

Host-pathogen interaction as a driver for evolution of animal influenza viruses: study on the molecular basis for adaptation and virulence of the virus and virus-mediated host response

The influenza virus is one of the most variable pathogens. It occurs in numerous antigenic variants and is capable of infecting many host species. Due to the high variety of virus variants and large spectrum of host organisms the disease can take different forms, from asymptomatic to very severe, which can cause death of an infected organism. During infection, the interactions between the virus and the host influence the course of the disease and the virus variants able to survive and be transmitted to other individuals. For this reason, research in the project involves two aspects: changes in the host organism during infection and changes in the virus during infection.

The first aim of the project is the detection and characterization of avian influenza viruses occurring in the regions of Poland and China with large number of wild birds coming from different parts of the world. Analyzing the sequence of identified viruses will allow to get information on the relationship of these pathogens to other avian influenza viruses found in other parts of the world.

The course of influenza virus infection depends on many factors, including the properties of the virus encoded in its genome. Viruses with very similar genomes can cause different course of infections, and these disparities can be caused by just one or more differences in the sequence of viral proteins. For this reason, it is important to gain knowledge on the mutations that can increase the virulence of the virus for a given host species. Therefore, in the project we will look for mutations in avian influenza viruses, which may be responsible for their increased virulence for mice, a model representing mammals, including humans. Furthermore, search for similar mutations affecting the virulence of the virus for ducks will contribute to better understanding of the role of these birds in maintaining and spreading viruses. One of the main mutations causing an increase in virulence is the change at the cleavage site of the hemagglutinin protein. Mutations in this region cause the emergence of viruses with high pathogenicity (HPAI), but the process itself is not well understood. For this reason, we will carry out the passage of a virus with the cleavage site that has an intermediate profile between low and high virulence and monitor the emergence of further amino acids in this region at the same time. These studies will determine the dynamics of the "transitional phase", which is very rarely captured in nature.

The next task is to evaluate the diversity of the virus that replicates in organisms of various bird species. This variety is very important for the adaptive properties of the virus. It is observed that some species of poultry (mainly quail) play the role of an indirect host that supports the adaptation of the virus to other species. However, the basis of this phenomenon is unknown. One of the factors may be the fact that the virus replicates intensively in these species, but the birds do not get sick, which allows the virus to spread "quietly". The generation of high virus diversity in these birds, which facilitates its adaptation to other species, may be another reason. In these studies we will assess how the host affects the virus. On the other hand, understanding the mechanisms of the host's immune response in the organs that are the main site of virus replication will allow a deeper assessment of the impact of the virus on the host.

Another factor that may affect virus replication efficiency is the modification of viral RNA by its methylation. Preliminary studies have shown that this type of modification plays an important role in infection with the subtypes H5 and H7. Further experiments will allow to better understand the influence and mechanism of methylation on the replication, virulence and pathogenesis of infections with various avian influenza viruses in the mammalian host.