Host-Pathogen Interaction (Immunology)
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Lecture: 29
Introduction of Innate Immunity-Physical, Bio-chemical and Microbiological Barriers

Hi, so in previous session, I have initiated the innate immunity and I basically gave you a very overview or introduction why innate immunity is needed and I have also talked how the if the pathogen in come in contact with the host then how this will be defended there are several layers of protection like anatomical barrier then if it breaches. And then there will be another set of immune cells mainly net immune cells they will come and remove.

And if it is further not removed then there will be an activation of those immune cell and they basically sense the pathogen associated molecular pattern and then that subsequently eventually these microbes will be transported to the nearest lymph node in order to develop more specific immune response which is mainly mediated by B and T lymphocytes. So, now let us move further about the innate immunity more precisely or more deeply in the innate immunity.

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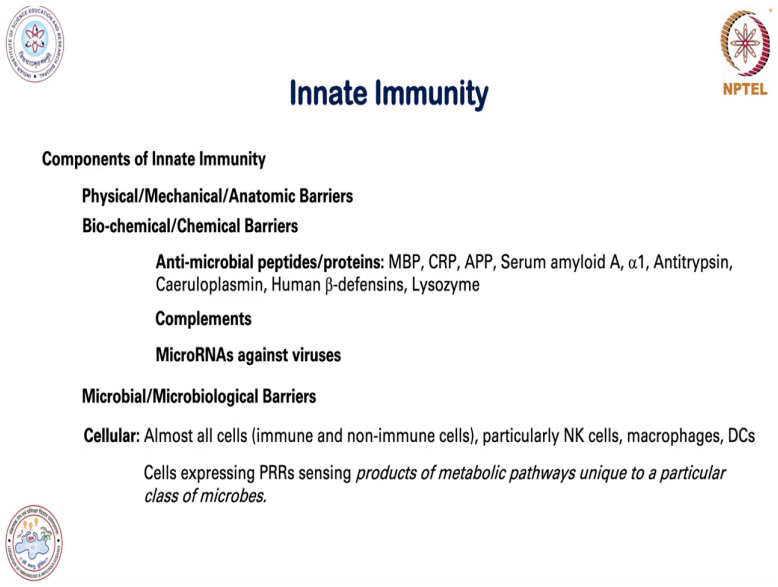

So, basically innate immunity is consists of various components. Components are like here you can see there is a physical mechanical or anatomical barrier. So, I will talk in great length about this physical, mechanical, orare anatomical barriers basically it is consists of our lining

the lining in the body if you know that the skin is the largest external organ in our body. So, over there is a variety of mechanisms are there which protect us from this microbial invasion- ~~region~~ there is a biochemical or chemical barrier.

So, it is a not just a kind of barrier it is not a like a wall of house the mechanical barrier is not only the mechanical barrier this is live they produce some or other kind of chemicals these this physical barrier and they defend against the entry of microbial pathogen. So, basically they the molecule which is secreted by this barrier we call it as a antimicrobial peptide or protein or sometimes we also call it as a antimicrobial enzyme there are some enzyme are also secreted.

So, these are basically here you can see MB~~D~~P it is a mannose binding protein and this is a basically a lectin family protein I do not know you may probably studied that lec~~ae~~tins are all those protein which is binding with the sugar molecule. So, those proteins we call it as a lec~~tem~~in. So, Mannose binding protein the name suggests that it is basically binding with the Mannose which is present in the microbial pathogen there is a CRP C reactive protein this C-reactive protein is a basically also produced in order to defend the microbial pathogen.

There is a APP this is nothing it is a acute phase protein which is mainly synthesized by liver and these proteins are also defending against microbial invasion. Similarly, there is a serum amyloid A Alpha One antitrypsin human beta defens~~e~~in in and there is a antimicrobial enzyme which is produced by a variety of cells which basically breaks down the bacterial cell wall probably you know that lysozyme act on peptidoglycan.

And this this enzyme basically breaks down the peptidoglycan and then they eventually kill the microbial pathogen. So, these are the various biochemical and chemical barriers. Another the most important biochemical barrier is complements. So, complements are the set of protein which basically synthesized in the liver and this complement basically do three things which I have told you in previous session also I will quickly tell that.

They basically induce inflammation, they also opsonize ~~optionize~~ the target microbes so that it will be readily phagocytosed by phagocytic cells. They will also make a kind of a complex which we call it as a membrane attack complex. So, this membrane attack complex basically

makes a hole in the microbial pathogen. So, that eventually this microbe will die. So, complements we will discuss in more detail in subsequent session in innate immunity.

There are some micro RNA's also against mainly RNA or DNA viruses only RNA viruses. So, there are some micro RNA's. So, micro RNA is nothing it is a non-coding small RNA this non-coding is small RNA plays a very important role in gene regulation expression of Gene regulation. They basically in general they bind to the three prime UTR of the transcript and they regulate the expression of or further translation of this transcript.

So, some micro RNA basically they either bind to the Genome of virus mainly RNA viruses and they basically reduces the replication of viruses this is one way. Another way is that when there is a virus infection this micro RNA can bind to the negative regulator of innate immune signalling pathway. So, when it will bind to the negative regulator of innate immune signalling pathway then what will happen it will activate or it will induce more antiviral expression of gene.

So, in this scenario the microbial pathogen or here I am talking RNA viruses will their replications will be reduced. So, these are some of biochemical or chemical barrier. Another barrier which plays a very important role is microbial or microbiological barriers. So, if you remember my previous session there are two kinds of interaction which is present in with the microbe that is commensalism and another is mutualism.

So, in commercialism and mutualism the bacteria or the microbial pathogen or microbes not pathogen I will not say pathogen they are microbes. So, they interact with the host and in some or other way they give a benefit to the host. So, microbial barrier is playing a reasonably very important role in defense. So, they grow in huge number and they do not allow to grow the pathogenic microbes.

So, their outnumber is also important in addition they produce some substance which basically inhibit the growth of pathogenic microbial pathogenic microbes. So, in that way this microbial barriers play extremely important role in defense. Another is the cellular component. So, this cellular component is basically when I say innate immune cells. So, basically all cells come in innate immune cell that includes immune cell as well as non-immune cells.

Particularly NK cells are so, these are professional innate immune cells like macrophages, NK cells, dendritic cells now you know there are so, many kinds of macrophages present in different organ. There is a two major kind of dendritic cells although there is a three but here I am telling two because they are playing important role in innate immunity one is that conventional dendritic cells and another is plasma-cytoid dendritic cells.

FDCS are playing important role in adaptive immunity. And these cells basically ~~e~~Express a germline conserved or germline and coded a receptor which we call it as a pattern recognition receptor. And this pattern recognition receptor basically senses the products of metabolic pathway of this microbe and then it will induce some kind of signalling and the result of this signalling will be production of inflammatory cytokine type 1 or type 3, interfer~~e~~on~~se~~ and so on.

So, we will discuss this in a great detail this pattern recognition receptor there are several families of pattern recognition receptor. For example, toll like receptor there is a ~~ring~~RIG-I-~~like this regard~~ like receptors, there is a NOD-~~nod~~ like receptor. So, we will discuss all this family of pattern recognition receptor one by one in subsequent session. So, now let us go back to the physical and mechanical or mechanical or anatomical barrier.

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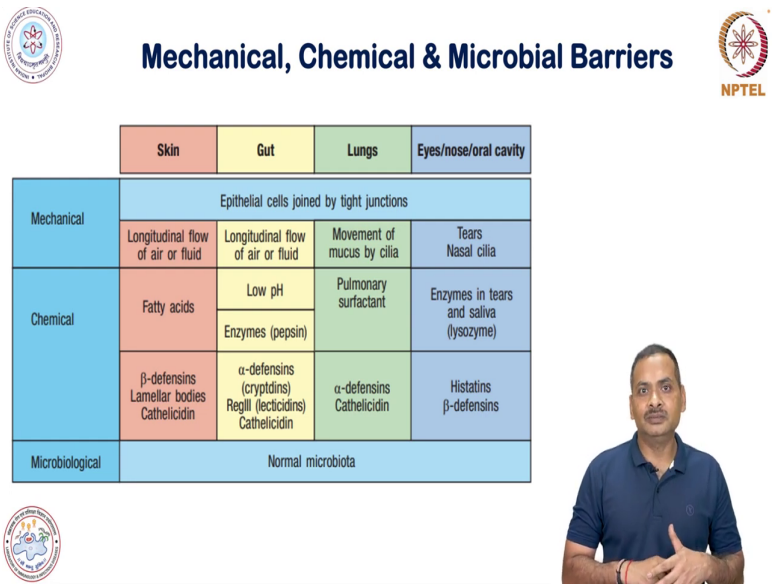

So, here you can see how this mechanical barrier is playing very important role in defense. So, this mechanical barrier in skin is basically constitute with this epithelial cells joined by a very tight junctions they are very tightly packed. So, microbe cannot enter it is a it is a quite

rigid it is it is like that the wall is very strong the wall of house is very strong nothing can just go even water cannot go if you make a proper wall.

It is something like that it is a wall or guard in our body. Besides this in skin there is a longitudinal flow of air or fluid that prevents the entry of pathogen in gut there will be a longitudinal flow of air and fluid we will discuss about the mucus. So, in our gut there is a continuous flow of mucus that prevents the attachment of microbe or entry of the microbe in lungs also there is a movement of mucus by Celia.

So, Cielia is keep on moving layer keep on doing this job and make the mucus flow that is another mechanical barrier. In eyes, nose and oral cavity there in eyes there is a tear this tear is keep on flowing and keeping a kind of to layer over our eyes and this tear basically consists of lysozyme if you if you maybe you have studied in nasal cavity nose there will be a cilia there will this is keep on moving.

So, this is providing a kind of mechanical barrier there is a chemical barrier in these places in a skin there are some fatty acids produced by microbe as well as the cells and basically this does not allow the growth of other microbial pathogen. There is a production of some antimicrobial peptide like beta defensin and there is a one more protein which is produced by these cells is cathelicidin and this is these molecules are present in some kind of some kind of structure which we call it as a lamellar bodies.

So, this is keeps on throwing. I will talk more about the denfensinifference in and this cathelicidine how it works in maybe in subsequent session. In gut we have you all are aware that in gut there is a low pH there is a production of hydrochloric acid which inhibit the growth of any microbial organism or any microbes including pathogen. There is a enzyme secreted In the gastric juice which you know there is a variety of enzyme peps-in, trypsin and there are some more enzymes.

So, this these things basically different against this microbe microbes or microbial pathogen in addition there is some antimicrobial peptide like alpha defensin which we call it as a cryptidines, regal which we call it as a lacticidine. So, all these antimicrobial peptides are also produced in the gut there is a some specialized cell you will see in subsequent session we call it as a panieth cell.

So, these cells will basically produce these molecule and different against these microbial pathogen. In lungs there is a movement of mucus by Cielia in gCut also there is a there is a continuous production of mucus there is a some specialized cell which is present in the gut we call it as a goblet cell I will discuss in more detail. In lungs there is a also production of mucus which is the movement is mediated by ciliary movement.

There is a some surfactant there is a pulmonary surfactant which basically. So, surfactant is which reduces the surface tension like if you um. So, you know the Maybe the concept behind cleaning of cloth we use a detergent. So, basically this will this will solubilize the fat and this has a both polar and non-polar group and they are basically acting like a surfactant they remove this dirt. So, something like that it is not precisely that but something like that.

So, pulmonary surfactants there are some molecules. This also produces a alpha defensein in and again cathelicidinecatholicidine is also present. In eyes and nose and oral cavities there are as I told you there are some enzyme in tear like lysozyme in saliva also it is present and that different against this microbes it is irrespective of pathogenic or non-pathogenic histatinmes are also present these are proteins or antimicrobial peptide and there is a beta defensin.

So, all these molecules are doing they are continuously doing their job that is why we do not fall sick we rarely false it right not every moment we are sickector right because these mechanical and chemical barrier are keep on working. In addition there is a microbiological barrier which has a normal microbiota probably you might be noticed when when you take antibiotic at that time this normal microbiota are destroyed some of them not all here but majority and that gives some problem stomach upset and all those things.

So, the doctor prescribes or now there is a lot of advertisement about the probiotics. So, probiotic is it is nothing just providing those microbes the sporets of those microbe in order to reconstitute or re remake this destroyed normal microbiota. So, you can understand the importance of this microbiological barrier.

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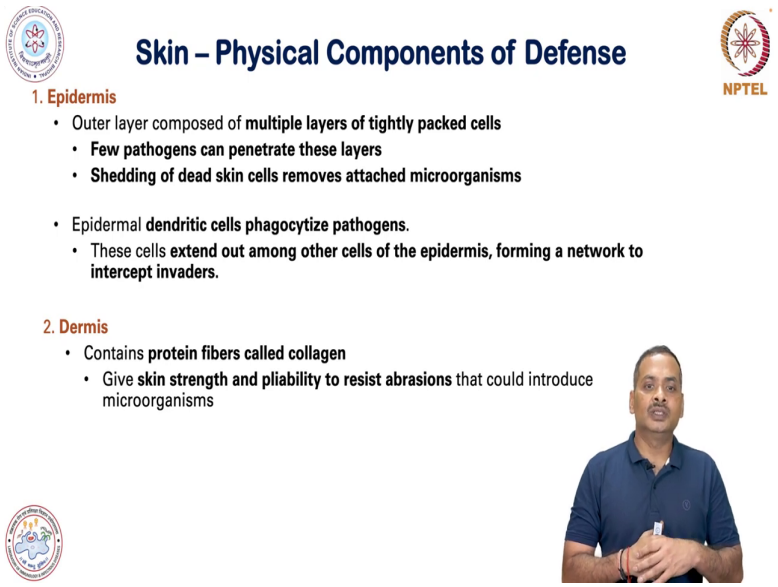

Now I will talk about the skin in more detail is physical component of difference. So, here you can see that there is a multiple layer of tightly packed cell which basically does not allow the entry of pathogen and this ~~is~~ ki~~neen~~ keep on shea~~da~~ping off its dead skin dead skin cells are keep on falling off and whatever if some microbe will attach then that will be also thrown out. So, in that way this is giving a protection and this is mainly in epidermis.

You remember that there is a one specialized phagocytic cells are there in a skin epidermal layer which we call it as a Langer~~-~~hang cell. So, that there is a presence of dendritic cells in the epidermal layer which phagocytose this pathogen and these cells are basically extended out among other cells in epidermis forming a network of intercept in invaders this basically intercept the invaders there is a dermis layer there is a you know the structure of a skin probably you may remember if not please take a look it is a simple structure.

There is dermis layer which contain a protein fiber called collagen and this basically this dermis is giving a skin strength and ~~palatability~~pliability to resist the abrasion that could be introduced by the microbe or microbial pathogen.

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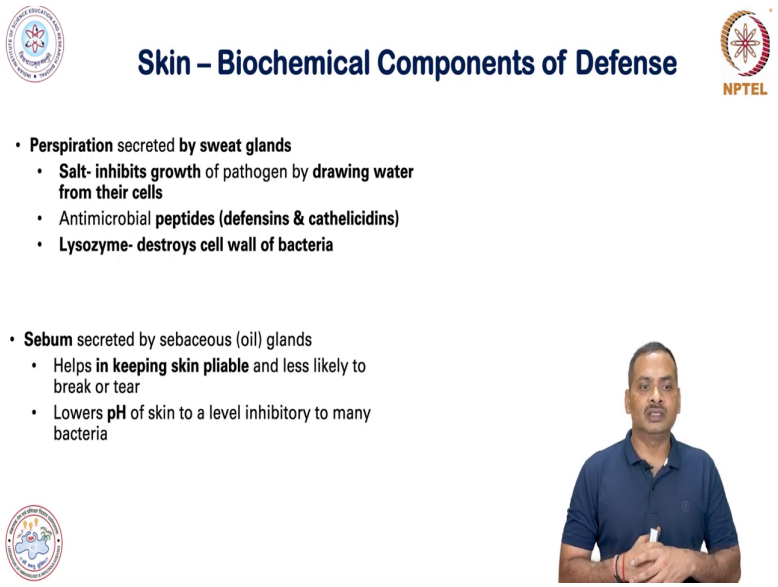

There is a biochemical component of defense in skin and basically it is a mediated by a perspiration basically secreted by sweat gland we have sweat glands and that produce some salt which will inhibit the growth of microbes by drawing water you know that concept of osmosis. So, if there will be more salt then this will draw the water from microbe microbial cells in that way this will also initiate some kind of killing or defending against the microbial pathogen or microbes.

There is a some antimicrobial peptide as I have told you in previous slide there is a di~~e~~fensin~~ference~~ cathelicidine ~~in~~ I will tell the mechanism in later session there is a anti-microbial enzymes like lysozyme which destroy the bacterial cell wall that is peptidoglycan there is a production of sebum secreted by sebaceous or oil gland helps in keeping skin ~~valuable~~pliable and less likely to break or tear this also maintain low pH in skin skin. So, that there will be inhibition of these microbes.

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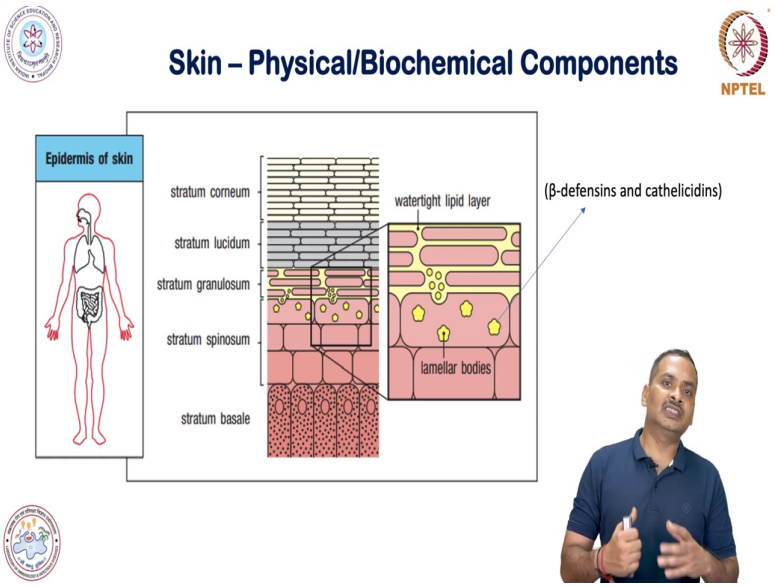

Here I will show you the skin is a one of the largest external organ and they have a several layers. Here you can see that there is a stratum spinosum, stratum granulosum and ~~spread a~~ stratum lucidum, stratum corneum. So, this is stratum corneum is keep on the it is a mainly dead cells stratum lucidium is basically below this cornea and stratum granulosum is in between lucidium and spinosum as you can see in this picture.

And here if you notice there is a yellow kind of laminar bodies and these laminar bodies basically contain the beta defensin~~inition~~ and cathelicidin and there will be a growth of this stratum spinosum and that is pushing out. So, towards terminal there is a dead cells which is giving a kind of mechanical strength and in addition this will also produce some kind of lipid layer its which is a watertight lipid layer and in that way the microbial pathogen cannot enter.

So, I will stop here for this session in next session I will discuss about the gut how what are the arrangements are there in the gut as well as in respiratory tract and I will take it further, thank you.