Immunology
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Lecture-10
Effector Mechanisms

Welcome back and welcome back to the immunology lectures. So, today it is the lecture 10 and we will be discussing about the effector pathways or the effector mechanisms in the immune system. So, over the last 4 lectures we have been discussing the different parts of the innate and the adaptive immune systems and particularly the mechanisms in the innate system and in the eruptive system the cells of the innate system the cells of the adaptive system.

So what we have seen is that the innate system which is the first line of defense has some specialized cells to deal with an pathogen or a pathogenic invasion. Like for example the macrophages the neutrophils the mast cells the basophils these are kind of this at the part of the innate machinery which is employed when there is an pathogen invasion. So, like for every battle so it is the immune system it is a battle against the foreign pathogens like some every battle you need the army.

So the person who will fight so those are the cells of the immune system and at the same time you would need the weapons. So, like the different weapons of the battle and the weapons of the battle are basically the effectors. So, who are actually working for the immune system? So, if you need to win the battles then you have to have some effectors because the cells by themselves cannot perform the function the cells are just the army men of the immune system.

So it requires the effector molecules some effector mechanisms by which this battle is won through who are those effector mechanisms or who are those effector molecules in the immune system. So, like in the innate system and in the adaptive system we have seen we have discussed the different mechanisms. How the neutrophils they migrate to the location and then they try to engulf the pathogen. How the macrophage engulfs the pathogen induces phagocytosis.

And then this after the pathogen is being killed then it can also present the peptides the processed peptides to the adaptive system. And there the cells of the adaptive system they are induced or they are activated and they do some things by which they basically kills or clears kills the pathogen or clears the infection or the invasion. So now what is this something what this something they do? So, that is the topic of today's discussion that is the effector mechanisms.

What are the different effector mechanisms that actually work for the immune system and leads to the winning of the battle or leads the immune system to win the battle. So, we will be telling very, very briefly about the different effector mechanisms and the effector molecules today and because these effector molecules as we progress in our lectures in their future lectures we will be talking about these effector molecules and the effector mechanisms very frequently.

So I will introduce you very quickly to the different effector mechanisms and the effector molecules that are involved in mediating an immune response.

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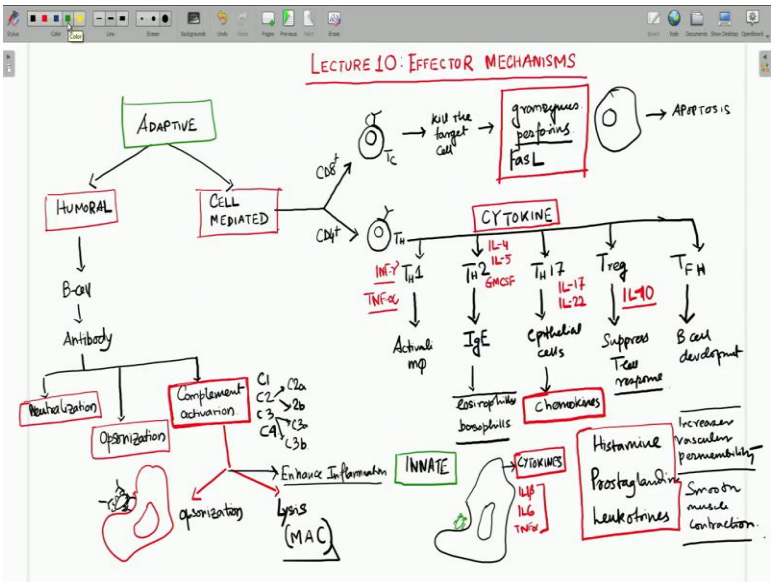

So, let us start from the adaptive system again where we left. So, in the adaptive system of the immune system the adaptive branch can basically be subdivided into two you know that is a humoral branch and the cell-mediated branch. So, these are the two main branches of the adaptive immune system the humoral and the cell mediated. And we have kind of discussed what are the; processes of activation of the cell mediated immunity?

The process of activation of the B-cells and all these series of events that occur in the adaptive immune system we have discussed very briefly. Now this humoral immune system effectively they produces it is the B cell mediated immunity and it produces antibodies we know it produces antibodies. In these antibodies now what these antibodies to the antibodies by themselves they cannot do any function. So, they need to they need to go to the location and then they can do some functions with help of other effector molecules.

So what do these antibodies to these antibodies can do at least three different functions. One they can neutralize, so neutralization. They can opsonizise the pathogen so it is also called opsonization or they can lead to activation of complements, complement activation. So, these are the three major functions that the antibodies to so they can either neutralize the pathogen depending on the different types of toxins that are produced by the pathogen.

For example the bacterias so they go and bind and by that but by that they can recognize the pathogen and induces killing of this pathogen. And then they can optimize so they can go and coat the surface of the pathogen. So, coating the surface of the pathogen and assist in the process of so they goes and coats the surface of the pathogen they recognize the pathogen surface coats the pathogen surface and then they can help in the process of phagocytosis and then you can also have complement activation.

So now this is something new what I told is complements these complements are one of the very, very important effector paths of the immune system they belong both to the humoral branch the adaptive branch as well as to the innate system. So, there can be complement activation which is antibody dependent complement activation there can be antibody independent complement activation. We will discuss about the complements in very details in our upcoming lectures.

But for the time being let us know that the complement activation is one of the important functions that is being carried out by the antibodies. And so the complement activation in turn can lead to two functions, it can also lead to two different functions. What are these? One is opsonization, again it can also lead to opsonization. So, antibody and complement they together

complement proteins so this call what are these complements? Complement proteins are primarily small proteins or like proteins which are being secreted from mainly the liver.

And they are kind of proteases which are activated and there is a cascade of activation events that occurs leading to cleavage of this complement proteins. So, these complement proteins they get cleaved they themselves are not active. So, the complement proteins are named like C 1, C 2, C 3, C 4 likewise C 4 complement here. So, they were their name are named as like C 1, C 2, C 3, C 4 and once they are cleaved they can form like C 2 if it is cleaved it can form C 2a, C 2b.

So, like this 3 can be cleaved into C3a and C3b so this kind of cleavage is occur and the complement proteins they get cleaved into smaller proteins or peptides and these actually assist in the process of the killing of the cells. So, and the cells can be killed by the complements by two ways one is by opsonization the other way is by lyses of the cell. So, they can also lyse the cells by formation of the membrane attack complex something which is known as the membrane attack complex are also known as MAC.

So this is what the complement proteins can do up upon complement activation and complement activation can be dependent on the antibodies it can also be antibody independent. It can be antibody dependent it can be antibody independent. So, it can be a result of recognition of the various oligosaccharides, mannose that is present on the surface of the pathogen is being recognized by some other complement proteins and then that can also lead to complement activation which is actually the antibody independent pathway.

And the antibody dependent pathway depends on binding of the antibody and recognition of the antigen and that leads to the cascade of events follows a cascade of events that leads to the cleavage of different, different complement proteins like C 2, C 3, C 4, C 5 and there is a long list. So, we are not going to discuss it in details now because we have lectures designated lectures for that so we will discuss there.

So just for the timing we just need to know that the antibodies by themselves alone cannot function, so they cannot do much they also require some other effector molecules they also

require some other effectors some receptors. That some kind of receptors or some kind of proteins that help them to opsonisize or kill the target cells or the target pathogens. So, this has to be very clear. And one of such effector mechanism is activation of the complements or complement activation and one of such effector molecule is the complement proteins.

So we got to know about the complement proteins and the complement proteins they can do again they can do 2 types of function precisely they can do 3 types of functions. One they can do opsonization they can lead to lysis by formation of the membrane at a complex. What they can also do is they can enhance inflammation, enhance the inflammatory response. So, how and in enhancement of inflammation if you remember from our previous lecture on inflammation and the migration of the neutrophils all these events then you will very easily recollect that I told there regarding the cleavage products of the complements.

So there are complement cleavage products like C3a C5a C4a which are also kind of chemo attractants they work as chemo attractant they are also known as sometimes they are also known as the NFL a toxins. So, they also help in enhancement of inflammation or inflammatory responses. So, this is another part this is another thing. So, primarily the complement proteins activation of the complement proteins can lead to opsonization or lysis of the cell by formation of what we call is the membrane attack complex.

Now coming to the cell mediated part. So, what is cell mediated part? The cell mediated part can again be broadly classified into two different parts one we know is the for the CD4, CD8 plus cells which finally develop into the cytotoxic T cells. so, the T cytotoxic TC and the CD4 plus cells which develop into the T helper cells. Now this T helper cell or the T cytotoxic cell they also help in elimination of the infection or the pathogen. Now how? So, the cytotoxic T cells as the name suggests the cells themselves they are cytotoxic.

So they can go and directly interact with the cell which is infected so for example the infected cell or the infected macrophage and it can kill that so it can kill that cell the target cell. So, it has a target cell it goes and kills the target cell directly. Now how does it do that? So, definitely there

are some effectors or effector molecules that helps in this killing by the cytotoxic T cells and for example there are effector molecules which help in destroying the pathogens.

For example the granzymes and this granzymes are basically proteases so they are pro proteases. So, the pro we use the term pro means they are not yet proteases but they get transformed into active proteases when they are cleaved. So, these granzymes are kind of inactive proteases and the when they are released into the target cell they become active proteases and they can do their function. So, that they can degrade the proteins and they can do a lot of functions.

So, this granzymes are released by the cytotoxic T cells and how do these granzymes they enter into the target cells they enter into the target cells by the action of another kind of proteins which are the perforins for example. So, the perforins which assists in the entry of the granzymes, so, that assists in the entry on the these granzymes into the target cell. So, let us say this is the target cell and this target cell is then it is killed or apoptosis is induced in these cells by the action of the cytotoxic T cells and some of the important mediators of this cytotoxicity is for example the perforins the granzymes.

And also you have the fast ligand the fast L the fast L which recognizes the fast so this is being expressed on the surface and then if it is recognized the fast which is recognized on the target cell and then it leads to apoptosis of the target cell. So, these are also certain effector molecules that are being released or expressed by the cytotoxic T cells which helps in recognition and killing of a target cell by apoptosis.

You will be learning about these in more details from our later lectures for the time being we are just trying to understand the different effector mechanisms that works in the whole immune pathway. So, now again so the weapons basically these are the weapons of the immune system. So, and then we come to that T helper cells now the T helper cells as I described when I started talking about the adaptive immune system the development and the activation of the T cells.

Then I have told already that the T helper cells when they the CD4 plus interaction occurs with the class 2 MHC molecules bearing the peptides of foreign peptides and I have shown this

interaction in the last class if you remember. So, when this interaction occurs then the CD4 plus cells they tend to differentiate into certain T cells subtypes and this is the effector. So, either they become the memory cells or they become the effector cells.

The effector cells means the ones who will directly in the will be directly present in the battle front so they will fight the battle. So, they are the effector cells and they are effector cells by because they has the ability to somehow release something or produce something that kills the cell that kills the target cell. As for example we have seen for the CD8 plus cells. So, the T helper cells they also are called the effector subset of this TD T helper cells includes the TH 1 T helper 1.

And as I also told you previously that these T helper cells of the CD4 plus cells they differentiates into the different subtypes depending on the availability of the cytokines. Now comes the name another effector molecule in the immune system a very important one the cytokines. So, we will be discussing about the cytokines in future lectures in very, very details I will be teaching you about the cytokines later on.

But for the time being let us understand that the cytokines they have a big role in the effector mechanisms of the immune system and the cytokines are released by most of the cells of the immune system they are released by most immune cells by the lymphocytes and all other cells are by the macrophages that if activated macrophages. They also release a lot of cytokines. So, cytokines are one of the very important effectors effector molecules of the immune system.

So depending on the cytokines what cytokine is present in the surrounding that actually decides which type of subset of the T helper cell will actually be produced. So, the T cells they the T helper cells there can be at least 5 different T helper cells subtypes have been identified and this includes the TH1, the TH2 the TH17, the T reg or the regulatory t cells and the follicular helper T cells the TFH. I have told you in one of my last lectures about these 5 subtypes.

Now but what do they do? Actually so what functions do they do? So, for example the TH1 cells they are involved in activation of the macrophages they activate the macrophages and leads to

the killing of the pathogen that is already there. So, they activate the macrophages and leads to the killing of the bacteria or whatever is present. The TH2 type cells the type to the TH2 cells they also do a lot of functions. So, one of the major functions is of course to help the B cell maturation sorry the B cell activation and in the class switching of the antibody types.

So this has a major role in class switching of the antibodies in the during the process of B cell differentiation and then the and mainly they are responsible for production of IgE immunoglobulin E you will learn about the IgE when we will be talking about hypersensitivity reactions later on. So, I think and they help in production of IgE leading to they can also help in the class switching of the antibodies on the B cells.

And the T helper cells they also activates the eosinophils, and basophils the cells of the immune system. They also help in the eosinophils, basophils and killing of different other types of bacterias and pathogens. The TH17 is one of the important T helper cells that are essential for enhancement of inflammation. So, one of the major functions of the TH17 is to induce the epithelial cells to produce another subset of cytokines known as the chemokines.

So they induce the epithelial cells mainly and which leads to production of the chemokines. Chemokines are also produced by many other cell types as well and so chemokines are basically the chemo attractants. I have told earlier as well what the chemokines are we have come across the chemokines particularly in the inflammatory response when we have this about the inflammatory responses. So, chemokines are also are very important class of cytokines they belong to the cytokine group family.

But they are mainly responsible for chemo attraction. So, attracting cells from one zone to another zone so cytokines are responsible for cell to cell communication and chemokines are primarily as responsible for cell migration. So, that is why they are known as the chemokines because they are that chemo attractants and helps in chemotaxis of the cell. So, they help in movement or migration of the cells.

So these TH17 cells they primarily synthesize the chemokines and these chemokines are responsible as I told they are responsible for the attraction of different leukocytes and primarily attracting more leukocytes more neutrophils into the area of infection or the affected areas. So, and then we have the T reg or the regulatory T cells. And the T reg cells are primarily their regulates the T cell responses. So, they basically they are the suppress the T cell response and thereby they are usually the cells which prevents the development of the autoimmunity .

We will be talking about the autoimmunity in the later lectures in the latter part of this course but for the time being so these T reg cells are one of the important cells which regulates or the T cell response and primarily they are inhibitory they has an inhibitory role. So, that they suppress the T cell responses. And the T follicle and help ourselves as we have discussed earlier as well they are important in the B cell development and the class switching of the antibodies they are helping.

So they help in the B cell development in primarily in these follicles in the in the germinal centers. So, they are responsible for the B cell development the class switching the affinity maturation all these processes these DF8 cells are responsible. Now let us quickly look into that as I told so these are the effector cells and the effector mechanisms by which the whole subset of the T cells they work. Now let us quickly look into what effector molecules these D cells they produce or that actually leads to these functions.

So the TH1 cells for example they are the major producers of interferon gamma we will learn about iron if gamma signaling later, so they produces interferon gamma and TNF alpha which is tumor necrosis factor-alpha. TH2 cells they produce interleukin 4 and interleukin 5 mostly which are the major cytokines that are involved in the class switching of the b-cells the antibodies on the b-cells and they also produces the GMCSF which the granulocytes macrophage colonel stimulating factors.

Then the TH17 it produces interleukin 17 and also interleukin 22 so these are the interleukin 17 is one of the major cytokines which helps in activation of the epithelial cells and leading to the production of the cytokines or they then they start producing the cytokines and IL 22 has direct

role in enhancement of inflammation. The T reg cells are primary producers of IL10 and IL10 is known to be one of the important interleukins or one of the most important cytokines that are involved in anti inflammatory responses.

So it is basically a also sometimes called an anti inflammatory cytokine or interleukin. So, IL10 is released by the T reg cells as they are the major cells which are responsible for suppression of the T cell responses. So, these are some of the effect molecules that have been produced by this T-cell subtypes or the T cells the T helper cells that mediate that actually mediate the function. So, these are basically we can where n we can draw an analogy and we can say these are the bullets basically which are being thrown by the immune system and the cells are the Warriors or they are the army men of the immune system.

And then you have more effective molecules, if we so these are the primary effector molecules that are involved mostly in the adaptive part of the immunity as well as in the innate part we also get in the cytokines are everywhere remember. So, the cytokines they are almost everywhere and in the innate part. So, the in the innate system so like we have the adaptive system and we have the inert system.

So in the innate system of the immune branch the of the immune system we also have different types of cytokines and they are primarily produced by an activated macrophage. So, an activated macrophages which has engulfed a pathogen for example so this is an activated macrophages which has phagocytosed a pathogen can also produce different types of cytokines. And which is also the effector molecule so they can produce many cytokines like the interleukin 6 the TNF alpha interlukin 1 IL1 for example interleukin 1, beta IL6 TNF alpha.

They can produce a lot of these effector molecules that does a lot of different functions in the unit part of the immune system. Apart from the cytokine so you can see that the cytokines has a big role in both the adaptive and the immune system in the communication the cell-cell communication. Another very important thing is the chemokines. The chemokines has a big role in cell attraction or cell migration so they can attract the different cells to different locations.

For example the dendritic cells so the dendritic cells are licensed to go to the lymph node and for that it the process is called the licensing of the dendritic cell and their chemokines has to play a very important role. So, chemokines they go and bind to the chemokine receptors. So, some cells they express the chemokine receptor on their surface and some cells that produce the chemokine. So, when there is chemokine in the surrounding that that will go and bind to the receptors and that will attract those cells towards that location.

So that is how the signaling occurs so the chemokines are the chemo attractants which attracts the cells expressing the chemokine receptors. So, the cytokines as I described here very quickly; So, it will be explained very, very elaborately in our in my later lectures about we will be talking about the cytokines but for the time being we get to know that cytokines are one of the major key players in the whole in the effector mechanisms of the immune system.

So, cytokines are involved in the innate pathways as well and as I told the complements are also present in the innate system as well. As there are other effector molecules I have told like for example we have the histamines the histamines, the prostaglandins and the leukotrins. So, these are also present and these are primarily these are also part of the immune effector pathways primarily the in it the innate pathway.

And these are also the word function they do is they increases the vascular the vascular permeability and they also lead to smooth muscle contraction. So, these are also kind of the effector molecules of the immune system that are mostly involved in the innate pathway. So, if we look into the whole picture the different effector mechanisms and effector molecules of this of the immune system we have identified among them are the complement proteins then we have of course the antibodies, the complements, the different types of small molecules enzymes like granzymes, perforins.

And then we have the cytokines we have the chemokines different cytokines different types of cytokines. We have histamine we have the prostaglandins the histamines which are mostly in enhancers of the inflammation. So, they are involved in the inflammatory responses. And also we have these cleavage products of the complement pathway or the complement activation

pathway. So, all of these molecules these effector molecules they work together to enhance or to amplify the signal.

So they are the effector molecule that actually effectively work on the different target cells and tries to kill the different target cells. So, we will be talking more elaborately or we will more discuss more and more about these effector molecules the pathways that are involved the effector pathways in our upcoming lectures. So, this much for today, it is this much and we end the lecture here, thank you very much.