Host-Pathogen Interaction (Immunology)
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Lecture – 22
Basics of Cytokines

Hi, ~~I~~in previous session, we have learned so many topics and if I see the major categories of topics which we have studied are first, you have studied the history of immunology how immunology field evolved? And then we have looked at how this innate and adaptive immunity communicate each other and then thereafter we have taken immune organs, various immune organs.

And these immune organs are playing very important role in defense in any part of the body please remember that thing. And then we have also learned about the various immune cell, which I will say that we have studied broadly key cell types of the immunity. There are further so many kinds of cells, but we will not take that deep insight in further divided or further subtypes of immune cell. We have discussed a major immune cells.

And now it is very interesting that how this immune organ and immune cells they communicate each other. So, you can consider a situation that suddenly there is a massive power loss in current scenario. And you cannot communicate with each other humans the whole world cannot communicate with each other. Then what will be the situation? It is a very h~~eav~~yway situation.

It is very difficult to control the things if there is no communication. So, similarly, the immune system is also communicating each other. The immune organs are communicating each other. The immune cells are communicating each other and this communication is mainly or only, I will say, mediated by specialized group of molecules which is produced by these immune organ or the cells which is present within these immune organ.

And we call these molecules are as a "cytokine". Let us look at how this cytokine works and various important aspects of cytokine.

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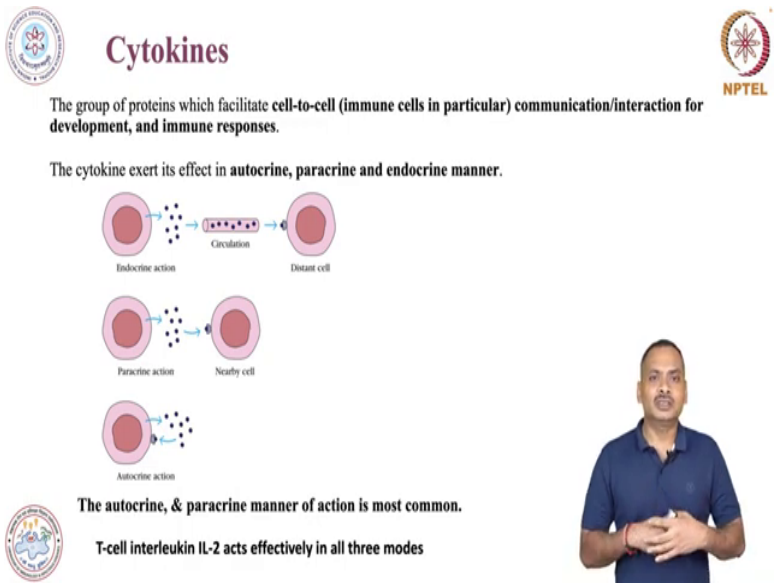

So, cytokines are basically a molecule which is secreted by cells. I will, I said cells it includes both immune and non-immune cells as well. So, this is a basically produced by mainly produced by immune cell but the non-immune cells do produce some cytokine or cytokine like molecules and they play important role in communication with immune cells. And basically, these this communication, why we need this communication?

So, this communication is playing very important role in development and various kind of immune response, development of for example, particular immune cells. As I have explained you in previous session, if you put the hematopoetic stem cell along with some cytokines, for example GM-CSF, if you remember then this cell will this hematopoietic stem cell will be differentiated into the dendritic cells.

So, these are the very important factor in order to develop to the particular immune cells. And it is also playing a very important role in development of further immune responses as we will go through this session, you will understand most of these points. And how this cytokine works? The cytokine works in various way it works in autocrine manner. It works in paracrine manner, as well as in endocrine manner.

So, how endocrine manner is taking place? So, basically, endocrine is nothing it is a there will be some cells which will secrete these molecules and then these molecules are transported through the blood vessels or through circulation and somewhere else. There will be a target cell and over there it will act and then it will exert their effect. So, this is a endocrine manner and if you have studied endocrinology the hormonal system.

So, all hormones follow this kind of production, as well as for their effect. So, the hormones are produced at particular site in the body or in particular organ which is, for example, a very common is like insulin. If you take the example of insulin, it is produced in the pancreas but it acts in variety of cells. It is moving through the circulation. And then it is exerting it is effect. So, this is a endocrine manner.

Another is a autocrine manner, so, autocrine manner of action is very simple the cell which is secreting these molecules, these active molecules, these cytokines, they basically act on same cell and then this will induce or this will develop a kind of response. So, this is autocrine manner, another is paracrine manner, paracrine manner of action is again very simple the cell will secrete these molecules, the cytokine molecules and it will act on nearby cells.

So, in that way they will induce the appropriate response. I the response could be activating response the response could be damping of response, so on so. So, this is the way by which cytokine acts in immunity. If you see very carefully the most of cytokines or these active molecules, act in autocrine and paracrine manner and this is the most common there are some cytokine which is also playing or acting in endocrine manner.

For example, there are some molecules known as thymosin which is produced by the thymus. And this thymus if you remember the immune organs, plays a very important role in T cell development and T cell differentiation. So, this is also a kind of endocrine, so thymosin is kind of a confused kind of thing it is a some people say it is it act like a hormone some people say it is like a cytokine.

So, it is little there is a debate for the thymosin. So, there is a one cytokine which we call it as a IL-2. So, this IL-2 is acting or the response or the action of this IL-2 which is produced by the T cells act on all by all these three modes the auto-crinme, the paracrine and the endocrine manner.

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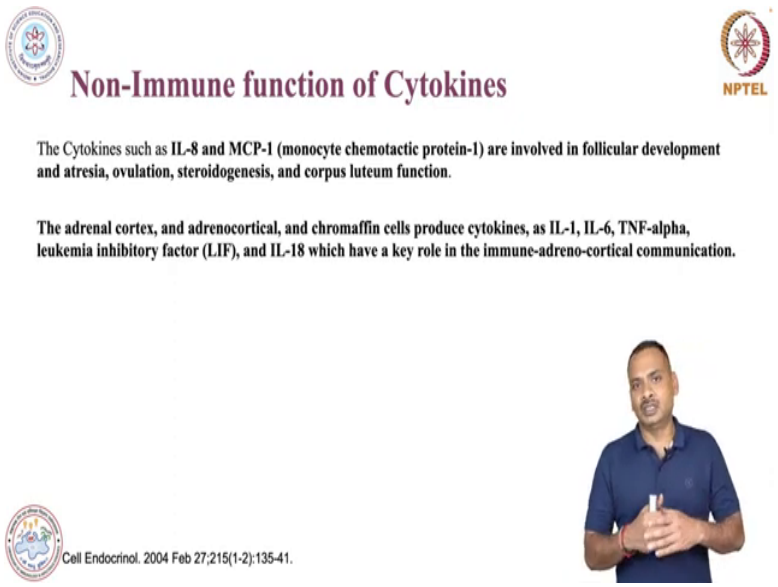

So, there are some non-immune function of these cytokines as you can see here, there is a cytokine known as IL-8 and MCP-1 this is monocyte chemotactic protein one. So, basically, this is involved in or this is acting on, the ovaries. They cause~~occurs~~ various kind of response, such as follicular development. It is playing important role in ovulation, steroidogenesis, the synthesis of steroid, molecule and corpus luteum function.

And this is also playing a very important role in narrowing. So, after ovulation there will be a some kind of void will be there and that void will be narrowed by the action of these cytokines IL-8 and MCP and that we call it as atresia. So, this is a non-immunological function of cytokine. Similarly, there is some cytokine, like IL-1, IL-6, TNF-alpha, ~~leukemia~~leukaemia inhibitory factor.

If you remember, I have discussed ~~leukemia~~leukaemia inhibitory factor in during the explanation about embryonic stem cells ES cells. And IL-18 which have a key role in the immune-adreno-cortical communication. So, these are little off from the cytokine. So, this is a non-immunological function it is not that cytokines are playing only role in immunity. There are some non-immunological functions as well.

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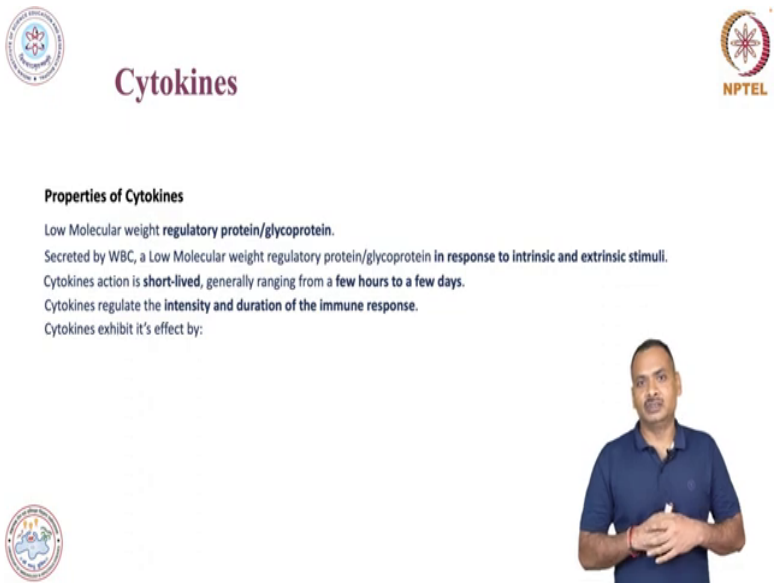

So, there are some properties of cytokine and they are basically low molecular weight regulatory protein or this could be a glycoprotein. In general, this is a glycoprotein again, you know in eukaryotic system the protein undergo post-translational modification and then there will be addition of sugar molecules. So, but there are different degrees of glycosylation. So, basically, these are low molecular weight and we can call it as a regulatory protein.

They are produced in response to the intrinsic or extrinsic stimuli. Intrinsic stimuli means within an organ. So, it is a so, for example, hematopoietic stem cells are there in the bone in bone marrow and there is a need of for example, production of, say monocyte. So, this hematopoietic stem cell will rejuvenate by themselves, divide in presence of some cytokine and then these cells will differentiate to the monocyte or macrophages in presence of appropriate milieu~~milo~~.

And this milieu~~milo~~ is basically consists of cytokine so, there is no external stimuli. Extrinsic stimuli is a very simple extrinsic stimuli is a the host when they are infected with some microbial pathogen and this microbial pathogen could be bacteria, virus, parasite as you know, there are variety of microbial pathogens. So, when they will enter then they will activate the immunity.

So, those are the extrinsic stimuli and when they will activate the immunity then these activated immune cells will produce some cytokines in order to clear or eliminate the pathogen. So, these are external or extrinsic stimuli. In general, the action of cytokine is a

short-lived it is not very long once they will produce it their action will be in few hours to few days, not more than that.

But if there is a some inflammatory condition will be there then the cells are keep on producing these inflammatory molecules and when they are keep on producing this kind of inflammatory molecule then the response will be sustained. However, their life is very short once they will produce within a few hours or in few days it will be de-gradated. The intensity and duration of immune response is basically regulated by the these cytokine.

As I told you, for example, if there is some very acute some pain so then in that situation there will be a spike of cytokine production. And in case of chronic, there will be a very little production for long duration. So, basically this cytokine regulates all this thing means the intensity and duration of immune responses. Now, how this cytokine exhibit it is effect there are several ways by which cytokine exhibit their effect.

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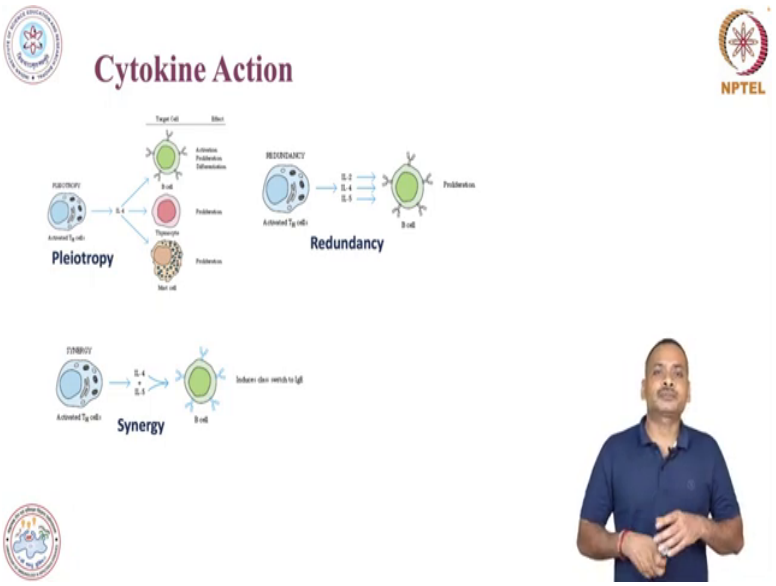

So, one and the most common is a pleiotropic effect. As you can see here, this pleiotropic effect means a cytokine is produced by some cell and this cytokine act on various different immune cells. Here you can see, there is a B cells, there is a thymocyte and there is a mast cell and the cytokine which is produced by activated T helper cell is IL-4. So, when this IL-4 will act on B cells then that will cause activation and proliferation and differentiation of the B cells.

However, when this cytokine act on thymocytes then that will cause the proliferation of thymocytes and when it will act on, say mast cell then that will cause proliferation. So, one cytokine act on different cell and the responses are the different that we call it as a pleiotropic effect or pleiotropy. Another is redundancy and this is basically the cell which is producing variety of cytokines but their effect will be the similar.

It is not, I will not say the same but it is quite similar. For example, here you can see the activated T helper cells producing IL-2, IL-4 and IL-5 and when this cytokine will act on B cells then that will cause the proliferation. Of course, there will be some difference but majorly the response will be the same and that we call it as a redundancy. Another is synergy, synergistic effect also we call it as.

So, here what is there? When the cell is producing, say some cytokine here. You can see there is a IL-4 and IL-5 and when it will act on B cells then that will induce the class switching. So, we will discuss class switching when I will take the B cells or antibody diversity. So, synergy means, for example, if there is a only IL-4 and this IL4 is giving a response in arbitrary unit.

For example, I am just telling a unit which is a arbitrary say the response of IL-4 on B cells will be say one unit. And when I am stimulating this B cells with IL-5, I am also seeing one unit response. But when I am putting the same amount of IL-4 and IL-5 over the B cells then I am seeing the response as a 11 or 10 or 20, something very big. So that what we call it as a synergy, or synergistic effect?

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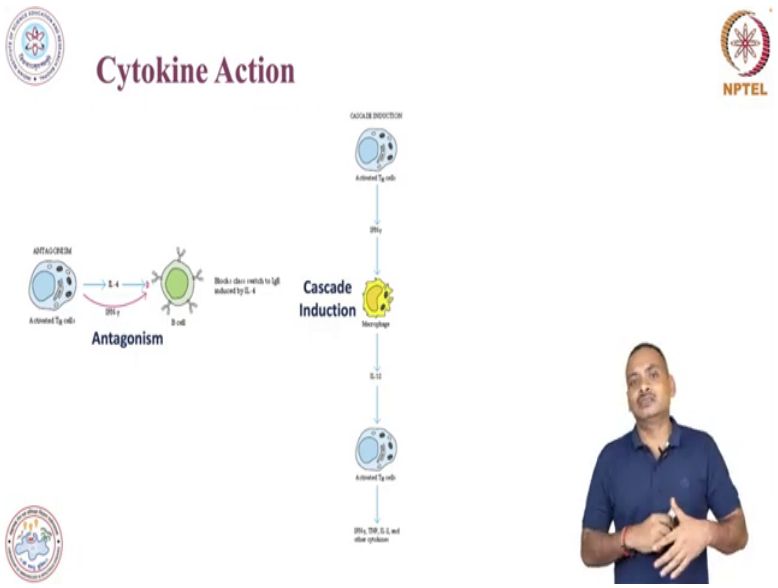

Another is a antagonism it is a so one, cytokine is inducing some effect over the cell, for example, activated T helper cells produce IL-4 and IL-4 basically promote the proliferation of B cells. But if there will be some Th2 cells will be there which is producing mainly interferon gamma. Then in that scenario this IL-4 effect will be reversed by interferon gamma. So that we call it as a antagonism.

And there will be a cascade induction for example, hair activated T helper cells are producing interferon gamma. Basically, when I say activated ThH cell, it is mainly the Th1 cell. So, currently you may not remember although I have discussed in very short when I was discussing the ThH cells. So, ThH cells basically produce interferon gamma and this interferon gamma basically acts on macrophages.

And then macrophages upon action of interferon gamma they started producing more IL-12 so that we call it as a cascade effect. So, there will be a one cytokine which is acting on the cell and that cell is producing another cytokine. So that we call it as a cascade induction. So, these are the ways by which cytokine produced or act.

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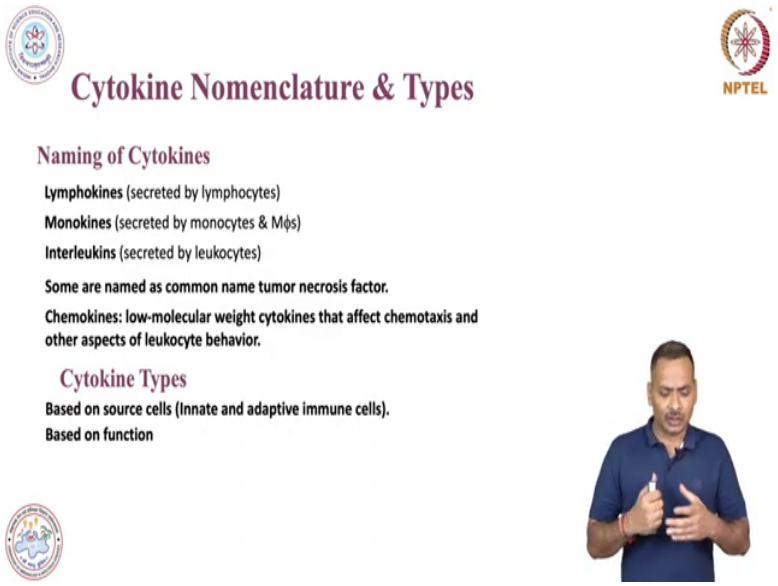

So now, we will talk about the cytokine nomenclature and types so, basically cytokines are in total these are the low molecular weight regulatory protein or glycoprotein. But there are different names if you see the literature, if you see the immunology book any immunology book, it is named by various wave. So, one of the most common way is it that it is denoted by lymphokines, although it is a little old system.

So, lymphokine word is also used and lymphokine and name basically arrived by the lymphocytes. So, the soluble molecule produced by lymphocyte are called as lymphokine. This is a little old system but still in books this word is used, monokine. So, basically the soluble molecules or soluble regulatory molecules produced by monocyte and macrophages we call it as a monokine.

There is a word interleukin, so, this is quite modern word the interleukin, so, all the soluble molecule produced by leukocytes we call it as a interleukin. So, this interleukin word is a quite frequently and much more predominant in our immunology textbook. Because there are so many molecules produced by the immune cells. And now we have a system, there is a immunology society and this immunology society basically came together.

And they started giving a name that we call it as a interleukin so, this is a like IUPAC system. So, interleukin is started from there and people do use some common name like tumor necrosis factor. So, this is a quite common name it started with tumor necrosis factor but still people prefer to use this TNF tumor necrosis factor. There is another set of molecule which we call it as a chemokines.

So, please remember this chemokine is also similar to the cytokine. They are also low molecular weight regulatory protein and basically, they are playing important role in chemotaxis. Chemotaxis means the movement of immune cell through the in our body when some molecule is secreted then the immune cells will move towards that cell where this cytokine is produced.

So, those molecules we call it as a chemokine if it plays a very important role in chemotaxis. And they are also playing important role in other aspects of leukocyte ~~behavior~~behaviour like rolling tethering and all those things. So, cytokine types are basically when we say the types, it is a in a very simple way we can distinguish in two major category. One is that innate immune cytokines or which is mainly produced by innate immune cells.

And adaptive immune cytokines which is mainly produced by adaptive~~,~~ immune cells like B cells and T cells. So, these are the various nomenclature and the types of the cytokines. Now, let us move on the function based on function these cytokines are of various kind.

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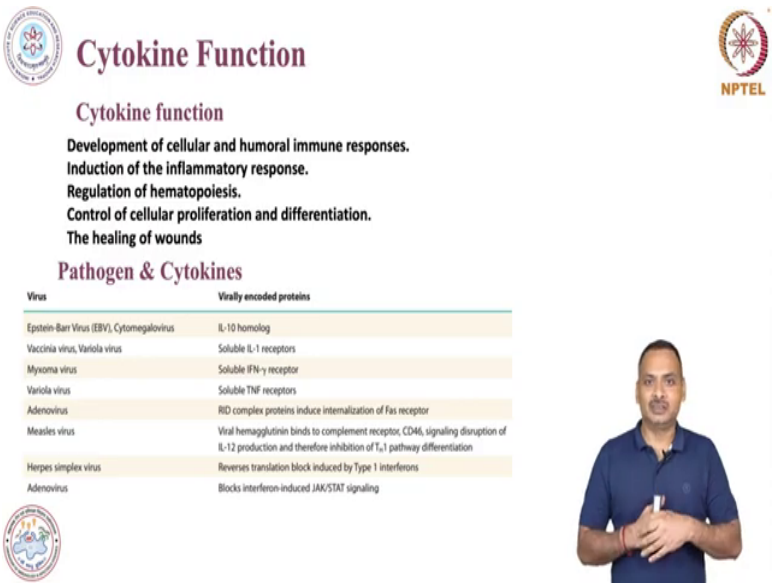

So, cytokine function is basically they play a very important role as I told you in development of cellular and humoeral immune responses or development of innate immune responses. And the most important thing which these days you are commonly hearing, is, it plays a very important role in inflammation. So, I will take a whole session now a couple of session about the inflammation in upcoming sessions.

And I will talk in great length about the inflammation. It basically control or regulate the hematopoiesis formation of blood cells. As you have seen, blood has a variety of immune cell that broadly, if you see the white blood cells, granularityocity, granulocyte, platelets, all those things. It plays a very important role in hematopoiesis control, cellular proliferation and differentiation.

So, cellular proliferation means if there is a hematopoietic stem cell. If the hematopoetic stem cells are increasing in number that is, we call it as a proliferation. But when this hematopoietic stem cell is converting to the say macrophages that we call it as a differentiation. So, these cytokines are playing very important role in cellular proliferation and differentiation.

The cytokines are also playing very important role in wound healing, if you have some scientific way to measure the healing process and to measure the cytokine production. You can very easily understand it is a very complex wound healing is a very complex process. And this basically taken over by the cytokines, as well as a variety of immune cell, including macrophages so, all dead cells will be cleared by the macrophages.

In addition, so now, I have told you all the positive things about the cytokines, cytokines are playing this that but cytokine also have a pathogenic effect if it is produced in unregulated form. If there is a too much cytokine that will cause the immunopathology the disease by the immune system and sometime, it result to the autoimmune disease. Similarly, this so, when I say cytokine there are activating cytokine, there are damping cytokines.

So, these activating cytokines are if it is unregulated that will cause immunopathology but if there is a damping cytokine which damps the immune response. If it is too much then that is also a kind of immune that also result to the development of disease or immunopathology. Therefore, some pathogen use this strategy to evade the immunity here you can see there are various viruses are there which produce a cytokine like molecule in order to evade the immunity.

For example, Epstein-Barr virus here you can see this produce IL-10 and this IL-10 is basically a damping cytokine and this damps the immunity. Like a vaccinia virus they also produce soluble IL-1 receptor. And here you can see there are variety of virus they produce the cytokine which basically damp the immunity or they also make a decoy kind of thing. They are like a cytokine but they will not function like a cytokine.

So, in this session I discussed in great length about the cytokine and their function, their naming, their action and so on. So, in next session we will discuss about the some more about the cytokine as well. As we will discuss some another class of molecule which is playing an important role in immune communication. Thank you.