Immunology
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Lecture No -34
T Cell Mediated Immunity

In this lecture we are going to talk about T cell mediated immunity. So T cell before T cell mediated immunity in last lecture or in the previous lecture we are discussing about the T cell development. So after developing from thymus the leaf thymus come into peripheral blood and from peripheral blood they enter into different secondary lymphoid organs. So bone marrow and thymus is called primary lymphoid organs and the spleen lymph nodes pairs patches they are called secondary lymphoid organ or the guard mould all this thing.

So from thymus to blood and then from blood to secondary lymphoid organ because there they are going to see the pathogen or pathogen presented by the dendritic cells mostly macrophage and B cells and after that interaction with a machine for a processed antigen they will be activated and do their job. But before interacting with because after maturation and entering into blood what they are when they are coming they do not see the they do not see the antigen yet what they are called? They are called naive T cell. They are called naive T cell naive naive T cell that means they do not yet saw or see any antigen.

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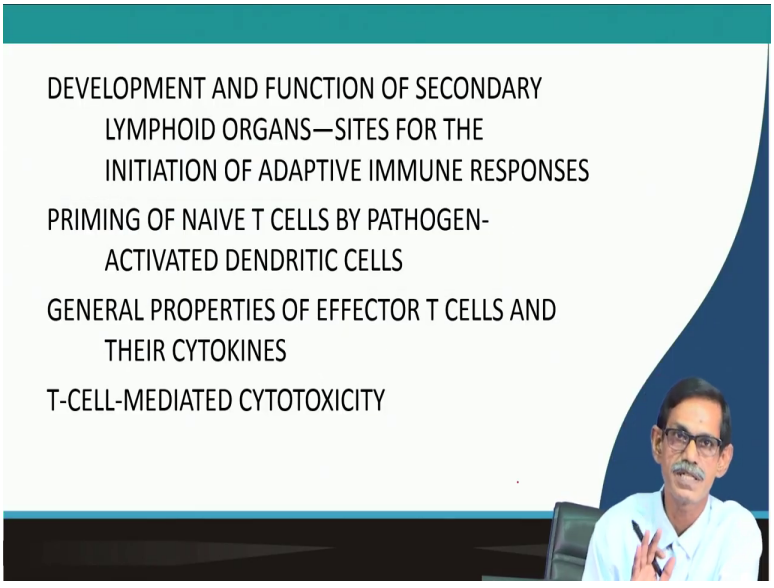

What we are going to discuss here the development and function of secondary lymphoid organs or how? Actually we are going to tell what part of the lymphatic organ this T cell visual stay priming because you need naive T cells primed by the pathogen otherwise they do not know or they will not decide what to do after seeing them who is presenting MHC1 or MHC 2 where it is presented depending on that the effector function will be decided.

And how they will understand everything almost everything are done in this system immune system or most of the system of our organ is by signal transduction. It is either direct contact of the cell that one cell attached with another cell by protein-protein interaction because of the surface protein of this cell surface protein of this cell interact this is one way or this cell release something which will go and bind to the next cell and activate this one.

It may be other way around this release something activate this one. So it is both and many times it happened many times it happened that cell, if this is the cell suppose this is nucleus this cell is producing some molecules and you know already this is supposed to be done in bio chemistry class. So this is molecule and they itself has a receptor. So where this will fit so when this thing happen the this released by cell itself and binding its own receptor it is called autocrine.

It is called autocrine. Same way if the cell releasing something and binds to the neighboring cell or very nearby cells it is called paracrine. Autocrine shelf paracrine nearing or neighboring cells and endocrine you know the hormone which release into the blood and work in distant place. So most of the time this property or the affected T cell function what will it will do how it will do this kind of modification their location is either mostly by cytokines lot of chemokines are also involved to attract them.

And also protein-protein or cell-cell interaction these three is the communication between cells and here all cells like antigen presenting cells are going to present the cell. So that cell-cell interaction through TCR MHC antigen peptide and many others that will see this interaction many other cell receptor and ligand interaction is important, chemokines are important, cytokines are important. Effect of all this who what kind of cytokines will be released and what will be the effect of that will decide actually the effector function of T cells whether it will kill or whether it

will help and helping means many things that we are going to discuss in this lecture or next lecture. And definitely T cell mediator cytotoxicity how it kills the cell.

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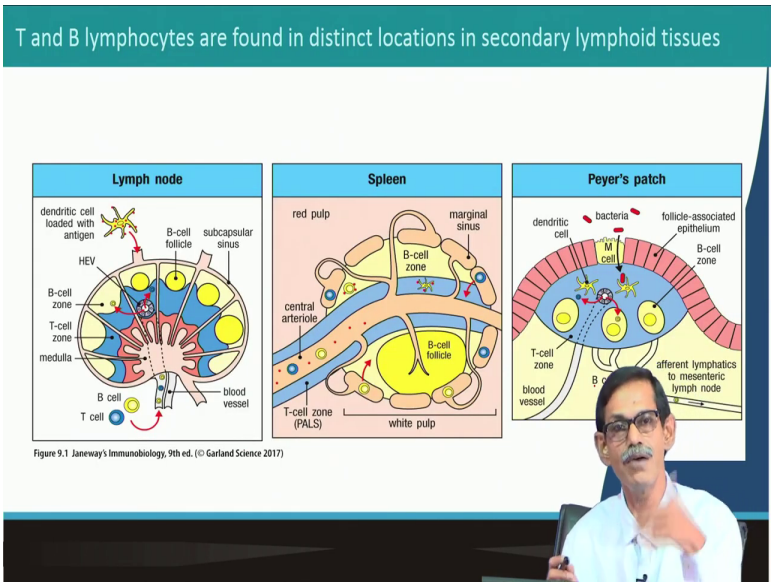

So now quickly I will just go through this and you know this. You know this because this is lymph node that you have seen the cross section, this is the spleen and this is a spare patch where the M cells are there and what why we are showing it again this blue zone is the T cell zone and yellow zone is the B cell zone. So it is distinct very distinctly look at it, so B cell is not everywhere and T cell is not everywhere.

But does not mean it is totally absent majority portion of the T cell is in this blue zone how it is happen it comes through this all B cell T shall go there and or it is coming through this venule and it is distributed that same thing happened here also. You see this is the blue region is a T cell region and yellow region is a B cell region. So all the secondary lymphoid organ where the; B cell will stay where the T cell will stay majority that is decided.

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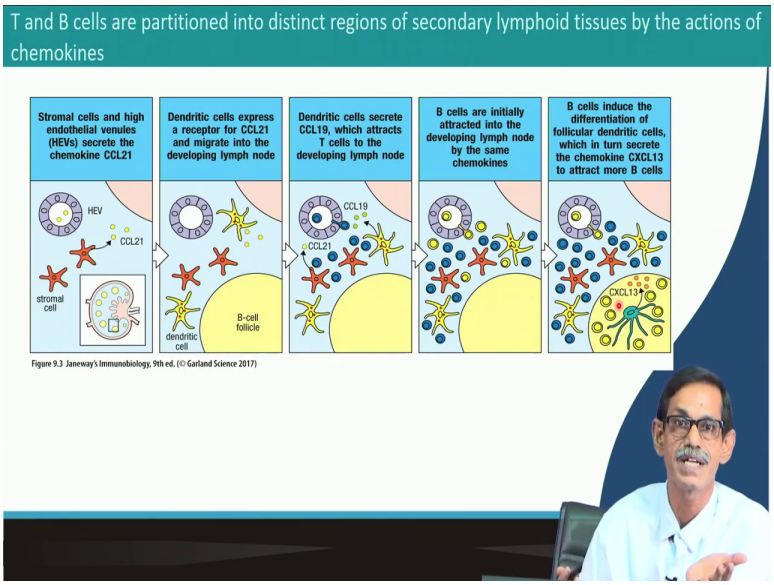

I am not going to go detail in this picture and who decided how it is happening? Again some chemokines. If you go through this slide com totally you can understand you do not have to remember the name but just to understand or get the feelings what happened you should go there. What is saying the stomal cells are high endothelial venule. So from where the B cell and T cell is coming they secrete one chemokine called CCL 21 that CCL 21 after dendritic cells that I mean this CCL 21 this dendritic cells are migrate to the developing limb node.

So this CCL one released by the venules of that secondary lymphoid organ which attract this dendritic cells. These dendritic cells again secrete another kind of chemokine that is CCL 19. CCL 19 brings or basically that attracts B cell and T cell both from blood. So now after coming here T cells stay in this region. So both are coming by the attraction of the CCL 2 19 released by the dendritic cells which is already activated by CCL 21 or both B cell T cell are here.

But another thing is coming this B cell T cell make this dendritic cells to secrete chemokine CXL13 in the this general center. So what happened this differentiated particularly this B cell I mean they interact between each other it is not one is doing another so B cell is also helping act activating the dendritic cells here which release CXCL13 and call all the T cell to the germinal center. So something is attracting both B cell and T cell and then from there B cell is also going to another part what happened ultimately what we see there is a strong I mean region which is more dense with B cell and one region which is mostly T cell.

So they are not exactly very much compartmentalized but their population is much more and it is happening by chemokines you know chemotaxis. So there are some chemicals and during that chemical cell get attracted migrate to that way and that is released by different cells epithelial cells dendritic cells even sometimes neutrophils at different points. But here dendritic cells endothelial when you secrete something and again activated dendritic cell attract the B cell that is how they were.

So why I am telling you do not have to remember I mean if possible definitely you can I am not saying purposefully you just forget it but the thing is just to get an idea how B cell and T cell are localized in different part of the different secondary lymphoid organ it is all by chemokines. If you remember this fact perfectly alright if you do not remember you have to remember that different chemokines are responsible for this kind of distribution of B and T lymphocytes.

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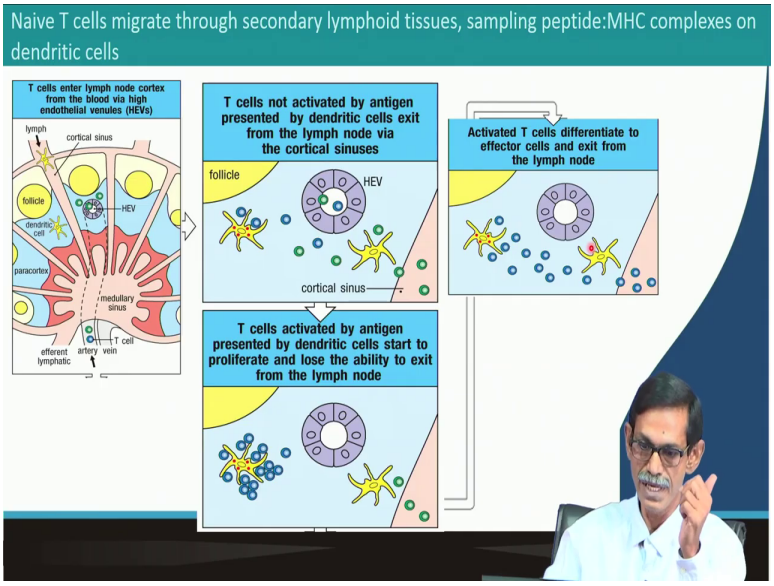

Now if you see what is saying naive T cell migrates secondary lymphoid tissue. So that whatever I said it is same or similar but here we are going to tell something different what is happening the T cell is coming here through this artery or through venule and there come what happened this picture it showed before also or similar picture during the basic introduction of the immunology what happened they interact.

With what they will interact they will interact with the antigen presenting cell mostly the dendritic cells they interact if interaction is strong here they get the signal to proliferate and stay there and if they do not interact they go away because what happened they cannot stay all the time. So after releasing from the thymus or after getting from the thymus they come into peripheral blood.

From there they coming to lymph node from lymph node they do not stay in one lymph node or once I mean in spleen or in pairs patches forever they keep on moving. So I then what happened after staying someday for there they come back to the peripheral blood or through lymphatics they go to another lymph node you can see it is a transferable job. They cannot stay in one place for throughout the life they completely rotate between different secondary lymphoid organ.

So what happened so once they are staying here the dendritic cells if it is infected or brought something from peripheral tissue they are presented. And if they interact they stay there attach there they multiply if those who are not interacting they are going out and once they are developed they become effector cells because they already know what to do now then this effector cells go to the peripheral blood and do their own job.

If it is a cytotoxic T cell it will go and find where the tumor cells or where the viral infected cells are there so it will go all over the body and do their own job so this is again a general phenomena.

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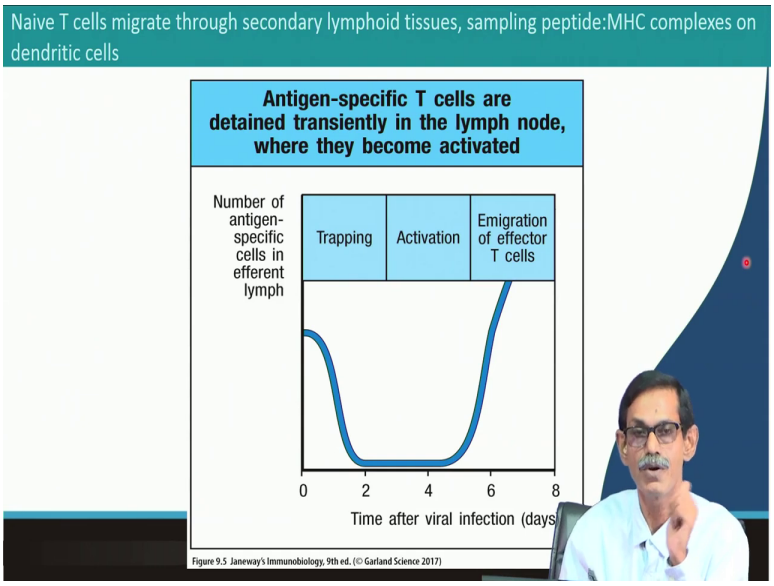

Like what is happening how long it is taking I mean whatever I said how long so this is just a timeline. So this is trapping, trapping means attaching with the dendritic cells then two to almost five days for activation. So, first two and half days for trapping. So if I go back so this trapping or attachment with this it because you know there are so many T cells and everything is not possible but their scanning is so much.

Suppose there are 100 students in the class and if I say that I mean then there is a corridor through which I enter into to take the class. And then I can go out in the corridor without touching and there is no interaction it will take the least time but if I say that I will shake hand with everybody whoever in each row I will go and shake hand with everybody and see who is there by name and what they are writing or what they are doing so what will happen it will take a lot of time.

So they are packed up T cells and each cell is scanning each one or most of them not a it is not possible each one but do not just extrapolate total in total to the classroom thing what I said but the thing is every time you interact with one student it will take some time. So trapping means scanning up of dendritic cells and all possible T cell in that region and which takes two and half days it is even I mean if I can imagine it is much less.

Two and half days if the scanning is done and they are so efficient and this scanning or trapping is done then they proliferate and activate when activation is done they release an immigration for affected T cells and to do their job.

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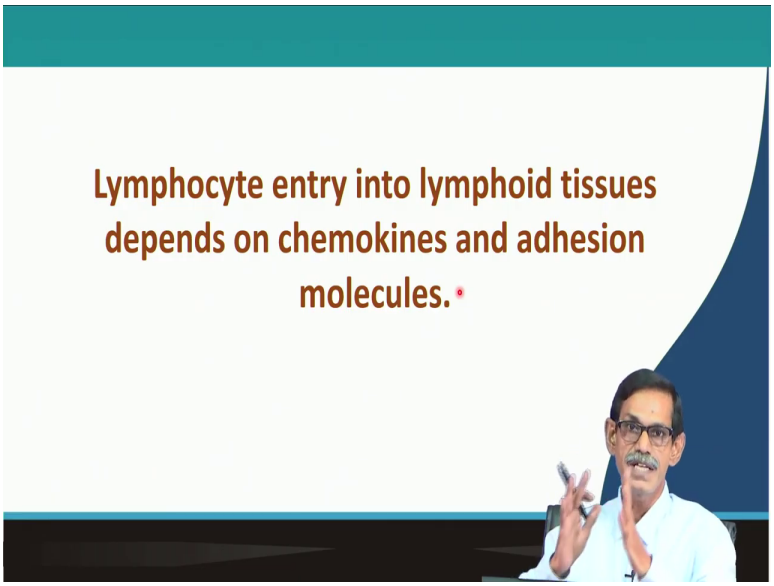

So this lymphocyte entry into lymphoid tissue depends on the chemokine and adhesion molecule chemokine. We already said like that how this endothelial venule release some dendritic cells release some chemokines and not only chemokines addition molecules are also there.

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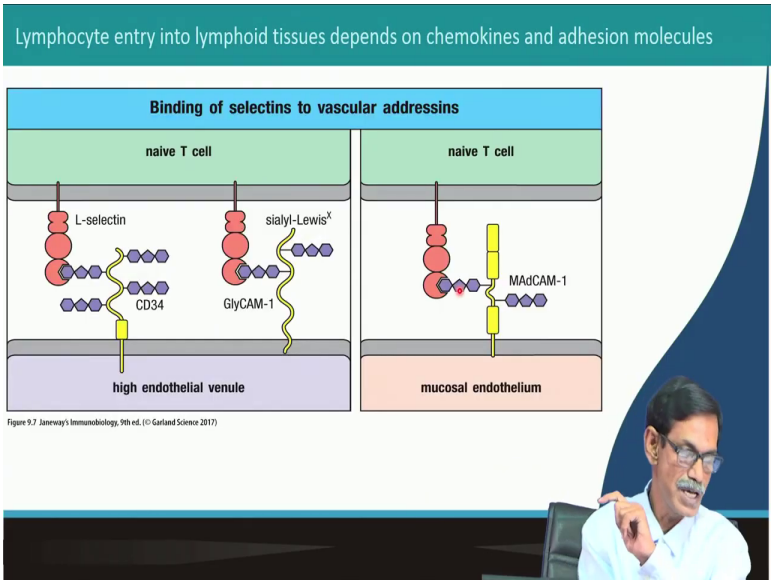

What are the addition molecules addition molecule means when I am saying that one cell is attaching or one cell is just interacting with other what is that, that means one cell should have a

receptor on its surface another cell should have a ligand of its so they interact that is how they interact they do not have any hand like us. So when two cell interacts what happened you see this is the naive T cell and when it is interacting with high endothelial venule has certain protein and there is not one type.

See this l selecting is one type of receptor and here this is CD 34 and glycamone these are the ligands and you see the protein part they are not interacting they are interacting with the sugar part carbohydrate part they are intact. So l selecting is interacting with the sugar. So and the same receptor so we cannot have so many I mean there is a limit how many receptor can be there. So there are some common receptors which can bind sugar we do not have that much variety of sugar molecule.

Glucose, mannose, fructose right and you can galactose. So, not that many; you can remember our name because there are much more variety in protein three dimensional structure. So that is much less diverse so if one receptor can bind with the sugar and if this sugar I mean all glycosylated protein can have a mannose right. So assume that all glycosylated protein or say 50% glycosylated protein has manners to expose.

And this is the receptor can find manners. So if this receptor can bind mannose it does not matter what protein it is. Any protein mannose is there it will bind. So in high endothelial failure venule it is binding with CD 34 glycam1 the same LC lectin of naive T cell in mucosal endothelium it is binding with another protein. Protein part is same by different but the sugar is same. So that will bring two cell together so that is what I was telling shaking hand.

It is you have to shake hand if the shaking hand if the interaction is very strong they will stay for a long time if the interaction is weak say can but they will not stay for long time move to the next cell not only that there are certain more addition molecule what are that you see here this is called I cam. Cam actually stands for cell adhesion molecule I cam, v cam, mat cam different kind of cam is a chemist cell adhesion molecule.

So this one is interacting with LFA variety of LFA is there LFA is there. Then LPAM then VLA all you see two sub unit you see one is beta another is alpha beta alpha beta alpha. So this is a heterodimer here the receptor is heterodimer and the ligand is there. In this case initially what was there initially the receptor was recognizing sugar. Now the receptor is recognizing the protein part. So these all are this is in general all these called LFL PAM.

So this is called integrin, this is called integrin sorry this is called integrin. So integrin and cell addition molecule interact why I am showing because all these; what we are going to see the cell mediated immunity is cell. Cell interaction after they are releasing something converting something so these are the protein which helps cell to attach with not only MHC and TCR it will come definitely this is one of the most important interaction otherwise it will not activate it.

But before that or along with that many other interaction is necessary and these are the proteins or the receptor and the ligands which actually play the role to be bring cells to two cells together to happen the cell-cell interaction and transfer the signal.

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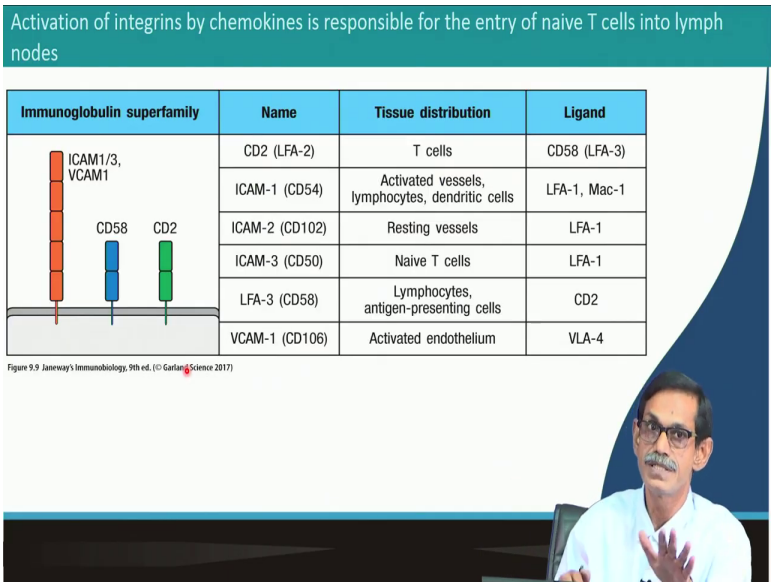

This is just a summary I mean not so many this is just few of this proteins and their distribution this is some super family. So what are the ligands? So this is the receptor and this is a ligand where they are present. So you do not have to remember I am just saying you can make this list very long. I mean if you possible but there is no point to understand immunology or immune

system this is fine those who are going to do research on this particular area definitely you have to remember. But to understand the immunology what you have to remember is that chemokine signaling.

You have to understand how what is chemokine how it reacts you do not have to remember hundreds chemokine names and their detail sometimes definitely but not always. Similarly here we have to remember that two kind of adhesion molecule one is that integrin is there which interact with the protein part another is there which interacting with the sugar part. Both receptor ligand interactions is very important for cell-cell interaction that is more important to understand immune system.

Not exactly all the names definitely you can its very good if you can remember but this is to understand the immunology or immune system these names but if it is with you as a reference that is why I am showing then you can go back if you need it you can get it in the book. But there are something I am not saying you forget everything something what we are emphasizing every time every now and then that is important.

You automatically you should understand what you should remember what is less important to remember not their function but their name.

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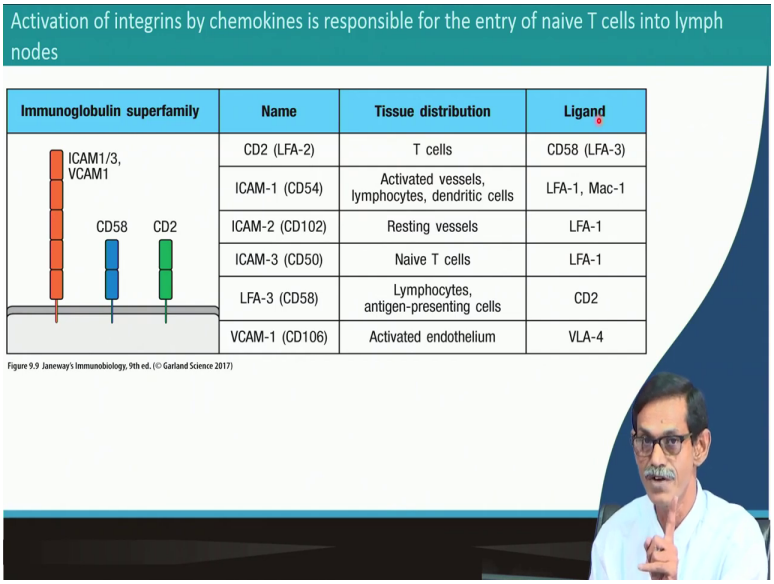

Immunoglobulin superfamily	Name	Tissue distribution	Ligand
	CD2 (LFA-2)	T cells	CD58 (LFA-3)
	ICAM-1 (CD54)	Activated vessels, lymphocytes, dendritic cells	LFA-1, Mac-1
	ICAM-2 (CD102)	Resting vessels	LFA-1
	ICAM-3 (CD50)	Naive T cells	LFA-1
	LFA-3 (CD58)	Lymphocytes, antigen-presenting cells	CD2
	VCAM-1 (CD106)	Activated endothelium	VLA-4

What actually this thing happening actually this interaction if you see this is picture so these cells epithelial cell has so many varieties of ligands you see glycam. Icam CD4 so and T cell also has variety of receptor here. So when T cell is coming that is a kind of handshake so these are series of cells so when they are going so not only they have multiple hands either side. So I mean if you say that both receptor ligands are two hands they are shaking hand.

So in epithelial cell there are multiple hands and T cell also has multiple hands so they not only one handshake. So they would like to shake their hand that means receptor like an interaction with wall one by one. So if one hand they just shake their hand leave it then another hand will automatically catch it. So they cannot leave the area or the manual this is bottom part is a lymph node and this is a venule.

So they when they are passing from here they cannot just go away they cannot flow away in fluid if there is like there is no interaction they have to continuously interact with this receptor. And if while this interaction is happening if this interaction is very strong like that you see so many interaction three interaction together. If this thing happened then it release something that is some changes are happening and this chemokine or this when this interaction will give the signal and this signal will release something which will tell the T cell not to go any more cross that enter into the lymph node.

So what I said at the beginning that the chemokines are releasing attracting them and they are entering into the lymph node it is not that from endothelial venule also this interaction is also very important. So chemokine is calling them they are coming but interaction with the cell addition molecule or selecting intriguing are very, very important that helps them to get in and that that is how they enter after that you know what is what happened I just told you.

So they interact with the dendritic cells they proliferate and then after maturation become getting the role what to do or becoming affected cells this effect results live. So once they get in they should have another mechanism to go out also right.

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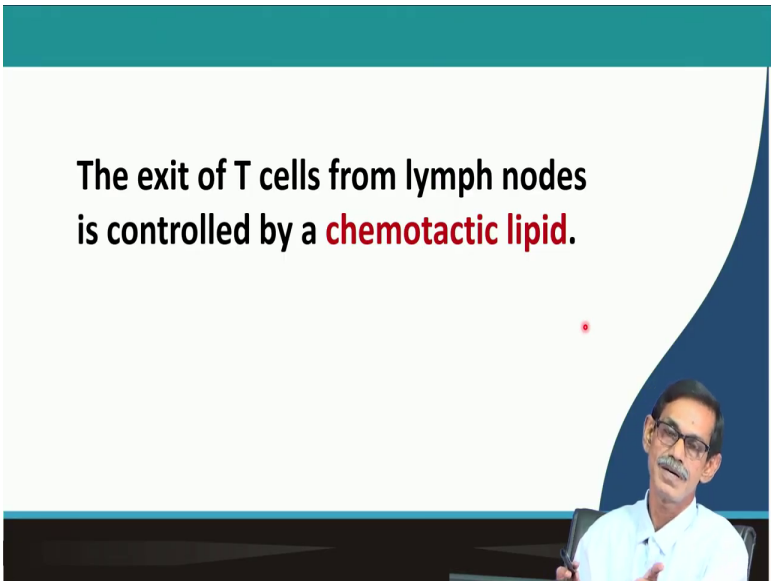

How they go out I am not showing that picture here just for your information the exit is not by this chemo kind exit is by a chemotactic lipid. Sso there are some lipid molecules which attract them towards out that is how they go out and come to the peripheral blood system. So getting in through chemic chemokine and goating out is chemotactic lipid. Because once they get in they have to go out when they mature or activated activated T cells or affected T cells should go out how they go out by lipid no chemo kind is involved.

At least mostly the chemotactic lipid at this system it is very hard to say like nothing I mean chemokine is not involved. May be there it is not reported yet. So better is controlled by chemotactic lipid is more technically right.

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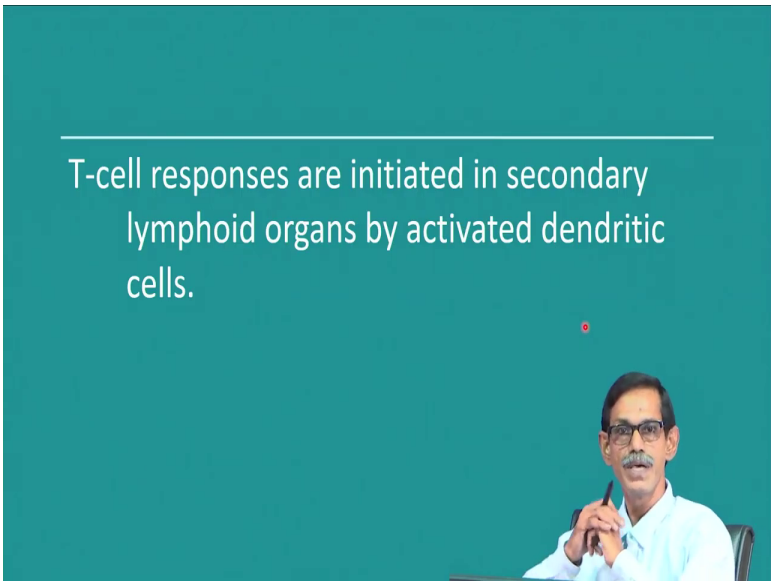

And T cell response are initiated in secondary lymphoid organs by activated dendritic cells you already know that because I told in when while I was discussing in the very early introductory classes that the dendritic cell is very important cell for activation of T cell in lymphoid organ particularly the secondary lymphoid organ.

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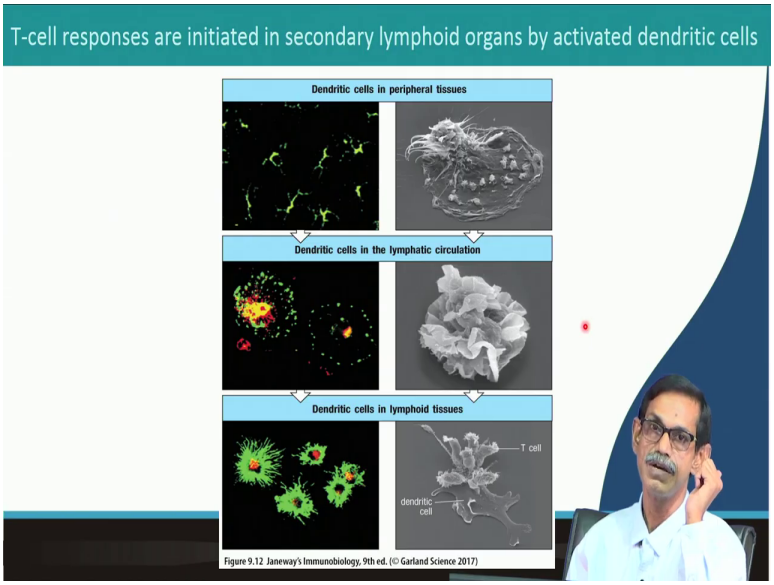

How it looks normally dendritic cells has lot of appendages you see so many and that is how the name is actually. And in this case this is the electron microscope and this is a fluorescence microscopy that what I told you. And the green color is basically the dendritic cells and red color which you can see here much better is the lysosome. Red is lysosome red is lysosome and green is dendritic cells.

So here what happened when their resting condition their lysosome and macrophage macrophages all over I mean they are I mean sorry the dendritic cells. And one thing I did not tell you during immunofluorescence microscopy there are software. If two proteins say one protein new level with red another protein you leveled with green. So if two protein and in two different place then you will see red is red green is green this is here.

So you see there; red is separate green is here you can see and if it happen then red and green are both in the same position or same location red and green mean suppose you DNA polymer is an RNA polymerase right two different enzymes both of them are present in nucleus. So if you make DNA polymer is red and RNA polymer is green what will happen, what you will see? You cannot see red and green separately because both red and green both are in the nucleus.

In that case in the computer screen or the software what you see is yellow. So if two protein co-localized and if we level them with green and red they are yellow. So what we are seeing here you see all yellow that means macro I mean the dendritic cells and the lysosome are all almost everywhere they are yellow. But here when they are coming to the peripheral blood from resting in the tissue it is like that when their lymphatic circulation they are coming you see there are so many folds slight change also here.

You see little part is co localizing that means yellow but most of the part green and red is separate. So lysosome is not doing anything they are not doing anything because they are floating when in tissue they have a role because they have to eat macroparanocytosis and as soon as they are eating lysosome is going to fuse right. But when they are in the lymphoid tissue that means when they are coming into the say lymph node you see red is completely distinctly visible that means they are they are not phagocytosis.

And doing phagocytosis anymore in tissue they are when in lymph node that part is done phagocytosis microfinocytosis they had already completed that part. They processed it this processing is done here now they are presenting it they do not need. So this is the immuno

localization and what in the electron micrograph is showing electron micro is showing that one cell there are so many T cell are attached.

So the appendages that means the MHC is exposed and the process antigen and so many T cells are attached. So this is just to give an idea that when we do the experiment or if you do the experiment you will get like this either by electron micrograph or if you say electron microscope even a fluorescence microscopy you will see this. But conclusion is coming that this activation start because you we can see the T cell attached to the dendritic cells that is a very first thing to happen to get activated

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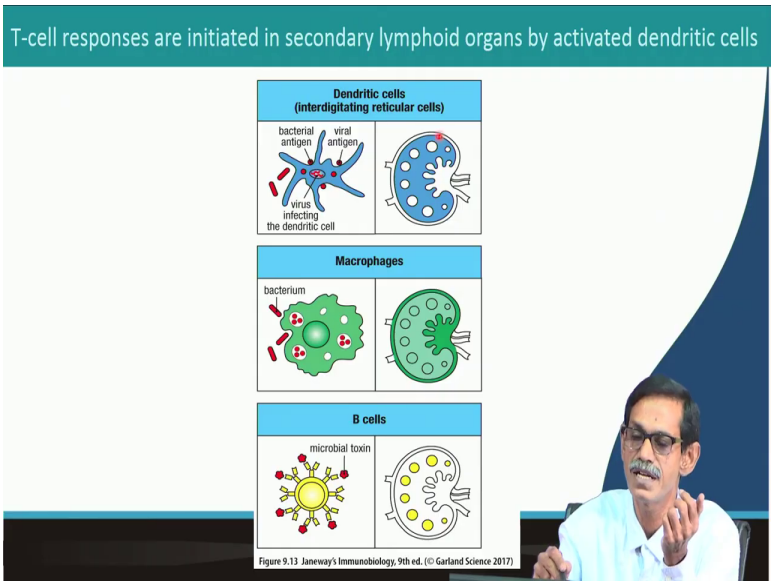

But in lymph node for example a dendritic cell is not the only cell there are all other antigen presenting cells are there. So if you see the distribution this is dendritic cells. So if you see the color it is almost everywhere except the germinal center right macrophage another antigen presenting cells. But not as active as dendritic cells to activate the T cells they are the most active and most efficient one microphage is also doing definitely.

So there this is mostly the virus and bacteria and this is mostly bacteria or dead cells. This macrophage is spreaded all over the lymph node so it is not only I mean like this so it is everywhere. But B cell only in the germinal center. So this is how it is distributed in the lymph node.

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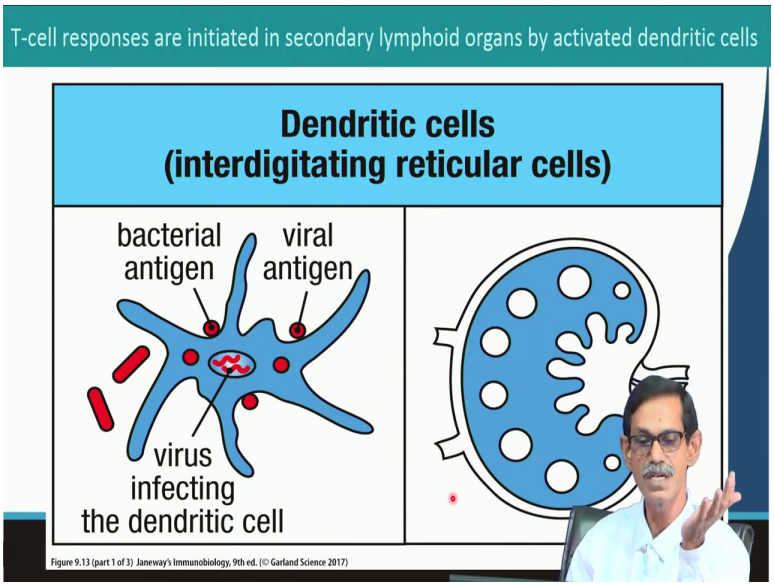

This is the same picture and in slightly enlarged form there are gender resource I just told you they very important but they have very two distinct function one is conventional dendritic cells conventional and dendritic cells they are almost everywhere.

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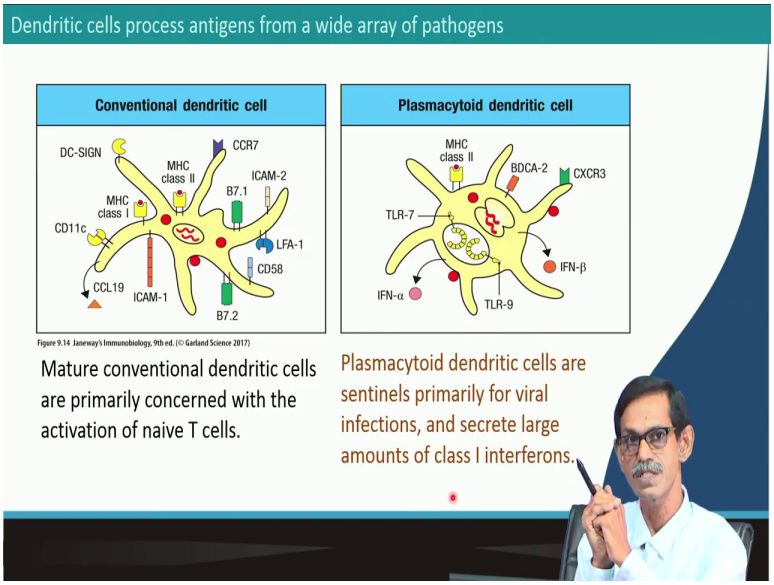

And what they are doing they are major job conventional this all you see they are expressing MHC 1 MHC 2 and all the protein you see a variety of protein and that intake dean and all other things are there and they release CCL 19 that is just they can. So, this one is mostly responsible for activation of the naive T cell in lymph node. So this is called conventional but there is a another one plasmocytoid dendritic cells what they are doing?

They are preliminary for viral infection because they handle the viral one if there is any virus infected cell that virus infected cell handling is their job. And they are not and they are they produce someone which is also written they produce a good amount of interferon class one interferon. Interferon will touch separately that what it is doing in different is very interesting you definitely will have a separate class for that.

So I am not saying but in general interferon helps to protect viral infection of the cell. Cell from viral infection so these particular that plasmocytoid dendritic cells are mostly responsible for handling the viral infections. By producing interferon as well as activating the cytotoxic tissue. But normally they are not as good as activation of the naive T cells. They are doing its not they cannot do but they are not as good as this.

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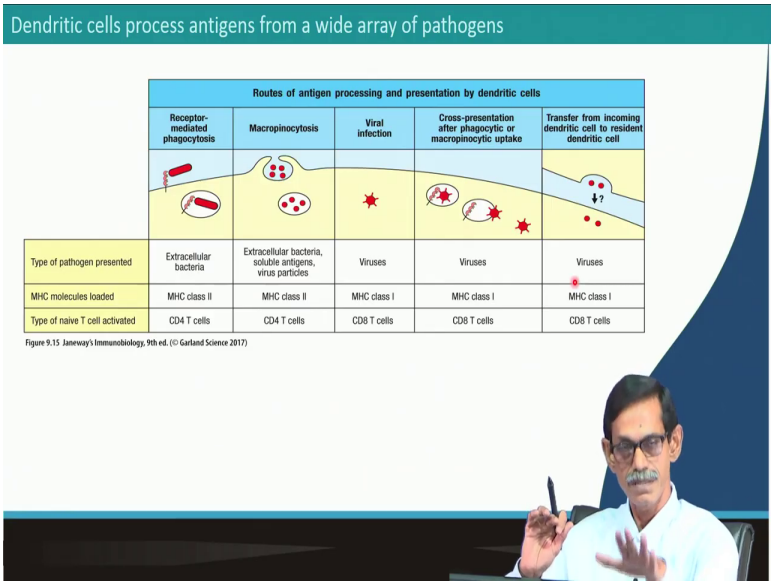

And this is for the last slide for today and the same I mean if you see, this I mean I do not want to repeat and read it for you but definitely they can phagocytose which if the phagocyte is something or macropinocitos something that is by class two that you know presented by. They can handle extracellular bacteria antigen toxin they can handle bacteria by receptor. Like TLR they can handle viral infection right that we already know because dendritic cells normally get viral infected.

And if they do not get virus infected then they eat the virus infected cell and then cross present that also we have discussed during antigen presentation. So cross presentation and transfer of incoming that is also we said sometimes if the mechanism is not known you can see this question mark here. So, one antigen is transferred to other dendritic cell. So this was within one dendritic cells and they transfer it exact mechanism how they do it is not known.

It is very common in lymph node because lymph node there are certain dendritic cells stay there. So, some dendritic cells bringing samples or the infection or the pathogen from outside and delivering to the existing dendritic cells so all these cases that will be presented by MHC 1 and activate or the affected cell will be CDH cells ok. So thank you for today, so in next class we will continue the T cell mediated immunity bye then thank you.