into the blood and then eventually it will come back to the lungs and from the lungs, it is going to be exchanged with the oxygen.

And at the same time, you also require the oxygen for running the electron transport chain remember that we said that the Krebs cycle is evolved into the eukaryotic cell because it is running it is present into the high oxygen level and because it has a high oxygen level, the organism could be able to run the Krebs cycle to enhance the energy productions. So, gaseous oxygen is required to transport from the atmosphere to inside the body. Iron containing hemoproteins such as the hemoglobin or the myoglobin has active site to bind the oxygen.

So, the hemoglobin what is present it is hemoglobin is present into the blood which is present inside the RBC whereas the myoglobin is present inside the muscle cell and both of these organs are very good in terms of carrying the oxygen because the muscle cells are required the oxygen to perform the different types of function whereas the RBCs are having the hemoglobin which have the function to carry the oxygen from the lungs to the different parts of the body.

So, the hemoglobin is present inside the RBC and the lung surface it binds the oxygen and then inside the body, it releases oxygen in a controlled manner to provide the oxygen for running the cellular metabolism. At the same time at the tissue site, it binds the carbon dioxide and release it to the atmosphere as the lungs surface. So, this is what it is going to happen. So, this is the lung, this is the lung where you are it is showing the alveoli. So, when the outer air you have a very high quantity of oxygen and very low quantity of carbon dioxide.

So, because of this difference into the concentrations, what happened is that at the lung side, there will be a very there will be in they will be the binding of the oxygen to the hemoglobin molecule. And you will see that the carbon dioxide concentration is very high from the deoxygenated blood.

So, when the deoxygenated blood is going to come it is going to carry the carbon dioxide and carbon dioxide concentration is going to be very high. So, when the carbon dioxide concentration is very high and the oxygen concentration is low compared to the outside the oxygen is a carbon dioxide is actually going to be dissociated.

And that so, what will happen is that hemoglobin carbon dioxide complex is going to be broken down and it is actually going to give you the hemoglobin plus carbon dioxide because

the carbon dioxide concentration is high, it is actually going to go into the atmosphere. At the same time, the same hemoglobin because the atmospheric hemo oxygen is high, it is actually going to take up that offseason and that is how the hemoglobin is actually going to form the oxyhemoglobin complex and that oxyhemoglobin complex is done going to transfer that oxygen to the different parts of the body.

For example, then the oxygen is going to carry through the arterial blood. So, in the arterial blood and then it is actually going to deliver that oxygen to the different parts of the body like the brain cells and at the brain cell side where the you see the carbon dioxide level is very high and the oxygen level is low. So, this high level of oxygen is going to be delivered. The same thing is going to happen, the HBO_2 is again going to be dissociate to form the hemoglobin and it is going to form the oxygen.

This oxygen is going to be delivered to the brain and at the same time this carbon dioxide is again going to bind to this hemoglobin and it is going to generate hemoglobin carbon dioxide complex and that carbon dioxide hemoglobin carbon dioxide complex is again going to be traveled through the venous blood and then it will again reach to the alveoli and that is how it is actually going to release the carbon dioxide.

And this cyclic event like where the hemoglobin is going to shuttle between the 2 events like in one case, the hemoglobin is actually going to carry the oxygen from the air and in the other event the hemoglobin is going to carry the carbon dioxide from the tissue is keep happening and that that is why it is actually going to be maintaining up healthy environment inside the body. And that is how it is actually going to give you the ability to detoxify the carbon dioxide what is being generated inside the tissue because of the metabolism and at the same time it is also going to give you the required oxygen for the running the metabolisms.

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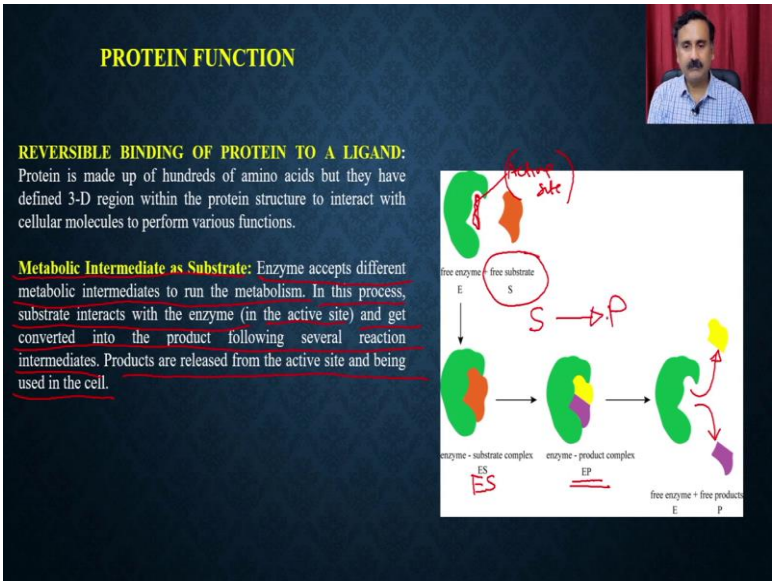

Now, apart from this the enzymes can also work as the metabolic intermediate. So, they can also work as the proteins are also can work as a metabolic intermediate as a substrate. So, the enzyme accepts the different metabolic intermediates to run the metabolism. In this process, the substrates interact with the enzyme in the active site and get converted into the product following the several reaction intermediates and the products are released from the active site and being used in the cell. So, this is what is going to happen.

You have a free enzyme and this is actually our is the active site. So, in this active site this is your this is the enzymes active site. So, active site is the area where the enzyme is actually going to interact with the substrate. So, when the substrate is going to come it is actually go and bind reversibly with this area, and that is how it is actually going to form the ES complex. Once the ES complex is formed, then there will be a lot of intermediate and because of that the enzyme is actually going to be get converted into the enzyme product.

Once the enzyme is going to convert the substrate into the product, the affinity of the products is going to be less and that is how these products are actually going to be released from the enzyme and this will continue big and that is how the enzymes are actually going to keep catalyzing the conversion of the substrate to the product.

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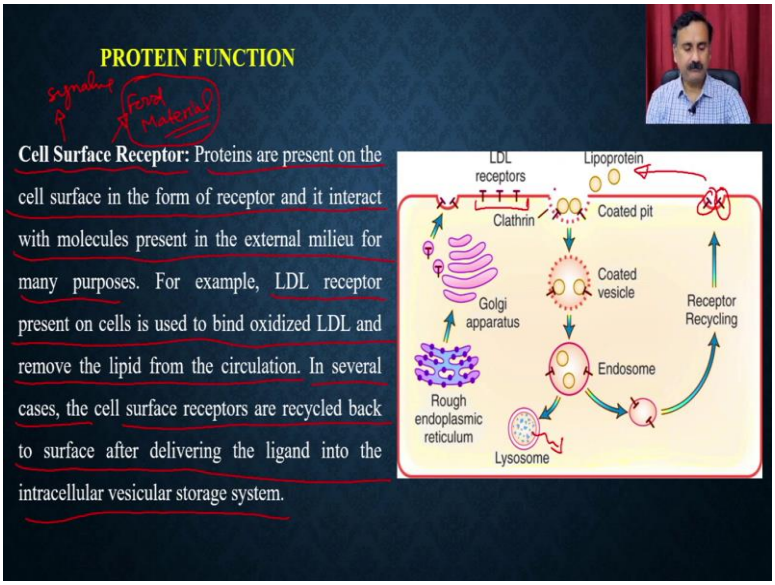

Now enzymes, the proteins are also going to function as a cell surface receptor. So, proteins are present onto the cell surface in the form of receptor and interact with the molecule present in the external milieu for many purposes. For example, the LDL receptor present on the cell is used to bind the oxidized LDL and remove the lipid from the circulation. In several cases, the cell surface receptors are recycled back to surface after delivering the ligand into the intercellular vesicular storage.

So, from the cell surface receptor, it actually can do many types of function. It can actually function as a signaling molecule where they can actually give the signal which are going to be received from another cell or it actually can also function as a food up the food material from the external milieu. So, in this case, I have given you an example of the LDL receptor which is actually going to work as a catching up the food from the external milieu. So, what happened is that the LDL receptor is present in the form of receptor onto the cell surface.

And when the oxidized LDL is going to interact with this receptor, it is actually going to be internalized into the vesicular structures, then these vesicles are actually going to fuse with the lysosome and when they will fuse with the lysosome the lipid part what is going to bind is actually going to be dissociated from these receptors, and that is how the lipids are going to be given to the lysosome and from here the lipids are actually going to be released into the cytosol.

On the other hand, these receptor molecules are actually going to go back to the plasma membrane and they are actually going to be expressed as the ligand again. So, these ligands

are again available for performing this function which means the with this recycling of the receptor will be continue and so it is actually going to be keep taking up the nutrition from the external milieu.

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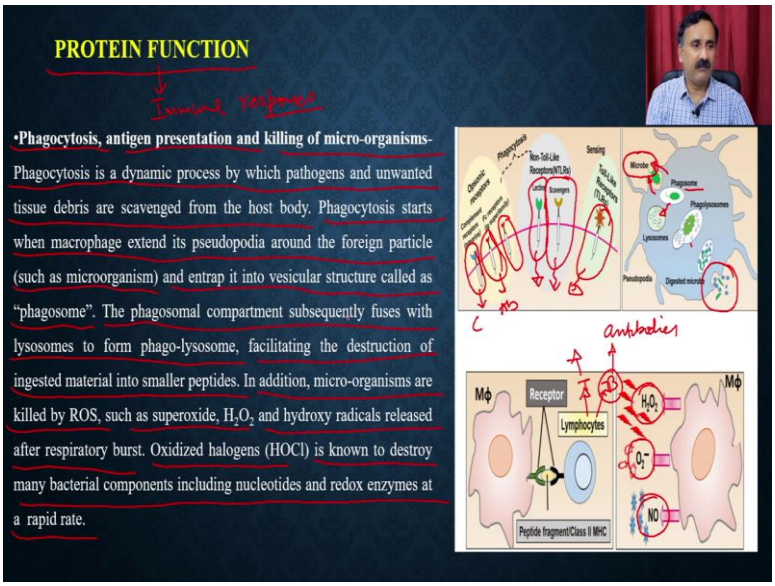

Then it also has the brain function to modulate the difference types of immune responses. For example, the phagocytosis, antigen presentation and the killing of the microorganism. Phagocytosis is a dynamic process by which the pathogen and the unwanted debris are removed or the scavenge from the host body. Phagocytosis starts when the macrophage extend its pseudopodia around the foreign particles such as microorganism and entrap it into the vesicular structure known as the phagosome.

The phagosome compartments subsequently fused with the lysosome to form the phago-lysosome, facilitating the destruction of the ingested material into the small peptides. In addition, the microorganisms are killed by the ROS such as superoxide, hydrogen peroxide and hydroxyl radical released after the respiratory burst. Oxidized halogens, such as HOCl is known to destroy the many bacterial components including the nucleotides and the redox enzyme at a very rapid rate.

So, this is what you are going to see. You are going to see that the cell has a different types of cell surface receptor like you have the complement receptor, opsonic receptor, these opsonic receptor is for the antibody, the complement receptor is for the complement then we have the another kind of receptors like the LPS receptors and also that then we have the non-toll like

receptor like the lectins, then we have the scavenger receptors and we have the toll like receptor, which are also called as the TLRs.

All these receptors are having their cognate ligands and that so, they are actually going to accept or they are going to recognize those kinds of ligands if they are present onto the pathogenic organisms. Once they see a pathogenic organism, for example, here you see that the bacteria is approaching towards the macrophages it is going to be engulfed. So, the cell wall, the plasma membrane is going to protrude from the bone and that is how it is going to engulf this into a membrane bound structure, which is called as a phagosomes, these phagosomes are then going to interact with the lysosome.

And that is how the degrading enzymes and as well as the low acidic pH is actually going to digest this particular microbe and so, it is actually going to be destroyed into the phagolisosomes. And then from here, it is actually going to be excreted out which means that bacteria are the killed bacteria is going to be thrown out. In some cases, it is and also be expressed in the form of the peptide and that is how it is actually going to amplify the immune responses with the help of the lymphocytes such as the T cells or B cells.

So, these lymphocytes could be the T cell or it could be B cell. Whereas T cell is actually going to secrete the antimicrobial agents whereas the B cell is actually going to secrete the antibodies. Apart from that the you see the macrophages in response to these particular events can also secrete the different types of cytolytic enzymes or different types of cytolytic chemicals for example, the hydrogen peroxide, superoxide radicals or the nitric oxide and all these are actually going to be anti-microbial in nature. So, they are actually going to clear up the infections.

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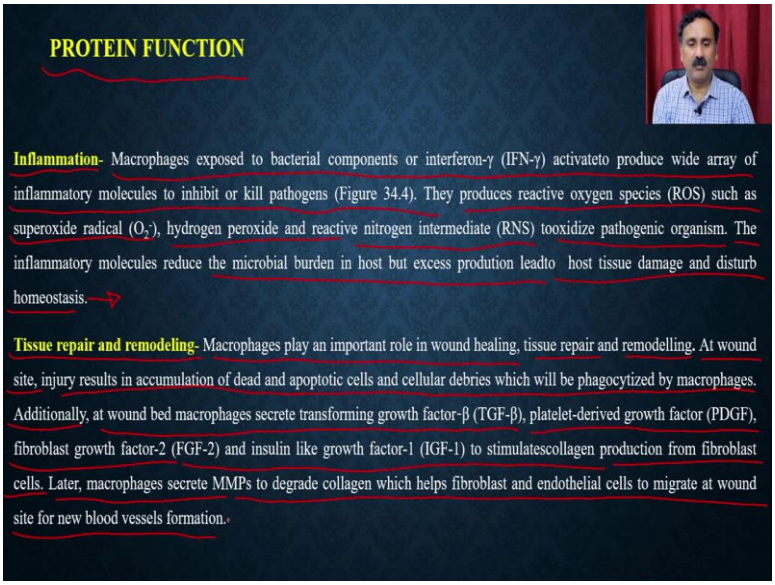

Apart from that, the proteins are also involved into the inflammation as well as the tissue repair. So, inflammation is required because the inflammation is like the swelling of that particular area. So, macrophages exposed to the bacterial component or the interferon gamma activate. Activity produces a wide array of the inflammatory molecule to innovate or kill the pathogens, they produce the reactive especially is ROS such as superoxide radicals, hydrogen peroxide and reactive nitrogen species to oxidize the pathogenic organisms.

The inflammatory molecule reduces the microbial burden in hosts, but the excess production leads to the host damage as well as the it disturbs the human status. So, inflammation is important because it reduces the microbial burden in the host and it also stop the infection at the site of injury. And on the other hand, if there are too much inflammation, then it is actually going to cause the tissue damage and as well as it is going to disturb the homeostasis.

Now, we talk about the tissue repair and remodeling, so macrophages play an important role in wound healing, tissue repair and remodeling. At wound site, the injury results in the accumulation of the dead and apoptotic cells and cellular debris which will be phagocytes by the macrophages. Additionally, in a wound bed macrophages secrete transforming growth factor TGF beta, platelet derived growth factor PDGF and the fibroblast growth factor FGF and insulate like molecules to stimulate the collagen production and from the fibroblast cells. Later the macrophage secretes MMPs to degrade the collagen which helps the fibroblasts and endothelial cell to migrate at the bone site for the new blood vessel formation.

So, when there will be an injury and there will be a tissue damage, then the macrophages are actually going to perform the different types of functions by T proteins. So, by different types of protein, whether it is a TGF beta, whether it is PDGF, fibroblast growth factors, insulin like growth factor, all these are protein molecules, which are actually going to participate into the different types of remodeling as well as the repairing processes. And that is how it is actually going to help the host or it is going to help the organism to repair the damages.

So, these are the some of the classical function of a protein, what we have discussed, what we have discussed? We have discussed about the functioning of the protein as the enzyme as an enzyme. We also discuss about the protein as an adapter molecule, whether they are part of facilitating the conversion of the substrate into the product or whether they are helping in terms of uptake of the lipid molecule from the circulations and also whether they are facilitating the sum of the immune responses. So, with this, I would like to conclude my lecture here and in our subsequent lecture, we are going to discuss some more aspects related to the living organism.

So, with this, I would like to conclude my lecture here. Thank you.