Immunology
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Lecture No -40
Effector T - Cells

Welcome back and let us welcome back to this immunology lectures and we will be talking today about the effector T cells. So for the last four classes we have been discussing about the maturation and activation of the B cells there is a humoral branch of the immunity. In one of my beginning lectures in the starting lectures I had already discussed a little bit about the adaptive branch of the immunity.

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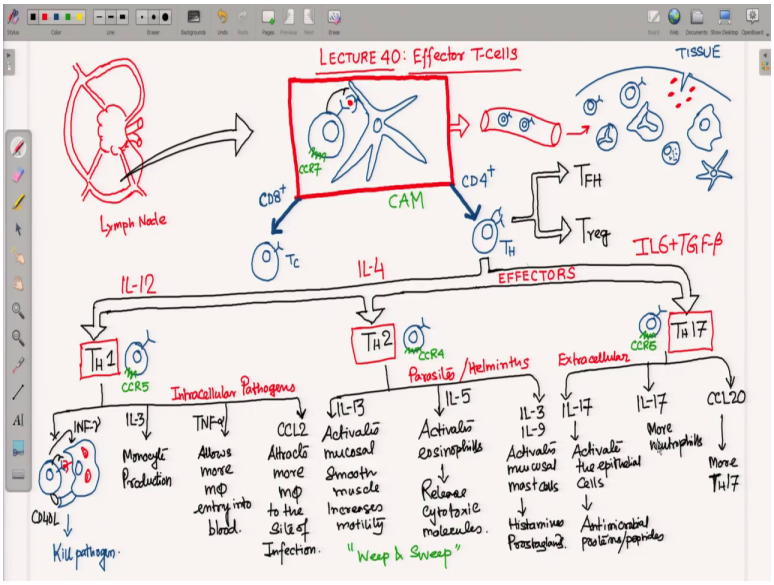

So the adaptive branch of the immunity comprises of signals that are processed from the unit cells which are primarily the antigen processing cells and they are being processed and presented. So these antigens are presented to the T or the B cells. And the adaptive immunity clearly has two branches one is the humoral branch which is the B cell mediated and antibody mediated branch and the cell mediated branch which is the T cell mediated or the T lymphocyte mediated branch.

So these antigens are usually carried by the dendritic cells or the macrophages which present it to the T cells there is a naive cells. The naive T cells or the night B cells and then activates them that their divots the adaptive part of the immunity. Now from the earlier lectures you have learnt quite some little bit about the T cell development the B cell development the T cell development auntie mode antibody mediated effector mechanisms responses that are generated by the antibodies.

We will learn more about the antibody responses we have not yet discussed about the complements the complement proteins the complement systems that we will be discussing very soon which are the antibody mediated effector mechanisms. So we have kind of learnt some of the effector mechanisms by the T and the P cells. And also the development of these two cell types like the T cells and the B cell developments their differentiation and all these things.

I have also introduced you a little bit to the T cell differentiation that is when a T cell a naive T cell is activated you remember the activation process how the T cell gets activated by the different types of interactions with the dendritic cell primarily or with the macrophages they get activated. So with a PCS with the antigen presenting cells and one of the major cell types of this this type of cell is the dendritic cell.

Because dendritic cell is kind of the cell that is connecting between the unit and the adaptive system so it is a cell of both init system adaptive system although there are very very classical differentiation between the cells of the innate and the adaptive system. So when we call the cells of the adaptive system we usually understand the B and the T cell when we say cells of the inert system we usually understand the neutrophils basophils mast cells macrophages these are the cells of the innate system.

I already you got an idea in the previous classes or I have already told you several times and discussed it that the two systems of the immune system the two systems the innate and the adaptive system they are very very well coordinated. So it is not that the inert system works discretely or the adaptive system works discretely. So they are very well coordinated there is a coordination between these two systems and they try to help each other.

So like the init system when it fails to kill a pathogen when it fails to destroy a pathogen and clear an infection it transmits that signal to the cells of the eruptive system. Once the cells of the adaptive system gets activated by the antigen presenting cells or there is macrophages dendritic cells they get activated once they are activated they again come back and help the cells of the init systems to clear the pathogen.

And these cells which actually help in the infection clearing or clearing of the infection levels which are involved in this immune responses directly or indirectly they are known as the effector cells. So they are the effector T cells. So for example T cells if you go back to the activation and differentiation of the T cells you will see that the T cells be it a CD8 plus cell or a city for plus L so CD8 plus cell will develop into a cytotoxic cell CD4 plus cell will develop into a helper cell be the CD8 or be the CD4 you have either the memory cells or the effector cells.

And the effector cells are those cells which ultimately helps in either they directly go and attack the pathogen and kill the pathogen or they will be involved in indirectly they will try to help the other cell types they can also help the cells of the adaptive system. So there are T helper cells that are responsible for helping the B cell development for example or B cell proliferation if you have; so I have discussed this in the last few lectures as well.

So you have seen how the T helper cells they help in the B cell development proliferation and activation. So they are help sells they help other cells in many ways they also help the cells of the innate system and that is why they are known as the effector cells that means the effector T cells they are the T cell effectors. Now how these cells of adaptive system they become affected T cells that is a big thing so that that has been so there has been a lot of research a lot of understandings of these mechanisms and people try to understand how these cells they actually become effector cells which were the cells of the adaptive system.

How they get activated and become the cells of the adaptive system you have learned the activation part by now. So if we quickly go back to our our immunological overview that we have discussed earlier we remember this this this picture where we have seen that our T cell a

naive T cell let us say it is this is a CD 8 plus or a city 4 plus naive T sell can interact with an antigen presenting cell like a dendritic cell.

By the presence of the MHC molecule on the APC on the antigen presenting cell which presents the antigen with TCR or the cell receptor and the co-receptor CD4 or CD8 co-receptor and there are many other interactions we are not discussing here whatever. So once these interactions occur then it is dis kind then it is committed to become R T cytotoxic or R T helper cell a T cytotoxic cell is also an effector cell and we know or we have learned in some of our earlier lectures how the T cytotoxic cells can they had directly have killing effects.

So they are the direct killers so they can directly go and kill they can inject enzymes they can inject bacteria siedel's or k pathogen killing materials into the cells into the infected cells and that is how they kill. So we have learned the effector mechanisms a little bit about the T cytotoxic cells now what are the effectors or the effector cells of the T helper cell type. So if we go and see what are the helper cell types and we will see that the helper T cells they can develop into different effector T cells as well as certain other T cells which are not really the effector cells.

But they are involved in some other processes like the TFH or the T follicular help ourselves we know them very well because we have learnt about their role in the B cell development process and the T rig or the T regulatory cells and they are also very important in regulate in regulatory roles. So they have regulator they are the regulators of the T cell responses. So you know these are the two different types which are not really involved in the effector mechanisms or the effector responses.

And the three major effector T cells that are involved in the effector mechanisms they are the TH 1 or the T helper 1 type the TH 2 and the TH17 we I already told you a little bit in in my previous lectures probably how these cell types they differentiate into different cell types. So it is primarily controlled by the presence of the cytokines the interleukins. So depending on what kind of interleukin or what kind of cytokine is present in the surrounding it will develop into at TH 1 or a TH 2 or TH 17 cell type.

So for example if there is a lot of IL 12 in the surrounding interleukin 12 then it will develop into a TH 1 cell type. If there is a lot of interleukin 4 IL 4 it will develop into a TH 2 cell type and if there is a lot of interleukin IL-6 and along with that not only IL-6 along with that TGF-beta together then it will develop into a TH17 cell type 17 and the TH17 is primarily named as TH17 because it is one of the major sources of the interleukin IL-17.

So these are the three major cell types or the effector cell types that are being produced in presence of the different cytokines. We will discuss cytokines very soon in our upcoming lectures about the different types of cytokines the mechanisms how they work what they do all these things. So for the time being let us just learn the names of the cytokines and their actions and their how the help in these effector mechanisms involved in this helper that are induced by this helper cells.

So now these T helper types 1 type 2 type this TH1 TH2 and the TH17 they can help in distinct mechanisms. So what are the distinct mechanisms that the TH1 cell is involved in? So the TH1 cell is primarily involved in clearing of intracellular pathogens that means what is intracellular pathogens or intracellular bacterias. Intracellular pathogens means those pathogens or bacterias that has been ingested or phagocytosed by a macrophage.

For example so in the tissue when there is a if you look at the tissue here in the tissue when there is a tissue damage or any insect bite or whatever then there is a lot of pathogens that is inrushing that is coming in. And these pathogens are first they make the cells of the inert system and then with the neutrophils the macrophages the mast cells and all this. So now this macrophages they can engulf the bacteria's.

So they once they end so that once these pathogens they enter inside the bacterias the cells of the unit the cells of the adaptive system for example this is TH1 cells they can help in activating the macrophages to become cytotoxic. So they themselves are not cytotoxic but I mean these T helper cells that themselves are not toxic. So they are not cytotoxic but they can release some cytokines give some signaling molecules.

So that they can turn these macrophages into cytotoxic cells and they can activate and enhance the killing by the macrophages. So these cells of the adaptive system they come to the periphery or come to this they get activated then they differentiate and then they move through the bloodstream and then they come to this damaged tissue area. So they infiltrate this damaged tissue area and there they start to show their effector functions.

How do these cells of the or what signaling or what exactly directs these cells to this site of action so these cells normally the naive T cells they express certain types of cell addition molecules. I have already discussed about the cell addition molecules a little bit in my inflammatory response classes. If you remember from that classes that can we have discussed about different types of cell addition molecules like the selectins the musings the immunoglobulin like CAMS the I CAMS.

So these CAMS are expressed or the cell addition molecules that are expressed on the surface of different cell types they are expressed on the surface of the endothelium they are expressed on the surface of the lymphocytes many other immune cell types. So these CAMS or the cell addition molecules they help in adherence and migration of the lymphocytes from one place to the other. So they are basically the helpers in migration and these cell types this maturefinally differentiated matured cell types developed T cells infected T cells.

They can express different different types of cams on their surfaces as well as they can also Express different types of chemokine receptors we will discuss what chemokines are for the time being let us understand from the name that chemokines are the chemo attractant that means they attract some cell types. So chemokines are small molecules which can attract a cell type by binding to the specific receptors present on the surface of the cell.

So for example a chemokines can bind to a specific chemokine receptor and so it is a it is a specific receptor ligand interaction. So the chemokinen is the ligand which binds to its specific receptor in attracts or pools that cells. So it is like a magnet to iron interaction that is occurring and this interaction is very very very specific. So it can draw the cells or pull the cells to a

specific location. So that is how these cells these cells of the adaptive system these T cells is fully differentiated and developed T cells.

They now start to express different types of chemokine receptors for example a ninth T cell usually expresses on its surface a CCR7. As soon as this naive T cell starts to differentiate into different types of T cells effector T cells their expression of CCR7 goes down. And then start they start to express different other chemokine receptors and different T helper cells may express different chemokine receptors.

For example these cells TH1 cells they express CCR5 the TH2 they express CCR4 and the TH17 they express CCR 6. So this they start to express that like the naive T cells they were expressing CCR7 and once this differentiates into the different T helper cell types like the effector cell types they start to express different different chemokine receptors like CCR5 CCR 6 on their surface and by virtue of that because of that they now start to move to different locations.

Different locations and start to show different responses different immunological responses, so what we were discussing about is that this cells this the TH1 cells they are primarily responsible for intracellular pathogens they are responsible for intracellular pathogens. Then we have the T helper cell type 2 which are mostly responsible for parasites for killing of parasites and Hellman's because they basically go to the they changes the mucosal smooth muscle motility.

And when there is a parasitic infection or a helminthic infection particularly in the stomach or in the intestine so they changes the mucosal or smooth muscle motility and tries to clear that helminthic attack or the parasitic attack how we will discuss. So these are the TH 2 type cell and the TH17 they actually elicit a class of responses which are responsible for extracellular pathogens. So like the TH 1 is responsible for intracellular pathogens these are responsible for extracellular.

So those which are not being internalized that has to be dealt with they are mainly dealt with the TH17 class of cell types the effector cell types. No more this TH 1 cell types they do primarily one of the major functions is that the activates our macrophage. So they can activate the

macrophage and how do they do that so these are for example a TH helper type 1 cell and this is a macrophage which has engulfed pathogens with a pathogen inside that means intracellular pathogen in here and that can present there has that expresses that MHC on the surface and that interacts with this T cell by the T cell receptor and T cell for co-receptor.

And as well as there is a because this matured this differentiated mature TH1 cells they express on their surface the CD40 ligand CD40 L we we by now we have known about the city for T and CD 40 L interaction from our B cell development processes so they express on their surface the CD40 ligand and this macrophages they express the CD40. So now they can now interact with the CD4 T + CD40 ligand interaction and after this interaction occurs.

They are of course there is signal transduction more our gene transcription downstream transcription of more genes and that leads to the production of different cytotoxic materials cytokines that will go and kill the bacterium or more efficiently. So this is one of the functions so they now kill the bacteria or the pathogen primarily the bacteria to kill the bacteria or the pathogen more efficiently.

And one of the major signaling in this inter process is that these these these T cells they starts to release a specific cytokine which is known as interferon gamma. So I have gamma we learn about these interferon's we learn about all these interference and the cytokines in our later classes very soon. So this day they start to express they start to produce this interferon gamma which is a very important role in activating these macrophages.

So now these macrophages they become activated a second mechanism by which this TH 1 cells they work is also they increases the production of the monocytes monocyte production in the bone marrow and that is primarily done due to cytokines like IL 3. Then they also produce a very important cytokine that is known as TNF alpha. We will learn about TNF alpha and its roles primarily in later in our cytokine classes.

But this T nif alpha is one of the very, very important signaling molecules they can activate the endothelium they can increase the vascular permeability and they allow more macrophages to

come into the blood they can increase vascular permeability. And allows more macrophage entry into blood now once more and more macrophages comes to comes out in the blood that has to go to the site of action as well.

So now macrophages which are coming to the blood there has to now migrate to the site of action and show their action. So they have to do direction do their function and for that you need some chemokines for example. So one of such chemokines is CCL 2 that is also released by the stage one cell type and they can attract more macrophages so CCL 2 is one of those chemokines that attracts more macrophages they can attract more macrophages to the site of action or the site of infection.

So the TH1 cells at least performs for different effector functions that we can summarize here that is they can produce interferon gamma they can activate the macrophages and induce cell killing bacterial cell killing more and more. They can also induce production of the monocytes they can also allow more macrophage entry into the blood and they can also attract those macrophages to the side of action.

Coming to the action of the TH 2 cell types for the TH 2 cell types as I told the primary action of the TH 2 cell types is to increase the motility of the mucosal smooth muscle. So they activate the mucosa of smooth muscle they activates the mucosal smooth muscle increases the motility. So increases motility and by that the helps in clearing of the pathogen primarily the hell means the worms the worms that infects our intestine for example.

So those are dealt with this kind of say this kind of TH2 responses type two responses and they can also they can also activate the EOC no fills and the basophils for example. So they activates activates the yoshino fills for example and activation of the eosinophils and the basophils would lead to the release of many cytotoxic molecules so they release a lot of cytotoxic release cytotoxic material or molecules that can clear the pathogens primarily.

The parasites so they deal with the parasites as I told and they also secretes a class of this interleukins like IL3 or aisle nine for example and they can activate the they can activate the

mucosal mask cells so they activates they activates the mucosal mast cells the mast cells this is another mechanism so this is another mechanism of amplification of the signal. They can activate the mucosal mast cells and that mast cells they are granulocytes so they will start releasing the granules like the histamines for example.

The histamines the prostaglandins and that will basically this release of this in these histamines or these prostaglandins. And so this vasoactive amines that would lead to also increase the fluid flow in the mucosa lumen so a basic mechanism by which this TH2 response works is sometimes also known as a whip and sweep mechanism so it is also called a whip and sweep mechanism weapen sweep mechanism. So they sweep out the pathogen from the intestine or from the body and try to clear that pathogen primarily.

The Hellmann's and the parasites and a third effector mechanism is the TH17 response and the TH17 response also it induces the in epithelial cells. So they induce the epithelial cells and tries to so as I told that these are the TH17 response primarily deals with extracellular pathogens. So the pathogens which has not been ingested or which has not been internalized so that means they help certain cell types for release of cytotoxic material or release of some bacteriostatic or bacteria siedel material so they primarily induces the so they produce interleukin 17.

As I told that they are the primary producers of interleukin 17 which activates they activate they activate the epithelial cells the epithelial cells and that leads to the production of the antimicrobial proteins. So produces antimicrobial microbail proteins and bacteriostatic and bacteria siedel antimicrobial proteins peptides and leading to bacteriostatic or bactericidal effect this also they also produce the a as they are the primary sea creatures of IL I told.

So, IL 17 also recruits more neutrophils neutrophils to the site of action neutrophils which are the fastest acting cell of the immune system so they go and infiltrate into the site of action or the site of infection. So IL-17 is one of those cytokines that can actually bring more neutrophils to the site of action and as well as they Prakrit this CCL 20 the CCL 20 witches are chemokine and the CCL 20 attracts more TH17 sorry.

So they attract more of this T helper 17 cells to the site of action so quickly a quick look into this entire picture is that that this effector cell types this the helper cell tiles they are the effector cell types. So there are the three different effector cell types the TH 1 the TH two and of course the TH 17 are the three major effector cell types TH 1 primarily is involved in intracellular dealing with the intracellular pathogens that means we the pathogens which has been internalized.

So they help the or activates the macrophages they help in monocyte production they allow more macrophage entry into the blood and also migration of those macro sites or of those sorry of those macrophages into attraction of those macrophages into the site of infection a second type of response is initiated by the TH two cell types they produce the one of the major producer of IL 13 for example one interleukin 13 and which activates the mucosal smooth muscle increases its motility and primarily by the production of the mucous by the goblet cells.

So they can activate the goblet cells and enhance the mucous production and by that they can also increase the motility of the mucosal smooth muscles they can activate the eosinophils then by that and recruit more you know fills and which can produce a lot of cytotoxic molecules that can clean up or clear the parasites or the Hellman's and this is primarily done by the action of interleukin 5 which is also produced from the TH 2 cells.

And then they also produce aisle three and IL 9 which primarily activates the mucosal mask cells and mast cells as you know are the major sources of the histamine this so mucosal mast cells are a small category of the mast cells that are present here. And they are activated by these TH 2 cell types and they can produce histamine or prostaglandin leukotriene all these molecules which actually helps in the valve which actually helps in the vasodilation.

And thereby increases the fluid flow to the lumen. So them to the mucosa lumen and then by that action they can actually sweep out the pathogen and thirdly the TH17 cell types they are mostly dealing with extracellular infection or pathogens extracellular pathogens so they activates the epithelial cell to produce a lot of antimicrobial proteins the induces the epithelial cell to produce a lot of antimicrobial proteins.

They also produce they are the major producer of the IL-17 interleukin 17 so they which actually attracts more neutrophils to the site of action and they also attract more of the TH17 cell type to the site of action. So we kind of today's try to summarize or get an overview of the different effector cell types I very I try to give a very preliminary idea about the three different effector mechanisms what they do.

What the major functions are you can get more details in the books. But we really do not have scope or time to go into more details so I will stop it here for the vector T cells primarily the T infect ourselves and we will stop the discussion here and we will try to learn more about the different effector molecules effector mechanisms. We will try to learn about the complement proteins the cytokines more in details.

And then we will see how they work in the different contexts. So how what are the major roles of the different cytokines in different contexts in the unit and the adaptive system what are their roles so we will discuss all those things slowly slowly in our upcoming lectures in more details. So, that is all for this lecture and thank you.