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Immunology

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Module No. # 01

Lecture No. # 03

Basic Concepts in Immunology

So, hope you enjoyed the last 2 class and went through books or internet for studying. So, before starting on my third lecture or this basic concepts in immunology in Module 1, I will just request one to all of you those who are new to immunology or studying for the first time: Please follow the class with books. And because everything is not possible to say in the class during this stipulated period of time, read any available books with you. Because this uh subject is very interesting, but there is a always a possibility, because similar names and similar cells are doing various kind of things.

So, when we explain, many times it happens; I am telling from my experience of taking the class to our student. Like initially, if you do not study or follow day by day, what will happen; If you want to study just before the exam or want to cover up everything together, you will remember everything, but when you will try to answer or defend the question, everything will be mix up. Okay. So, this is my suggestion. I will not repeat it. So, please follow.

I mean, you do not have to read much for each lecture, but read just after the lecture, you read the book. Any book, but that chapter, you, hope you understand. The cartoons or the figures may not match, but you will see everything or you will find everything in almost any book. But, I am following the Janeway's mmm Immunobiology. So, you will, if you have this book, it is only better, because the slide we will also see the same slide. Okay. So, next class today.

(refer time: 02:11) So, the point of adaptive immunity was the interaction of antigen with antigen receptor induces lymphocytes to acquire effector and memory activity. How this lymphocyte looks like? This is this is the lymphocytes in blood; how it looks likes. And this is a electron micrograph; how this lymphocytes. So, seeing them, it is not much to understand, like how exactly. But this is just to show you how the lymphocyte looks like under microscope, regular microscope and electron microscope.

So, what they have. (refer time: 02:53) So, both lymphocytes, B and T lymphocytes, they have a receptor. That you already know. So, this is the B cell receptor, this is this is the B cell receptor, how it looks like. Okay. So that, why this is not a receptor? So, it will be a receptor, if it is integrated with the membrane. So, this is the B cell receptor, when it is integrated into the membrane. So, what is happening? If you see this, if you see this receptor, you see there is Y like structure.

I will discuss much more detail of this. And this is a structure of antibody also. In detailed, in uh future classes, when you will read or when we will discuss the antibody in uh specifically. So, for today, if you see, so, (the) this region, this region is known as variable region. And this part, actually actually this part is constant region; or it is responsible for effector functions. And variable region; so, this region variable region, particularly this site. So, if you see this, this region is responsible for antigen binding.

So, when it is attached with the membrane of the B cell, if this is B cell, then it is B cell receptor. Okay. So, after interaction with the antigen, after interaction with the antigen, it gives signals. And the same cell converted to plasma cells and produce the same molecule, but without this part. Okay. So, what is going to happen is, what is going to happen is, they will not have this thing. Okay. So, this molecule is now free or secretary molecules. This same receptor molecule which will produce without the transmembrane domain, which anchored them with the cell, will release in blood.

And then, this will serve as antibody or this is actually known as antibody. So, this antibody has 2 very specific distinct domain. One, we call the variable region, which is responsible for antigen binding. And this, this part only the antigen binding part. And this part is constant. It is not very much variable. And this is responsible for effector function, like what next. Antigen attached, antibody attached the antigen and what to do next. So, this is the effector function.

Same way, if you see the T cell receptor, this is the T cell receptor. T cell receptor also, very similar, but not exactly same, because it is much smaller. It also has a constant domain. This blue region is the constant domain. And the upper part is a variable region, which is antigen binding sites. Here, only 2 chain. One is alpha, another is beta. So, alpha, beta, 2 different chains combined. And they are attached through this transmembrane domain. They always remain attached.

They never secreted like the B cell receptor as antibody. So, they always remain attached. And these 2 alpha and beta also linked by a disulphide bond; this black lines what you see. Here also, there are 2 different protein. First is, there is a big chain and a small chain. Okay. This is one peptide, this is another peptide. So, there are 2 big peptides and 2 small peptides. So, one big and one small peptides are attached by a disulphide bond; this (ba) black one.

And this unit, like one big, one small, is also attached with a disulphide bond. Okay. So, they are this thin line is a hinge region. And hinge region helps, basically they can bend together like that. This is the antibody. They can go up to this, 180 degree to 0 degree almost. Okay. So, that that the hinge region helps. So, if antibody is here. So, an antibody has antibody has 2 binding site; one here, another here. So, 1 antibody, 1 antibody, if this is the antibody can bind 2 antigen at a time, but, T cell receptor can bind only 1 antigen at a time.

(refer time: 07:35) How this antigen binds? Say here; so, this part is antigen, the yellow. This is a protein part. So, this is the antigen. So, antibody molecule, the same antibody (mol), slightly simpler way it is done. So, this is the antigen binding site. If you see, it interacting with the antigen, a small part of the antigen, not It is, like if this is the antigen. If some if say this pen is the antigen. It is not hold the whole pen like that. It is holding a small part of it. Okay.

So, this small part of it, this antigen molecules, if you see here, this is only this blue part of this antigen. This whole molecule is the antigen or the protein. A small part, the blue part, is interacting with the antibody. Same way, here this red part is interacting with the ah another antibody. Okay. These 2 are completely different. So, 2 antibody recognising 2 different part. So, if whole molecule is antigen, the part of antigen which is recognised by this antibody molecule is known as epitope. Okay.

It is known as, this blue or the red part. So, the segment of antigen which is recognised by the antibody antigen binding site is known as epitope. Okay. So, this is known as epitope. So, the part of antigen which is recognised by the antibody is known as epitope. (refer time: 09:25) But the part of antibody which is recognising the epitope is known as paratope. So, the antigen binding site of antibody is paratope. And the antigen part which is recognised by antigen or recognised by antibody is epitope. Okay.

So, you can understand from this figure, like whole protein is not interacting with antibody. A small segments are interacting. But in case of T cell, what is happening? (refer time: 10:06) In case of T cell, it is slightly different. And and importantly different, which we will see, which we will see later. But in case of B cell receptor, what do we see? Mostly, the outer

part of the, outer part of the protein, outer part of the protein is interacting with the antibody.

In case of T cell, it may happen that the epitope part; this again, it is also epitope. The epitope part, which is recognised by T cell receptor, may be buried or inside the protein molecule which is not seen in the 3-dimensional structure of that protein. Okay. Because, T cell epitope or T cell will not recognise the whole antigen. It need to be processed. T cell cannot recognise the antigen as a whole. Okay. So, if this is the antigen, suppose my hand is the antigen.

So, antibody can interact here. Okay. Only this part, antibody can interact. But T cell cannot interact like that. So, for T cell what we need? For T cell, we need that antigens should be processed. That means, first, if this is the antigen, the linear one. It should be chopped in pieces. So, it will be chopped in pieces. You can see, it is different fragments. And these fragments should fit. There is another component. Another terminology we have to remember now onwards is known as MHC.

MHC is major histocompatibility complex. Major histocompatibility complex, which we will discuss again in later. What it is, what it, what this MHC? MHC is a protein. MHC is a protein. MHC is a protein that is just like a receptor molecule. Okay. This MHC present. There are 2 type of MHC. We will discuss later. But for the time being, the MHC is a protein which present as a receptor, mostly in the antigen presenting cells, in this case. So, this MHC, have a space. Okay.

This also has a cleft. That cleft will be occupied by this epitope. So, what is antigen will be processed into pieces. One of these piece will go and bind to this epitope. Is going to bind this peptide binding cleft of this MHC molecule. And T cell receptor. T cell receptor can recognise this antigen. The red part is now antigen. Okay. Just the perspective is different. So, the red part is antigen and yellow part MHC molecule. So, T cell receptor can recognise the antigen only when it is presented by MHC molecules.

So, the T cell receptor binds to a complex of MHC molecules and epitope of an antigen. Okay. So, here is the difference. B cell receptor can bind antigen unchanged or as a whole. I mean, whole antigen, you need not to, it not to be processed. But in case of T cell receptor, antigen should be processed into different pieces or fragmented. One of the fragment will fit into the uh fit into the cleft of the (anti) uh MHC. And the whole complex of MHC and antigen will be recognised by T cell receptor.

So, here is the difference. And after this interaction happen, this signal will go inside. This signal will go inside the T cell. And that, then T cell will multiply, proliferate and do its function or the effector function, what it is supposed to do. (refer time: 14:09) I already told this. Antigen receptor genes are assembled by somatic rearrangement of incomplete receptor gene segment; which is little complicated for this time being. And we will discuss in much more detail later.

How this receptor, how this variety of receptor which can recognise variety of antigen or epitopes; we will discuss later. (refer time: 13:33) Okay. So, lymphocytes activated by antigen, give rise to clones of antigen specific effector cells that mediate adaptive immunity. Okay. So, these activated antigen gives us the clone which is mediated adaptive immunity. But we already discussed, these B cell or T cell do not develop any adaptive immunity against our own cells.

So, how this thing happen? This thing happen actually that a single progenitor cells, the hematopoietic stem cells can produce multiple cells. These, these cells can produce multiple cells. So, these multiple cell will have variety of receptor. This variety of receptor, this uh is what. Receptor is means: If the antigen is look like a triangle, the receptor will be like this. If the antigen looks like a sphere or circle, the receptor will be like this. If it is a square or rectangle, the receptor will be like this.

So, that is how the receptors are. And this is cartoon for different; only 7s are given here, because, just to make you understand. So, what is happening? All these 7 receptors, all these 7 receptors are containing cells undergo development or the training period, what I personally prefer. That you have, they have, they need to be trained that what to do or what not to do future. So, what will happen? During this developmental stage, if they interact with our own protein.

So, all these reds are different self-antigen. So, if they interact. If the receptor or B cells or T cells interact with our own protein, they will get a signal that to die. Okay. So, they will, these 4 will die. Listen carefully, any B cell or T cell interacting with our own protein or self-antigen during the developmental stage, they will get the signal to die. So, in this case, 4 different lymphocytes interacting with self-antigen, they are going to get the signals to die. So, only 3 will survive.

So, these 3 mature lymphocytes which does not interact yet with any antigen, will come to the peripheral blood. Here, in this stage, any of these 3. If any one of them interact with foreign antigen, this one will multiply. Okay. So, this one will multiply and do the adaptive immune response; or do the job to perform the adaptive immune response. All these

phenomena is clonal deletion or clonal selection hypothesis. (refer time: 17:29) Okay. This is very important, because this is the key principle of saving our self-cells or self-antigen; not to do any harm of self, but do harm to the foreign or pathogens or the microbes.

What are the the postulates of this clonal selection hypothesis? It is, each lymphocytes bears a single type of receptor with unique specificity. That is very important. That means, 1 lymphocyte, whether it is B or T, it will produce only 1 kind of receptor. If it interacts with a triangular antigen, it will always interact with a triangular antigen. And all the receptor will interact with the triangular antigen. So, 1 B or T cells will produce a single type of or unique receptor with unique specificity.

That means, their antigen specificity is unique. They will not cross-react with others. Interaction between a foreign molecules and a lymphocyte receptors, capable of binding that molecule with high affinity leads to lymphocyte activation. That is the last stage. What is this? This, if it interacts with foreign antigen strongly, it will gives a signal to multiply and proliferate. The differentiated effector cells derived from activated lymphocytes will bear receptors of the identical type or identical to the parental cells which lymphocyte was derived.

Coming back. So, this one, the yellow one is interact with the antigen and it is proliferating. You see all. So, from 1, now it is 5. But all looks identical. So, they will not change the receptor specificity. So, 1 receptor interact with antigen, that particular B cell or T cell multiply into many cells. But their receptor molecules will be same. So, it will interact with the same antigen in future. And the last one is the first part of this previous picture. The lymphocytes bearing the receptor specific for ubiquitous self-molecules are deleted and at an early stage of lymphoid development.

So, they are absent from the repertoire of mature lymphocytes. So, now I am giving uh a small home task, just to understand. Normally, we say library, cDNA library, genomic library, in case of genes. Right. Here, we are saying repertoire. What is the difference between library and repertoire? We will find in net or dictionary, anywhere. You just see what is, what is the library and why it is repertoire. Is a similar kind of library, but we do not say it library. Okay.

So, this, this is, that means, if you interact with the self-deletion, I mean if you interact with the self-molecules, that particular stage will uh cell will be deleted in the early stage of cell development. That is this part. Okay. So, all this event are, together we call clonal selection hypothesis. That is very important or the basic principle of adaptive immunity. (refer time:

20:42) Lymphocytes with self-recep uh receptors are normally eliminated during; that we already discussed uh just or it is functionally inactivated.

Even if it is not deleted, we say that, okay, they will get a signal for death, they will die. They may not be dead, just in case if they do not get the signal. But they will be functionally inactivated. Okay. We call it anergic. So, we will discuss later. They will not do any further activity in future. So, they are other machinery will be blocked. (refer time: 21:19) And after this what will happen? So, what what we discussed? We discussed cell developed in bone marrow.

They then they get trained. So, all the cells are developed in bone marrow. So, this is shown bone marrow. This is under the femur. But not necessary, bone marrow is present only in femur. Bone marrow is present all the bones. Okay. This is just for the cartoon. So, bone marrow, it will produce. Then B cell will develop or get the training here or mature here. And T cell will developed in that thymus, which is the yellow. This is the yellow thing, the thymus, which is located behind the heart.

So, T cell will migrate from bone marrow to thymus. They will develop there or mature there. After maturation of B cell and T cell, what I said, they will migrate to the secondary lymphoid organ like lymph nodes. All the blue small dots are the lymph nodes, which is present all over the body. Okay. So, they will go. And another thing is the spleen. The spleen is another secondary lymphoid organ. And there are some uh mucous associated lymphoid organ.

Also we will see. So, they distributed. So, it is kind of; see, it is a defence system. So, defence system cannot, or the members of the defence machinery cannot sit in one place. Right. If like, in a local police station, what we see is, there is a main police station to maintain the law and order; main police station. And there are lots of local thanas in different places. Right. So, different places, lot of local thanas. So, what happen? Main police station is here.

They are controlling everything and they are getting the information. But local thanas are taking care of their small area of their capacity. Here, lymph nodes are this kind of local thana. Okay. Or a a good number of police personnel like B cell and T cells are sitting there. If there is any person doing any crime, what will happen? There are certain person in police department. They catch and bring it to the (lo) nearest thana or the police station. Right. Here also, that lymph nodes are the local police station.

And macrophages, dendritic cells, they are covering or scanning the whole body. If there is any infection, they bringing them or catch them and bring (tem) bring them to the local police station, like the lymph node. And lymph node is taking care that; okay. Check them, because, at the initial part, if the innate immunity already can handle this at the tissue level, it is fine. But some of the information of that particular pathogen or the pathogen as a whole, they will bring it to the nearest lymph node.

So, the immune system will take, I mean, take the initiative for the adaptive immunity. If it is already managed by innate immunity, they will not much response of adaptive immunity. But, if it cross the innate immunity, then adaptive immunity will make a specific target based weapon like antibody; or T cell definitely will help to make the antibody. And that antibody will go and manage the infection. Okay. So, it, these lymph nodes are all over the body and it will take care of the future, I mean, infection states, what it is doing.

(refer time: 25:25) What is happening. So, you see immature dendritic cell resides in the peripheral tissue. So, in skin or some other peripheral tissue, immature dendritic cells are lying in between there. So, if there is any cut or anything happen, any infection happen here, dendritic cells are there. They can do the macropinocytosis and they will form a macropinosome where they will capture this bacteria or other pathogen, whatever it is there. So, from there, they will bring it to the lymph node. Okay.

So, this is the lymph node. I will come, what is the lymph node, maybe today or maybe in the next class. So, in this lymph node, this dendritic cells, they will present the antigen. Listen carefully, in the lymph node, they will present the antigen to the B cell and T cell. Okay. So, because infection happen in tissue, somewhere else. So, the dendritic cell take that candidate or the pathogen, bring it to the nearest lymph node. And at that lymph node which is packed with B lymphocyte and T lymphocytes.

So, they will show, see, this is the culprit; do whatever you want to do or you can do. This kind of presentation. So, what will happen? These dendritic cells; here, what I am talking like, the kind of uh conversation between 2 humen. In 2 cells, they do not talk like that. I am sure you know. They talk between; I mean, any kind of interaction or signaling or cross talks between cells are happening between protein and protein. So, one protein is in the surface of the dendritic cells.

That is why we call it antigen presenting cells. So, they present the antigen on their surface, which T cell can see. So, what is going to happen? There are lot of T cells here. So, some T cells can see, if specific T cell binds here, they remain attached and they replicate. You see from 1 to 2, 2 to 4, they are increasing. And these T cell, activated T cells will ultimately do

the job. (refer time: 27:42) Okay. Dendritic cells, actually the uhm middle man between innate immunity and adaptive immunity.

Because, in innate immunity what happen? Neutrophil, eosinophil, basophil, monocyte; monocyte means in tissue we call it macrophage. They are taking care. They are eating, phagocytosing, they can kill it, they digest it. Okay. And they do all the releasing all the cytokines and chemokines which brings more neutrophils and macrophages. So, they are handling this at the site. But dendritic cells, they are staying at the site, while they are, these group of cells are taking care of the infection, the dendritic cells bring some of the antigen to lymph node, while B cell and T cell see them and do their job.

What is doing? B cell will be activated, produce (ant), sorry. B cell will be activated, produce antibody to tackle and T cell will help B cell in some case. In some case, it helps. That we will see uh uh in next class. And T cell, there is another type. I told in the um uh previous lecture. There are 2. One is cytotoxic T cell, one is helper T cell, another is cytotoxic T cell. So, in case of uh helping like B cell activation, helper T cell is coming. If the virus infection happen, then cytotoxic T cell will be activated.

Because virus infection, you cannot kill just the virus because virus grow inside our own cell. Right. So, I, you have to kill the cell to stop their growth. So, cytotoxic T cells recognise which cell is virus infected, go, identify them. And after identification, they kill that particular virus infected cell. So, the virus cannot grow much or more to infect neighbouring cells or furthermore. So, that is how the virus infected cell, NK cell also helping them.

So, this way, from the site of infection where innate immunity playing a major role, dendritic cells, bringing them to the nearest secondary lymphoid organs, mostly lymph node, it may be spleen or other cells and make a bridge between innate immunity and adaptive immunity. Normally, in the previous slide, (whatis) what I said; or previously also. Dendritic cells are efficient in macropinocytosis. Pinocytosis means, drinking liquid. And phagocytosis means, eating the solid material, like bacteria or something. Okay.

But dendritic cells in tissue are phagocytic. So, they are specialised to display their antigen at the cell surface. Okay. That means, this is also antigen presenting cells. There are 3 types of antigen presenting cells or 3 antigen presenting cells are there in the immune system; dendritic cells, macrophage and B lymphocytes. So, they not only do the job for immune system, do their job, this is also a part of immune system. Not only do their own job like killing them or phagocytosis them, they also present the antigen to T cells.

So, B cell is doing their own job like production of antibody. But at the same time, it is also presenting antigen to T cells to for their recognition. Similarly, dendritic cells doing its job, phagocytosis or micropinocytosis. Macrophage is eating the bacteria, killing them. At the same time, they are also presenting. So, these 3 cells, dendritic cells macrophage and B cells are also called antigen presenting cells or professional antigen presenting cells. Okay.

So, this is for today's lecture, I hope uh you remember it. And in next lecture, we will discuss more on adaptive immune response, what is happening; how the B cell and T cell helping; or how the T helper cells and cytotoxic T cell works. Thank you for today.