Immunology
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Lecture No -25
Summery of Immune System

Welcome to this lecture so now I am going to summarize whatever so far we discussed. Let us see just to recapitulate what exactly happening just to link all of them together. So what happened I mean what happened in immune system, I mean why immune system is there? You know to protect us from infection or mostly for a common infection. So what is happening there is the first line of defense.

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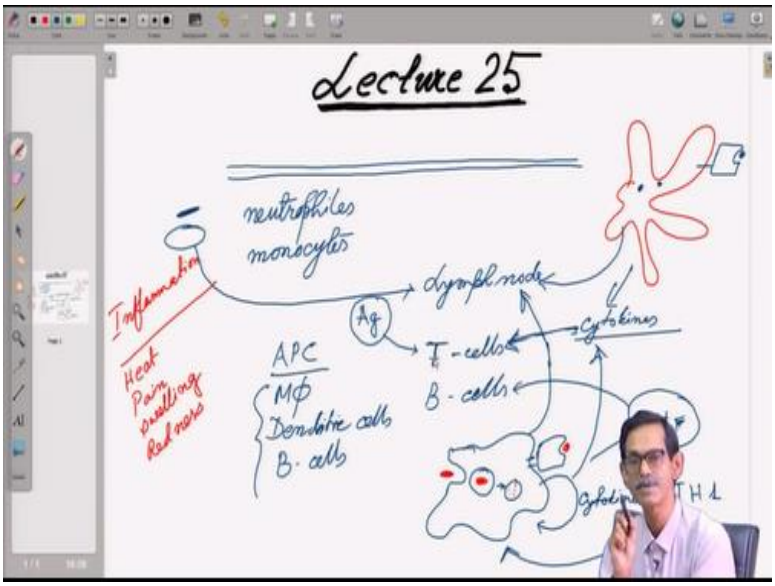

So there is a first line of defense and in this defense what we have, in this defense we have many things; we have our skin, we have mucous immediately they are taking care. So if there is any pathogen, it is not so easy for the pathogen to enter into our system. So what is happening if any pathogen if there is a cart, that I am just going to repeat exactly what is happening if there is a cart and in that cart, so there is a suppose there are infection suppose they are bacteria.

What is when the first reaction happened the first reaction is going to happen that there will be inflammation and that inflammation will you know that that inflammation will make lot of difference in the immune system that will actually cause or to inform the immune system exactly that what is going to happen. So what are the immune cells there, there are

neutrophils there are monocytes right there are other cells like us eosinophils, basophils they are must cell.

So many things are there and from there from the site of infectious tissue I mean a tissue infection site tissue or skin whatever you have there from there this antigen or the pathogen will bring to the nearest lymph node. In lymph node what is there? In lymph node there are T cells there are B cells. So when this thing is going to come if our innate immune system which is supposed to take care the very beginning are failed.

If the primary line of difference just breached and then this adaptive immune response will come. So this antigen is going to be presented by presented to T cells by different APC antigen presenting cells which are macrophage we also write macrophage like M phi we have dendritic cells, we have B-cells here also as antigen presenting cells so these and macrophage or dendritic cells what they are going to do suppose I am talking about the macrophage.

So in macrophage what is going to happen what I just discussed right in the last lecture is that the antigen will come and it going to be internalized and suppose if I take this color as red it will be internalized and this internalized vesicle will be in the vesicle that will be chopped into pieces that will be chopped into different pieces which will go with MHC 2, so ultimately it will be presented by MHC 2 this is one thing happening.

And during this inflammation during this fact that inflammation what is going to have a lot of cytokines are going to happen cytokines, chemokines which will bring all this thing I mean all the different cells into the site and what is this symptoms of inflammation just to recapitulate again that is heat, pain, swelling and redness. These will tell you that some mean I mean if all four or any at least first three like heat, pain and swelling is there you will see that inflammation is happening inflammation means there are infection is there.

So this antigen processed in case of external pathogen and in case of internal or cytosolic pathogen then the suppose the dendritic cells are going to take care and that antigen or the viral antigen are going to be presented by MHC 1, both these dendritic cells and macrophages are going to lymph node what they are going to do they are going to release lot of cytokines they are going to release lot of cytokines.

What these cytokines are going to do? these cytokines are doing two things; one they like I mean they will I mean control the macrophages and dendritic cells called auto-clean regulation that auto-clean regulation will activate the macrophage a lot of molecule will come one I mean will come again when you see the T cell activation how what are those molecules co-stimulatory molecules will come so this molecule are newly expressed which was not there in macrophage.

So cytokines will produce and they will activate itself. So the cytokines, cytokines both in case of dendritic cells and macrophages they will activate itself at the same times the cytokines also the cytokines also activate B-cell and T-cell, so first this macrophage is going to even better to this T-cell part first I mean this both the dendritic cell as well as macrophage produce cytokines that is going to activate T cells depending on their activity.

Like dendritic cell the MHC 1 will activate cytotoxic T cell macrophage AC 2 will activate T helper cells so that T helper cells this macrophage the T helper cells are of two types one is going to make the TH 1 response that TH1 response again activate macrophages to kill the internal pathogen or intracellular pathogen inside it and there are one T follicular T helper follicular cells which is you are going to learn in much more detail that.

This T helper cell is going to help the B cell this one very important thing is there in immune system because there is always a possibility that either T cell or B cell can do the mistake because if there is no control so that is why every are both the activation of T-cell and B-cell it is important, that both that B-cell and T-cell should get two different signal.

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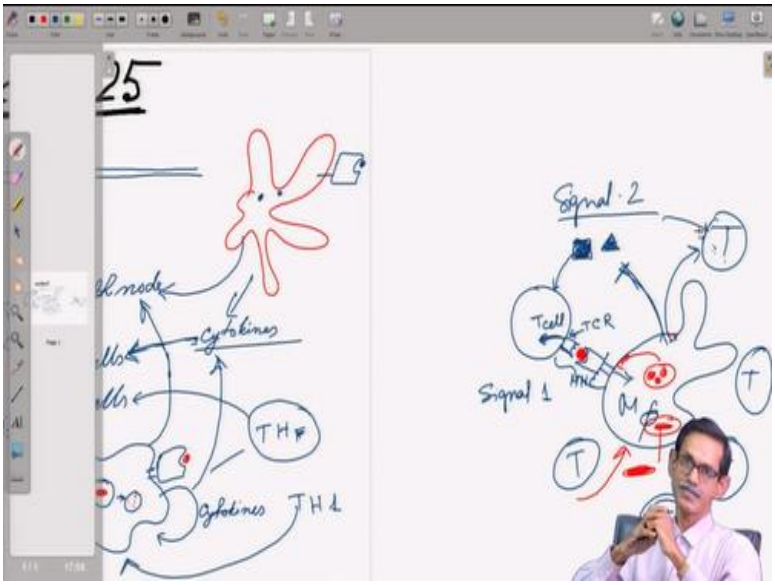

What is this? two different signal what is this two different signal two different signal means suppose this is suppose this is the T cell, so what is happening these T cell is this receptor is there, if any antigen binds here with presented with the MHC this is the MHC molecule this is macrophage, so this interaction this is TCR, this is TCR, this TCR and MHC this interaction will give one signal.

Suppose this is signal 1, this interaction is going to give a signal to the T cell that this interaction is happening if this thing happened only then T cell will not be activated because there may mistake it can happen because so many because we are in lymph node what is happening there is so many T cells this is packed and there are so many lymph nodes are there this is packed. So when one antigen presenting cell is going it is interacting with many T cells so some weak interaction can happen anytime, so this is not going to activate the T cell.

So these interactions should stable for some time and this interaction this activity I mean this I mean how this antigen is presented let me make the different color so how this antigen is presented how this antigen become here in on top of MHC molecule this antigen is processed because it is already taken up the whole bacteria was taken up into vesicles and this vesicles is make this antigen into small pieces this is presented by MHC 2.

So during these process macrophage get activated, activated macrophages is what they are going to do activated macrophages are going to release some small molecules really some small molecules they are mostly cytokines and chemokines in this case it is cytokines. So

these also will activate, this will also activate. So both this if this is signal 1 suppose this is signal 2 both signal is very, very important.

Either signal 1 or signal 2 is not going to do any change in the T cell because you imagine one macrophage is there and lymph node is packed, so there are many T cells there are many T cells surrounded by this macrophage all are T cells, so this cytokine is a molecule so if this cytokine released by the macrophage it is not only specifically I mean there is no person is there then go and feed there so these molecules can go either this side or can this side.

So cytokines can go and bind to this T cell but if this means if this is the signal 2, it is not going to do anything to this T cell because this interaction signal one is not there, so even it is going bind and giving the signal to T cell will not be activated. So these is very, very important so both the signals simultaneously is required to activate the T cell whether it is cytotoxic or it is T helper cell.

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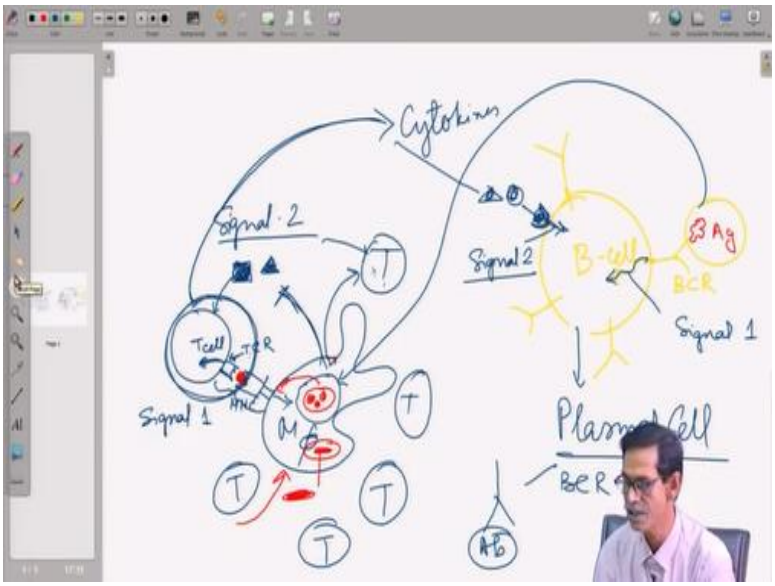

Same way if we see B cell, if B cell is there so let me change the color if B cell is there, so this B cell this is B cell all B cell has their receptor looks like antibody because they are basically the antibody molecule, so this antibody molecule can bind the antigen freely that antibody molecule can bind the antigen freely. So they are attached to it, so antibody interaction with the antigen.

So this red is antigen this antibody interaction is the antigen also give some signal and this all the receptor when the antibody is receptor they have some cytoplasmic tail. So as soon as this

thing binds to antigens to the antibody or the B cell receptor rather. So this is B cell receptor, it will also give a signal. So this is again signal 1, so these signal 1 can happen any time. Because antibody B cell receptor can bind to many things, which is not that strong binding or some self antigen is slightly similar.

And to the B cell receptor may interact for a while for very short period time less efficient or less affinity but these signal even if it is there B cell will not be activated. Even this is a very one more thing we will discuss it is, if this signal 1 or the interaction with B- cell receptor and antigen happen only, so if there is no other signal then that B cell will be anergic. So only signal 1 if happen, if this signal 1 is very strong.

That means this interaction is very strong, if this thing happened this B cell will be anergic. Anergic means they will not work any further throughout their life. They will be totally silent or irresponsive to immune system. So they are basically out of the immune system. So that nonspecific interaction, somehow it happened that B cell will be gone. So this thing is only this thing is not possible, so what is going to happen?

These thing there this activated T cell so see, same antigen is presented by the macrophage and if this is MHC 2 then this T cell will be activated, these T cell, activated T cell I mean there they are in lymph node, they are very close. It is not that much space like the way I am drawing, these T cells, activated T cell will also release some cytokines and these small molecules these cytokines will also act on this B cell.

So these will give a, because this is also there is a receptor where it will bind, so this will give a signal 2. So one signal will get from the antigen B cell interaction, another signal will come from this cytokine which will give the signal 2. In B cell activation both signal 1 and signal 2 is very, very essential. If this thing does not happen then we will not see any B cell activation. B cell activation means what?

The B cell activation means this particular B cell will be converted to plasma cells and in plasma cell what will happen, as soon as it becomes plasma cell this B cell receptor BCR will be spliced separately that we have said in reading the antibody diversity and antibody processing time. So it was like initially, it was receptor and the same antibody molecule will be produced which does not have any symmetry domain by alternate splicing.

That will release the antibody in the blood. Again, this what kind of antibody whether it is IG, first antibody will be IgM and I already told how it is switched and what the IgM, IgD, the alternate splicing. So this whole process is going to take time and that is why the first thing. So in this case when it is when we are saying it is very simple and straightforward. It is not, because all this antigen processing part we have discussed.

So when at the very beginning and the introductory class we have discussed all this thing. So the antigen processing, both the case of viral antigen or tumour antigen or extracellular antigen or the pathogen that processing, so this one line thing antigen processing means you know there are almost one hour lecture what thing is happening.

This T cell activation like, what is happening we will discuss in next class, how exactly T-cell happening these B cell activation also will be discussed. So this is the summary like, what we have discussed so far. So what we know, we know how this BCR are generated, why we need so many antibody or BCR or so many antibody of TCR because there are so many different pathogens. So each one each one is responsible for a specific peptide. So that peptide is generated from where, that peptide is generated from antigen.

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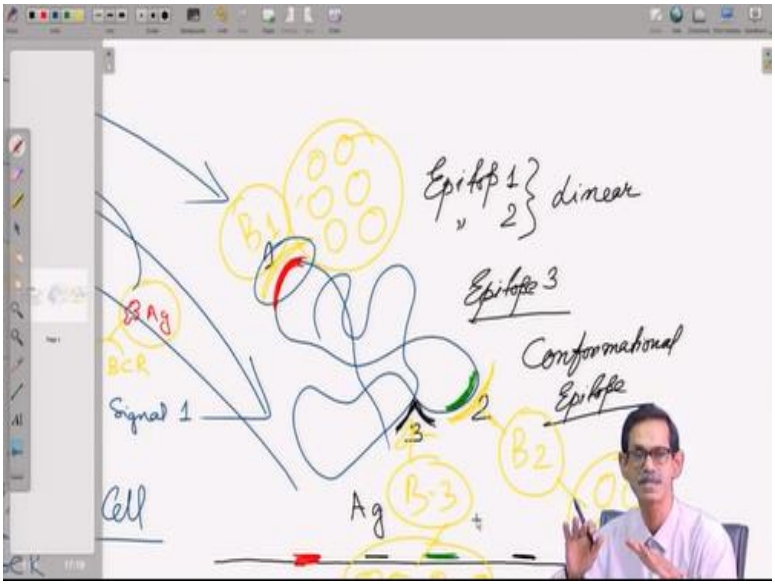

So this, what is this antigen actually now? What is this antigen if we see so suppose this is a protein. So this is a protein and this protein this part is one epitope, what is epitope; we know that which part of the aminoacid or protein is recognized by the antibody. Then it may be an different epitope, clear again this may be an epitope, what is the difference

between this red, green and black.

What is that this three epitope suppose this antigen suppose this is 1 antigen antigen has epitope 1,epitope 2, epitope 3, what is the difference difference is, I mean if you see carefully this is the three-dimensional conformation if you see this. Now if you make a straight line suppose this is the primary sequence of the peptide now what will happen you will see red is here, then we will see green is here, but where is the black, black you may find some here, some here why? Because you see these part actually contributed by fold.

Because two part of the protein come together and make a structure which is recognized by the B cell actually. In T cell it is not going to happen. T cell is always one type receptor, because it is chopped but B cell receptor can recognize the whole protein. So if this is the case, so then in case of 1, on epitope 1, epitope 2 you see it is a continuous sequence, this case it is called linear epitope.

But in case of epitope 3, it is generated because of a particular fold particular conformation, if you denature it will not be there because there will be spread like this, this is called conformational epitopes because it is generated by 3- dimensional structure of the protein. So now, once this is a protein it is not that one B-cell reproduce, so once one T cell is activated here, that T cell present and in lymph node there is not only one B-cell.

There are so many B cells. These will continuously try which can fit into that because in this case there is no question of here the B cell receptor can recognize the whole antigen. You do not need to chop it. So what is going to happen, so it is possible I am taking the B cell again. So it is possible that one B cell, this is B1 can recognize this another B cells that is B2 can recognize this, another B cell suppose B3 can recognize this.

So what is happening, one antigen entering into our system brought to lymph node presented to T cell and we shall also can see. So what is going to happen, one antigen can activate many B cells each one will produce, I mean each B cell will happen they will activate, they will multiply again many in number, all are identical. Here it will all be one there it will multiply again, it will multiply two.

So each one will some of them will be converted to plasma cell and each group of each

cluster basically, each type of B cell will produce antibody, they are different but can target the same antigen. One particular activated T cells or one class of T cell, what will happen after activation they will also multiply. If you see, if you remember that on side of dendritic cells they are multiplying so each one each activated T cells against that particular antigen.

Against that particular antigen can come and activate each one B1, B2, B3 because this is common, this particular set is common for particular antigen. So these T cell can interact with different B1, B2, B3 cluster can activate and because that is why we need more T cells. So each activated T cell will go and look which B cell is at attached with the antigen. So what will happen initially, it may the same that is why it takes few days to process initial part that is 7 days.

Once it is activated, immediately what is going to happen? Once it is activated, it is activate many B cells that many B cells may be of different type. May be B1, B2, B3, B4 because some antigen has only one epitope some antigen may have multiple epitopes. So more epitopes better for immune system, bad for pathogens but what we will see multiple type of B-cell is active are activated they are produced variety of antibody some are very good, some are less but ultimately whole antigen will be taken care.

And this is how the whole immune system works and there are many other things and then this B-cell will that antibody will do the effector function, then complement activation optimization, neutralization, many other things and then I will see the effect. So far whatever we have discussed, how the diversity of this receptor of B-cell generate, how antigen processed and initially that you already know the innate immunity part how this thing happened and you know the complement system by now.

And then how these things generate B cell activation, also you know so gradually or if you don't know you will know very soon and ultimately the whole system error attack. So innate immune system will taken care, if it fails then adaptive will come, but one side have to be is there it will take care of most of the infection and that is why we do not see ourselves sick all the time.

Even we are living in an environment everywhere microbes are there. Our water, our air, whatever we are touching, everything full of bacteria evens our skin so many bad bacteria

are there. But we are still safe because our immune system is working.