

Host-Pathogen Interaction (Immunology)
Prof. Himanshu Kumar
Laboratory of Immunology and Infectious Disease Biology
Department of Biological Sciences
Indian Institute of Science Education and Research (IISER) - Bhopal

Lecture: 28
Introduction of Innate Immunity

We have finished about four weeks and we have learned very important topics like history of Immunology we have learned about various organs of immune system we learned about various cells of immune system. And we have also learned all those small molecules or the substances which coordinate all these systems which we commonly called it as a cytokines there are several names right.

So, let us begin with innate immunity and innate immunity we also call it as a natural immunity and it plays extremely important role in all aspect in all aspect means try to understand every moment we are exposed to the I do not know numerous microbial path microbes it is not necessarily the pathogen but we are continuously exposed to the numerous microbe and our innate immunity is basically defending all those microbes and we are basically surviving.

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Survival of the fittest theory

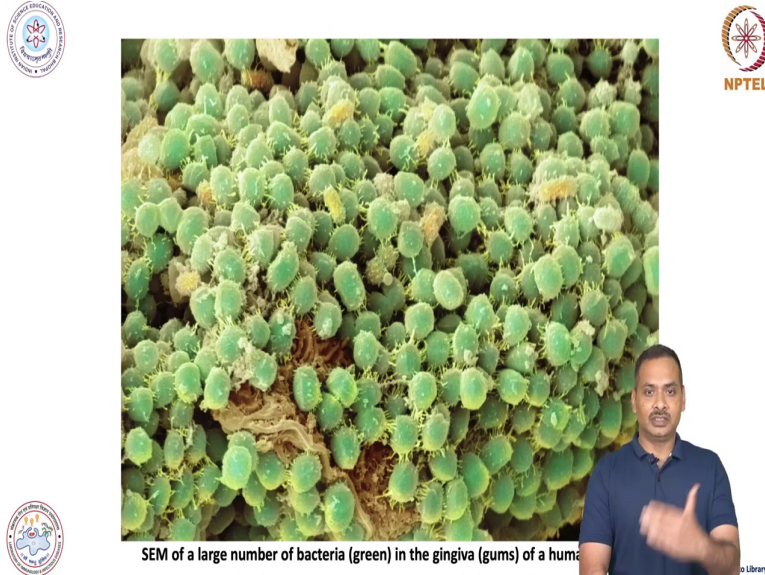
British naturalist Charles Darwin (1869)



So, here I just want to start my this innate immunity session with this very famous you are very well aware about this concept survival of the fittest theory which is given by the British naturalist Charles Darwin. And he basically said that the organism best adjusted to their

environment are most successful in surviving and reproducing. So, this is very much true. We are the host is basically present in such a way that it is a the most fittest way. I will convince you with I will convince with this statement in subsequent slide.

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Here you can see this is a simple scanning electron micrograph of large number of bacteria which is shown in green. In gingiva which is basically gum of human mouth and here you can see there are so, much microbe right.

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Is the human body human?

No

Why?

Microbe are 10 times more then number of human cells
Luckey, T.D. Introduction to intestinal microecology. *Am. J. Clin. Nutr.* **25**, 1292–1294 (1972).

9.1 % Human cells

Bacteria are 1.3 times more then number of human cells (37.2 Trillion)
Sender, R., Fuchs, G., & Kloos, R. Are we really vastly outnumbered? Revisiting the ratio of bacterial to host cells in humans. *Cell* **164**, 337–340 (2016). Rosner, J.L. Ten times more microbial cells than body cells in humans? *Microbe* **9**, 47 (2014).

43.5 % are human cells

does not include fungi, viruses, and phages & it will an order of magnitue) and it will come around 9.5 %

And when you see this outnumbered microbe then we have a one very simple question that is human body is human. So, if you look at with the scientific information. So, the answer will be no. The human body is not human and the ~~ok~~ why I am saying this thing because if you

look at the microbes which is present in our body this is 10 times more than the human cell which is which is a which is in major majority right the microbes are 10 times more.

So, basically we are more micro rather than a human body right. Well this observation was given in 1972 at that time the tools and techniques for estimation of these microbes as well as human cell is not so, developed. So, I reviewed a lot of literature and then I found out that this. So, when I say 10 times then it is only 9.1 percent human cells are there. So, after reviewing of literature I found out some article which is quite recently published in 2014.

And that article is also saying that bacteria are 1.3 times more than human cell and the number of human cell is 37.2 trillions. So, if you if you look at this observation then here you will notice that the workers reported only about the bacteria. And in this scenario the human cell is still less about 43.5 percent but here they did not included fungi, virus, ~~fudges~~ phages. And if you just make a simple estimation it will be in a huge number an order of magnitude.

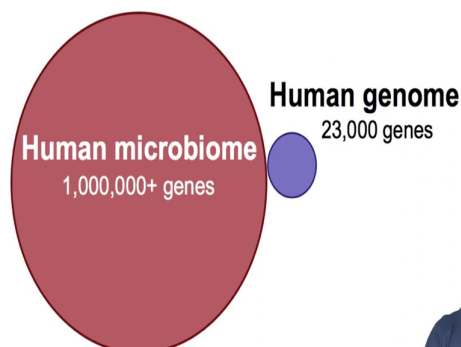
And if you overall again look at then you will find out that about the human body is containing about 9.5 percent cells. So, why I am giving all these introduction that because this human body or the host is basically very closely associated with microbes. And these microbes are some of these microbes are useful some are not useful and those microbes which basically evade our system we basically call it them as a pathogen.

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Additionally.....

Genes are approximately 200 times more than the host genes.



Turnbaugh, P.J. et al. The human microbiome project. *Nature* 449, 804-810
Gilbert J, J.A. et al. Current understanding of the human microbiome. *Nat M*



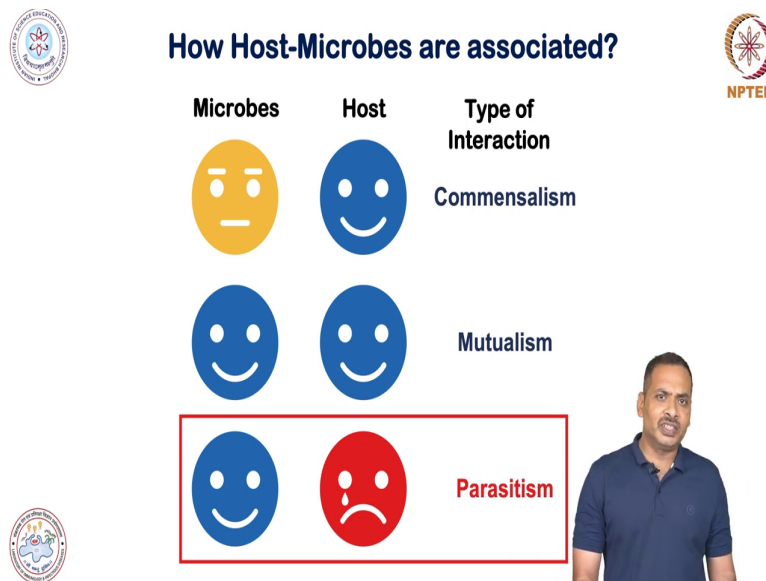
So, here this is additional information it is not only about the number of cells the gene pool which is present in our body is about 10 in our body the we have about 23000 gene or 23 to

30000 generally this kind of prediction is there. But if you look at the microbial gene pool this will consist of again a huge number about 10 lakhs. So, again I would like to say that this microbial dominance is major dominance which is about 200 times more right than the host Gene.

So, neither we are more in number in if you look at the number of cells not our genetic pool is bigger than these micro. So, under this scenario the host need to be survived and then reproduce as per Charles Darwin Theory right? So, this is very, very I am highlighting this point because here the innate immunity comes in a big picture innate immunity enables us to survive and then it is important for the continuity of life.

So, this is a philosophy behind this introduction. Now let us look at how these microbes are associated.

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So, this is probably you have studied in school time there are several kinds of association of these micro with the host and here you can see one is commensalism. So, in commensalism the microbe is either harmed by the host or not benefited by The Host but the host is may be benefited. So, this kind of Association we call it as a commensalism there is another Association which we call it as a mutualism in which both the microbe and the host are getting benefit from each other.

So, this is a mutual mutual benefit this is also fine commensalism and mutualism both are fine to the host. Another association is basically the parasitism we call it as a parasitism. The

microbe is basically benefiting a lot or they are harming the host or host cells or host and this kind of association we call it as a parasitism and this is the point of concern point of concern in terms of immunity.

So, for this concern the host developed variety of mechanism variety of things cell there is a whole system which we call it as an immune system and there are so, many things.

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Innate Immunity evolving with Pathogen

Now
Adaptive immunity
-450 my
Innate immunity
-700 my

MHC, Ig, TCR, FcγR
Lymphocytes

Toll-like receptors
Complement system
Phagocytosis
Anti-microbial peptides

Host
Pathogen

❖ Innate immune genes evolve slowly while pathogens evolve rapidly.

❖ Many of host restriction factors undergo positive selection to resist the evading mechanism of pathogens.

Innate immunity evolved 700 millions years ago since the origin of Sponges.
Adaptive immune system evolved 450 million years since the first jawed vertebrates (fish).
Clin J Am Soc Nephrol 10: 1274–1281, 2015.

So, we will basically if I will sum up everything then I can say that this innate immunity basically evolved with the pathogen here you can see that the innate immune things such as if you see there is a a pattern recognition receptor which we call it as a toll-like receptor we will study in a great detail in innate immunity in subsequent session about the toll-like receptor there is a complement system and there is a phagocytosis an antimicrobial peptides.

So, all these innate immune kind of a sensor or system or this these are basically a set of molecule or proteins or some phenomena all are evolved quite long back, it is about 700 Millions-a years ago. And you know that now we have a more sophisticated mechanism which we call it as adaptive immunity. And this adaptive immunity is not that old compared to the innate immune things.

And this innate immune things were evolved about 700 million years ago since the origin of sponges. Sponges are quite early right if you see the origin of life whereas adaptive immune system or mechanisms or molecules they are evolved 450 million year ago and this was

basically started when there is a first jawed vertebrate was there that is when the jawed fish the fish with jaws.

So, this makes the innate immunities much more older and if you see that an innate immune genes evolve relatively slow while pathogen evolve very rapidly here you can I have depicted in this cartoon. So, another or one very live or in current scenario there is a one live example which you can understand that the infection of SARS covid2. The SARS covid2 infection initially that caused lot of lot of death.

Then this pathogen is getting evolved in evolving with the host then there are several other strains came and this and that. So, you can see that pathogen can evolve quite rapidly many host restriction factors undergo positive selection in order to resist the evading mechanism of pathogens. So, so overall the message is that innate immunity is quite old and they are evolving quite slow compared to the pathogens.

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**Outnumbered microbes
Genetic/Gene pool-derived from microbes
&
Faster evolution of microbes**



So, if I sum up everything then I can say that outnumber microbes they're they're the number of microbes are more compared to the human cell Gene and genetic pool derived from microbe is also very big and fast revolution of microbes.

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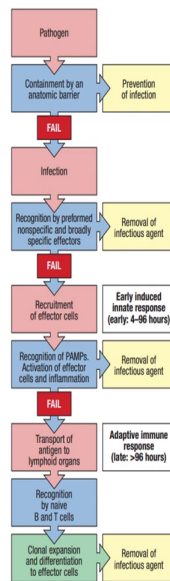
Results to

Innate Immunity as a first line of defense against plethora of microbes



Basically result to the development of innate immunity and innate immunity is a first line of defense against plethora of a microbial pathogen.

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Pathogen entry & Immune responses



Now I will explain you what happened when some microbe come in contact with the host okay?:- So, basically when the microbial pathogen come in contact with the host there will be a containment means the pathogen will be not allowed to enter in the host and basically this is achieved by anatomical barrier which we also call it as a mechanical barrier which we also call it as a physical barrier. So, these are the different names.

So, pathogen when they come in contact with the host. So, these barriers basically stop the entry and most of microbes are prevented and this will stop the further infection but if it fails then what will happen. So, if the pathogen breaches this barrier these anatomical physical

or mechanical barriers then there will be a recognition by pre formed non-specific and Broad specific effector molecules are there.

So, there will be a some kind of sensors if they will breach and enter further then these this these preformed non-specific broad sensors will come in picture and they will try to remove the microbial infection. But there is a possibility that the pathogen will again breach or break this barrier then what will happen if it will further enter then there will be a recruitment of effector cells or immune cells.

And generally this takes about the time which is which is taken by the pathogen and the host in order to induce the immune response it is about 4 to 96 hours and we call it as a early induced innate response. So, if it breaches then there will be a recruitment of effector cells and effector cells means like a phagocytic cells and all those things they basically recognize the signature molecules of this pathogen.

I will discuss in great detail about this signature we which basically we call it as a pathogen Associated molecular patterns for example gram positive bacteria has a peptidoglycan which is not present in human cell or animal cell. So, this will be recognized and then there will be a trigger of inflammation I have discussed in a great detail. So, inflammation will be triggered and then the more recruitment of immune cells will be there and then eventually the microbes will be removed.

So, this in at this level also the microbe can be removed but the microbe is a if it is a professional pathogen then probably it may not removed. So, what will happen basically if it is not removed then these microbes will be transported to the nearest lymphoid organ you probably remember there is a peripheral lymphoid organs over the these microbes will be transported. And then there will be a development of more pathogen specific immune responses will take place.

And basically it is mediated by lymphocyte a granulocytes if you remember the B cells and the T cells then these B and T cells which is a naive in the in the lymph nodes they will basically become a pathogen specific and then there will be a clonal expansion. So, this clonal expansion will result to the generation of more pathogen specific B cells which eventually differentiate to the plasma cell and produce antibody.

And there will be a clonal expansion of pathogen specific ~~t-shirts~~T-cells and eventually the micro will be cleared from the host. So, this is a just a simple scheme or a simple and this is a simple schematic which explains what is the course or steps of pathogen entry and how our immune system take care of this thing. So, here I will stop and in next session I will talk about more innate immunity we will take various here you have seen there are anatomical barriers. So, I will discuss in great detail about the anatomical barriers, thank you.