Immunology
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Lecture No -31
Development of T Lymphocytes

Welcome, today's class so last few classes you had varieties of techniques. So we were kind of in a break from all this immunology detail of the and biology part of the immunology or the life the immune system so we are discussing about different techniques so I hope you had a break from all this B-cell, T-cell, macrophage, lymphnode and all this thing. But we have to come back to again into our main immune system to know what is going on in different part of the immune system.

Because so far whatever we discussed I am just if I tell very quickly we know what is in that system we know what is adaptive immunity and then what are the components we know B-cell T-cell, cytotoxic T cell and T helper cells, macrophages, neutrophils, inflammation more or less you complement different effector functions everything you know an antibody structure. How the diversity of B-cell, T-cell receptor arrived to that many varieties of different kind of B-cell.

These parts we have discussed right we have discussed as much as little possible or within the scope of this course because there is just no limit because you can study even more detail. But as it is going like too many times we are kind of kind of discussing MHC antigen processing also you know right. So now the thing is all the components of immune system are known. Now we have to learn how immune systems understand to protect us not to making any harm to ourself.

But we have to handle the foreign pathogen or the pathogenic or material or toxic material that body's handling which is coming from outside. So we first will learn different components then we will learn now in some lecture that we are going to listen that how immune system learn how to recognize which one is foreign which one is not and what happened what time because whatever we discussed before now we are going to discuss with time.

So we are going to start with development of T lymphocyte development of T lymphocyte first then we will discuss development of B lymphocyte and then we will see that how they learn and there are a lot of places you will see it is not known and it is mystery. Mystery means not discovered yet exactly what is happening but still we will try without going much detail as much as possible to discuss right. So before going to detail I will just I mean it is not possible at this moment to know what is your feeling like how much you understand how much you remember.

I am sure many of you read novel write in novel what happened there are so many varieties of characters. So if this is new if you were not aware of this trouble all the characters are new to you do not know their name so gradually will learn different names and gray and then you learn their character depending on the writer or the author you the way the author or the writer explained their character you learn who is good who is bad, who is the hero who is not.

So in any mini story will find there is a Robin Hood kind of character who is very helpful doing and somebody is protecting somebody's a head of the family or a head of the society. So many ways and that story goes in such a way and continuously there are a lot of interaction with different people immune system is just like that. There are many characters initially will find so many complexity like not remember but gradually you go you will learn them you know their character you know their job then only you have to just like story what I mean me?

If you ask me when I am reading a story whenever I am reading about any character automatically an image of that person building my brain like how he or she will look like what he is doing how he is doing that is my imagination. So if you remember if you can visualize the whole immune system just you know that story this is a story assume that immune system is a story of variety of character and they are doing the different job.

So what will happen if you close your eye and can imagine what they are doing and you give the shape and size of the character and then imagine this is this he is doing like that or it is doing like that they are interacting how they are interacting not like exactly human being so may be slightly change your idea like how cell behave you have to you know how cells behave. So same way if

you if you are reading a story just the book then your imagination is 100% your imagination and when there is a jungle.

You imagine a jungle how it will be that complete your imagination. But as soon as you go to comic what will happen the artists imagination is implies on you. Like you can see the jungle the way artists side you will see the person the artist think about him or her same way of showing you the different cartoons here in immune this immune system story. So how the basal look like how the macrophage look like how the dendritic cells look like.

So that is the artists imagination you can completely ignore that you can think of your imagination and think the story in your own way or you can imagine like a comic book that we are following the slide. So like how they look like then if you know the story gradually even the name you find complicated many of you have read the Harry Potter. So you when it come for so many characters so many varieties of name but still you like it and there are so many complicated things are happening.

Initially you might have problem to remember the name and their relation and all this a magic world but gradually when series came one after another you know everybody's character you feel I mean you can feel for them you can think for them you know how they look like but as soon as you saw the movie the image in your brain change. Now you cannot think how the Harry Potter looks like because you have seen him right in this case sale also if you are working with it when you see the sale under microscope how exactly it will look like your imagination will be like that.

So what I will suggest every chapter every book think this is a story there are B cell is one character macrophage is one character encastle is one character, helper T cells, cytotoxic T cells are one character they have a communication that communication is between a code or signal that signal is the cytokines. So they are some Robin hood-like T helper cells which is helping everybody there are a fighter like cytotoxic T cell.

So imagine that story and think the whole immune system will be very, very simple and straightforward once you can chuck a whole communication thing or the table in your brain then you will see everything is so easy and simple. Do not try to understand discrete away that part is over so we explained individually what is antigen processing, what is MHC, how it is fit into MHC and how it is happening so this part it is already shown right.

Now it is up to you how you can understand. So now you have to imagine in your own way keeping everything you remember and try to link them so then you will enjoy the whole story ok. So this is my suggestion that is how you can remember the immune system what you will find like what I am going to do or I am doing rather or rather we are doing is just we are telling story like things. So this thing happening that thing happening something we know something is I will tell ok.

We will know later because some every suppose there are four or five things happening in a story parallely. So what is happening you cannot so in a movie all five things together so you have to show serially sequentially particularly in any detective story this is very common. This is also because here some cells are there were spying all the time figuring out where the pathogens are so they as soon as they got they are doing something all things or many things happen paralleling until unless you imagine together then you would not get the fun.

See if you want to have fun and understand nicely learn the character first then try to link them together and see what is happening if there is an attack and our heroes like B-cell T-cell macrophage all of them are very particular about they do not want to do any harm to our own cells. So they are so specific about the foreign and if there is any problem then there are already diseases. So that training part is very, very important and that is why we are going to go one by one first we will discuss about the T-cell development.

Then you will see B cell development it is not possible simultaneously one by one we have to teach right. So B-cell and T-cell lymphocytes you know they are coming from the same progenitor, lymphoid progenitor what they synthesize? The synthesized in bone marrow right. So

in bone marrow the B-cell synthesize and T lymphocyte precursor is also synthesized but B-cell developed or get the training or mature.

Mature means they understand how to know which is cell and how to distinguish from self and non-self training is we call it development during that development receptor is also formed. How the receptor form VDJ recombination DJ recombination and that we discussed already here we are not going to go detail. We will just say when this VJ recombination is happening when this VDJ recombination is happening we are not going to go determine just mention it because you know much more detail now how this thing is happening.

So B cell most of the B cells are developed in bone marrow so that training or maturation is called development I am repeating again. So B cell developed in bone marrow and T cell precursor after synthesizing in the bone marrow they migrate to through blood to another organ called thymus, clear. So that in that thymus T cell mature or T cell development happen. T cell is not the passenger of in thymus so they are not just going in thymus.

So they control the thymus also so both the cases they need rigorous training or screening rigorous screening for both B-cell and T-cell, why? Because if the screening is not done properly or if there is any faulty screening what is going to happen they will not recognize our self protein as cell. If somehow they miss this thing or if the our own protein the start understanding so know this is foreign then what will happen our immune system will try to kill us.

So that rigorous training is very, very important. Many part of that rigorous training is not yet clear but something which is clear we will discuss as much as possible. In case of B cell one thing you have to remember that though you will learn later B cell produced throughout our lifetime B-cell produced throughout our lifetime. But T-cell producing thymus those thymuses after puberty are shrinking down. So the property is not that no T-cell is produced but the production of T cell or maturation of T cell slows down very much.

And it also have seen that after puberty in Mouse particularly after puberty if you take the thymus out so if you cut the thymus or upper to the thymus out from the mouse nothing much

happened to immune system immune system is equally working that means before puberty most of the T cell are mature and after maturation they remain in our system they divide and maintain the specificity or the variety or the diversity is that clear. Anyway if you I mean so far whatever we discussed we are going to meet in life session.

So I hope many of your doubt no I may not clear all the doubts but most of you doubt whatever we discuss I hope it will be clear in the live session very soon so do not worry for that. So if you have question will be there. So now so this B cell continuously produced third the lifetime. So if there is an imagistic that there is a chance of mistake can be over like because these B cell every cell has a lifetime. So B cell will die new B cell will come so if there is a mistake that may be short term if there is not very bad mistake.

But in T cell it happens before puberty most of the things happen and in T cell development I also should tell you the T cell development whatever we know it is we know mostly from Mouse. And I already told you in one class Mouse immune system and human immune system are very, very similar right. So most of the information that we are going to give or discuss in the class it will be from Mouse only very little information and human information where it came if any individual is defective in any organ or something then only we can tell you what happened in Mouse.

So what happened I am telling you initially the both B cell and T cell Part, B cell receptor B cell have grow they make the receptor. If any receptor binds to our own protein that cell will die that you know from clonal selection hypothesis right but in T cell receptor what happened? In T cell receptor so T cell is there so this is the T cell then the receptor grow, so from T cell receptor grow like this and fourth thing is it should interact with our own protein because T cell cannot recognize antigen without MHC and that MHC's my own MHC, clear.

So if T cell receptor does not react with MHC that will die. So this in case of B cell what we said if it interact with our own protein that cell will die that is a clonal selection we hope you remember this is called a negative selection. That means as soon as you remember a recognize you have to die but in case of T cell first selection is what? Selection of our own protein, so if

this is the MHC the T cell receptor and MHC should interact and antigen should be in the middle right.

So antigen and I told you MHC is very not stable and MHC 1 and MHC 2 both are presenting our self antigen also but that cannot activate T cell right. So first T cell after generation of T cell it should interact with MHC so that is what MHC my own protein in B cell if it interact it will die but in T cell it should interact this is called positive selection. So first you have to select positively so after BDG and BG recombination so many variety of receptor will form but all receptor we do not need I am talking our T cell.

Now I will not talk much about the B cell. So T cell receptor after BGD recombination in the beta chain and BG recombination in the alpha chain there is so much variety of that kind of cells and in the receptor only those receptor will survive which will interact our own MHC that is self MHC that is called positive selection. So in this case interacting with cell protein not really kill them that will select them.

So then what we want then we want that same receptor we survive. Survive means which can recognize our own MHC those will only survive and those T cell which has the receptor which passed the positive selection now interact with our own protein. If it interact with the self antigen they will die. Now you see it is so complicated initially I am saying if it interacts then we will survive with the self antigen. Second I am saying that he would interact with the self antigen it will die that is the negative selection.

So in case of T cell receptor both positive and negative both the selection are there. So now if you calculate that way positively selected cell means they react to it so self antigen then negatively negative selection means they also react with the same antigen. So if you calculate both so all positive please selected send interact with self antigen will die that means there should be no T cell. Listen again positive selection means it is going to interact with our own protein then only they will survive otherwise all will die.

So the T cell receptor which can recognize our own protein will survive. Next time I am saying if it is interact with our own protein it will die. So that means whatever selected before also dying and there should be no T cell receptor. So this part is still very hazy that is not but there our hypothesis will come what is happening what are the provable thing that is very interesting. So discovery of this thing is very interesting I will try to tell you as much possible to discovery part.

Just because if I tell you; just the information like these diseases there will be 10 points and you have to memorize the 10 point. All they say in 15 20 points I can tell you this thing happened in this thing happening I can show you slides where lines are line up the line will be written I will read out or you can read the book but you cannot remember that. So if you remember experiment behind it how this thing or how this line came after what experiment if it is possible not all as possible.

Then what will happen even if you have a big story against one thing in your life also you will see if there is only one if you somebody say do one thing you may forget but if there is a background of anything a lot of things then it is hard to forget because some even as soon as you remember something rest of the party can remember that is that is the reason I will try to tell you some experiment by which you can remember or at least chance of forgetting the things will be less.

Many experiments you may not understand because now neither I am in a position to explain you much or you are not in a position to understand better because many thing you are not in a position at this moment at this stage of your course maybe in fourth year at the end of other courses over molecular biology and all this thing when everything will be known you may understand but at this moment you may not understand.

Do not worry I will try my best to explain as less complicated way as possible but you have to understand that experiment I will tell why I am telling all this thing not telling much about the immunology. I am telling him immunology because I told the immunology is the story. So I will just keep on initial part was description of things what is happening now I am going to tell you story one after another you have to just remember the story.

And if you it is like a different chapter of a story you just have to put them together to complete the whole story or the whole novel whichever way you understand. So how this positive selection and negative selection happened that will understand and simple thing. Now all of you know every book it is written I am also telling and told you so many times T cell maturing thymas how it was known? And how suddenly all the part of the body someone will see that T cell is going to thymus and it is mature there.

It is discovered even before the B cell, B lymphocyte and T lymphocyte is discovered B lymphocyte until inference I discovered it was discovered before. It was accidentally discovered that in Mouse if some of the thymus was removed their immunity goes down that time B cell T cell was not known it was not discovered. So that just by that discovery it was identified that means thymus has some role in it in immune system.

What is that role? It was not known. Same way there is human disease digest syndrome. Now in the digest syndrome it was found that something is wrong. So B-cell population is perfectly all right but T-cell population is low. So this discovery sometimes it should be true disease or some accidental discovery. So it is no one can suddenly from all the body parts why thymus it is not known. It was not known now everybody knows what is happening in B-cell and T-cell development.

There are one differences in B cell there is no positive question of positive selection is because B cell receptor directly can recognize antigen but T cell we have to recognize the MHC right T cell receptor should recognize. So that is one difference another difference just I mean what is the B-cell and T-cell difference? B-cell T-cell differences definitely their life at one is it is through lifetime it is happening and T cell mostly it is happening before puberty.

In Mouse what happened thymus maturation thymus, thymus maturation continues up to three to four weeks after birth. But in case of human at birth I mean before birth you can say just before birth or when we are born before that thymus maturation is complete. In B-cell and T-cell both some portion of the cell some portion of the cell is mature not mature in bone marrow, clear.

That is why at the very beginning I said most of the B-cell mature or developed at bone marrow most of the T-cell mature and developed in thymus.

There are some cells which is not maturing timers in case of T cell there are some cells which not mature of mature in bone marrow in case of B cell. There is one more very difference in B cell B cell receptor is only one type right what is there to heavy chain to light jets. But in case of T cell what we have in T cell receptor most of the T cell receptor is alpha and beta type that we already told most of the receptor is alpha and beta type but there are certain receptor which is Gamma Delta type.

So the two type of receptors are present in T cell which is not in case of B cell so this all I am while telling if you consider that I am telling like a story no slide nothing. So this is also I am giving you information careful about it so two type of receptor present in T cell alpha beta and gamma delta but in case of in case of B-cell we have only one type of T P cell. But there are certain T cells also less variant or in variant natural killer type T cells, T 17 cells, T regulatory cells.

So not only cytotoxic T cells and just in general T helper cells there are some more sub population of T cells which you will learn not now. In this lecture I mean in continuation of this lecture because it will continue few lectures T cell development and T cell immunity next few lecture we are going to discuss. We are; I am particularly going to discuss mostly the alpha-beta T cell receptor development and partly gamma delta T cell receptor development.

T cell development not the receptor, we already discussed the receptor. So T cell development will mostly contain the T cell with alpha beta receptor and little bit of Gamma Delta receptor and rest of the T cell receptor thing we are not going to touch much until unless it is necessary in some future cases. Something we need and that time will tell what is that not much detail is known also and we are not going to make this course that complicated because then there is endless actually.

So this is just I can say this is the introduction of T cell development. Real T cell development discussion will start in the next lecture, see you then. Bye.