Host-Pathogen Interaction (Immunology)
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Lecture: 31
Introduction of Innate Immunity-Mucosal Surfaces and Microbiological Barrier

So, in previous session we have discussed about the mucosal surfaces~~ervices~~ we have taken the gut and we have taken the respiratory tract. In this and we have discussed about antimicrobial enzyme that is lysozyme. So, I will continue this antimicrobial peptide and their function and then I will talk about the microbiological or microbial barrier.

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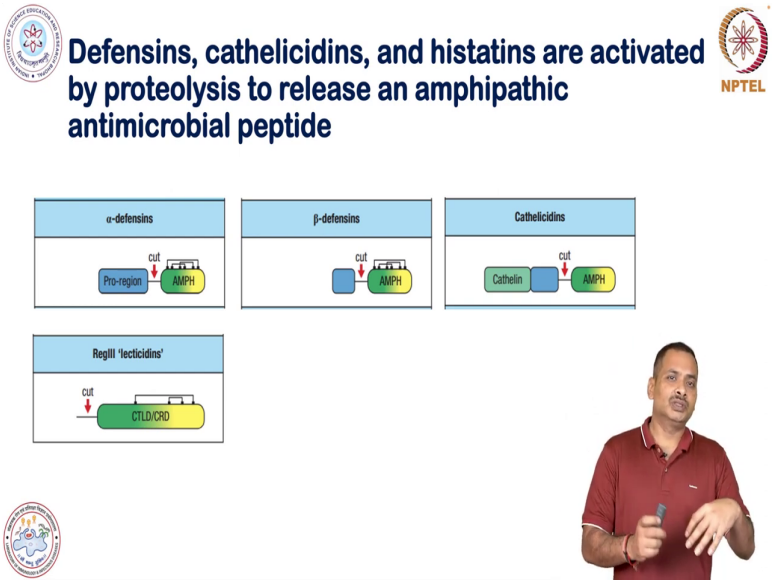

So, there are various proteins like a defens~~e~~in in cathelicidins, histatins and basically all these proteins are produced in inactive form in pro form. And these proteins upon activation they generate kind of amphi~~empty~~pathic antimicrobial peptide which has about polar and nonpolar region here you can see amp~~l~~hipathic~~fication~~. And here you can see that Alpha defen~~ee~~sin in which has a pro region and when it will be enzymatically cleave then that generator active Alpha defensin.

And this pro region is short in case of beta defensin and this upon cleavage it also generates the amphipathic beta defensin. In case of cath~~ee~~licidins there will be cathel~~i~~ens~~e~~ domain and there is a some pro reason which is again cleaved and then it will generate amphipathic active cathelicidins peptide and it is true for Regll~~dragly~~ or lacticidine for a protein. And basically

this overall once this amphipathic peptides will be generated for for all these cases like a defensein in different defensein in cathelicidine and lacticidine.

So, after this amphipathic peptide basically it will be attracted towards the microbial membrane system and once it will be attracted to the my microbial membrane it will basically go and deposit in such a way that it will make a pore.

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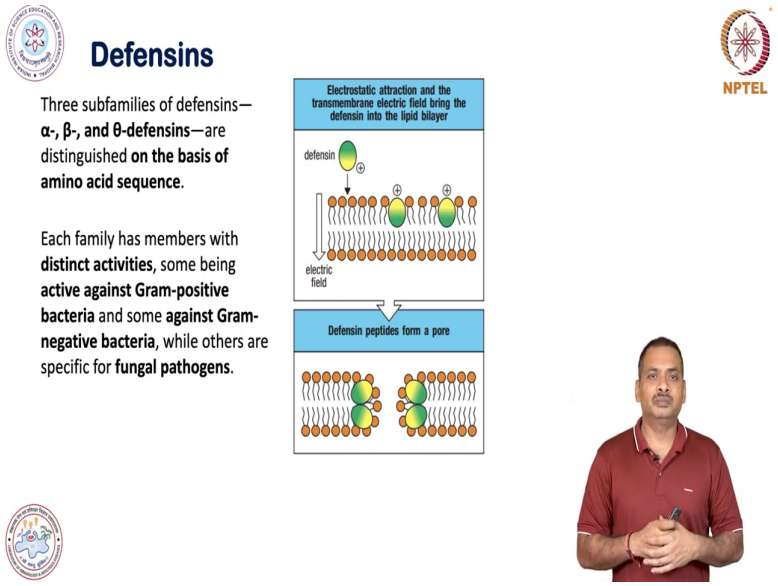

So, here you can see this mechanism I will show but before that I just want to say that defensinsve has a three members. So, there are three subfamilies that is Alpha, Beta and Theta defensinse in and these are distinguished based on the amino acid sequence. So, there are three major subfamilies of defensins. And each family member has a distinct activity and some are being active against gram-positive bacteria and some are active against gram-negative bacteria and some are playing important role against fungus they have antifungal property.

And how it works as I have explained you they are attracted towards the membrane of microbial pathogen it could be a bacteria gram positive negative or fungal membrane and then they are deposited in such a way that they will create a hole here you can see. So, this is electrostatic attraction and transmembrane electro electric field bring the difference in too close to this membrane and lipid by layer of the microbial pathogen and it will be deposited in such a way then that it will make a kind of pore here you can see. So, this is the way by which defensin act it is it is a quite common for other peptides also.

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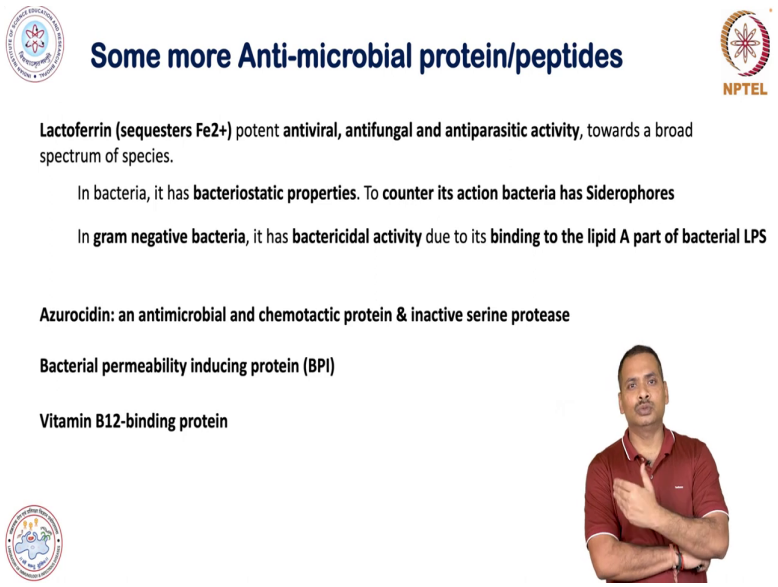

There are some more antimicrobial protein and peptides let me explain lactoferring. So, lactoferrin is a protein which is a predominant in breast milk. And the key role of lactoferrin is to sequester the iron ion and they are quite potent against viruses means they have antiviral activity they have antifungal activity and anti-parasitic activity as well. So, so this lactoferrin is a basically sequestering iron from the microbes ~~microbes~~ or microbial pathogen.

And then so in order to once the iron will be sequestered from this microbial pathogen then their activity will be significantly reduced. So, they have basically in bacteria they have a basically bacteriostatic property they stop the growth of bacteria and the bacteria to encounter this or to overcome this problem they have a variety of mechanism by which they can get the iron in order to maintain their multiplication or growth.

So, they have a like a Siderophores which is iron binding protein this is in bacteria. So, these hydro force basically take the iron and keep it with them and slowly they will transport inside the cell in order to protect from this lactoferrin thing. So, this is a very interesting that how this bacteria's keep iron by having this protein Siderophores~~syndroforce~~ this is one way. Another way is that they will develop some kind of receptor which will specifically bind with the iron which will attract the iron.

And then they will transport inside the cell in order to maintain their cellular activities in gram-negative bacteria this has some bactericidal activity as well basically it binds with lipid~~ase~~ A. So, lipid a if you remember the lipid structure sorry LPS structure not lipid if you

remember the lipopolysaccharide structure there is a one reason known as a lipid a and this lipid A basically it has a quite a strong immunogenic property among whole lipid.

So, in case of a gram-negative bacteria this lactoferrin can bind with the lipid Aa and somehow they will disrupt the outer membrane and then they can kill the bacteria as well there is a another protein known as azeuroci-sedine it has also antimicrobial property and chemotactic this is a chemotactic protein and having some serine protease activity it is also synthesized in inactive form.

And upon activation the serine protease activity get activated and they basically break down the proteins of the target entity that is anti-the microbes there is a bacterial permeability inducing protein. So, this is a the name itself is explaining the property. So, once this protein will bind then this will this will enhance the permeability with various ions there is a basically this will disrupt the permeability overall if you see carefully.

And in that way there will be a loss of iron loss of nutrient and then there will be a death of microbe. There is a vitamin B12 binding protein it seems it plays a very important role in in antimicrobial activity. So, some microbes may need a vitamin B12 for their growth. So, vitamin B12 binding protein is also playing a very important role as an antimicrobial peptide or protein and this is basically also sequestering the vitamin B12 and which is needed for the microbe to replicate.

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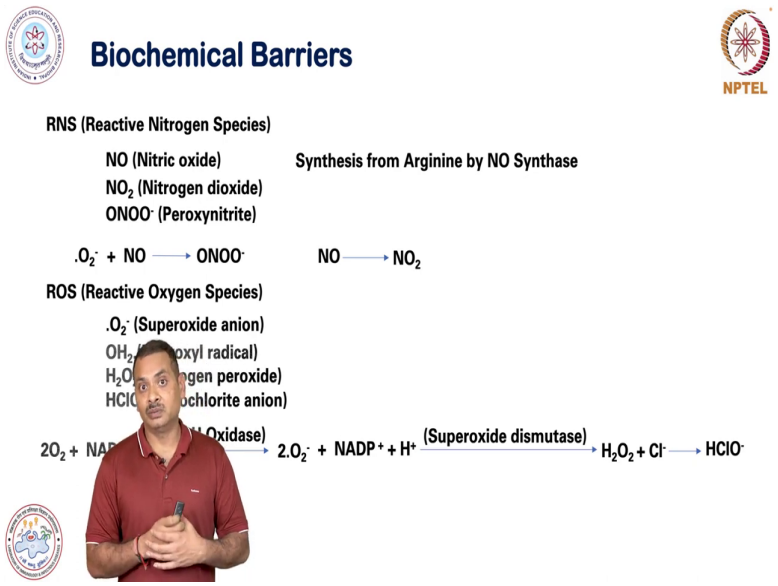

Now I will talk a few more biochemical barriers and which I have discussed in great length in neutrophils. So, I will just quickly move on to this slide. So, there are reactive nitrogen species you know there is a nitric oxide which is which is produced in the cell there is a basically it is synthesized by nitric oxide synthase and using arginine and there are nitrogen dioxides there are peroxy nitrite. So, all this makes a hostile environment inside the phagocytic cells.

And how this this is synthesized basically this superoxide ion react with nitric oxide and then this peroxy nitrite is synthesized from nitric oxide the nitrogen dioxide is synthesized. The ~~right~~ reactive oxygen species also present in these phagocytic cells and this is superoxide anion that is hydroxyl radical, hydrogen peroxide, hypochlorite anion. And there is a this is this superoxide anion is produced by the action of NADPH oxidase I have discussed in a great length in previous session.

So, I will not explain anything more that will generate the superoxide anion and by the action of superoxide dismutase~~tributes~~ this hydrogen peroxide synthesized which react with the chloride ion and then this gives a hypochlorite anion. And all these species these reactive nitrogen and oxygen species are very potent antimicrobial or it it can react you can know you know by the knowledge of chemistry they can react with anything and then they can destroy. So, this is one of very important kind of biochemical barrier.

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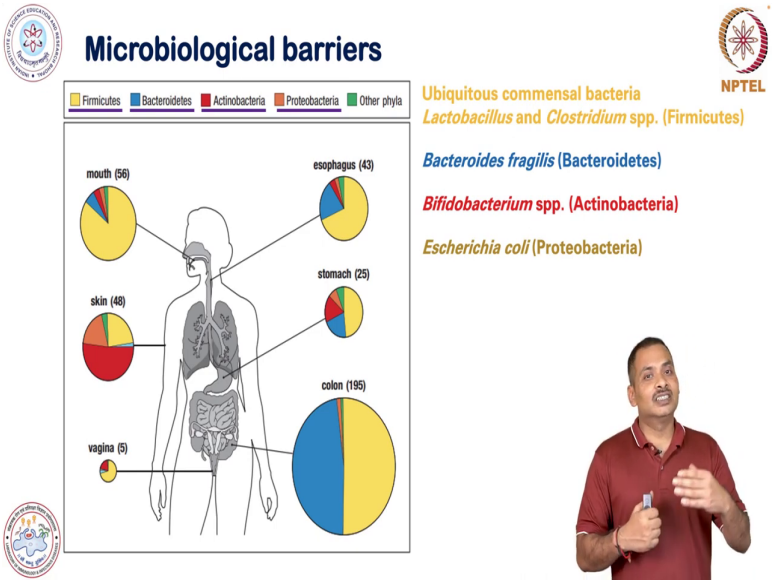

Now I will move to the microbiological barrier and this image is quite sufficient to explain a whole microbiological barriers here you can see there are there is a huge number of microbes

present in different region. Here you can see there is a in mouth there is a big amount of this Fermi-cuties this is a family of microbe. And it is not only present in more amount in mouth it is also present in esophagus stomach and colon and vagina.

And this make this constitute a huge amount of biomass as well and another is a there is a bacteriaoi-dietes and actino-bacteria and proteobacteria. So, so what is this Fermi-cuties. So, basically this is a commensal bacteria which is a basically species of lactobacillus and close-tridium and that constitute such a huge mass it is present on skin also. Another is a there is a bacteroides fraudgilisy-list which constitute another big mass of bacteria that is bacteria dits.

And the third one is actinobacter and actinobacter is a baffido-Bifidobacterium species and this also present in quite good amount if you see very carefully it is present in huge number in skin there is a proteo-vbector basically this is a E coli species and their number is more in esophagusoesophagus and stomach and quite less in Colon and vagina also and mouth also but these are also present. So, it is very interesting that E coli is present in our body.

So, these are the basically commensal bacteria and you know if this commensal bacteria are disturbed by taking antibiotic then that will disturb the whole gut system. So, that is how doctor prescribe probiotic along with this antibiotic. Another thing is that sometime due to some immunological problem our immune system start reacting with these commensal bacteria. There are so, many reasons it is a huge topic.

So, in that scenario this there will be a the individual will develop a inflammatory bowel disease and this inflammatory bowel disease is quite complicated it is it is really very have-Painful disease. So, they whatever they will eat then there will be some pain or cramp and all those things and this there are so, many inflammatory bowel disease one is Crohn's disease.

So, over there this basically in that scenario this anti the immune our immune system is start reacting with commensal bacteria and that creates a problem. So, this is all about the microbiological barrier and with this I will stop here and in next session I will take you in great length about the pattern recognition receptor which is a quite a huge field which is recently discovered and if you remember my previous session this work also received the Nobel Prize.

If you remember there are two key workers who received the Nobel Prize one is Bruce Butler and another is a Julie Hoffman in 2011. So, we will discuss their work as well as we will discuss the work of two major researchers that is a ~~Ruslan Madguitov~~ Ruslan medzhitov and Shizuo Akira. So, I will not take the precise work but I will give you overview about the pattern recognition receptor and we will discuss every family of pattern recognition receptor, thank you.