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Interactions of selected alphaherpesviral glycoprotein B homologs with the endosomal-exosomal pathway proteins and MHC class II molecules

Herpesviruses are one of the most widespread pathogens, causing infections in humans, as well as farm and wild animals. The classification of herpesviruses into subfamilies: alpha-, beta- and gammaherpesviruses is used to identify the evolutionary relationship and summarize the unique properties of individual members of the *Herpesviridae* family.

During the infection with herpesviruses, a very complex immune response is observed: viruses can interfere with the host's immune system and cause latent infection - resulting in a transition to a latency state, in the case of alphaherpesviruses. Viral proteins play an unquestionable role in modulating the immune response, and recent literature reports also point to the role of extracellular vesicles (EVs) released by cells in the formation of antiviral immunity.

The aim of the doctoral dissertation was to investigate the interaction of glycoprotein B (gB) of selected alphaherpesviruses with proteins of the endosomal-exosomal pathway and MHC molecules class II as a component of the immune system in order to better characterize the described mechanism and to test proposed an additional, immunomodulatory, function of gB.

Three representatives of alphaherpesviruses were selected for the study: herpes simplex virus type 1 (HSV-1), bovine herpesvirus type 1 (BoHV-1) and pseudorabies virus (PRV), which allowed to assess the degree of evolutionary conservation of the examined mechanisms. Experiments based on the use of stable mammalian cell lines with constitutive expression of gB genes and virus-infected cells were carried out.

One of the most important results of this work is the demonstration of the incorporation of mature forms gB to extracellular vesicles and the differences in the degree of inhibition of MHC class II molecules on the cell surface and in the vesicles by the three studied gB homologs. Additionally, for the first time, the vesicles released during BoHV-1 and PRV infection were characterized, confirming they contain gB.

The knowledge obtained about the interaction of gB of selected alphaherpesviruses with endosomal-exosomal pathway proteins and MHC class II molecules during alphaherpesviral infection may help to better understand the immunobiology of herpesviruses and thus contribute to indicate the direction of the development of new therapeutic strategies and viral infection control.