Bioinformatics
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Lecture - 4b
Protein structure and function II

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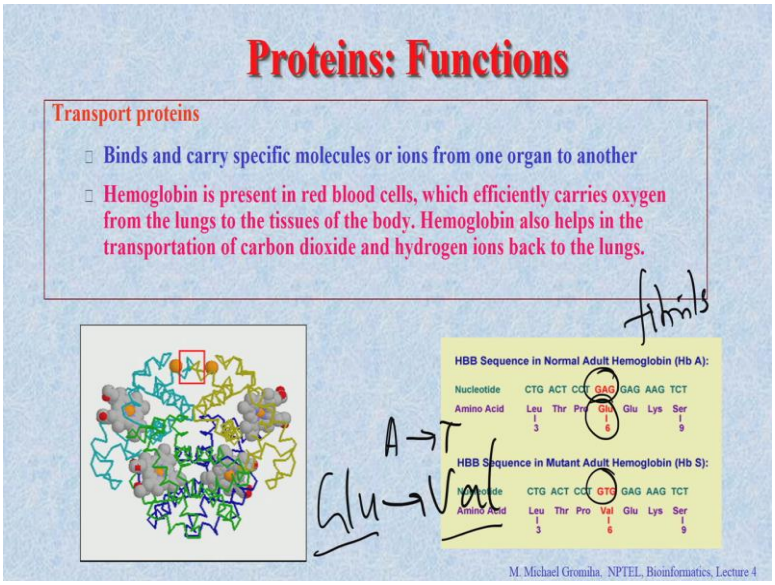

Now, this is a next one we will talk about transfer proteins and this is a very famous protein, this is very important. So, we everybody needs this protein right. So, which what is the protein involved in this transport oxygen transport.

Student: Hemoglobin.

Hemoglobin, right.

So, here hemoglobin is present in red blood cells right which efficiently carries the oxygen from the lungs to tissues of the body right then hemoglobin also helps in the transportation of the carbon dioxide and hydrogen ions back to the lungs. So, this is the protein right hemoglobin has how many subunits.

Student: 4.

4 subunits 2 alpha subunits and 2 beta subunits and the b subunits they contain a specific residue called the glutamic acid right. So, this is the structure of the hemoglobin b chain;

they look like this, if there is a change in the nucleotide or the change in the amino acid. So, this will affect this transport right for example, here if you see this is GAG right. So, GAG is code for glutamic acid if it is converted to GTG, right. So, A is changed to T right, then you change glutamic acid to;

Student: Valine.

Valine; so we change to glutamic acid to valine. So, now, just we; now we discussed about different characteristics features which type of amino acid residue is glutamic acid.

Student: Charged.

Charged negative charge right, so about valine.

Student: Hydrophobic.

Hydrophobic right. So, if you convert mutate glutamic acid to valine what will happen.

Student: It changes.

It changes; right. Now, they form the hydrophobic environment. So, if you do the hydrophobic environment. So, this amino acid residue valine tries to interact with the other the hydrophobic residues in another chain right in their hydrophobic packet because of this interaction. So, it is not able to get proper interaction. So, it tends to form fibrils right because of this fibril.

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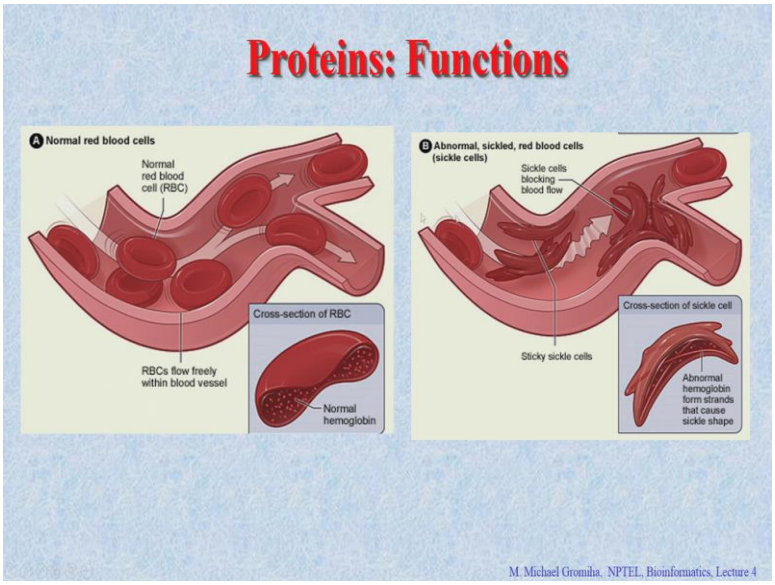

So, they change the shape like the regular one into sickles; now this is a regular shape and if you make the sickle cell, now this will block this transport of this oxygen. So, this is one form the sickle cell anemia. This is mainly found many people in Africa.

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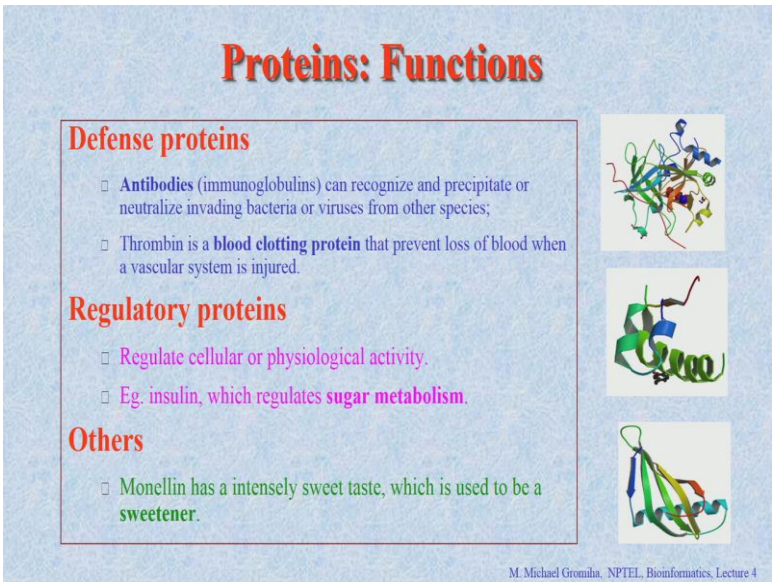

So, now this protein is very important for the carrier of oxygen right now there are other proteins called defense proteins, so what is called defense proteins.

Student: Antibodies.

Antibodies; so because we defend ourselves because we have to be safe from the environment right from the bacteria or virus are all anything. So, like immunoglobulins right. So, this can recognize and precipitate or neutralize the invading bacteria or virus from the other species then there is another protein called thrombin right this thrombin is also very important because it is a.

Student: Blood clotting.

Blood clotting protein, then because when we get injured; so this should be clotted right. So, if this is the one which helps when we get injured. So, to prevent the loss of blood right in the vascular system right then there are some proteins they are acting as regulatory proteins right this regulates the cellular or physiological activity for example.

Student: Insulin.

Insulin, right, this is a well-known example. So, it regulates sugar metabolism. So, if you are having diabetes. So, right we need to have insulins, right. So, this is the one which regulates the cellular or physiological activity and there is a lot of other proteins they are having different functions one example is a monellin, it is a protein which is also used to as a sweetener, right if it is safe for then also other proteins nutrient proteins right this is the one usually people know.

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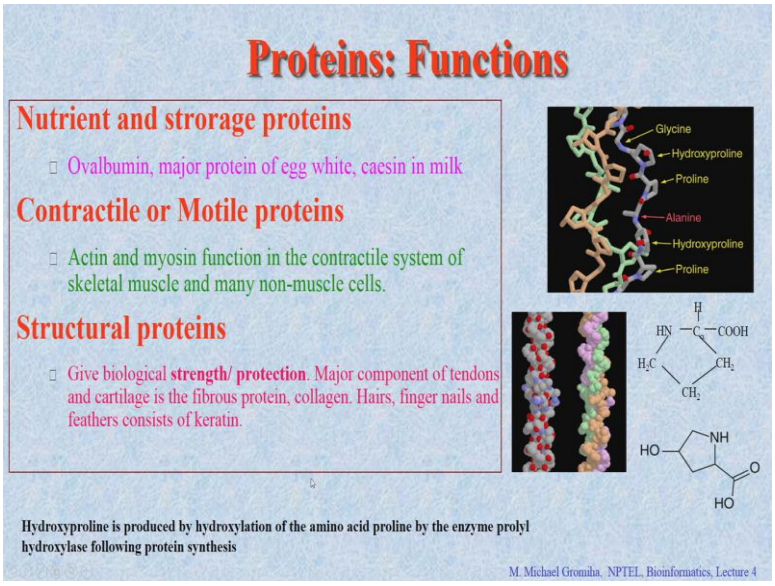

If you talk about the proteins then immediately they will about what are the proteins means they will tell about the (Refer Time: 03:56) eat beans. So, we will get lot proteins. So, there are various nutrient proteins like ovalbumin that is available in egg right like the egg white and the casein in milk and so on.

So, there are various proteins, they have different functions in living systems and we have these proteins for the proper function of our body right and all the cellular processes, then if you have different types of structural important proteins, right or this is called contractile proteins or the motile proteins right. So, for example, this Actin or the myosin; then function the contractile system of the skeletal muscle, then these are structural proteins right which gives the strength and protection for example.

Student: Keratin.

Keratin; right. It is a fibrous protein. Also the collagen right, for example, you can find this in hairs and fingernails, right and the feathers, right. So, you can see these proteins and this protein; they have some specific combination of amino acid residues like they have the combination of this hydroxyproline glycine and proline.

So, about this is the higher contribution of this protein. So, you can see the one third this is about the glycine and hydroxyproline as well as the proline. So, this gives the elongated shape to this structural protein like the collagen or keratin and so on, fine.

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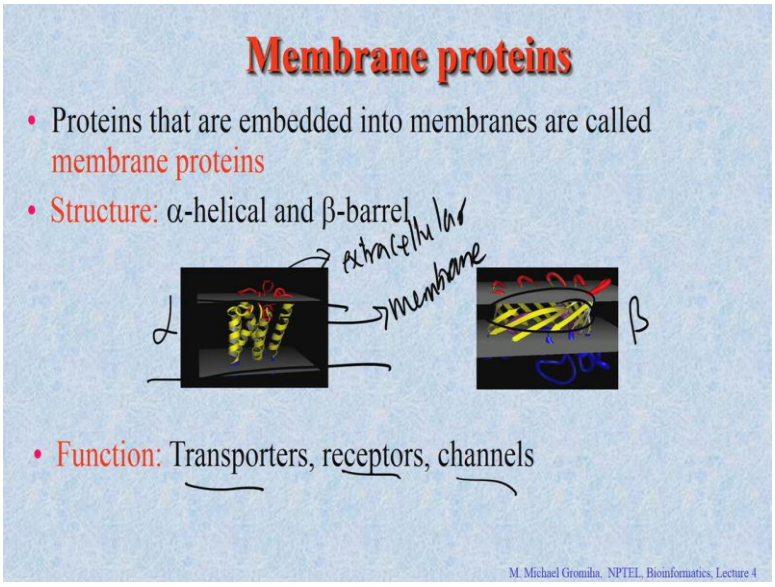

Then; first we discussed about globular proteins and the fibrous proteins and next step the membrane proteins right as you discussed earlier membrane proteins are embedded in membranes.

Student: (Refer Time: 05:39).

So, if you see; I give 2 types of proteins here this is a membrane and right. So, I have the membrane surface because here; this is the membrane and these are the proteins which are embedded in the membrane. So, this is the outside the extracellular space and here this is the membrane right and these proteins are as we have discussed earlier 2 types of proteins here, this is alpha and this is beta right you can see this is a beta-barrel conformation.

So, these proteins also go for various functions like the transporters or receptors and channels and so on.

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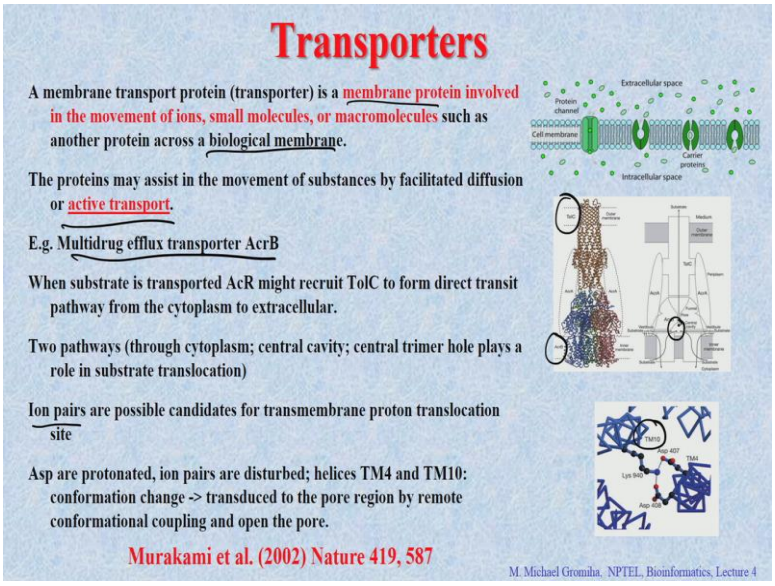

Just I will explain with this with few examples. So, here is one example for the transporters; right what is the transporter generally.

Student: (Refer Time: 06:25) transports a molecule.

Transports molecules; so you can say the transporter is a membrane protein which involved in the movement of ions or smaller molecules or macromolecules such as

another protein across the biological membrane. So, this transports right mainly these transports assists like the substance right mainly by the active transport right from the lower concentration to the higher concentration.

Then, for example, multidrug efflux transporter oh here is an example I give for the multidrug efflux a transporter AcrB right here how the transport happens here you can see the molecules. So, here this is the inner membrane right here this is the periplasm and this is the outer membrane. So, this is the protein involved in outer membrane is 12 c this 12 c and here the inner membrane this is the AcrB.

So, if you have this substance here right if the substrate is here right you can see the substrate you cross the membrane and the during this transport this transmembrane helix like transmembrane will extend right these are the residues which are involved in the electrostatic interactions like the Asp 407 and Lys 940 and Asp 408, they are disturbed right because these are the ion pairs are possible candidates for the translocation they are disturbed. So, the helices transformation helices will extend would change the conformation.

And goes here and due to the pumping mechanism, this will be pulled out through their outer membrane to the outside. So, this is how the; do the transport mechanism likewise there are various transporters which are known in the literature and they have different mechanisms to transport ions and the molecules across the membranes.

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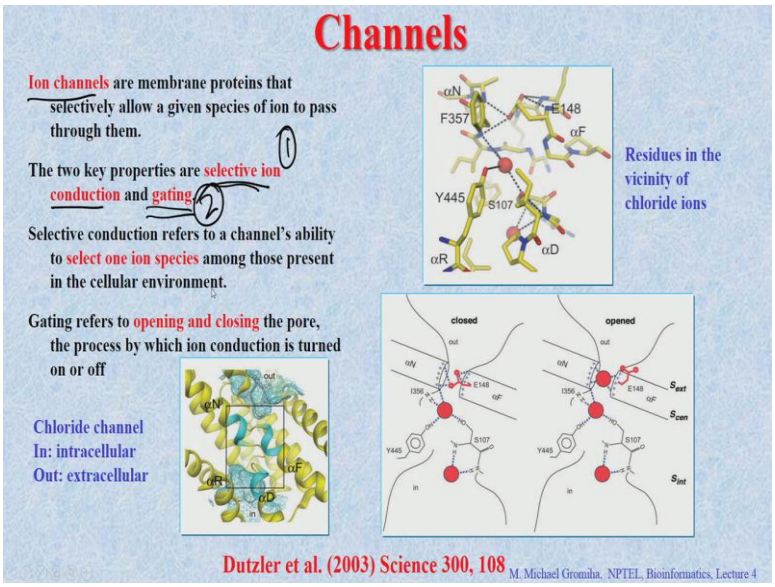

These are also membrane proteins, for example, ion channels right there are different types of ion channels right potassium dependent ion (Refer Time: 08:18) channel, chlorine dependent ion (Refer Time: 08:20) channels and so on.

And these proteins also they cross the membrane right selectively they cross the membrane there are 2 properties for this transport. So, one is the selective ion conduction and the second one is gating. So, one is selective ions means this will select only some ions, for example, they select a potassium, but not chlorine.

Likewise, they have they select some sort of selectivity. So, you should allow only to some ion and the second one is the gating; gating means for some cases it will open the channel. So, it will allow passing through and some cases it will close the channels. So, in this case, nobody can the molecules they cannot enter into these channels right ok.

So, if you see this example. So, this is the example of the closed and opened confirmation. Here if you see the molecules here the ion is here they want to transport through this membrane. And, here if you see this is glutamic acid 148 this 148 is here inside the membrane. So, in this case, it blocks the transport right now change the conformation and here this E148 moves away from the membrane to outside.

Now, the path is open and now this ion can pass through this membrane right this is the in this is out. So, here it is blocked and here; this you have space. So, it can go right. So, there are 2 different aspects one is the selective and conduction they will allow passing only specific ions and the second one is the gating. So, it has opened and closed confirmation right it changed the confirmation to allow to pass through into the membrane.

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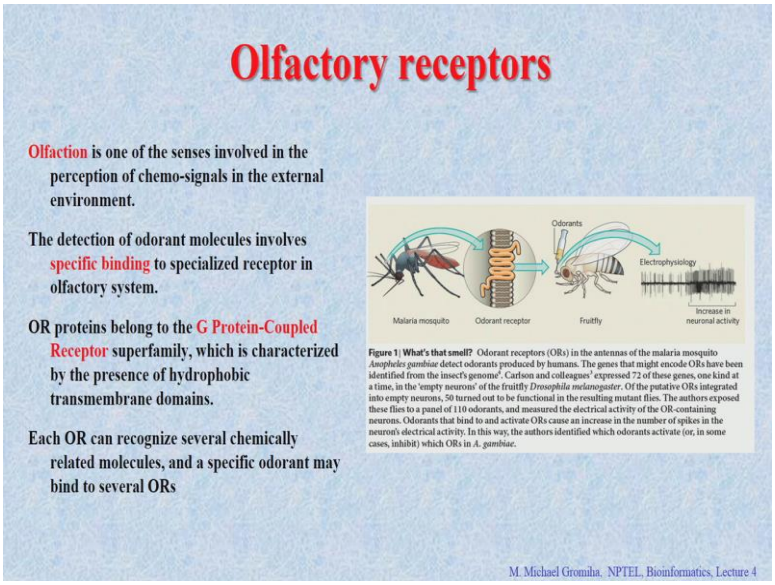

This is another example of olfactory receptors. So, olfaction is one of the senses involved in the perception of the chemosignals. So, how to get this olfaction?

Student: (Refer Time: 10:21).

To smell right. So, if you see malaria. So, it is one of the major causes because the mosquitoes can recognize human. This is why mosquitoes bite and then cause malaria. If mosquitoes cannot get this olfaction cannot recognize human, then we do not have any problem. Now, they try to understand whether this mosquitoes antenna contains some of the olfactory receptors because. So, they take the electrophysiology experiments they try to see the olfactory receptors in the antenna they found most of these receptors. This is how they recognize the human.

Also instead of the morning time, if you compare the evening time it can easily recognize human this is why they have a lot of mosquito bites in the evening, right. So, now, there are several research is going on to understand the olfactory receptors mainly in the GPCRs, see there are several methods they develop to identify these receptors and see how the mosquitoes can recognize; this type of receptors and what is the correspondence between the proteins in the mosquitoes and the proteins in the human and see how; what is the correspondence between these 2 to understand the olfactory receptors and address the issue of malaria.

So, now if we look into these functions right there are various functions, we described can you remember some of these functions still we discussed till now.

Student: Antibodies.

Antibodies.

Student: Structural proteins.

Structural proteins, enzymes.

Student: Transporters.

Transporters, regulatory proteins, receptors, transporters, right channels. So, we discussed various functions right and the functions of these proteins mainly depend on the structure right structure means I can say, here I can show one of the structures right how a structure looks like, this will help to dictate the function.

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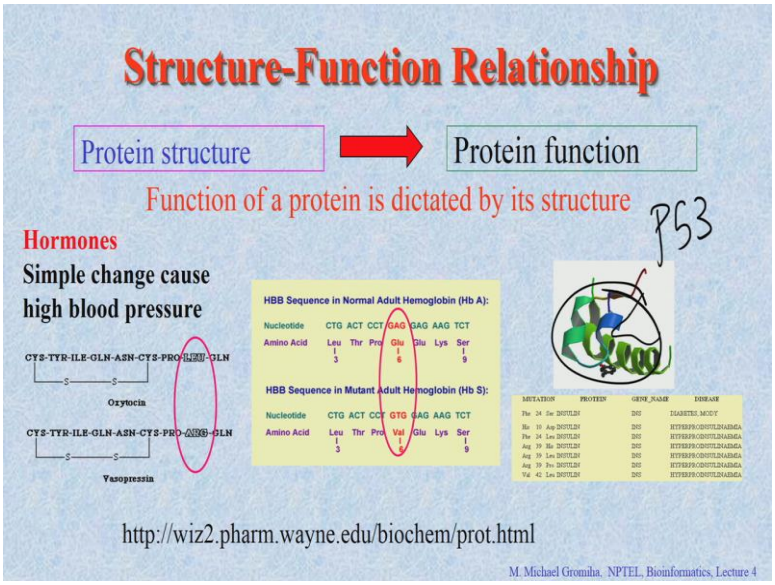

For example, I discussed about the enzyme, the active sites. So, if you look into the structure the active sites are not located inside the structure right because inside the structure it is completely compact, right. So, you can see where you can see the probable active sites. So, that the ligand molecules can enter and interact or any other molecule can go and interact.

So, if you go to the structure, if you see this only you can see a kind of pocket here, right. So, if you have a different structure right, now from this structures you can understand the probable active sites and where ligands can interact as well as inhibit the activity. Currently, we know that we have suffered (Refer Time: 12:59); various types of new diseases, right cancer and HIV and you can see the chikungunya, dengue and all; right. So, all these diseases they are targeted by some of the specific targets, proteins, right.

So, when you try to design the inhibitors they would like to have the structures because the function is dictated mainly by the (Refer Time: 13:20) structure. So, in different levels. So, it is as explained earlier. So, (Refer Time: 13:25) in case of the hemoglobin right the glutamic acid (Refer Time: 13:28) 6 is mutated to valine. So, it causes the sickle-cell anemia likewise a small change in the hormones like the leucine to arginine, it causes high blood pressure like in the case of several proteins like the insulin there is some changes cause diabetes and like the p53 you can see right. So, here is small changes, it causes which disease? Cancer.

So, if you understand the functions and if you understand the cause of the different diseases it is important to know about the structure.

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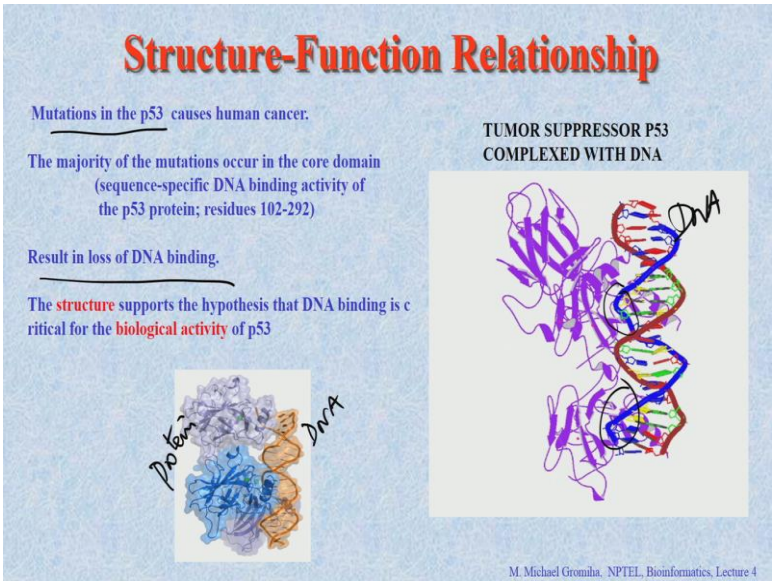

So, if I say one example; this is the p53, right where you can see a protein is here and you can see DNA here this is a DNA here you can see the protein it is a DNA binding

protein. So, the mutations in the p53; say if you make small changes mainly the replacement of arginine right it causes human cancer.

So, now how to understand what why these specific mutations cause cancer; what is the relationship between this function as well as from the structure, right. So, in this case, it needs to get the structure information because the structures are known. So, you can see the proteins right and this is a DNA and you can see the sites where the proteins can interact which is a DNA site.

You can see here the region where the proteins can interact with the DNA right. So, when you mutate these amino acid residues which are binding with the DNA and see how their activity changes or how they increase or decrease the binding free energy or the binding specificity. So, whether you see the DNA binding with the proteins and this will help you to understand how this specific mutation or the structure is important to understand the binding specificity of this protein DNA binding complexes as well as how this will effect to the diseases for example, in the case of cancer.

So, likewise, they try to get the features they try to understand the molecular mechanism or the basis of the diseases based on this structures. So, to understand the function this is essential to know about the structures and this is the reason why it is much emphasis has been given to understand different structures.

So, when you look into the protein structures. So, there are various levels of proteins structures.

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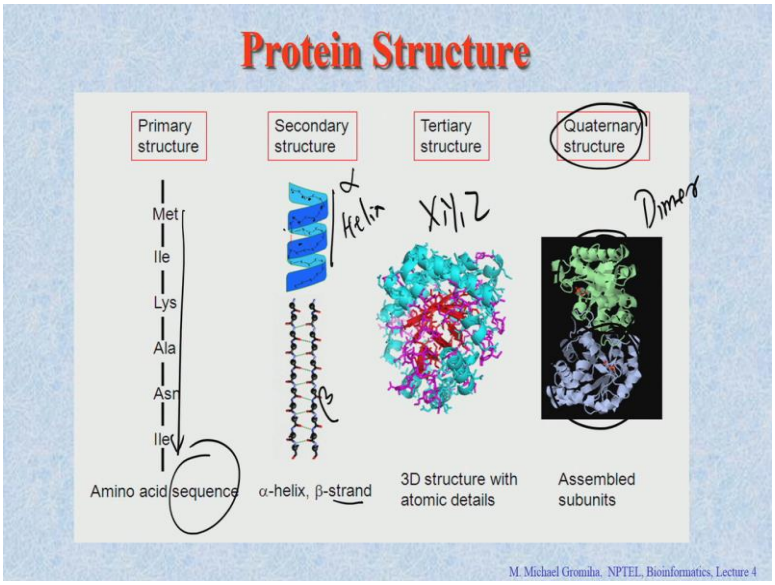

So, primary structure, secondary structure, tertiary structure and the quaternary structure just I will mention these names and we will discuss the details in the next class right

So, what is the primary structure primary structure deals with the combination of amino acid residuals? So, we can get the combination of amino acid. So, first is this methionine second is this isoleucine third this means lysine right. So, we can get this information and go to next level right here you can see the arrangement of this residues right here if this is the just the amino acid sequence right and when how these residues are arranged right. So, this will give you the next level of information. So, this is why they called a secondary structure.

So, here if you see they are kind of a helical shape like a spiral shape. So, this is why they called this as helix right and then the second one you can see there is this kind of a ladder. So, it is a kind of ladder. So, in this case, they put this is a strand. So, the first letter is Greek is alpha. So, they mentioned helix as an alpha helix and the second letters beta. So, they put beta sheet.

This is a secondary level and then go to a tertiary see if you see the secondary level tertiary level you can get more information here exactly how a protein looks like how the residues or the atoms are arranged in a 3D structure. So, It gives the complete picture of all the atoms mainly in the case of the coordinates like x, y, z coordinates right; this will give a tertiary structure then we go one step further

So, several tertiary structures they forms subunits they collectively form the quaternary structures right say if we say this is one chain this is another chain right the biologically they perform the functions once they form this a oligomers then if it is one is this monomer and it is more than one chain we call this as oligomer right. So, here you can see the 2 molecules right they are called a dimer right. So, they are very important for the function right. So, these type of structure this assembled subunits they are called a quaternary structures.

So, in the next class, we will discuss more about the primary structure secondary structure tertiary structure and quaternary structures and what are the information we gain from the primary structure or the secondary structure or tertiary structure, and how this information will be transferred to understand the mechanism as well as to understand the function, fine.

Thanks for your attention.