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-Bhopal

Lecture-65
Influenza Virus and Disease-3

Hi, in previous session we have discussed about various aspects of influenza virus. Now in this session we will discuss how the influenza virus infect the target cell what are the molecular events are taking place, but before that we will just look at the composition of influenza virus.

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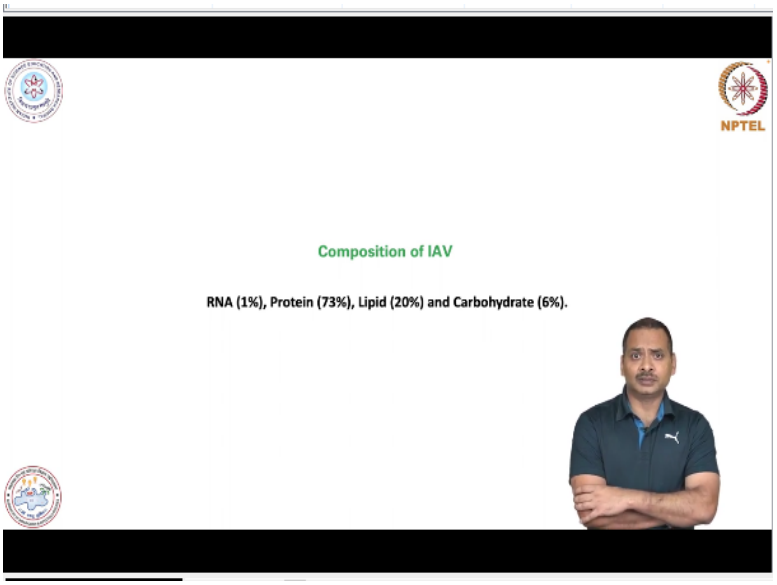

Here you can see that this viruses consist of one percent RNA, it has 73 percent protein component and 20 percent lipid component. So, try to understand this is a envelope virus and this virus receives the envelope from host cell and it has also carbohydrate about 6 percent.

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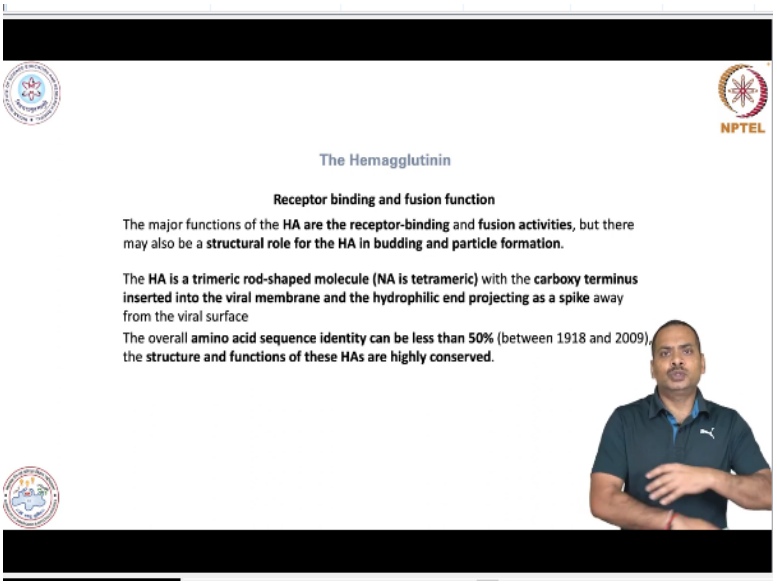

So, it is very interesting to understand the hemagglutinin protein, the HA hemagglutinin is HA which is basically interacting with the host molecule known as sialic acid, it interacts with sialic acid and then this will trigger the binding of this virus with target cell and then there will be, this HA protein plays a very important role in receptor binding as well as fusion, membrane fusion is taking place and then this RNPs are transported inside the cells.

So, their major function is a receptor binding and membrane fusion, but they may also have some structural role for HA in budding off after a virus replication there is a release of virus or egress of virus. So, they may play important role in budding of virus and particle formation. So, HA is basically primary protein, there are three subunits.

The functional unit is trimeric in contrast NA has a tetrameric, there the four subunits are coming together and that makes a functional NA and HA is there is a three subunit they come together and make a functional HA, with c terminus inserted in the viral membrane and hydrophilic end which is present on the spike of this virus which is away from the viral surfaces.

So, overall amino acid sequence identity if you see it is less than 50 percent, if you compare the influenza virus of 1918 and 2009 and the structural and function of these HA are highly conserved. So, although the sequence is not very less similarity but the overall structure and function of these HA protein is highly conserved.

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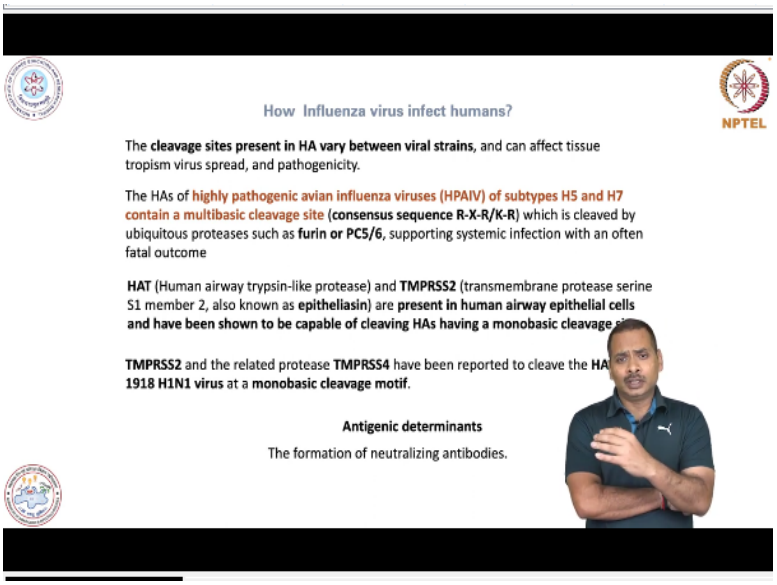

How influenza viruses infect the human or human cells? Basically, it is started with the cleavage. There is a cleavage site present in HA, which is veriesy between viral strain to strain and can affect the tissue tropism. So, some virus infect particular cells, another virus infect another cells. So, all these things are basically depend on this HA. So, tissue tropism and that will result to the pathogenicity.

If some virus is targeting very important cell for example epithelial lining of the lungs then that will cause more fatality. So, HA's of highly pathogenic avian influenza virus, we also call it as a HPAIV of subtype H5 and H7 contain multi-basic site, the consistent sequence here you can see that R-X-R oblique K-R which is cleaved by the ubiquitous proteases. So, ubiquitous protease is present in the body fluid like a furin and PC5 oblique 6, supporting systemic infection with an often fatal outcome.

So, here you can see that there is a multi basic cleavage site and these cleavage site is cleaved by these host enzyme and once it will be cleaved then this virus become a very active and if this enzyme is present ubiquitously then that will cause more fatality. There is another enzyme HAT, it is a human airway trypsin like protease. And there is another enzyme TMPRSS2, this is transmembrane protease serine S1 member 2, also known as epitheliasin.

And they are present in airway epithelial cells and have been shown to cleave the HA protein having a monobasic cleavage site. So, over there you have seen there is a multi basic cleavage site and if there are so many consensuscious sequences will be there then that will be multi basic. And if it is only one then this is a monobasic cleavage site. TMPRSS2 and related

proteases, this is another proteases TMPRSS4 have been reported to cleave the HA of this Spanish flu H1N1 which caused the pandemic in 1918, virus at this monobasic cleavage site.

So, these enzymes are basically created or cleaved this HA protein in this H1N1, this Spanish flu virus and it has a monobasic cleavage motif. So, HA is a very important antigenic determinant and if we mask this HA by some monoclonal antibody or by other mean then we can prevent the infection. And as I told you if we have a neutralizing antibody for HA then the infection can be very easily prevented.

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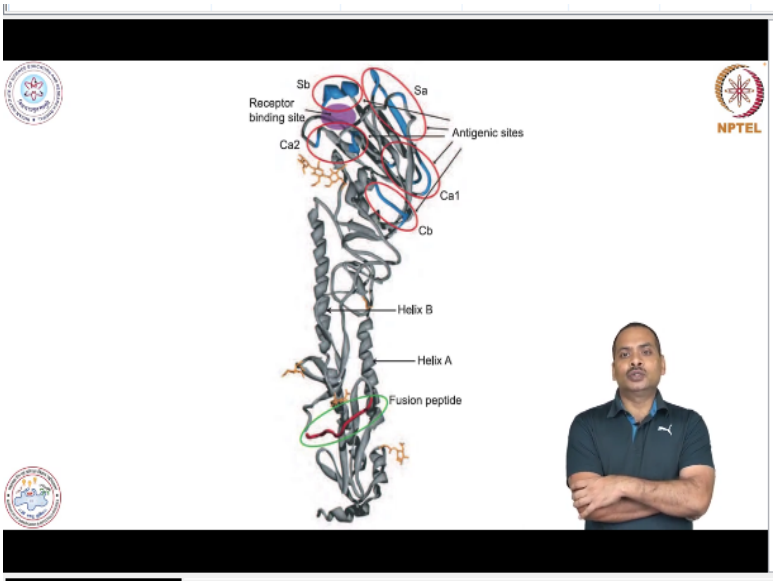

So, here I will show you the structure of HA protein. Here you can see this is a very complex as well as elegant structure and here you can see there are globular domains and this globular domain is playing very important role in kind of various function, there is a fusion peptide, this fusion peptide basically helps in fusing the membrane of virus with the host cell.

So, with this I will stop here and in next session I will discuss about how the molecularly**,** this fusion and cleavage; all these things are taking place and that result to the productive infection. Thank you very much.