

2ND INTERNATIONAL SYMPOSIUM ON INFECTIOUS DISEASES AND VIROLOGY

November 14-15, 2025 | London, UK



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A transvirion functional axis – HA0-HA1/2-M2-M1-RNP – regulates virion integrity and resistance to thermal inactivation of influenza A virus: virological and medical significance

We have described a novel biological phenomenon: the survival of the influenza virus during heat treatment due to non-infectious virions containing the uncleaved receptor hemagglutinin protein HA0 (mol. wt. 80 kDa). These virions were found to be more resistant to the standard pasteurization temperature regimen (72 °C -15 sec), whereas infectious virions containing cleaved HA1/2 (mol. wt. 55 and 25 kDa) lost their infectious properties to infect target cells under these thermal conditions. This is a major finding of our recent investigation [Zhirnov & Chernyshova, 2025]. Earlier, we reported a similar differentiated resistance to acidic pH treatment (pH 4.0–5.0) in virions with uncleaved HA0 compared to those with cleaved HA1/2 [Zhirnov et al. 2016]. Based on the obtained data, we concluded that there exists a transvirion structural-functional axis – HA0-HA1/2-M2-M1-RNP. This cascade-type regulatory axis is suggested to determine both the structural integrity of virions and the functional cooperation of these subviral components during virion uncoating in target cells, enabling the virus to realize its infectious potential. The obtained results have an applied aspect, shedding light on the mechanisms by which the influenza virus may evade thermal inactivation via virions containing the HA0 protein, under conditions used in industrial pasteurization of food products. This is especially relevant given the current pre-epidemiological situation, where contamination of milk and other meat and dairy products with highly virulent avian influenza viruses (such as H5N1 strains carrying dangerous human-specific mutations) is escalating. Further studies remain to be performed in real industrial pasteurization settings – an important step toward preventing the spread of dangerous viruses in both natural environments and among human and animal populations. The modern study of dangerous viruses – such as avian influenza and other yet-unknown “Disease X” threats – requires tight international cooperation among scientists to design effective solutions to combat these highly pathogenic agents and novel diseases of humans and animals.