Immunology
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Lecture-8
Adaptive Immunity

So, welcome to the immunology course and lecture on adaptive immunity. So, in our last lecture we started describing about the innate immune system which we described as the very first response of our body against any pathogen or any external invasions. So, the innate system as I described is the first line of defense and then when the innate system is unable to respond or unable to contain that infection or restrict that infection then it tries to transfer the message to the adaptive system.

Now who is the adaptive system and how does the optic system work? So, we will try to get an overview of how the innate system and the adaptive system works together and how this message from the innate system is being processed by the adaptive system and the cells of the adaptive immune system they start to work. Now who are the cells of the adaptive immune system primarily the lymphocytes the T and the B lymphocytes.

So, again the adaptive immune system can also be divided into the cell mediated part and the humoral part. So, the cell mediated part is mainly mediated by the T cells and the T cells again are of the T helper type and the cytotoxic T cells we know that. And we have the B cells which is the humoral part of the immunity there is a humoral immunity that is antibody mediated. So, this is the very broad classifications now we have to look how the cells of the innate system they bring the; or carries the message from the innate system to the adaptive system.

And how that activates the adaptive system of the cells of that active system are getting activated. So, of course let us start again from the beginning where we have seen that the adaptive the cells of the adaptive system like the antigen presenting cells. Now these antigen presenting cells are the main connectors between the two systems. Who are the antigen presenting cells? The antigen presenting cells are mostly the macrophages or the dendritic cells.

These cells they engulf the pathogen so grossly the idea is like this, that these cells they engulf the pathogen and then they process it and chops the protein components into small peptides and they present it on the surface by two classes of MHC molecules either class 1 or the class 2. Now it depends on what type of antigen it is presenting depending on that it uses class 1 or the class 2 of the MHC to present the antigen.

So now these cells of the innate system expressing MHC class 1 or class 2 carrying the antigen will enter the adoptive system and will activate the cells of the adaptive system. As I told the cells of the adaptive system are the T cells and the B cells. So, in this lecture we try to summarize or try to see how it activates the T-cells.

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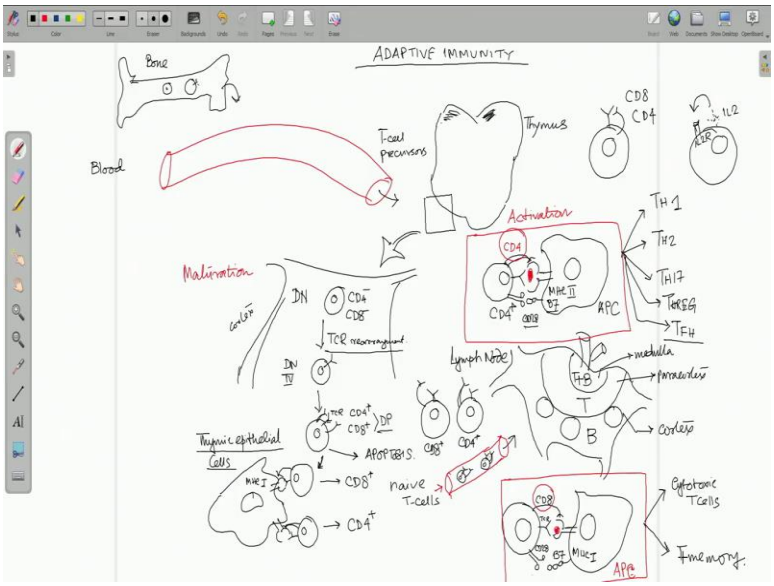

So, if you look into the picture here it is the bone marrow which is the site of starting point. So, all the cells of the immune system are coming from there so that T-cells the B-cells they are their progenitors. So, for example they are called the lymphoid precursors. So, now this lymphoid precursors they in turn from they leave the bone marrow and they enter into the bloodstream and they migrate. So, we have discussed a little bit about migration of the cells in our class of in our lecture on the inflammation mostly the migration or the extravasation of the neutrophils.

Similarly this other lymphocytes or leukocytes other lymphocytes they also migrate and these T cells or the T cell precursors we call them the T cell precursors because we do not call them the

T cells they have not yet become mature T cells so the first stage is their maturation. So, they have to make sure to get become the T cells. Now what is the mature T cell a mature T cell should have what we call our T cell receptor.

So it should be expressing a T cell receptor and along with it a co-receptor which is which can be a CD8 or a CD4 co-receptor this are required for recognition and binding to the MHC molecules. So, this mature T cell has to be first produced and this is produced in the thymus. This maturation process starts in the thymus. So, this precursor cells the T cell precursor we now call them the T cell precursor. So, now this t cell precursors they enter into the thymus.

And inside the thymus you can if you see have a magnified view of this then you will see there is a cortex region and para cortex region. So, this maturation primarily occurs in the cortex region. What happens here this precursor cells when they enter into the thymus they neither express any of the CD4 or the CD8 nor they express the T-cell receptors. So, they are not yet T cells, T cells or mature T cells. So, there these cells they start to get mature inside the thymus.

And since they are not expressing either of the two co-receptors like the CD4 or the CD8 that means these cells are CD4 minus CD8 minus. So, the CD4 and the CD8 are the markers of these T cells. So, we call them the markers to identify what kind of T cells they are or finally to what kind of T cells they will differentiate into. So, CD4 and the CD8 minus T cells are also called the double negative because they are negative to both the CD4 and 8.

So they are also called the double negative cells. The next stage once they enter the thymus. The next stage is they will start to get mature and they will pass through several double negative stages. So, we call them like double negative 1, double negative 2 that means the cells are still not expressing the CD4 or the CD8 co-receptors on the surface. And in the meantime what happens is there is rearrangement of the T cell receptor.

So there is TCR you will be studying about T cell receptors and T cell receptor rearrangements in details later on but for the time being just for your understanding so there is a T-cell receptor rearrangement during this double negative stage. So, it rearranges and at the stage when the cells

are still double negative that is DN 4. At this stage they start to express the T cell receptors. Now they are expressing the T cell receptors but they are still not expressing the co receptors.

So that means they are still double negative they are CD8 negative CD4 negative. Now these cells start to express on their surface both the CD4 and CD8. So, and of course the T-cell receptor so this is the TCR and they are CD4 plus as well as CD sorry as well as they are CD8 plus. So, now this stage is known as double positive stage. So, that means they are not anymore double negative they have started expressing on their surface the T-cell receptor as well as both the CD4 and the CD8 co-receptors which means although they are expressing the co receptors.

But they are still not destined they are still not destined to bind a specific class of MHC molecules. Now they have to be selected for that. Now who is doing this selection someone has to select these double positive cells and finally end up in either CD4 class cells or the CD8 plus cells. So, who is doing that? So, inside the thymus we have the thymic epithelial cells. So, this thymic epithelial cells they express the different MHC molecules the class 1 and class 2 molecules on their surface.

Now this timing thymic epithelial cells they are kind of helping these T cells to mature and select one of the; either selected as a CD4 plus or selected as a CD 8 plus cells. So, these cells as I told they are expressing the MHC's on their surface this thymic epithelial cells they are expressing on their surface the MHC is so depending on the type of MHC molecule it is interacting with; so if this double positive cell is interacting with an MHC class 1 then it is going to become a CD, it is going to become a CD 8 plus cell expressing the CD8 co-receptor only.

If it is interacting with a class 2 MHC by the CD4 co-receptor then it is going to be a CD4 plus cell. Now what happens to those cells which do not interact with thymic epithelial cells? So, it is a process of selection. So, that means there are also cells which might not interact with those thymic epithelial cells. So, those cells which are not so these are the cells which are interacting. Those cells which do not interact with the thymic epithelial cells they are not selected and they will die by apoptosis.

So this cells will then die by apoptosis. Now these cells which has been selected as CD8 or CD4 plus cells these are still the naive T cells so they are the naive cells because they have not yet encountered with any foreign antigen. So, they have not been activated. So, now these cells they still have not encountered with any foreign antigen so that is why we call them as the naive cells. So, these are the naive T cells.

Now these naive T cells after being selected as the CD8 plus and the CD4 plus cells there can undergo a second round of selection and this selection occurs usually by the help of the macrophages or the antigen presenting cells. So, they can undergo a second round of selection and those which are selected as CD4 or CD8 class cells they will now leave the thymus so these are the naive T cells expressing either CD8 or CD4. So, they are the naive cells expressing either CD8 or the CD4 they will now go to get activated.

Where do they go for activation? So, now they will migrate to specialized organs like the lymph node for example. So, let us see how what happens in this lymph node? So, this is kind of a picture what we see in the lymph node and the lymph node is also having 3 major regions one is the medulla, the para cortex and the cortex. So, the medulla is mostly filled up with T and B cells the mature B cells and the naive T cells.

This para cortex is a site for T-cell activation and the cortex is primarily the site for B-cell activation. So, we will talk about this cortex area or the B cell activation when we study the humoral immunity. So, for the time being let us concentrate on the pair cortex where the T-cell activation occurs. Now this lymph node also apart from containing this T and the B cells of the T cells and the B cells in the cortex, para cortex they also contain the antigen presenting cells like the dendritic cells and the macrophages which are presenting the antigen on their surface by class 1 or the class 2 MHC molecules.

Now this these T cells as I told now they are kind of destined so they have on their surface T-cell receptors as well as either CD4 plus or the CD8 co-receptors, so, the CD4 plus CD8 plus T cells. Now for the activation of the T-cell it has to meet the MHC molecule. The activation of the t-cell requires a make meeting between the MHC molecules and the T-cell receptors and the co-

receptors. And this interaction is vital for activation of the T cells and further differentiation into different T cell types.

So what happens here is inside the lymph node a T cell interacts with an antigen presenting cell which can be a macrophage or even a dendritic cell which is expressing the MHC molecules it can be an MHC class 1 or MHC class 2. Let us take an example of the MHC class 2 from here. So, let us say this is the MHC class 2 and this is a CD4 plus T cell and this in this is the T cell receptor and a CD4 co-receptor.

Apart from these interactions the CD4 plus or the CD8 plus the T cells the naive T cells they also express another marker on the surface which is the CD28 and this can interact with the B7 on the surface of the MHC on the surface of the macrophage or the dendritic cells that means antigen presenting cells. We call it in general as the APCs. So, basically we see there are 3 different interactions occurring one is the TCR or the T cell receptor.

MHC carrying the antigen of course and a co-receptor the CD4 or the CD8 depending on the type of the T-cell and along with that a CD28 to a B7 interaction. This interaction is particularly vital for the activation of the T cell. So, we call this the activation. So, this part is the maturation and this part is the activation. So, now the T cell is activated after all these three interactions are complete, so it gets activated.

Something similar happens with the CD8 plus cells as well. So, the CD8 plus cells will interact with antigen presenting cells which are expressing MHC class 1. So, this is MHC class 1 and then this is the CD8 co-receptor the T cell receptor the TCR and of course there is the CD8 and B7, CD28 to B7 interaction. So, this is a class 1 MHC this is another antigen presenting cell APC so this is the class 1 MHC interacting with the CD8 here this is CD8 and this is CD4.

So the cells which are expressing on the surface the CD8 co-receptors they will finally form either the cytotoxic T cells or the T memory cells. They will finally differentiate into the cytotoxic T cells or the T memory cells and this which interacts those which interacts by their

CD4 co-receptors with the MHC class 2 molecules presented on the surface of the APC's they will finally produce different subsets of T cells.

So the T helper cells, so they can give rise to TH1 TH2 or TH17 or TH the T reg cells or the regulatory cells as well as a specific class of T cells which are also known as TFH or the follicular helper T cells. And these TFH cells and also the other T helper cells they are required for helping in the activation of the B-cell. So, they are also required in the humoral part of the immunity so they will they are not really the effector T cells. So, the effector T cells if we see the effector T cells which actually give the cell mediated immunity or which actually performs the cell mediated immunity or the TH1 and the TH2 cells and the cytotoxic T cells.

So the cytotoxic T cells are the class of T cells which directly can interact with the pathogen and can kill the pathogens. So, they have that mechanism they express certain effector molecules which leads to after direct interaction with the pathogen that can lead to the destruction of the pathogen directly. So, these are the effector cells so either the class TH1 or the TH2 cells or the cytotoxic T cells and then you have the memory T cells.

So this entire process occurs inside the lymph node the para cortex of the lymph node and the T helper cells now this these T cells so depending this depends on what type of cytokine is actually present in the surrounding. And depending on that they start defect differentiating into the different types of T cells the TH1 or the TH2 or the TH17 or the T reg or the TFH cells. So if we look into the whole picture once again starting from here in the bone marrow.

So the T cells and the B cells the progenitor cells or the precursor cells they enter into the thymus the T cell precursors they enter into the thymus inside the thymus they get matured. So, they initially these T cell precursors they mature through different stages where the T cell receptor are rearranged the T cell receptor rearrangement occurs and during this time it does not express on its surface either of the two markers CD4 or CD8 and that is why they are known as the CD4 minus CD8 minus or the double negative cells.

This DN cells are the double negative T cells then gradually start developing or expressing the T cell receptors on their surface. They now start to express these T cell receptors on the surface and at this stage double negative 4 they express the TCR or the T cell receptors and then they suddenly start expressing both the co receptors that is the CD4 and the CD8 and they become CD4 plus and C Plus.

So, now this CD4 plus and CD8 plus T cells are called the double positive cells. Now this double positive T cells they have to be selected. Then now who does this selection? It is the thymic epithelial cells primarily who can express class 1 and class 2 MHC's on their surface and the select for the CD4 plus or the CD8 plus cells. So, from the double positive cells now they become single positive.

So it is either a CD4 plus or a CD 8 plus now they are further subjected to another round of selection by mostly the macrophages or the antigen presenting cells which expresses the MHC's on their surface class 1 or the class 2 MHC's and then finally the cells which are selected they proceed to the lymph node for activation. And those cells which are not selected that is those are those are not selected by the thymic epithelial cells they get destroyed or they are killed by the process of apoptosis programmed cell death.

And then this CD4 plus and the CD8 plus cells the which are still kind of naive T-cells they have not yet met with any antigen yet. So, now they will go into the lymph node and then there they will encounter with the antigen presenting cells which are presenting the antigens by class 1 or class 2 MHC molecules. So, this is an interaction here showing the class 2 interaction or class 2 MHC interactions with a CD4 plus cell.

And the class 1 MHC molecule which interacts with the CD8 plus cells, so now the make the basic of the interaction is kind of similar so MHC class 2 interacts with the T cell receptor and the CD4 co-receptor. Along with there is another co-stimulatory interaction so this is called a co-stimulatory interaction between the city 28 and the B7 which is expressed on the surface of the antigen-presenting cells and the maturity cells they start expressing the CD28.

So this CD28 to B7 interaction is also important for activation of the T cells. Now these T cells are now kind of activated and what also happens here. So, these T cells they now start to express on their surface the receptors for cytokines for example IL2 are and the secret IL2 or interleukin 2 and this in turn leads to their differentiation. So, that class of interleukins this helps these cells to differentiate into different types of effector cells or the memory cells.

So either they will produce effector T cells which are the TH1 TH2 or the cytotoxic T cells and they produce the memory T cells as well. So, now this interaction between the CD4 plus T cells and the antigen presenting cells having the class 2 MHC that is which are mostly exhibiting the bacterial or the exogenous antigens presenting those antigens they will be presented and these T cells will get activated and they will now give rise to different subsets of T cells which will be either effector T cells or will produce the memory T cells.

Similarly the CD8 plus T cells they interact with class 1 MHC molecules. So, class 1 MHC molecules are usually displaying viral antigens or self cell antigens. So, these class 1 MHC molecules carrying that antigenic peptide bound class 1 MHC molecules they interact with CD4 plus T cells. And once this interaction is complete along with this co stimulatory interaction here shown for the CD28 and the B7.

Once this inter interaction is complete it can develop into the cytotoxic T cells which can directly affect the pathogens which can directly go and kill the pathogens or the cells the target cells. So, they can directly go and kill the target cells or they can also develop the memory T cells. So, this is kind of the cell mediated part of the adaptive immune system. So, it is the cell mediated part of the adaptive immunity that we discussed or focused on today.

And in the next class we will try to understand the humoral part of the immunity which is the B cell mediated. So, this was the T cell mediated adaptive immune response and this is the cell mediated part of the adaptive immune response. In our next class we will try to describe the B cell mediated humoral immune response, thank you very much.