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Immunology

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Lecture-5

Basic Concepts in Immunology (Contd.,)

So, welcome in lecture number 5 of basic concepts in immunology. In last class we discussed the effector mechanism of antibody what happened, how they are doing?

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Now I am going to discuss about effector mechanism of T cells like what these cells are doing the effector mechanism of immunity T cell actually orchestrate the cell mediated immunity and regulate B cell response to most antigens. T cell I mean we will see in next half an hour what T cell is doing and how many ways it helps the adaptive immunity. Because T cell also need to be activated specifically against the pathogen or antigen it is not in general like innate immunity.

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We already mentioned but again today we will see that what is slight more detail will definitely go in much more detail in much more detail in this T cell part. Let us go and recapitulate what we said about the MHC. MHC is the major histocompatibility complex why we need that because if you remember I already told that T cell receptor cannot recognize antigen in native condition or alone.

The antigen should be present by either MHC class 1 and MHC class 2, to T cell receptor. So, T cell receptor recognize antigen with MHC together the complexes recognize B cell receptor can recognize directly the antigen directly the organism or pathogen but T-cell is not. There are two types of MHC. Two types of major histocompatibility, compatibility complex one is MHC class 1 and the other is MHC class 2.

We will discuss later what is their detail function of this MHC 1 and MHC 2 but now if you see this picture the cartoon you see there is very similar looking thing they are very similar ok but immediate difference what I can see and I am sure you can see this yellow line in this case of MHC 1 there is only one. This is a transmembrane domain so only one transmembrane domain attach them with the cell membrane.

In case of MHC 2, 2 transmembrane domain attached or anchored with the cell membrane in case of MHC 2 and the red part is the processed antigen ok. In previous lecture, 1 of the lecture previous lecture we see that antigen is processed ok.

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So what is this processing? Here what we are going to explain now is this is a virus infected cell we all know that virus grow inside the cell host cell. So, this is a virus infected cell, what is happening? The virus is replicated within the host cell and after replication they are producing their nucleic acid either RNA or DNA and then they just bulge out and making more virus from here. And this virus will go and infect the neighboring cell.

So, new virus will come out and infect a new cell but if you see the virus infected cell express some protein which is like spiked type of protein on the cell membrane. So, in normal cell this viral proteins, the Spike protein is not present. So, as soon as the virus any cell infected by virus they will express a specific protein which was not there before. So, this new protein, our adaptive immune system can recognize they can recognize that this is not our own cells so something happened.

So as soon as this new protein come out cytotoxic T cells can recognize them. So, cytotoxic T cell can recognize this new surface protein as soon as they recognize or bind or attached specifically they gives as they give a signal. What kind of signal? These cytotoxic T cell after this attachment will be activated and tell that particular cell by cytokines are by cytokines that something happened.

And these cytokines, the cytotoxic T cell will produce cytokines replicate and then in this attachment they will produce if you remember the previous class also they are producing lots of killing things. Killing thing means they produce perforin kind of protein which can make perforate the cells that means they can make holes in cells they express some kind of proteins which induce apoptosis that means programmed cell death kind of signal.

So we will come later at the beginning we do not have to worry about that. so, if we remember just now the cytotoxic T cell T cell can recognize virus infected cell and give signal to this virus infected cell to die. So, it will die then. See if there is no I mean if the cell in virus infected cell die then they cannot grow inside. So, automatically the virus inside the cell will also die. But this recognition is not that simple.

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This is the whole slide where we already discussed it what happened in case of T cell the antigen is chopped into different pieces. One of these piece fit into the MHC and this MHC antigen complex is recognized by the T-cell receptor. So, same thing happened here also what happened the virus infected cell produce lots of protein inside the cell.

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So, this is a big cell they see themselves if we make a big way this big way you see inside the cell there is nucleus, there is endoplasmic reticulum. So, all the viral protein is also synthesized inside the cell, I mean inside the cell in the cytoplasm. So, during this protein synthesis what happens will come again later in a more detailed way. Any protein synthesized in our body that all proteins are not properly folded there are some incomplete protein.

So all this miss folded or incomplete proteins are degraded inside the cytoplasm there is a system called proteasome. So, same thing happened because virus replicate very fast, so they are also doing lot of mistakes during protein synthesis. They are misfolded protein they are incomplete protein so all these misfolded protein and incomplete proteins are processed into small pieces. The previous slide and this one of the small piece or this small piece will enter into the endoplasmic reticulum and where MHC 1 is located.

So MHC 1 will be packed with this piece of viral protein and these MHC 1 from endoplasmic reticulum will go to the surface of the virus infected cell.

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So, what we see here just spike it is not really spike it is like this so the spike protein or the viral protein rather viral protein will go outside the cell or express the membrane of the cell along with the MHC 1. The cytotoxic T cell, TC which is what this is the simplified picture or the cartoon but if you see closer view of this it is this junction is actually looks like this. So, the viral protein along with MHC is going to recognized by the T-cell receptor.

In this case it is MHC 1 so any intracellular protein or any protein synthesized inside the cell is going to be presented by MHC 1. And MHC 1 cytotoxic T cell and cytotoxic T cell recognize MHC 1. So, I am just summarizing one thing to remind you and you are I mean I will tell them anytime but again there are two type of T cells one is cytotoxic T cell another is helper T cells. Cytotoxic T cell cytotoxic T cell has cytotoxic T cell has CD8.

And helper cell helper T cell has CD4, helper T cell has CD4 helper T cell has CD4. So, that is why many times instead of cytotoxic T cell we calls CD8 cells and T helper cell we said CD4 plus. So, we normally CD 4 plus and CD8 plus. Cytotoxic T cells CD8 also recognize this MHC 1 so two thing we have to remember one cytotoxic one, cytotoxic T cell express a co-receptor along with the TCR a co-receptor called CD8.

This is number one, number two cytotoxic T cell recognize MHC 1. Cytotoxic T cells recognize MHC 1 ok and T helper cell express a co-receptor CD4 and it recognize MHC 2. Cytotoxic T cells CD8 plus and recognize MHC 1, T helper cell CD4 plus recognize MHC 2. So, the viral infected cell express viral protein or present viral protein through MHC 1 which is recognized by which is recognized by TCR along with CD8 and kills the viral infected cell by giving the signal of apoptosis.

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Now CD4, CD4 cells means T helper cells you see THI will come to that one. So, T helper cell having CD4 which is recognizing you see this is a MHC 2 there are 2 transmembrane domain. So, antigens presented by MHC 2 are recognized by T helper cell receptor along with CD4. What it is doing? It activates macrophage. You see this picture and then I will show you later.

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What is happening those which are intracellular bacteria parasites a *Mycobacterium tuberculosis*, *Mycobacterium leprae* what they are doing normally macrophage eat Mycobacterium also just like other bacteria. But Mycobacterium somehow they know that tricks that they manipulate the macro vesicles what is happening in in when one macro bodied bacteria, so there phagocytose internalize then lysosome is they are inside already.

So lysosome is full of proteolytic enzyme, so the lysosome sitting inside phagosome come they fuse together so these two vesicles these two vesicles are there one is lysosome another is phagosome so which is full of proteolytic enzyme they mix become one. So, this proteolytic enzyme present here will kill and chew all the material inside this phagosome

which we have seen like in the neutralization, in case of opsonization the whole thing is completely chewed up.

But *Mycobacterium* or similar kind of intracellular ah parasite and bacteria this somehow managed the macrophage in such a way so these lysosome this violet vesicles are not fusing with this phagosome. So, what is happening *Mycobacteria* grow inside the macrophage. So, macrophage do not realize that they are growing inside or not doing anything even they realize they do not do anything.

But if our immune system is strong enough and if this thing goes then the disease will progress. You see there are; in this is the microscopic image see there are so many bacteria inside all these red cells. So, this is a tissue section so there are so many cells in some bacteria inside. But when Mycobacterium are growing inside what they do not have the control is that the micro actual protein are expressed or presented outside the surface of the macrophage by MHC 2 which was not there before.

So these MHC 2 presenting *Mycobacterium* protein are recognized by T helper cells. So, these T helper cells understand something is different because this protein was not our own protein. they This if it is our own protein the T cell receptor of this helper cell would not have recognized them because they are already eliminated. We know from the clonal selection hypothesis or clonal deletion method.

So as soon as they recognize that means something is there. So, this interaction will activate this helper cells so they release some cytokines which is here interferon gamma and this interferon gamma will tell the macrophage , see you are doing mistakes which you are basically allowing them to grow they are not very good thing so what you do, lysosome should fuse with them and kill them. So, this signal will tell the macrophage to fuse the lysosome and all the intra- vesicular bacteria will now chopped up.

This is called TH1 response. So, normally we are exposed to TB patient or we are having the micro bacterium inside our body because it is airborne. But if our immune system is strong as soon as they start growing TH1 cell recognize them and this recognition is through this MHC 2 and they tell them to kill it. So, we do not see any infection. So, this is how T-cell have the adaptive immunity because this T-cell receptor this takes time.

And if you see this case when it is you see in this case in normally we do not see any bacteria inside this tissue. So, this is called TH1 response of T-cell.

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T's this is this TH 1 is also TH means this is also helper but another important function of the helper cell is what? Another important function of helper cell is helping B cell because B cell alone can interact with the antigen free they do not need to be processed but B cell only interaction in the antigen is not going to activate it. So, B cell if you interact only with the antigen they are not going to be activated. But it also needs another signal from T helper cells.

So this called T follicular helper cells. You learn it much more detail when T cell development will see our T cell the sorry B cell development will read or will study the B cell mediated immunity, how B shall confer the immunity when we discuss that we will discuss this part much more detail. But here what happened I told you there are 3 type of antigen presenting cells macrophages, dendritic cells and B cells.

So after engulfing or taking the antigen inside by receptor mediated endocytosis they also present this antigen the B cell is also going to present the antigen through MHC 2. So, I am repeating one more time one is any internal or endogenous antigen that means any protein synthesized inside our body inside our cell is presented by MHC 2*. Anything coming from outside say bacteria or bacterial protein or toxin or any foreign agent from outside to inside by phagocytosis or receptor mediated endocytosis they are presented by MHC 2.

(*Please read MHC I)

So B-cell internalized antigen from outside presenting by MHC 2 recognized by T helper cells receptor along with CD4. So, these combination are giving the signal to T-cell this interaction is giving the signal to T-cell which in turns activate the B cell and telling that now you proliferateand convert to plasma cell and produce antibody.

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So, now they were going to this innate and acquired effect. So, what is in summary B-cell activated by T helper cell and going to produce antibody intern antibodies showing it is effector function in 3 ways neutralization, opsonization and complement activation. And T-cell not only helping the B-cell to activated and produce the antibody it is also helping the immune system by killing virus infected self as well as it is also helping which is not mentioned here or the tumor cell also.

The cancer cell is also producing some new protein which is not present normally in our body is also presented by MHC 1 and same way the viral protein was recognized by

cytotoxic T cell was recognized by cytotoxic I mean the tumor cell also recognized by cytotoxic T cell and killed by cytotoxic T cell. And TH1 response what it is doing if there is any intracellular pathogen which is growing inside they recognize that and tell the cell to kill the intracellular pathogen.

So if you see I mean if you remember that slide that we have for type of pathogen virus, intracellular bacteria, extracellular bacteria, extracellular bacteria is mostly taken care by the antibody. Intracellular bacteria by TH 1 response most of the types of they kill by inside killed inside the cell. Virus is taken care by the NK cells and cytotoxic T cell which we already discussed that is the effector function.

And the parasite what happened if it is smaller then, antibody can take care antibody can bind and also and if it is intracellular then TH 1 response is going to kill them. And if it is big then you already know that antibody coated parasite is killed by your eosinophil. So, eosinophil will also make hole and kill the bigger parasite if it is antibody coated. So, these are the affected functions. So, if there is any mistake here whatever I told that is how it is protected.

But if it is any mistake in that that either we can occur in our lifetime any defect in immune system or immune system defects can be inherited and which cause several problem.

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What are these problems? So, infectious agent virus or bacteria this normal response is the protective immunity. You normally do not see the disease but if it is deficient in some way I mean there are many way it can happen. So, what we will see a recurrent infected infection. So, if any individual will see that they are infected I mean recurring infection happen their immunities know or protection is less.

Innocuous substance that is normally the allergen which cause allergy, now it is normal response is allergy if there is a defect there will be no allergy some of it is good. Grafted organ is not the natural process but if we want to graft or implant any organ okay, transplantation so if there is normal response immune system is then it will not be accepted by our body but if it is defective then it will be accepted. These 2 like allergy and rejection is non-pathogenic most of the time.

If there is a defect in immune system that cannot recognize our own protein or own organ then autoimmunity will happen but if there is deficient self tolerance. This is normal

response organ if immune system responsive to the self organ that caused another disease called autoimmunity. And tumor just I told if there is a tumor or cancer normal response tumor will be cleared by our immune system but if there is a deficient or for some reason the T cell or NK cell cannot recognize the transformed cell or the cancer cell the progression will be the disease, the cancer.

So this is if immune system works and how it works in general B cell T cell in and immunity how it happened. But if you want to do something what is the best protection what is the best protection, how we can induce our immune system then we just discuss little bit.

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But the best protection to induce our immune system is the vaccination. So, we can prepare we can trained our immune system against a particular disease. Medicine can cure the disease but disease will happen but vaccination will protect us from the happening of disease. So, if the vaccinated properly and proper time then disease will not happen. So, immune system will not have to work or even if we work we will not know.

So it can manage by itself but unfortunately not always vaccine is available there are many diseases very effective vaccine is discovered but there are many diseases in today for like HIV malaria we do not have any vaccine particularly there is no vaccine is developed against any parasitic disease. But some viral disease some bacterial disease vaccine very good quality or protective vaccine is discovered.

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And just I am giving you 3 examples like diphtheria till 1945 till 1945 we have the cases of diphtheria you see is going on this but when the vaccine developed or the vaccination not; vaccine development is not the only the proper vaccination is also require. A proper vaccine does not happen you see suddenly it goes down and 1955 onward or 54 onward the existance or the recurrence of this diphtheria is very, very low.

There are very few cases where either vaccine does not work or immune system is not working properly even after vaccination very low. So, vaccine can almost eradicated the diphtheria but not as good as a smallpox.

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Same way polio also, polio has 2 different type of vaccinations recently what we are using is the oral vaccination. So, it is now we are giving the many of particularly in India all of you have heard (FL: 26:36) right there are many ads every time you listen polio day anybody below 5 years should have two drops of polio vaccine this is just oral. So, but what you see it was up and down but before the vaccine discovered or vaccination process or immunization process initiated it was kind of not very low right.

And gradually it is decreased and now you see it is almost disappeared this is the result of 1990 if you see the latest result that the polio cases are very, very low.

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Same way another vaccine is the measles. Measles are also goes down to very low it is going up and down but now it is going down and slowly it is almost not there. Not only measles there is a disease called subacute sclerosing panencephalitis which is a brain disease that is late consequence of a measles infection that means it appears after the measles is over measles. So, that case also it happens when this measles goes down automatically the SSP that the subacute sclerosing pancephalitis it also goes down and it is almost zero.

So, what we can say is that if that immune system normally works perfectly or fine many times we do not see any disease and this is one of the most wonder because if you study what happened to the AIDS patient where the immune system is goes down almost there is no immune system you see what I mean what kind of infection is going, are happening in case of AIDS patient, you will be surprised.

But staying in the same environment or staying in the same ocean of so many pathogen micro organism most of us not having any disease most of the time it is really a wonder and that wonder I mean the credit total credit should goes to immune system. And this immune system as much we study because many things we do not know exactly how it is happening and that is the most important thing are important reason for studying immunology.

Like more we study not only studying I am not talking about this kind of course more research I am talking about. More we will know more we can handle or more we can control or manipulate our immune system and we can develop more vaccines more effective vaccines newer way of vaccination and we can protect ourselves more and more and so that there will be no disease. Because you know bacteria we have antibiotic and these antibiotics are not good but even we can have antibiotic to kill bacteria.

But the more dangerous thing is in case of bacteria or more severe problem that we are seeing right now is antibiotic resistance strain. So, we cannot I mean may be near future we cannot kill bacteria by antibiotics. So, only thing we have to understand the immune system so we have to do something to activate the immune system so the even the bacteria infect us or get inside the body or somehow it enters into our body that cannot do much by our immune system.

So that way immune system is very much important to study to know even if you do not know our immune system will work right. So but it is very interesting; that way and research is also very important. And one should think about to study the immunology and proceed further or immunology research to protect ourselves from disease and any kind of infection and cancer also.

So, this is the today's class I hope you have cleared the basic concept whatever I told is the overall immunology that we are going to teach in next few modules. Like we are going to go detail about many of not much detail but as much as possible within the scope of this course will discuss whatever I discuss in last 5 lectures I will discuss and rather we will discuss or in little more detail to understand in much better way, thank you.