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Immunology

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Module No. # 01

Lecture No. # 01

Basic Concepts in Immunology

Welcome you all to NPTEL online certificate course on immunology. Myself, Sudip Ghosh, Department of Biotechnology, IIT, Kharagpur. I firstly, I must thanks NPTEL, Ministry of Human Resource and Development for giving me this opportunity to take this course. And, there will be another professor with me, Professor Agneyo Ganguly. He will take some classes as well. So today, I would like to introduce what I am going to teach and what is the immunology subject means, basic concepts of immunology.

Immunology is a study of our immune system. So, from the name, you can understand that any system is not working as a single component. So, there are many components in a system. So, immune system means to protect ourselves from invaders. So, when one system works, all possible way to defend the intruders or the pathogens or any kind of foreign attack from our body which immune system can handle; they work as a whole. So, first we have to understand what are the components of the system; how it works; and how exactly they communicate between each other.

Everything is the system. So, I will go slowly. And just for all the students I am telling. Normally, when I am taking the class, this is usually a third year course. So, already the student have the knowledge, basic knowledge of biochemistry, cell biology, molecular biology and genetics. So, a basic idea of all these subject is required to understand the uh immunology fully; and of course, to enjoy the subject. So, I hope, whenever it is required, you have to go back if it is not there.

You have to go back and study some part of the basic biochemistry, molecular biology, cell biology and microbiology. So, before I start, I will just try to show you some books. There are number of good books. And I will show you some books and uh give you as a reference. So, any of the book is fine to follow the course. (refer time: 02:50) The first is basic immunology

by Abul K. Abbas and Andrew H. Lichtman. (refer time: 03:01) Second is Immunology, by David Male and co-authors.

(refer time: 03:08) Kuby Immunology. (refer time: 03:13) And the fourth one is Immunobiology. I mean, the picture I took from the different edition. So, you can have any edition. Or the latest edition is always better, because immunology is a very dynamic subject. Everyday new research articles are publishing. So, every new edition, you will find many new information, which may not be there in the old book. So, latest (ed) edition of the book is always better.

But for your information, throughout the course, I will follow this book, Janeway's, Immunobiology. Most of my slides are from this book. So, if it is possible, you can follow this. Or, whatever I will tell, maybe the figures are different, but it will cover the whole thing. You will find; any any immunology book, you will find the information. (refer time: 04:09) So, immunology. Immunology is the study of immune system. The study of all aspects of host defence against infection and also of the adverse consequence of immune response.

What is immune system? Immune system means, the tissues, cells and molecules involved in innate and adaptive immunity. So, those who are new to this subject, innate immunity means, in our body, we have a general protection mechanism. I will come later in little detail. That means, any infection happened or any attack happened from outside, body has a immediate mechanism to protect that. That is innate immunity. And adaptive immunity is when innate immunity fails, if the infection still exists, body has another system which takes some time, but make a definite or specific weapon to protect the infection.

So, it adapt or prepare a specific or infection specific mechanism to solve the problem or combat the disease or the infection. So, that is called adaptive immunity. (refer time: 05:42) Basic concept or theme of our immune system is: kill the pathogen, but do not harm the host. This is most important thing for the immune system. Because, by same mechanism, if one system can kill oneself, they should have the same capacity, they can kill also ourselves. But this is a very big issue that immune system knows, that we are not supposed to; I am talking about immune system; they are not supposed to do any harm to our system, if the immune system is working perfectly.

So, what they are doing? The first thing is, protection against the infectious disease. Second thing, they have to understand what is self, what is non-self; and eliminate potentially destructive foreign substance from the body. (refer time: 06:39) To understand any mystery; like, how immune system works? how this thing works? to understand, any mystery, you

have you have to ask few questions. What are these? Why? When? Where? What? and Who?

So, when we will discuss the immune system, we will also (ans) try to answer these questions. May not be in this sequence like why, when, where and who and what. But, you will find the different, (wh) I mean, why immune system is working; when it is active; where it is working; against whom it is working. So, all these questions, we will try to answer through this course. (refer time: 07:20) Immune system, they protect us from the attack, but not attack from these big animals.

They are not that much threat to our body. (refer time: 07:32) But, this nice looking cute pet is always risky, because they can carry some of the infection. Because we go very close to them, so you have to careful. But real threat for our body or immune system is: (refer time: 07:48) are these. They are microbial organism like virus, bacteria, fungus, protozoan parasite. All these microorganism which we cannot see but can cause serious damage of our system or body; immune system can see them.

(refer time: 08:15) But this immune system or (immuno) immunity; the concept or the notion of immunity came long time back. In ancient Greece, it was also known that, those who survive from the disease confers great protection against it later. That means: if someone is somehow survive from a disease, next time, the same disease cannot make that much harm with respect to a person who is attacked by the, for the first time. Okay. Another thing was Variolation.

The inhalation or transfer into superficial skin wounds material from smallpox pustules. That practice is uh known since 1400, in Middle East and China. So, that means, the superficial skin of a smallpox patient, if you inhale, that gives you some protection. Edward Jenner (refer time: 09:16) knew all this thing. And what he had observed, that the relatively mild disease cowpox or vaccinia are; seem to, are seem to confer protection against even more fatal disease of smallpox.

And many of you may know the story of that how he discovered the vaccine against smallpox. And he is the person who named this technique as a vaccine. And it is still, we are using the same term. In (ni) 1880, Louis Pasteur devised a vaccine against cholera in chickens. (refer time: 09:58) And more interestingly, he also developed a rabies vaccine that proved to be a spectacular success, upon a first trial in the (ba) in a boy bitten by a rabid dog.

And we are still using this vaccine till today. In fact, the beginning of immunology as a science is usually attributed to Edward Jenner for his work, because he is the first person who demonstrated that we have a system in our body. That time, it was not known (whr) whether it is a virus infected or something else. But we have a system in our body that can protect or that can generate a specific protection mechanism upon infection. (refer time: 10:47)

So, let me go through uh the smallpox or the vaccine. Smallpox vaccine, he first demonstrated in 17 or last 18th century exactly, I mean date wise. But, World Health Organisation declares that there is no smallpox in earth or smallpox is eradicated in 1979. It is almost 200 years it took. Okay. (beca) Because, that time it was not known. First thing is, vaccine was not that popular. And vaccine, when developed, people were not usually know that what is this, how it is going to work.

So, there are lot of volunteer organisations used to put lot of posters; in the new years, you should take vaccine first to protect your (sem) self from the smallpox. Even in my school life, when I used to go school, around 1975, 76, 77, that time. So, there are lot of poster in the lamppost, (refer time: 11:54) in a wall; that, okay, if you find any smallpox candidate, you will be uh rewarded 1000 rupees. Or there will be 1000 rupees award for giving a report. If your report is proved to be true, then you will get 1000 rupees.

And that is, I am talking about around (se) 1975, 76. But, so, that time, WHO knew that there is no smallpox, because the last (refer time: 12:22) person who survived in smallpox is Ali Maow Maalin of Somalia. He is the last survived of smallpox, in 1977. So, after that, there is no smallpox reported. Though smallpox virus may be stored in some laboratory or somewhere, but it is not in nature so far. I mean, no more new cases. (refer time: 12:46)

As introduction in this whole course, basically in the basic concept of immunology, first few lectures, what I am going to cover is: the origin of vertebrate immune cells, those who are responsible for immune system; principles of innate immunity; principles of adaptive immunity; and the effective mechanism of immunity. (refer time: 13:12) So, the origin of vertebrate immune cells. All the cellular elements of the blood, including the cells of the immune system, arise from pluripotent hematopoietic stem cells in bone marrow.

So, they divide in bone marrow. They divide or they produce 2 different kind of cells. One is common lymphoid progenitor. Another is common myeloid progenitor. Common lymphoid progenitor produce 4 type of cells. One is B cell or B lymphocytes; T cell or T lymphocytes; NK cells or natural killer cells; or innate leukocyte cells, ILC. Similarly, common myeloid

progenitor produce immature dendritic cells, one way; another, granulocyte macrophage progenitor and megakaryocyte erythrocyte progenitor.

So, these erythrocyte progenitor makes megakaryocyte and erythroblast. Megakaryocyte produce platelets. And this granulocyte are produce all the white blood cells we know, like neutrophil; eosinophil; basophil; mast cell precursor, which is not known yet; monocytes. Dendritic cells, from immature, it become mature. And from this unknown precursor of mast cell, cell produce mast cell. And monocyte become macrophage in tissue. In from, common lymphoid progenitor B cell in (ly) they, all these; their produce come into the peripheral blood.

They reach into the lymph node where; I mean, I will come later what is lymph node and how it looks. So, B cell, T cell, NK cell and ILC, the innate leukocyte cells; all of them are normally resides into leukocytes, where they interact with the antigen; and they become effector cells. B cells having a receptor on their surface. They (pro) convert it to plasma cells produce antibody upon infection. T cells, they also have receptors specific to antigen, by which they recognise the antigen.

They become activated. They have different functions. Or they are called activated T cells as effector cells. Again, we will discuss it later. NK cells and ILC, they do not have any specific receptor to recognise the antigen, but they are very similar to the cytotoxic T cell. I will come again. So, before I go to detail, there are few terms you will find in the whole lecture. And initially, these term may be new to you, but it will gradually, in within the uh discussion of the introduction part, we will say what is what?

So, NK cells (al si); in T cells, there are 2 types. One is helper, another is (ju) cytotoxic. Cytotoxic means, it can kill the cells. So, NK cells are very similar to cytotoxic T cells, but they do not have any recognition receptor. And ILC, the activated ILC, they are very similar to different form of T cells. So, instead of helper cells also they have a different form. So, different ILC: ILC 1, ILC 2, ILC 3, ILC 4. They are very similar to different functions, but they also stay in lymph node to see the infection or to find out what is the infection is or what to do with that.

(refer time: 16:48) So, this is a few slides or whatever we saw in the last slides. This is in the bigger format. (refer time: 16:53) So, there is no point. You can go through and see carefully what I told so far. (refer time: 16:57) So, now I will start the principle of innate immunity. So, first thing, I already told you that immunity, we can divide into 2 major ways. One is innate immunity, another is adaptive immunity. So, innate immunity means, immediate protection.

And adaptive immunity takes some time. It makes specific arrangement or specific device or specific cell become activated to protect specifically that organism. So, our cell our our system, immune system has is immediate protection mechanism. That is called innate immunity. So, (emen) innate immunity; there are few points are there. I am just going through one by one. And then, try to explain again one by one. First is common cell organism. Because, in our (ce) body, you know that there are lot of (mico) microbes stay inside our body.

Like our gut, which is full of microbes; our nasal cavity, mucosal cavity, ear. So, all, there are few microbes, they stay inside our body, they are beneficial. It is not that they do not make any uh damage of our cell. They are, they can do, but they are very less. So, the common cell organism cause little host damage, while pathogen damage host tissue by a variety of mechanisms. Anatomic and chemical barriers are the first defence against pathogens. The immune system or the innate immunity is activated by inflammatory inducers that indicate the presence of pathogens or tissue damage.

The myeloid lineage comprises most of the cells of the innate immune system. I will come one by one, when I will try to explain a little more detail. Sensor cell express pattern recognition receptors that provide an initial discrimination between self and non-self. (refer time: 19:08) And number 6, sensor cells induce an inflammatory response by producing mediators such as chemokines and cytokines. This is also 2 new vocabulary for immune system.

And innate lymphocytes and natural killer cells are effector cells that share similarities with lymphoid lineage of the adaptive immune system; or they are also taking part in innate immunity. (refer time: 19:39) So (com), I just show you few pictures before also. The microbes, microbes, they vary greatly in size and lifestyle. Not only that, that nature, I mean, in the lifestyle, their nature, where they will grow and how they will stay is also varies. Like virus, all of you know, they grow inside the cell.

Bacteria, they are may be inside, they are may be outside. Right? Here, in this picture, you can see the bacteria is uh, this is Listeria, this is inside the cell. And some extracellular bacteria, archaea and protozoa stay normally outside the cell. Fungus and the bigger parasite like uh ringworm or hookworm or helminths group of thing. So, body, after seeing them, immediately they try to kill them. (refer time: 20:33) How? What is the component of innate immunity?

First is the anatomic barriers. Okay. So, when anything comes, the host can adopt 3 strategies, normally, to deal with the threat posed by the microbes. 1, avoidance. So, make some mechanism, so you can avoid these microbes or make some resistance so that they cannot grow or do the harm or tolerance. That means, allow them to grow or tolerate them. So, tolerance is normally not the way of protection, but sometimes our body do. So, anatomic barriers, which is the first line of defence is skin, oral mucosa, respiratory epithelium, intestine.

So, they do not allow directly the microbes to enter into the inside of the body. Then, in blood. If there is any bacterial infection or anything, there is a antimicrobial protein present. And there is a system called complement, which is uh, you are going to learn in much more detail. Complement is a protein which is heat labile, but they non-specifically can target bacteria and kill them. Okay. There are few innate immune cells, that we just mention it, but that will go in little more detail.

Like macrophages, they can eat them; they can do phagocytes and kill them. Granulocyte, natural killer cells; normally they kill the virus infected cells. So, these innate immune cells complement antimicrobial proteins anatomic barriers. These are the components of immune system. So, when infection, if it crossed that part; like, infection somehow managed to handle this innate immunity, they start growing. Then, adaptive immunity come into picture.

So, then B cells activate it and produce antibody. T cells help them to produce antibody. If the infection is a viral infection, then cytotoxic T cell comes into picture and kill the all virus infected cells. So, adaptive immunity part will come later. (refer time: 22:47) So, third point that we are telling, that the immune system is activated by inflammatory inducers that indicate the presence of pathogens or tissue damage. So, what are the inflammatory inducers?

Inflammatory inducers are bacterial lipopolysaccharide, ATP, urate crystals. One thing we have to remembered that macrophage is not only cleaning or killing the (pagos) uh microbes. Macrophage also clean up the mess. Mess means, all dead cells, they are eating. uh uh After infection there are lot of immune cells, they are dying. They also clean the mess. So, normal regular cleaning procedure also macrophages are doing. So, this back, but normally that do not.

The normal, regular, our body cell, when they phagocytose our normal body cell after death, the immune system is not activated. But, when there is an infection, our body can understand which, which is pathogen, which is non-pathogen. We will come how. So,

bacterial lipopolysaccharide, ATP, urate crystals. Sensor cells, like macrophage, (neu) neutrophils, dendritic cells. They are the cells which can recognise which is foreign, which is microbes. And they go and eat them and kill them. Okay.

They are also mediators. How they understand? So, if one of the cells eat one bacteria, they get activate; understand that, okay, something foreign comes. So, they release some chemicals or proteins which are the mediators like cytokines and cytotoxicity. Cytokines, oh sorry. Cytokines and also there are some cytotoxicity develops by uh ILC. Okay. And the target tissue are production of antimicrobial, where the mah infection happen. Antimicrobial proteins, induction of intracellular antimicrobial antiviral proteins killing of infected cells.

So, somehow, this is going to happen when any infection is happen in our body. It may be, infection can happen in the damaged tissue; cut site of the body; or through food; or direct contact in blood. (refer time: 25:16) The phase of, phases of immune response. Okay. So, what happened? So, there, I mean, if you see or follow the table, there are response; typical time after infection to start of response; and duration of response. So, innate immune response, which is mediated by inflammation, complement activation, phagocytosis, destruction of the pathogen, which starts within a minute.

It can continues up to days. But the adaptive immune response; there are several components. You can see here. Like interaction between antigen-presenting dendritic cells and antigen-specific T cell recognition of antigen; adhesion; co-stimulation; T cell proliferation; differentiation; activation of antigen-specific B cells, which in turn going to produce antibody; formation of effector cells and memory cells, memory B cells and T cells, both; interaction of T cells with B cells, which convert the B cells to plasma cells and memory B cells for the (pro) and produce antibody; emigration emigration of effector lymphocytes from peripheral lymphoid tissue to organs.

Like, when exactly, because antibody is going to produce in the lymph node. That, we will see later. But, the antibody should go to blood and go to the target tissue where it will work. Elimination of pathogen by the effector cells and antibody. Effector cells means, effector T cells. So, all these things, the initial starts with hour. Sometimes, it initiates days. Sometimes, few days, but it will continue or the duration of response depending on normally the weeks.

But it depends; if the infection persists, the response also, you can see the responses is also exist. And immunological memory is a maintenance of memory B cells and T cells, because B cell and T cell recognise, recognise the antigen, specifically by their receptor. So, there are

few B cells. Not all B cells or all T cells are going to work, to fight against a specific antigen. There are few B cells and T cells. We will see (al) in later classes, why I am (ta) telling few B cells.

So, so these B cells and T cells which (res) was activated due to a specific infection, they remember how their enemy looks like. So, that remembrance help them if the same pathogen attacks again, so that they can fight much quicker way or much quicker time. When antibody production normally takes 7 days; 6 to 7 days. So, from day infection; if the first day of infection, you take 0; then, antibody production takes 7 days. So, but the same pathogen if you attack for the next time or the second time, it will take only 3, 4 days or even less than that.

So, that memory cell help them. And this memory cell, in many cases, it may be lifelong. Okay. So, it, days to weeks; and it may be lifelong. Because, there are many case, like the pox, what we already told. The pox, once it is vaccinated, it is very rarely, one individual; even for the chickenpox also; very rarely you can find that one individual have chickenpox twice in their lifetime; normally once. Or, many of them, many of us; we do not have chickenpox, because we have the vaccine.

So, these memory, many disease, it is lifelong. In some cases, it is not that long. Okay. So, for today or this lecture, it is end, this is uh, here we (Sto); I mean, I would like to stop here today. And in next class, we will see how the components of blood or immune system; or, what are the components of immune system which plays a role in both innate as well as adaptive immunity. Thank you all.