Host-Pathogen Interaction (Immunology)
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Lecture – 21
Cells of Immune System and its role in Host Defense – B and T cells

Hi in this session we will discuss about B and T lymphocytes and we also call it as a B cells and T cells. In previous session we have discussed a kind of subtype of T cells which we call it as NKT cells and it is role in recognition of lipid and lipid derivative and tease and here we will take up this B cells and T cells.

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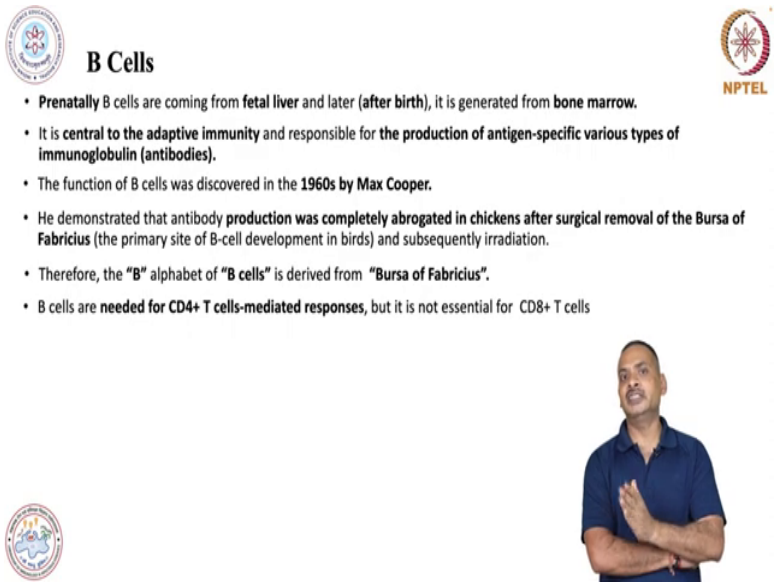

So, let us begin with B cells, so, B cells are one of a very important cells. As you know I think most of you are aware about the B cells and antibody. So, all these antibodies are produced or derived from the B cells. There are different stages of B cell development and the terminal stage which we call it as a plasma cells and these plasma cell, basically secretes the antibody against antigen or microbial pathogen or any kind of foreign entity.

So, I think I have explained to you this B cells are basically produced by fetal liver, prenatal condition or prenatally it is produced by the fetal liver. And subsequently after birth this is basically produced by the bone marrow cells. I have explained you during the bone marrow when we have taken the immune organ that is bone marrow. So, it is in adults, it is produced from the bone marrow.

It is a key component of a specific immunity or you can call it as adaptive immunity and they produce antigenous --specific antibody and I have discussed, if you remember when I was taking the properties or Hallmarks of immunity that there is a the immune response or immunity can distinguish or they can recognize a family of molecule which is innate receptors and they have a very strict specificity as well.

And this strict specificity is basically achieved by the antibody. Antibodies are also called as immunoglobulin and just for your note. Immunoglobulin is a highly glycosylated protein. Please remember this is a highly glycosylated protein and this glycosylation is very much essential for their structure for their function and for their stability under physiological condition. So, antibodies or immunoglobulin is highly glycosylated.

Just remember that thing the function of B cells was discovered in 1960 by a great scientist. His name is Max Cooper, and the B cell word is basically came after his work. So, he basically demonstrated that antibody production was completely abrogated in chickens after surgical removal of if you remember, there is a one a specialized organ which is present in the birds which we call it as a bursa of fabricius.

So, basically what he has done, he surgically removed and then he irradiated the chicken. And then he found out that the antibody production was severely reduced or almost completely abrogated. So, by his work it was a known that this organ is playing a very important role in B cells production, as well as antibody production. And after this work these cells were called as a B cell, there is a B word B alphabet.

This B alphabet is basically derived from this organ name and this B cell is B stand for bursa or fabricious and this from that time onward we call these cells the antibody producing cells as a B cells. B cells plays a very important role in CD4 T cells-mediated immune responses. If you remember that I have told you, there are three major kind of antigen presenting cells. One is dendritic cells.

The dendritic cells can present the antigen and these antigen presenting cells basically express the MHC Class II molecules. So, the dendritic cells is a one, another is macrophages and the third one is B cells. So, B cells plays a very important role in development of CD40

T cell mediated immune responses but it is not playing any role in CD8 T cell mediated immune responses.

After a short, while I will tell there are two major kind of T cells. That is CD4 positive T cells and CD8 positive T cells. And they play a variety of role I will explain you in a in a short while.

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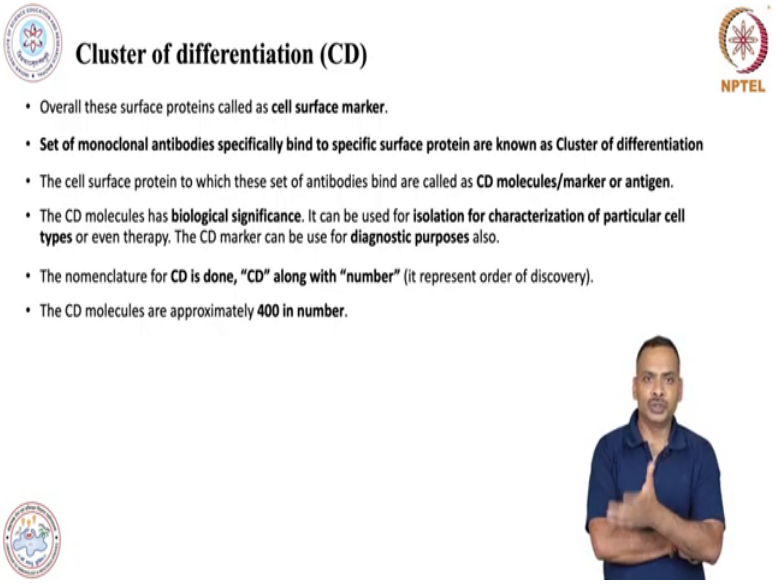

So, before, going to more detail about the T cells, I would like to introduce a very important a notation which we commonly use in immunology and I want to discuss the importance of giving this notation. And this notation we call it as a cluster of differentiation or we can also call it as a CD. Now, let us look at what is CD? So, CD is so, if you take out the lymphocyte or PBMC from the blood.

And if you observe under the microscope after staining and then you can distinguish ~~in~~ two major kind, one is granulocyte and another is agranulocyte. And if you look at a granulocyte there are variety of cells. So, agranulocyte contain B cells and T cells but under microscope or morphologically or phenotypically. You cannot distinguish which cell is T cells or T Th cell or Tc ~~C~~ cells.

A cytotoxic T cells or B cells by looking by simple looking and just by looking the morphology or phenotype, phenotypically, you cannot distinguish those cells. So, there is a need of some system by which we can distinguish. This is a B cells, this is a T cells, this is a

NMKT cells and this is the macrophages. Every time you cannot observe under the microscope. Because when you do the experiment or when you investigate something.

If you always observe the cells under microscope then you cannot conduct further experiments. So, since these cells are functionally different and is functionally different. So, it is quite obvious that these cells must be having different surface proteins. Over the surface, the protein must be different. And these surface protein are could be maybe this is a some receptor for some ligand and this ligand could be a soluble or it is present over the cell.

This could be some signaling molecule. This could be some adhesion molecule, sometimes cell need to adhere with say, blood vessels or something So, this surface proteinase, we basically are could be different and this is different from different cell types for example, B cells, T cells, macrophages and so on. So, forth, so, additionally, this there is a possibility that for example, there is a resting, macrophages or resting T cells are there or naive T cells are there or naive B cells are there.

And when they get activated then their surface markers will change or surface proteins will change. So, if we track the surface protein then we can distinguish This cell is naïve, this cell is activated or this cell moves from this stage to this stage. So, we need to find out some way to track this these events in the cells. So, overall these these proteins which is uniquely expressed at particular stage of development or activation or non-activation, we call it as a cell surface marker.

And overall, this cell surface marker is playing a very important role in various immunological or biological processes. So, how we can distinguish these cell surface markers. So, there is a set of monoclonal antibody. I will tell you what is monoclonal antibody, so, there is a set of monoclonal antibody which basically orare specifically bind to a specific protein and we call it as a cluster of differentiation.

So, let me explain what is monoclonal antibody? So, when there is a monoclonal there is a also there must be or there must be polyclonal. So, monoclonal antibodies, the antibody which can look at only one antigenic surface. And this antigenic surface or antigenic determinant we call it as a epitope. So, monoclonal antibody can look at only one surface and then this can bind. So, monoclonal antibody are very specific to their target.

So, there will be a set of, for example, if there is some protein this has a several three-dimensional structures. So, one monoclonal antibody will bind to one of the surface. There are so many surfaces, or one portion of the surfaces. So, all those set of monoclonal antibody which is binding to one specific surface protein. We call it as a so, this the set of antibody we call it as a set of monoclonal antibody.

And this will bind to one molecule which has a many surfaces and we call it as a cluster of differentiation. So, the cell surface protein to which this set of antibodies basically bind we call it as a CD molecule or CD surface marker, or CD marker or CD antigen. Anything you can call it. This CD molecule has some biological significance and it is used for variety of processes and this the CD. The CD molecule was developed from ages.

Now, we have so many CD molecules. So, this has a some biological significance. For example, you want to isolate some from PBMC for example, you want to isolate the B cells. So, if you have those set of antibody which is uniquely binding to the molecule which is uniquely expressing over B cell, you can use that antibody in order to isolate those B cells or visualize those B cells. And rest you can discard or you can use this B cell for further experiments.

So, this has a very important role in biological system as well as this is also playing a very important role in for example, therapeutic as well as diagnostic. For example, in previous session, I have discussed about the NKT cells. So, if I want to isolate NKT cells from the individual, I can use those CD molecule, the specific CD molecule which is expressing over NK cells. I can use those set of antibody and then I can isolate the NK cells.

And then I can use this NK cell for various treatment and later on, I can infuse to the patient in order to say overcome the viral infection or to overcome the cancer. So, this has a lot of significance this I was explaining about the therapeutic. There is also significance in diagnostic, for example, in some blood cancer the B cells are not moving from stage A to stage B. So, we can easily find out using those set of antibodies, unique set of antibody.

So, this has a wide range application. The CD molecule is basically, this naming is done along with a CD and there will be a some number and number is based on the order of

discovery. So, for example, in B cells or T cells, some molecule was discovered so that receive first that number and later on people found out okay in T cells there are further different kinds of T cells, so, they receive another number or higher number.

So, the CD molecule, the naming is like that for example, CD3. CD3 is present on T cells. There is a CD4 T cells, so, CD4 T cell the CD4 molecule was discovered later. There is a CD19 on the B cells. So, CD19 was discovered quite later to compared to the CD3 and CD4. So, this is a one of a convention and it is adopted in in case of CD and numbering or CD nomenclature.

So, far about 400 approximately 400 CD molecules were discovered and these molecules are used in our various kind of studies.

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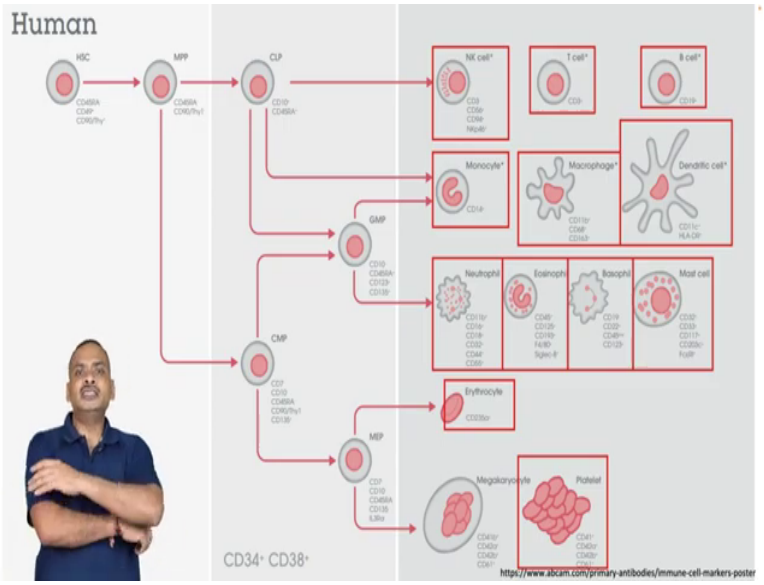

Here I have a one simple scheme which this is in case of human here you can see that lot of CD molecules are written. CD45 are A – CD49 and all those things in on hematopoietic stem cell. Basically, this hematopoietic stem cell is positive for CD34. I think I have explained when I have taken the hematopoietic stem cells. So, here you can see that there is a unique CD marker over the erythrocyte platelets and neutrophil, eosinophil, basophils, mast cell and monocyte macrophages, dendritic cells, NK cells and B cells.

So, if you see there is a some unique marker. Here, I just want to tell one more very important technique which we are using or a concept, not precisely the technique the concept. For example, if I want to isolate B cells and I want to culture those B cells and further study. So

then there will be a two choices. One is that I should isolate the B cells and then perform the experiment which we call it as a positive selection method for isolation of B cells.

Here what I will do? I will take the antibody which is uniquely binding with the B cells, particularly CD19 molecule and then I will pull out those cells and then I will culture and perform the experiment some functional experiment. So that is not so good. The another way is that you take the blood and remove all those cells which is not needed for your experiment. We call it as a negative selection.

So, negative selection is you remove everything, except what you want in that way the B cells will be untouched and this can be further used for any functional studies. Positive selection is fine over there when you are when you are doing some basically, you are disintegrating that target cell for example you want to measure some transcript or expression of some gene in the B cells.

Over there you can use the positive selection method because the antibody will touch those cells and you are not further performing any experiments. So, you are immediately after isolation, you will break this cells and take out the transcripts and measure the amount of transcript. So, over there positive selection is okay but where you are performing the functional studies of target cell over there it is strongly recommended that you should perform the negative selection method in order to isolate the target cells.

So, here I gave you the concept of CD and here there is a T cells I intensely put this T cells towards end~~N~~ because I will talk about the T cells now. So, T cells has a unique one, common marker which we call it as a CD3. So, they are CD3 positive and then this CD3 positive cells are differentiated into two main lineage. One is T helper cells and another is a cytotoxic T cells.

Cytotoxic T cells are basically recognizing the antigen proteinaceous antigen, along with MHC class I molecule and upon recognition they basically li~~y~~yeses the target cell. Like NK cells, I have explained you NK cells in great session in a great length in previous session, So, CD~~A~~8 T cells has a cytotoxic property. They play a very important role during virus infection, as well as during the development or during elimination of this transformed cells.

On another hands is T helper cells they recognize the antigen, along with MHC class II molecule which is expressed by a very specialized cell known as antigen presenting cells. I have explained you antigen presenting cells on several occasion in previous session. So, they sense the antigen along with MHC Class II molecule and then they will differentiate further in order to develop appropriate immune response, particularly adaptive immune response.

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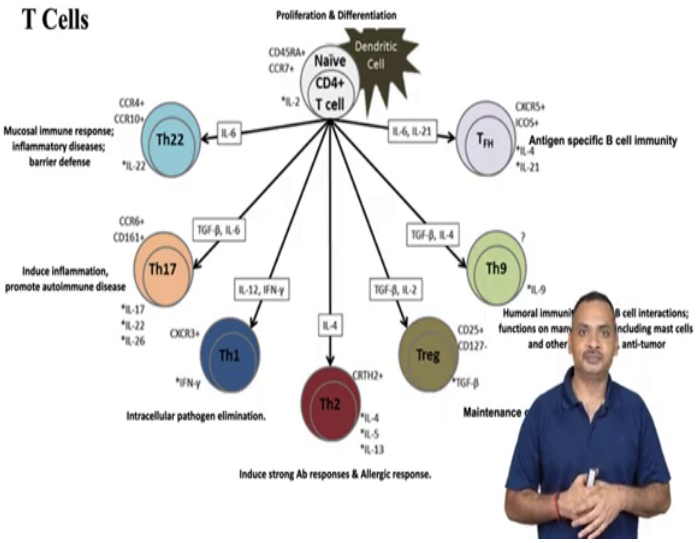

And this T cells are this Th cells or T helper cells are of several kinds and they have a huge range of function. For example here you can see that there is a Th1 cells. They play a very important, important role against intracellular pathogen for example, mycobacterium, tuberculosis or listeria infection. They play a very important role and basically activate those cells and kill those pathogens.

Another is Th2 cells. This Th2 cells are very important in development of B cell dependent immune responses. And here you can see, there are some unique cytokine produced by these differentiated Th cells. For example, in case of Th1 it is a interferon gamma, IL 12 and in case of Th2 it is IL4 and upon activation they also produce the same cytokine along with other cytokine. In order to establish that kind of immune response.

For example, Th2 produce IL4. Then cell differentiate into the Th2 and then this Th2 cells will proliferate and then they will produce more IL4, along with all those cytokine which is needed for the development of B cell mediated immune responses. They play important role in allergic responses. Another here you can see that Th17 cells this basically induce inflammation and they basically involve in autoimmune diseases.

There are Th22 cells. This Th22 cells are basically play important role in mucosal immune responses. You remember, I have discussed various in various immune organ. The mucosal associated lymphoid tissues. So, over there I have told you there must be a very good balance between tolerance and immune response because if it will be disturbed because food is a all foreign thing but there is a no immune response.

So, over there is a tolerance and tolerance plays a very important role against this but if this food contains some pathogen then our immune responses get activated and clear and clear that microbial pathogen. So that is a very delicate balance between tolerance and immune response. So, over there, this Th22 cells are there and they play a very important role. And there are some diseases for some inflammatory bowel diseases.

And all those things over there these cells are also playing probably these cells get dyisregulated. So, this is not my research field, so, I cannot tell too much about that. There is a TFH cells. Basically, this TFH cells plays a very important role against this antigen specific B cell immunity. Th9 cells they are basically very important against tumour. And they are also involved in in one or other way, in activation or in function of the mast cells.

There is a T-Rexreg cells so far I was talking about all activating things but there is a need of damping of immune response. Because if the system will keep on activated then that result to the autoimmune disease, so, there is a cells known as T-Rexreg cells. These are T regulatory cells. So, these T regulatory cells basically damp the any over activated T cell mediated immune responses. With this I am completely finishing the immune cell and it is function in immunity, various immune cell we have discussed.

And we have also studied their role in immunity and in some or other cells. We have also studied the how these cells are involved in in disease. So, in next session I will take you to the soluble component of immunity. So, we have discussed the organs of immunity. Then we have taken the cells. Now, we will study the molecules which is playing a very important role in immunity and later on, I will discuss how everything get integrated. Thank you. Thank you very much.