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Immunology

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Module No. # 01

Lecture No. # 02

Basic Concepts in Immunology

Welcome back to my second lecture. In last lecture, we ended up in uh response time and of adaptive and innate immunity. Now, we are going to (refer time: 00:31) speak about the myeloid lineage that comprise the most of the cells of the innate immune system; what are those cells. Okay. So, myeloid cells in innate and adaptive immunity. And very briefly, what they are doing. What you will see here, you will see in the left side, there is a cartoon. In the right side, there is a microscopic image.

So, this left side cartoon, we are going to use the same thing in throughout the course, in my lecture. Like, uh say for example, the macrophage. (refer time: 01:10) This is the cartoon. So, we are going to use this throughout all the slides or presentation what we are going to see. So, what this macrophage is doing? It is basically do the phagocytosis and activation of bactericidal mechanism. And they also do antigen presentation. I will come later, what is this antigen presentation is, which is very, very important. Okay.

So, this antigen presentation is one of the major role phagocytosis. Macrophage is also doing the cleaning up of mess that we already told in the last class. Same way, the macrophage, (refer time: 01:54) there is another cells which is also a antigen presenting cells. Is known as dendritic cells. It uptake the antigen from peripheral sites by, normally by macropinocytosis. And by that, it presented the antigen to B cell and T cell in the lymph node. (refer time: 02:20) Neutrophils: This is again a phagocytic cells.

It can eat bacteria and it is very, very bad that way. It is a very (ba) good killer. Okay. So, activation of bactericidal activity mechanism is mostly initiated by the neutrophils, in that site of infection in the tissue. (refer time: 02:41) Eosinophil, which is also present in blood and it is responsible for killing parasites. And which kind of parasites? Which is already coated by antibody. That means, after infection, antibody will generate. That will coat the parasite.

And if parasite is coated with antibody, then it is killed by eosinophil. (refer time: 03:10) Then it, basophil, which promotion of allergic response and augmentation of anti-parasitic immunity. Okay. So, basophil, you can see, there are lot of vesicles filled with it. And these vesicles contains different chemicals which used to do this or show this immunity. (refer time: 03:35) Mast cells: This is also involved very much in active immunity, that these granules which we see here; these granules is full of histamine.

If anybody already aware of what is the role of histamine; histamine is responsible mostly for allergic response. Okay. So, when there is allergy, we see, this is a major component of allergic response is this. This is uh the mast cell is doing it. (refer time: 04:09) So, now, how this sensor cells like macrophage, dendritic cells recognise that which is foreign. They have a pattern recognition receptor. So, normally macrophage, most of the cells, if you see in our system, all cells has lot of receptors on the surface, because cells needs lot of communication between cell to cell or environment to cell.

So, they can understand what is going on outside or what to do next. So, that information from outside to inside of the cell are transmitted through the receptor. So, most of the cells in our body have different kind of receptors or different sets of receptors depending on their functions and role in regular physiology. But these immune cells, the macrophage also has a special kind of receptor; macrophage and dendritic cells; which recognise which one is pathogenic or which one is foreign or outsider.

They are mostly TLR 1, TLR 2. TLR stands for toll-like receptor. 1, 2, TLR 4. And then glucan receptor, mannose receptor. All these receptor are exposed outside the cell. Okay. So, outside the cell, by this. Outside cell, the receptor is there. So, if anything foreign comes, they can hold or touch or sense or what next. (refer time: 05:38) So, now, what we are telling in the last slide. Like, macrophage is explicit number of receptors that allow them to recognise different pathogens.

What are those receptors? They are the mannose and glucan receptors. They are toll-like receptors. So, I already told, there are, every cells of our body has different kind of receptors. So, macrophage and dendritic cells, they have this kind of receptors to recognise the foreign pathogens or infectious pathogens. What these receptors are doing? The mannose and glucan receptor glucan receptors and the scavenger receptors bind cell wall carbohydrates of bacteria, yeast and fungi.

The toll-like receptors, the TLRs are an important family of pattern recognition receptors, present on macrophage, dendritic cells and other immune cells. The TLR recognises different microbial components. For example, the heterodimer of TLR 1 and TLR 2 bind certain lipopeptides from the pathogen such as gram-positive bacteria, while TLR 4 binds both lipopolysaccharides from gram-negative and (la) lipoteichoic acid from gram-positive bacteria.

Which is not present in our own cells. Right. So, the LPS and the lipoteichoic acids are not present in our own cells. So, if there is a receptor in macrophage, which can recognise those, they can immediately figure out that whatever cells enters or whatever the organism enters, they are not our own cells. So, that receptor can recognise and get the signal that they are foreign. (refer time: 07:23) So, now, another important thing which we are going to discuss now.

Which is, these sensing, like dendritic cells or neutrophils and the macrophage, when they uh understand that something foreign came. And I already told that they have a capacity to phagocytise the cells. Phagocytise mean, they can eat the cells. Which we already know in the class 6 or 7 that amoeba can phagocytose the bacteria or the food, so they can make pseudocode; put them together; and internalise the cell. And by which they, but how they recognise which is foreign.

That is, those receptors which just I told in the last slides. So, what is happening? The first macrophage eat bacteria, by recognising by those cell receptors. As soon as they eat bacteria, they understand something is new and they are activated. An activated macrophage produce some molecules. It may be cytokines and chemokines. Chemokines means which, the chemicals which attract the chemotactic activity. That means, it attracts other cells into that particular site where they eat.

So, what happen, in tissue; suppose this yellow part is the tissue. There are bacterial infection. Suppose there is a cut in hand or somewhere or uh some nails, just uh entered or any kind of damage, tissue damage; some bacterial infection happen here. So, there are macrophages and dendritic cells here. So, the macrophage will see these bacteria, recognise them, eat them. After eating, they will be activated. An activated (ma) macrophage will produce cytokines and chemokines.

So, these cytokines and chemokines, they have different roles. That, you will gradually see in different, I mean future classes. But for today or now, these cytokines and chemokines, what they are doing? This is the blood vessels. Okay. This is blood vessels. So, there are a lot of say RBC, neutrophils, uh T cells, macrophage are there. So, these blood vessels are very

tightly packed, so that blood cannot diffuse to the tissue. Okay. But these particular cytokines and chemokines, what they do?

They vasodilate these blood vessels. Vasodilate means, if you see carefully, these cells are not as tightly packed as before. So, there are some gaps. So, from these gaps, neutrophils and other cells are attracted by the chemokines and they reach to this site of infection. So, this site of infection, with time, you will see lot of cells. And it is a very common practice. I mean, uh many of you wide apart. sa Suppose there is a cut or something happen, what we usually tell?

Usually tell, okay, now it is fine, but tomorrow morning you can have or you will have pain or swelling. Okay. So, these swelling, pain are the immune reaction. This is called inflammation. Okay. This is the inflammatory response. So, these inflammatory response are initiated by this macrophage and other. So, then all these cells enters. And this inflammatory response means, what you, all the cells will migrate to this particular site, which will swell this place.

There will be some heat. Or that particular place will be slightly hotter than rest of the body. And there will be a pain. Another thing is coming, the redness. Okay. So, heat, pain, redness and swelling are the 4 ta 4 symptoms which describe clinically as inflammation. Okay. That redness depends on, definitely depends on the skin complexity. But heat, pain and swelling is very easily distinguished simple from normal skin. And those who have this cut; and many of us or most of us have experienced this.

And so, this is the first response of immune system, that something happened. (refer time: 11:49) Okay. Another innate lymphocyte component is the natural killer cells. Also the innate lymphocytes and natural killer cells, that ILC and natural killer cells; they are also component of innate immunity. Okay. So, this innate lymphocytes and natural killer cells are effector cells. That is, they are the similarities with lymphoid lineage. Lymphoid lineage means, B cell and T cell.

They are very similar. Their functions are very similar. But, they also helps in the adaptive immune system. But they can recognise a foreign pathogen and kill them; like NK cells, which has lot of small granules, you can see. So, these granules are loaded with killer or materials or the poisons. Okay. So, if they touch any cells, they will release this granules, material inside the granule. That will come later in detail, like what they are doing. So, they release this.

So, after releasing this toxic or the poisonous material, the neighbouring cell with which they attach, they will die. So, they release the lytic granules that kill, what kind of cells? Virus-infected cells, as well as, which is not also written here, the tumour cells. Okay. So, any cells converted to tumour cells or virus infected cells are recognised (b) by this natural killer cells and they kill them. So, this is more or less the components of innate immunity. So, inflammation is a part of innate immunity, but initiation of adaptive immune response.

(refer time: 13:33) Now, now, we are going to talk about the outline of the adaptive immunity. What is adaptive immunity? We already told that adaptive immunity means, when some pathogen interact or invade the tissue or infect us, then innate immunity initially try to combat this infection or the attack. But innate immunity or innate part of immunity are not enough always to solve the problem. So, we have a backup mechanism which is more powerful and more specific, which is again take help from the innate (com) immunity part; and they make themselves ready or make the weapon specifically for that particular pathogen. Okay.

So, which will take time? In last class, we see, it takes days to days to week. Right? So, now, we are going the, going to say that, outline that what is adaptive immunity. And gradually, we will discuss. And I I am sure that you will have many questions in between, like innate immunity. There are lot of components or lot of terminology. You have listened for the first time, those who have not studied immunology before. So, what is going to happen?

There are many question will come; how this thing happened; how that thing happened. But I am sure that you will get the answer with the progress of the course. The problem of teaching immunology, let me tell you a few thing. Problem of teaching (immunel) immunology is: Immunology is a system. It is not always like I talk one by one, so you study one by one and understand whole thing. Whole system in it, when any infection happen, everything jumps together, whatever possible way the immune system can handle them. Okay.

So, it is not 1 or 2 things. And when you study immunology, it is not possible to study everything at a time. Right? So everything is written chapter wise. So, we have to (unders) read every chapter, understand every chapter to understand the whole immune system. And which is not possible at the beginning. So, what I am trying to do is, I am just going to give you a very brief outline of almost everything what is happening, in just maybe 4 or 3 to 5 lectures, right, total.

So, to give an idea, what are the components of immune system; what are the type of immune system; how it works. So, initially, please bear with me. So, I am not going to go in

detail like what is what. But eventually, we will see. And whatever we are discussing in the first 3 or 4 lectures, we are going to explain in much more detail with respect to the initial class. And then, many things will be cleared. And there are many questions that nobody can answer, because it is not known yet. Okay.

Let us starts the principle of adaptive immunity, which is just we are going to, I am going to outline what are those. So, first point. The interaction of antigens with antigen receptor induced to acquire effector and memory activity. That we have told little bit. So, for that; so, what is this receptor, I told. So, if this is the cell. And this is normally B and T lymphocytes. Say for now, I am saying B or T cells. So, B and T cells has receptor. Okay. So, these receptor; this is particularly, that is, this kind of y type of receptors, we draw for B cells.

And for T cell receptor, we can draw like this. So, this is for T and this is for B. Okay. So, this B and T cell receptor, this B and T cell receptor, these receptor can recognise. Suppose, this is the receptor. They can recognise a foreign antigen. And these antigen receptor, when it binds, it induces. So, the signal from this receptor goes inside. Okay. So, something binds here. That gives the signal inside. And which will mmm tell the B cell and T cell that something came, so you take care of that. Okay.

So, the interaction of antigen with antigen receptor. So, B cell and T cell or B lymphocyte or T lymphocyte as a specific receptor, which interact with antigen, which induce the lymphocyte to acquire or to convert them to effector cells. Now, a new term came. Now, a new term came. oh Now, a new term came, antigen, okay, which is not, we (d) did not explain it. Antigen is the molecule. It may be small molecule, big molecule. By definition, anything antibody can bind is antigen.

Anything antibody can bind is antigen. And what is antibody? Antibody is a protein molecule produced by B cell, which we will see very soon. A quick presentation of antibody. So, antibody has a binding antigen binding site by which it can bind antigen. Okay. There is another term. I am just telling now, which is immunogen. I will discuss it little later. So, antibodies and the T cell receptor are composed of constant and variable regions that provide distinct function.

We will come very soon, what is this. Antibody and T cell receptors recognise antigen by fundamentally different mechanisms. Okay. Just remember. So, binding up antibodies with the antigen and binding up T cell receptor of, with antigen, are slightly different. That we will see. Antigen receptor genes are assembled by somatic gene rearrangement of incomplete receptor gene segments. I am repeating again. Antigen receptor genes are assembled by somatic gene rearrangement of incomplete receptor gene segments.

So, why this thing? This is not that easy to understand at this moment. And I will take at least 3 to 4 class or lectures, just to explain this slides. So, for the time being or for the basic concept clearing session, what I can say is: See, there are so many varieties of microbes available in earth. And we are always exposed to many of them. Right. Air, water, solid surface, our skin, full of different microbes. But they are not doing anything. And we are, most of us are normally healthy all the time.

So, our immune system always fighting with them and clearing them so that we do not feel sick or we do not have any infection or you would not face any problem having disease. So, if you see, antigens, any; say for example, any anti-proteins present in earth may be antigen; any carbohydrate, nucleic acid, any biomolecules can act as an antigen. So, there are so many varieties. And every organism is a different protein. An antibody is also a protein. Right.

So, if antibody is a protein, I am assuming antibody is a protein. And I hope all of you know that protein is synthesised from or the protein information is written in a gene. So, 1 protein or 1 antibody is developed from genes. Actually, 2 genes are responsible. I will see later. So, even for simplicity, if I consider 1 antibody, 1 gene. And there are millions of possible antigens. So, that means, each and to understand again the interaction, for each antigen, we should have a different antibody.

That is why they are so specific. And that specificity is like lock and key. Okay. Very rarely 1 key works with different locks. Right. So, so, 1 key, 1 lock is very specific. Rarely, 1 key can open another lock. That is, one kind of specificity. Another specificity is the gloves. When you wear a gloves, it will fit exactly to the hand. So, the specificity is like this. It is very tight. Very tight interaction between antigen and antibody. And so, the antigen is different means, antibody is also different.

So, if there are; for example, if there are 1 million antigen present, technically, there should be 1 million antibody. Those, if the (anti) 1 million different antigens are present, that means 1 million different antibody we need. But I hope you know, by different prediction or different algorithm, the number of genes present in human is only 25,000 to 35,000s. Varies, because different software's or different algorithm's prediction is different. So, if it is, even the, if we go the maximum, say 35,000 genes we have, even all these, I mean, all these genes are producing antibody.

That is also much less. Is, with respect to 1 million antigen, 35,000 is very, very little. So, how; and you know that all genes are not producing antibody. Many of our own proteins are produced by our own gene. So, 35,000 includes all proteins present in our body. And out of that, very few are responsible for producing antibody. So, these few genes, how they are producing so many variety of receptors? I am talking only about antibody. The same thing or similar thing is equally true for the T cell receptor.

They also are very specific. 1 T cell receptor normally does not bind to another one. We did early. Like 1 key is good for 2, 3 different locks are very rare. Similarly, 1 receptor can binds 2, 3 different antigens are also very rare. So, same way. So, if you consider both the variability or the diversity of antigen receptor for B cell, as well as the T cell receptor, the number is not matching. The number of genes and number of receptor variability are not matching.

So, how these diversities open? So, it is a, it was a very big question before. But now, we know what are the mechanism (it) of it. So, just, of all this thing, if we write one single line that antigen receptor genes are assembled by somatic gene rearrangement. That means, some rearrangement is happening. So, we do not have that many genes. We have some segment or component. Some rearrangement is happening. And that rearrangement makes that many variation.

(refer time: 25:12) Now, lymphocytes activated by antigen give rise to clones of antigen specific effector cells that mediate adaptive immunity. So, the lymphocyte, which have a specific receptor, bind with a specific antigen. That interaction makes their number more. More and more number is; so, 1, this is 1 cell. It binds with something. It get activated. So, 1 cell is not enough to handle so many bacteria in; And, because, normally, infection does not happen with 1 bacteria or 1 virus.

So, if this, if this virus, if this virus is 1, it is fine; nothing will happen. Because, to cause a disease, we need a (num) certain number of organism. So, (na) when we see the disease happen, that means, more number of infection or more number of bacteria or the pathogenic agent is there. So, 1 cell is not enough. So, suppose, there is 1 B cell, 1 receptor. It interact with 1 antigen. So, that interaction will give the signal to this cell. This cell will multiply, so that they can handle.

So, we have, suppose there are 100 different cells. Only 1 cell interact. Then these cell (on) only are going to multiply and tackle the problem. And this multiplication will make them also slight different. It is not just like resting cells or if there is no interactions, all other B or T cells, they are slightly different. They converted to effector cells. This effector cells

mediate adaptive immunity. So, what we see, the final mm protection from the immune system is actually mediated by the activated clones of antigen specific adaptor cells.

Lymphocytes with self-reactive self-reactive receptors are normally eliminated during the development and functionally inactivated. Now, this is also saying, if receptor of B cell and T cell can bind protein as antigen and can get activated, why not they are interacting with our own protein? At the very beginning of the first lecture, we said that, okay, the immune system means, fight with the pathogen, but do not harm the self. So, immune system should not harm our own cell.

But our own cell also made up of protein. There are so many receptor proteins. There are so many free proteins, hormones. But they are not interacting. Why? Because, what point 13 is saying, the lymphocytes with self-reactive receptor. That means, the receptor which can interact with our own protein are eliminated during the development. So, if there is any B or T cell, which can recognise our protein or my own protein or your own protein is eliminated during the development.

So, there is no receptor left. Normally, the immune system is not defective. No receptor left which can binds to our own protein. That is how it is not causing any harm to our own cell. Lymphocytes mature in the bone marrow. So, the lymphocyte, either B or T cells, they produce in bone marrow and then come into the peripheral blood. So, in case of bone marrow; so, lymphocytes mature in the bone marrow. What kind of cells mature in bone marrow? The B cells.

And another type cells, lymphocyte is T lymphocytes. They mature in thymus. Thymus is a gland. We will see later. And then, congregate in (limpoti) lymphoid tissues throughout the body. That, we will also see. Okay. So, they produce in bone marrow. A part, B cells are mature in bone marrow; and T cells are matured in thymus. Then they come, work in a peripheral blood; and they resides on a lymph node. That, we will see later. And from there, they do their job.

And adaptive immune response are initiated by antigen an antigen presenting cells in the secondary lymphoid tissue. Okay. So, the cells or the lymphoid tissue are 2 type; primary lymphoid tissue and secondary lymphoid tissue. Where these B cells and T cells are produced and developed or modified or trained, rather, they are called primary lymphoid, like bone marrow and thymus; bone marrow and (tha); bone marrow and thymus. They are the primary lymphoid tissue.

After maturation or after getting the training, what to do; and they migrate to secondary lymphoid organs. Secondary lymphoid organs: they, where they live throughout their lifetime or in some cases our lifetime. Okay. So, the secondary lymphoid organs are lymph nodes. We will see what is that; spleen. Okay. So, lymph node, spleen, there are many other lymphoid tissue. We will see later. I mean in, may be in the next class or next lecture. Okay.

So, adaptive immune response are initiated by antigen and antigen presenting cells in secondary lymphoid tissue. I just told what is secondary lymphoid tissue. (refer time: 30:50) So, a text. The lymphocytes encountered and response to antigen in the peripheral lymphoid organ. So, the peripheral lymphoid organ are the lymph nodes and other spleens. So, they are the lymphocytes. So, after producing and maturation, they go to the lymphoid organ, secondary lymphoid organ, where they interact with the antigen in uh or the pathogen in the secondary lymphoid organ.

Mucosal surface: So, I am talking; the lymph nodes are present inside different body. But there are lot of mucosal region in our body; like mouth, nasal, intestinal, intestinal or the alimentary canal. So, the mucosal surface also have a specialised immune structure, that orchestrate response to the environmental microbe interaction. Because, our face is, we are, many thing we are eating, right. And that foods or sometimes even the clean in water, where it is not clean enough or pathogen free.

So, they are always in encounter with the different pathogens or foreign. They may not be pathogen, but foreign bacteria. So, they also have a specialised lymphoid tissue. That, we will see later. And lymphocytes activated by the, by antigen proliferate there. That I already told. So, once they interact, they proliferate into more number. And peripheral lymphoid organ, they happen. They generate the effector cells. Some cells fight for to combat the pathogen invasion or to kill them.

And some of the proliferated effector cells converted to memory cells, which we do not know completely at what is the mechanism how they remember the pathogen structure or their proteins or their things. It is not clearly known, completely known actually. So, that immunological memory protect us from future infection. So, this is the part of or the outline of adaptive immunity. So, in next class, we are going to discuss slightly more detail of these points. Okay. Thank you for the day. See you in next class.