Immunology
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Lecture-6
Innate Immunity

So, welcome to the lecture 6 of this immunologic course and myself Agneyo Ganguly and I will be also teaching you some parts of the immunology course along with professor SK Shosh. So, we will start discussing about the whole network of the immune network and we will start discussing with the innate immune system.

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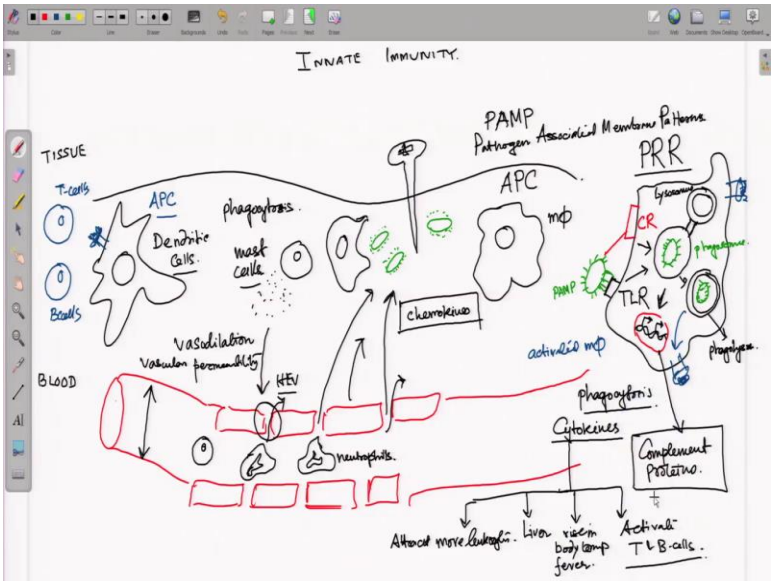

So, what is the init immunity and how does the init immune system works. So, before we start with the discussion about the init immunity let us try to understand how the different branches of the immune system actually works and how the coordinates. So, whenever let us say whenever there is an invasion in the body what are the initial barriers that a pathogen has to cross. So, initially whenever there is a tissue damage or an invasion.

So, the first barrier a pathogen would come across is the anatomic barriers for example like the scheme the mucous membrane so that it will not be able to penetrate. Now if it crosses this kind of anatomic barriers then it has to face the physiological barriers. Now the physiological barriers

clearly includes certain very important things that we come across whenever there is a infection you see rise in body temperature.

So the body temperature rises so that most of the pathogens they do not survive in this temperature and the acidity of the stomach for example so the stomach is highly acidic so most of the pathogens they do not survive there. So, this is the second barrier that is the physiological barrier and then there are many other, chemical mediator which also immediately come into play and try to restrict the pathogen from attacking our body.

So this is a kind of physiological barrier and then we have the phagocytic barriers. So, now the phagocytic cells that is the cells of our immune system the very important cells of our immune system are the phagocytic cells they will immediately come into that site of action and they will now try to engulf those pathogens and kill them. So, that clear the pathogens from the system and finally you can have an inflammatory response.

An inflammatory response means you will have some mediators of inflammation that are being released and then you will have swelling redness and many other acute inflammatory symptoms that will immediately start. So, this entire thing that occurs in the very first phase of an pathogen invasion or an immunological challenge these are all from the innate immune system. The innate immune system is the first line of defense of the body.

When this innate immune system cannot clear the pathogen or let us say the fact it is new for the body. So, the body has never seen that pathogen before let us put it in this way so in that case the innate immune system will not be able to clear the pathogen and now it is job is to transfer the signal from the unit to the adaptive system that means the cells of the adaptive system. Who are the adaptive system cells? The cells of the adaptive system are the T and the B lymphocytes.

So the signal will now be transferred from the innate system to the adaptive system and now the T and the B cells will be activated and you will have either a T-cell mediated response or a humoral response there is a B cell mediated response. So, this is kind of a very well coordinated

network. So, initially the init system tries to fight the pathogen with all its possible weapons and its weapons are mostly the phagocytic cells, various chemical mediators, complement system.

We will discuss all these things in details later on one by one. So, the complement systems the cytokines there are many chemical mediators which are working in the init system so they will try to clear the pathogen first they will try to clear the infection. If it fails it will transfer the signal to the adaptive immune system and this signal transfer primarily occurs via some antigen presenting cells.

Now the name you can already understand from the name that they are presenting the antigen. So, they are antigen presenting cells they will in some way they will try to present a new antigen to the eruptive system and then the adaptive system cells will get activated and either they will produce antibodies like from the B cells or they will activate the T cells and will kill those pathogens. So, now let us see how this innate immune system actually works.

If you look into the board here so you see here that whenever there is an infection or a tissue damage there are bacteria's or pathogens that are coming into the site of action. So, these green ones these are the bacteria's for example and if we consider this as the blood stream this part this is the blood stream so the blood is flowing and many immune cells the cells of the immune system they are present here like the mast cells, the neutrophils and there the neutrophils the mast cells they are all present here.

So now these cells will start immediately they will start to migrate to the site of action. How will they migrate there is a specific mechanism by which this cell starts to migrate to the site of action and then you have tissue macrophages, the macrophage cells. There is the tissue macrophages that are already present the tissue mass cells these are already present there. So, now these cells which migrate there will try to engulf the pathogen by a process called phagocytosis.

And the first cells or the immediate acting cells which immediately go to the site of action are this neutrophils. So, the neutrophils are kind of the first acting cells of the immune system that means they are the fastest acting cells and they immediately go and try to engulf or phagocytose

the pathogens or eat them up. Other than that there are also some other chemical mediators and chemical proteins which actually they mediate this migration that means they try to attract more and more of the cells of the immune system to go to the site of action.

They are for example the chemokines we will discuss them in details later on just for the time being I am just using the terminology. So, like for example the chemokines there are other mediators as well. So, is chemical molecules they are chemoattractant so they will attract more and more of these cells of the immune system like for example the neutrophils the mast cells they will move to the site of action.

And then there are a lot of signaling going on in this region we are not discussing them in details right. Now for example these mast cells what are the mast cells do? The mast cells they contains granules inside them and these granules are full of histamines. So, whenever there is an infection for example the histamine is released and this release of the histamine one of the primary action of the histamine is to do Vasso dilation.

And increases the vascular permeability so it increases the vascular permeability and there by that is why it allows more and more of these cells of the immune system to migrate to the tissue. So, by that more and more of these neutrophils the macrophages more mast cells they move to the tissues and there are also the tissue dendritic cells present here. This dendritic cells are one of the most important cells of the immune system.

So these are the dendritic cells so what do these dendritic cells to the dendritic cells has a very very important role to play. The dendritic cells are actually one of the major cells that connects the innate system to the adaptive system and the macrophages as well. So, these cells primarily the dendritic cells and the macrophages they are also known as the APC or the antigen presenting cells so they present the antigens.

Now how do they do that so as I described here if you look into the picture again there is a insect bite or a tissue damage or an nail piercing the tissue and then there are bacteria's coming in. Now these bacteria's are the initial function of the immune system is to send the cells or the

phagocytic cells to this region of infection and leading to engulfment of the bacteria. So, the bacterias or the pathogens that have entered are engulfed by the phagocytic cells.

And then there is also release of histamine from the granulocytes like the mast cells and leading to vasodilation vascular permeability increase and leading to migration of more of these cells going or moving to the site of action. Now how do the cells of the immune system they actually recognize these bacteria's or the foreign pathogens. So, there is our specific feature on the surface of the bacteria's which we describe as P A M P which is also known as pathogen associated membrane patterns.

Now these patterns are recognized by specific receptors which are known as pattern recognizing receptors. So, these are the PRR's. Now this PRR's they can recognize this pathogen associated membrane patterns on the surface of the pathogen or on the surface of the bacteria's. So, one of those specialized cells who can recognize this PAMP's are for example the macrophages. And this macrophages so let us see what exactly a tissue macrophages doing in this situation.

So let us say this is a tissue macrophage and this tissue macrophage expresses on its surface a receptor specific receptor or this PRR kind of receptor like the toll-like receptor the TLR and this toll-like receptor is one of those important receptors which can recognize the PAMP's. The PAMP's that are present on the surface of the bacteria's. so, here you have the PAMP's which are recognized by the toll-like receptors.

And then there are also the complement receptors the CR's so by virtue of these compliment receptors and the toll-like receptors these macrophages they can recognize the foreign bacteria's. Now what happens there is a process called endocytosis. So, now it eats up the foreign pathogen or the foreign bacteria so it is been eaten up by the macrophage so and it is being internalized so then the process is called phagocytosis.

And it has been eaten up and the bacteria is then internalized and this is called a phagosome what is formed is called a phagosome. And then inside the cell there are acidic compartments which are known as the lysosomes. So, the next event that occurs immediately after this cell eating is a

fusion between this phagosome and the lysosome leading to the formation of a phagolysosome this is called a Oh phagolysosome.

So now this a phagolysosome is being formed which contains this bacteria which is being internalized and now it degrades the foreign pathogen and degrades all its components like the proteins the carbohydrates everything that has been internalized everything is being degraded and chopped up into small pieces into small peptides. And these small peptides are then displayed on the surface they are now being displayed on the surface of they are displayed on the surface of the macrophages.

Thus peptides are these bacterial peptides they are now displayed on the surface of the macrophages by a specific class of MHC molecules and which is actually required for transferring the signal to the adaptive system that is for activation of the T and the B-cells. So, this is what this entire event that we described in this part here actually shows it for a tissue macrophage. Now this macrophage is now is an activated macrophage so it is activated.

So it is an activated macrophage. Now what does this activated macrophage do? This activated macrophage actually does a lot of things. So, this same thing we can see also in case of a dendritic cell. So, the dendritic cell is also an antigen presenting cell and whenever there is this kind of a response the dendritic cell is also able to internalize or phagocyte those bacteria's and pathogens and they can also present on their surface the peptides processed peptides from those bacterias or from those pathogens to the cells of the adaptive system.

And these dendritic cells by a process called licensing because normally the dendritic cells they cannot enter into the or these antigen presenting cells they cannot enter into the adaptive system. So, whenever there is an immunological challenge and the unit system first try to face that immunological challenge try to clear the pathogen from the system. If it fails to clear the pathogen from the system it starts a process usually by help of this antigen presenting cell it starts phagocytosis primarily by antigen presenting cells like macrophages or the tissue dendritic cells.

Now these dendritic cells and the macrophages they then go to the lymph nodes and by going to the lymph nodes there they meet the B cells and the T cells. So, there are the T cells and the B cells but these are naive that means they have not yet met any foreign pathogen. So, this are the naive T and the P cells that are usually present in the lymph node waiting for the signal to come from the antigen presenting cells and from the innate system and then they are activated and then antibodies are produced and other humoral responses and other cell mediated responses are triggered.

So let us see what happens in this part. So, now this activated macrophage the macrophage which has already internalized or already phagocytosed a bacteria or a pathogen is now activated and inside that leads to in the in the nuclei that leads to expression of certain genes. So, there is gene expression. So, there is expression of certain genes leading to secretion of a class of molecules which are known as the cytokines. Cytokines are very important effector molecules in this immune system.

So they are the effector molecules of the immune system and they can do a lot of functions they can do a lot of functions by activating the B cells and the T cells they can do many other functions. So, we will discuss about this cytokines in specific classes. And this cytokines and the downstream signaling can also lead to the secretion of another kind of protein which are known as the complement proteins.

Ao what does this cytokines actually do? This cytokine can lead to or they can attract more leukocytes to the site of action as I told before they can attract more leukocytes to the site of action. So, for example the chemokines which is also a class of cytokines so they are also involved in attracting more of these cells to the site of action. They can stimulate the liver and lead to secretion of specialized proteins like the complement proteins they can also lead to a fat hypothalamus leading to rise in body temperature.

So you have fever for example and they can also activate they can also activate the T and B cells. So, the cytokines has varying roles in the downstream in the downstream pathways. So, the cytokines are one of the major effector pathways. So, if we look into this whole picture again

very carefully the innate immune system starts with the immediate invasion of a pathogen in our body as soon as it crosses the anatomical barrier. For example there is a nail piercing or an insect bite and the pathogen enters into the space into the tissue.

And then there are the cells of the immune system primarily the neutrophils which are the first acting cells of the immune system and they are very fast they go to the site of action very fast. In our next lecture we will describe how the cells of the I mean the neutrophils they move very quickly to the site of action. So and then there are the antigens presenting cells we have the antigen presenting cells the macrophages and the dendritic cells and you have the mast cells also the mast cells.

Or the and then immediately there is release of histamine which leads to vasodilation, vascular permeability increase in the vascular permeability leading to opening up of this high endothelial venules or the HEV's thus facilitating more migration of more of the neutrophils and the other cells of the immune system to the site of action. At the same time there is phagocytosis initiated by the tissue macrophages and this is primarily initiated by the pathogen associated membrane patterns that are present on the surface of the pathogens which is recognized by some specific receptors that are present on the surface of the macrophages.

So the macrophages by this presence of their toll-like receptors they can recognize the pathogens and then they can internalize or eat them up. Once they internalize the pathogen then it forms the phagosome which then fuses with the lysosome and Franz the phago lysosome and inside the phago lysosome the pathogen is kind of degraded in all its protein carbohydrates and all the components of the pathogen is degraded and chopped up into small peptides.

Now these small peptides are then displayed on the surface of the macrophage on the surface of the macrophage by specific classes of MHC molecules and this has been primarily required for activation of the adaptive system. So, now this antigen presenting cells as the name is given because the present antigen. So, now the present these peptides or these antigens to the cells of the adaptive system that is the B and the T cells and activate them.

Apart from presenting antigens in the this an activated tissue macrophage also secretes a certain class of proteins or the this effector molecules that are the cytokines. Now the cytokines have varying function and they can do a lot of functions of which initially they try to attract more nuclei sites into the site of action they activate the lever thereby producing proteins and primarily the complement proteins.

The complement proteins are also very important in the innate system we will describe complement proteins in our upcoming lectures and then leads to rise in the body temperature so you have fever and also tries to activate the T and the B cells. So, this is kind of an overview that we discussed today and try to understand how the immune system initially tries to respond to our tissue damage and an attack by a pathogen a foreign pathogen.

And leading to and then it starts to generate an inflammatory response what we call an inflammatory response. So, and that is a complex process an infant inflammatory response involves a complex process starting from migration of more and more of the neutrophils more degranulation of the mast cells release of histamine and release of other mediators of inflammation. So, we will slowly gradually what exactly we mean by inflammation and how exactly it is mediated by these specialized cells of the immune system.

So, for today we will stop here for this lecture and we will discuss more on the innate system as well as the inflammatory responses in our upcoming lecture. So, thank you very much.