

Pathogenicity of highly pathogenic avian influenza H5N8 subtype for mallards and herring gulls - influence of homo- and heterosubtypic immune response on clinical manifestation, replication dynamics and genetic diversity of the virus.

Influenza viruses are among the most variable pathogens found in nature. Since the consequences of variation remain unpredictable, periodic occurrences of novel variants of flu virus raise justifiable concerns. One of the new flu virus variants, designated as H5N8, has caused an epidemic of sizeable magnitude in wild and domestic birds throughout Europe (including Poland) in 2016-2017. The virus came into being in the process called '*reassortment*' that is mostly about the reshuffling of genome segments between flu viruses of different origin, in that case: H5N1 highly pathogenic virus and low pathogenic viruses that naturally circulate in wild fauna. The emerged virus is a "hybrid" of unfavourable features: on one side it is well-adapted to certain species of wild birds, in which it does not induce clinical signs and can be carried over long distances, but on the other hand it maintains a high virulence for poultry. Hitherto, the species of wild birds that could play a role of asymptomatic carriers have not yet been identified although, based on previous experiments with H5N1 virus, wild mallards are on top of the list of potential candidates. On the other hand, field observations indicate that the herring gull is a susceptible bird species. However, the only apparently healthy wild bird in which we found the infection with H5N8 during the 2016/2017 epidemic was a herring gull captured by ornithologists in Northern Poland. It seems plausible that not only is susceptibility dependant on bird species but also on pre-existing immunity resulting from previous infections with viruses of low pathogenicity. It cannot be ruled out that prior contact with such virus, especially if it belongs to the same so called "antigenic group" (e.g. low pathogenic avian influenza H5 virus) can mitigate disease course in individuals which, if fully susceptible, would not survive the infection. Additionally, little is known about the response to H5N8 in individuals previously exposed to low pathogenic viruses of non-related subtypes like H3N8 (very common in mallards) or H13N6 (prevailing in gulls). Another scientific area that requires exploration is the influence of pre-existing immunity on the selection of new variants of the virus.

The objective of the project is the assessment of pathogenicity of the novel H5N8 avian influenza virus in mallard ducks and herring gulls, both in fully susceptible birds and those with prior contact with viruses of low pathogenicity. We will study clinical course, duration of viral excretion and target organs for the virus. Application of a modern technique called "deep sequencing" will allow for tracking the emergence of novel variants of the virus.

The undertaken studies will deepen our knowledge about the role of wild birds in the spread of H5N8 virus and gain insight into creation of new variants. The results will help to better design wild bird surveillance, more precisely forecast the epidemic and better organize preventive actions in relation to poultry.