Immunology
Prof. Agneyo Ganguly
Department of Biotechnology
Indian Institute of Technology, Kharagpur

Lecture No -45
Cytokines Introduction

So welcome to the lectures on immunology and welcome to today's lecture on the topic cytokines. So the term cytokines you might have been very well acquainted with by now because most of the processes or the immunological processes that we have described so far some way or other there are involvement of the cytokines. So you have come across several names of these cytokine molecules by now like the interleukins or the chemokines I myself have taught you in some of the classes in the earlier classes on innate immunity or an adaptive immune system.

The overview when we described the overview of the innate and the adaptive immune system this term cytokines have we have come across several times. And so we need to know in details what these cytokines are actually and how do they act. So before we go into what these cytokines are or how they act upon on. So we need to know what they are what these cytokines are so these cytokines are one of the most important effector molecules in the immune system.

And they are relevant in both in case of our innate system as well as in case of the adaptive system. So be the init or be the adaptive systems the cytokines are very, very important. We have seen the rules of the cytokines particularly in case of T cell and B cell activation maturation activation and differentiation had there been no cytokines these events would not have occurred. So for these events we need these cytokines. What are these cytokines?

So the cytokines are basically small proteins or very small glycoproteins even they are glycoproteins or proteins which mediates this kind of action by communicating between the different cells. So say they are basically important molecules that are required for the communication between the cells. So their cell to cell communication molecules there are small molecules small proteins or glycoproteins that are required for cell to cell communication mostly

secreted by the leukocytes but not that only by the leukocytes but they are secreted by other cell types as well.

But they are mostly secreted by the leukocytes so and that is where the name originates from that we have come across the names like the interleukins. If you remember we have several times use the term interleukins. So the interleukins as the name it suggests it comes from the fact that these cytokines or these interleukins to be precise they are produced or secreted by one leukocyte and they act on another leukocytes.

So that is why they are sometimes designated as interleukins that is connection between the leukocytes they are the connecting molecules between the leukocytes so that is why they are called the interleukins also sometimes not all cytokines are interleukins. So a big class of them are interleukins there are also chemokines and other factors like interferon's the tumor necrosis factor these are all they have all fall under this broad classification of the cytokines.

Now the thing is before we start knowing about the cytokines their mechanisms of action and all these things we also need to know how these cytokines they actually work.

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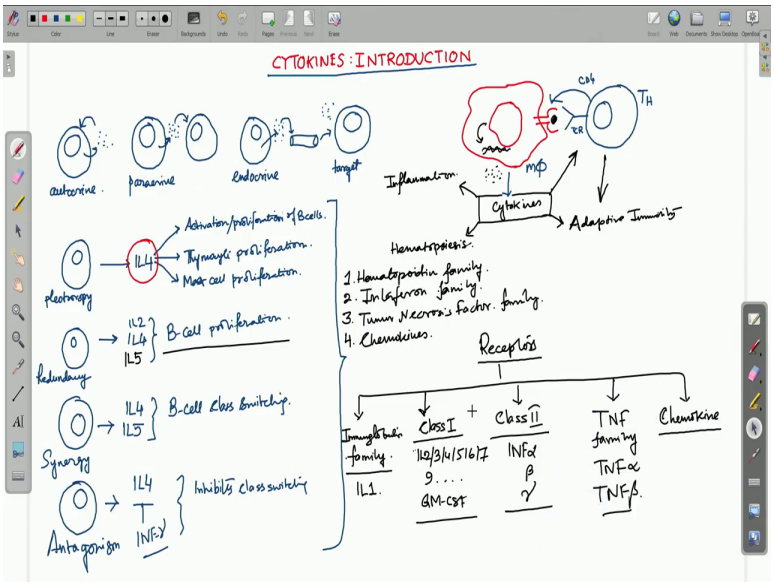

So the cytokines they can work in primarily in three different ways one is they can be auto crime. So auto crime means it is secreted by one of the leukocytes or the cells and it acts upon the same

cell. So it works on the same cell so if you remember interleukin 2 for example secreted by the T lymphocytes and they work on the T lymphocytes are the same on the same T lymphocytes. So, that that is an autocrine example of an autocrine secretion.

So it can be autocrine it can be paracrine that means they are secreted from one cell and the target cell is located in the vicinity. So close to it so it works on another cell which is located in a close vicinity to that cell so that is a paracrine and it can also be endocrine some of them can be endocrine. Which means that they are secreted from one cell type enters into the bloodstream and they act on a cell which is distantly located from this cell so that is an endocrine.

So the target cell this is the target cell this is always called the targets. So the target cell is distantly located when the target cell is located in the vicinity or next to it that is a paracrine and when it is located distantly that is endocrine. So that means it has to travel through the circulation and then it works on the target cell. So now these cytokines they can mediate their action in at least three different ways what we have seen is the cytokines can exhibit different types of action.

What are the different types of action that means they can be pleotropic that means one single cytokine can work on many target cells or do many functions that is called a pleotropic. It can show redundant function that means more than one cytokine can exhibit the same type of function or it can be synergistic that means one of the cytokine is helping the other cytokine in mediating the action that is a synergism or a synergy or it can be antagonistic that means one of the cytokines can inhibit the action of another cytokine.

So that is an antagonistic action. So there are at least four types of actions that the cytokines can do one for example pleotropic. So one cytokine for example interleukin 4 can mediate at least 3 different activities like activation of and the proliferation of the B cells activation or proliferation of B cells for example they can also help in thymocyte proliferation and they can also help in mass cell proliferation. So this kind of an action mediated by a cytokine for example like interleukin 4 for example it exhibits pleotropy that is a single cytokine can exhibit more than one function so that is a pleotropic.

Then more than one cytokine can also some time exhibit same function and that is called redundancy of function. So that is a redundant function that means more than one cytokines it can be two three four cytokines they can help in same kind of action. For example interleukin 2 IL-2 IL-4 IL-5 they all help in D cell proliferation. So these cytokines like interleukin 2 interleukin 4 or interleukin 5 this is 5 or interleukin 5 they all can perform the same function like B cell proliferation.

Again cytokines like IL-4 and IL-5 so this is known as redundancy and they can also exhibit synergy. For example IL-4 and IL-5 interleukin 4 interleukin 5 they both together that means in case of there is a there is a basic difference between redundancy and synergy what is that? In case of redundancy the two cytokines they exhibit independently. Independently the two cytokines they exhibit same function or they perform the same function.

But in case of synergy it is a synergistic action so that means they together perform one single function and that is called a synergy. So for example they these two cytokines interleukin 4 and interleukin 5 they together can help in class switching for example B cell class switching. So they both together can help in synergistically they can help in B cell class switching and again a fourth situation can be antagonistic.

So antagonistic situation is like interleukin IL for the action of IL-4 in B cell class switching sometimes is inhibited that is inhibition inhibited by INF gamma interferon gamma. So this can be inhibited by INF gamma and that is called antagonism or inhibition also. So that is also inhibits the class switching. So it inhibits or antagonizes class switching so as we have seen at least in case of the cytokines the mode of action of the cytokines can be at least divided into four different ways like the pleotropic action redundant action synergistic action or antagonistic action.

So pleotropy means our single cytokine can perform many functions like for example inter nuking for can perform at least three different functions like activation or proliferation of the B cells, thymocyte proliferations or even mast cell proliferations redundancy. So interleukin 2

interleukin 4 or interleukin 5 all of them can perform same action like B cell proliferation. Synergistic action involves interleukin 4 and interleukin 5 for example they can together they can also do functions like class switching in B cells.

And antagonistic action is for example interleukin 4 the activity of interleukin 4 or class switching of the B cells can be inhibited by INF gamma. So that is an antagonistic or inhibited reaction now coming to what type of functions these cytokines they do as I described in the beginning or told in the beginning that they can perform, so they are the main molecules that are required for cell to cell communication.

And they can perform a lot of functions so by now we have already read a lot about the inert system adaptive system the very initial phases of innate immunity inflammatory responses and we have seen that in almost all of these cases we have involvement of cytokines, if you remember my one of my initial classes where we described about activation of the macrophages and the phagocytosis. And then the macrophage is activated and a macrophage is a major source of cytokine.

It is a major source of cytokine it starts immediately it mediates its action by secretion of different types of cytokines in all these cytokines that are being secreted they mediate different different actions they can mediate different actions like even they help in the T cell activation and development they can help in inflammatory responses they can help in systemic responses like they can help in or in induces production of complement proteins from the liver.

They can help in hematopoiesis so there are lots of actions that immediately starts when there is secretion of cytokines from this activated macrophages. So let us see what are the different functions that cytokines can perform when there is secretion of cytokines from in response to a invasion or a tissue damage. So whenever when there is a tissue damage if you remember one of our initial classes initial lectures we describe it like a macrphage.

And the macrophage is a one of the antigen-presenting cells so it can present antigen for example so it can also present antigen and it can activate a T cell a naive T cell for example a T helper

cell. So if this is a TH cell or the CD4 plus cell so it can interact with this with its T cell receptor and with the CD4 core receptor and the TCR the T cell receptor and this macrophage is an activated macrophage. So this is a let us say this is a macrophage there is an activated macrophage.

And this will then start to produce so there will be internal signaling within the macrophage and there will be gene expression transcription gene expression and that would lead to secretion of the cytokines the cytokines would be secreted. Now once the cytokines are secreted so the cytokines that are secreted that can perform a lot of different functions. So now what are the functions that they can perform?

One they can enhance inflammation or inflammatory responses they can activate the adaptive immune system, they can activate hematopoiesis and of course they can help in T cell activation and this in turn will also help in the adaptive immune system. So if you look here in this picture over here the cytokines are secreted or they are produced from this kind of an activated macrophage and this activated macrophage it has the ability to present the antigen of the foreign antigen to our T helper cell and activate the T helper cell in that to is mediated by the secretion of cytokines.

So this activated macrophage is now competent to produce Express the different genes for the genes that encode for different cytokines and those cytokines will be produced and those cytokines can now mediate a lot of functions. What are the different functions that these cytokines can mediate it can enhance inflammation it can do hematopoiesis it can activate the adaptive immune system. So adaptive immune system means it can activate the T cell mediated as well as the big B cell mediated or the humoral immune system as well.

And it can also help in that T cell activation and differentiation. So these are this is kind of a very brief a very general overview what a cytokine from our activated macrophages can perform. So as I told that these cytokines are mostly we can but I mean the most of the cytokines they have been named like this IL’s if you look here the IL’s though they are the interleukins that means they are produced from one of the leukocytes and the work on another leukocyte.

So that is why they are known as the interleukins. Now the thing is apart from the interleukins there are other cytokines as well it is not only the intelligence it is true that the interleukins are the major class of the cytokine. So there are in IL 1 2 3 4 5 6 7 8 9 10 a lot of IL's different IL's or the intelligence and they have varied rules. We have already studied some of those roles while we went through B cell maturation differentiation and all those things.

Also in case of T cell activation and maturate and differentiation so we have already seen how these cytokines they help in T cell activation as well as formation of different T's and subtypes. So, different T cell subtypes; they produce different cytokines or they express genes of different cytokines and that mediates different actions. So these things we have already known a little bit. Now these so how these cytokines have been classified. So these cytokines are mainly broadly classified into four different classes.

So what are the four different classes of cytokines one the hematopoietic the human protein class of cytokines or the hematopoietic family of cytokines. Secondly the interferon family we will discuss about the interference later. So interferon family of cytokines is a very important class of cytokines because interferon class of cytokines are one of the first line of defense of the body against a viral invasion. So when there is a viral attack this interference are kind of the first lines of defense of our body against a viral invasion.

So whenever there is a virus attacking our body it is the interferon molecules that tries to cope up or tries to defend. So apart from the high metropolitan family the interferon family we also have a third important family as the TNF or the tumor necrosis factors the TNF family and finally that we have already told several times maybe the chemokines. These chemokines are another class of cytokines which we have been discussing several times from the beginning of our lectures that these chemokines are involved mostly or they mediate mostly chemo attraction.

So that means they attract they help in attracting the cells we have seen the role of chemokines for example in neutrophil extravasation, in inflammation, in role in inflammatory responses. So chemokines has varied roles and also we have seen in the role of the chemicals in licensing of the

dendritic cells in the B cell activation in the B cell development activation processes from movement of these B cells from the dark zone to the light zone.

So chemokines have various activities they are mostly they are described as the chemo attractants which can attract one cell from one zone or one region to the end of the region. So they help in migration of the cells and that is why they are they help in chemotaxis. So that that is the chemokine group of group of cytokines. So now so these are the four broad families of the cytokines and this particular distribution is based on the structure of the cytokines.

So it is a structure based classification but if we look into the cytokines as I described in the beginning also that these cytokines how they how they do their function. So cytokines primarily bind to cytokine receptors are present on the surface of the target cell and if this is the cytokine molecule it goes and binds to the scepter and then there is a downstream signaling pathway that helps in mediating its action, so that is a very simple thing.

Although it is simple it is it is not really that simple. So we will we will describe we will try to make it simple and use it how these cytokines they actually act on or they actually perform their functions based on their receptors. So let us see what are the different receptor families of the sub families of the cytokine? So these are the receptor families the receptors the cytokine receptors what are the different cytokines receptors that are present on different cell types?

So there are at least five different classes of cytokine receptors and cytokines their functions are actually in in principle they are classified according to the receptor to which they bind. So there are at least five different types of receptor and the first type of receptor is the immunoglobulin family of receptors in one of the major cytokines is interleukin 1. Then comes the most broad type of cytokine receptors that is kind of ubiquitously present in many cells or most of the cells.

And most of the cytokines they bind to this class of resistors there is a class one receptor so this is the major cytokine receptor that is expressed in most of the cell types because they offer binding to these different types of interleukins like IL-2 3 4 5 6 7 9 everything so these are also

known as the hematopoietic class of cytokine receptors. And they bind to for example interleukin 2 3 4 5 6 7 9 and many other GM-CSF all of these cytokines they bind to the class 1 receptor.

Then we have the class 2 receptor we have the class 2 receptors and these so class 2 receptors they actually bind to the interference the INF interferon, interferon alpha beta gamma interferon alpha beta gamma and all this they bind to these are the class 2 receptors. Then we have the tumor necrosis factor receptors or the TNF family of receptors the TNF family receptors and they bind to the TNF that TNF alpha the TNF beta.

And finally of course we have the chemokine receptors the chemokine receptors and these receptors they are particularly a bit different from the rest of all the cytokine receptors that we have seen so far particularly in the way they transduce the signal because the chemokine receptors are mostly associated with G proteins. So they are G-protein coupled receptors if you have read about the G-protein coupled receptors in your in your cell biology or molecular biology backgrounds.

So you must be knowing what these GPCRs are the G-protein coupled receptors are so these chemokines are mostly associated with the G proteins chemokine receptors. So now these are the different the four different classes of the cytokine receptors and the chemokine receptor. So there are five different classes of the cytokine receptors starting from the immunoglobulin type the class 1 the class 1 is one of the most widest or the widely bound receptors among the cytokine receptors.

The class 2 you know which is the interferon class of receptors or the INF alpha beta gamma receptors then you have the TNF family receptors that is a TNF alpha beta they bind to the TNF family receptors and also you have the chemo kind research. So the cytokines they bind to this different types of receptors and mediates their action and this action means there is our signaling downstream of receptor ligand binding.

So when this ligand is the cytokine here so the cytokine molecule the protein or the glycoprotein that is being that is being secreted that cytokine molecule is a ligand and that binds to the

receptor. So due to the advancement of molecular biology recombinant technology recombinant DNA technology many of the cytokines and the receptors their structures has already been very well established.

And it has been very well studied how or what kind of binding occurs between the cytokines and their corresponding receptors. And since this is known or these things are now being very well studied so we already have a fair idea how this cytokine binding to the corresponding receptor actually works and what kind of signaling is actually working downstream of that receptor ligand binding. And that helps in understanding or explaining many of the phenomenon's many of the things many of the things that the cytokines do.

For example this redundancy the synergy or the antagonism that the cytokines exhibit in their action that can be very well explained by this binding of the receptors and the downstream signaling that actually occurs. So from the receptor structures from the receptor ligand interactions the affinity between the receptor and the ligand. So whenever there is a ligand and the receptor the term affinity comes. So if there is an affinity depending on the affinity how high the affinity is or how low the affinity is there are different signaling.

So these can be very well explained and we will try to understand in our next lecture that how depending on these different receptor structures the cytokines can exhibit their functions like redundancy or antagonism. So for today this much is that is where we end and we will be talking about the cytokine receptors and their modes of action in our upcoming class, thank you very much.