The main goal of this study is to discover the influence of pH modification on intracellular molecules transport. Research on this subject will be based on the example of two viruses that pose significant healthcare risk for humans: human coronavirus OC43 (HCoV-OC43), which frequently causes upper and lower respiratory tract diseases, and Zika virus (ZIKV), which causes infection that may be associated with severe neurological disorders such as microcephaly in newborns and development of Guillain-Barré syndrome in adults. Both of these pathogens exploit for host cell infection the endocytosis process, which in physiological conditions is used by the cells for nutrient and signalling molecules uptake.

The onset of infection is as follows: viruses attach to the surface of host cells and interact with the receptor proteins found there. As a consequence, they trigger a number of factors that cause the cell membrane to build up an invagination at the viral attachment site and deepen it until eventually intracellular virus-containing vesicles are formed. In order to be able to replicate viral RNA and to create progeny virions, viruses must escape from the vesicles to cytoplasm. The studies outlined in this project will characterize the ZIKV pathway in intracellular structures, up to the site of the viral envelope fusion with the host membrane and release of their RNA into the cytoplasm.

Interestingly, it has been noted that the internalization process of both ZIKV and HCoV-OC43 is highly sensitive to pH changes and the pretreatment of the cells with NH_4Cl, an intracellular pH boosting agent, lead to viral accumulation on the cell surface and ~100% inhibition of infection. It was hypothesized that NH_4Cl could affect intracellular transport, so that viral-containing vesicles may cease to target their standard compartments, and their recycling into the cell surface may be induced instead. An alternative explanation for the observed phenomenon could be viral arrest on the cell surface, achieved by blocking their introduction into the endosomal compartment. The implementation of this project will help to clarify this issue and therefore will bring understanding of the mechanism of inhibition of infections caused by the respective viruses.

The proposed research on HCoV-OC43 and ZIKV intracellular pathways will let us understand the molecular background of infections caused by these viruses and identify potential antiviral targets, therefore contributing to the development of other branches of science, for example chemistry. Analysis of viral transport inside cells will also broaden the knowledge of cell biology concerning the endocytosis process course and regulation. Moreover, it will bring advances in the general understanding of virus-host cell interactions, as up to now the inhibition of virus entry into cells by alkalizing agents has been seen only in the context of prevention of structural changes in viral proteins that are needed for fusion, whereas this research may reveal another possible role of the pH: to regulate the entry of viruses into the endosomal compartment or to drive their recycling to the cell surface.