In eukaryotic cells mitochondria are organelles that are involved in many important processes. The most prominent role of mitochondria is the cellular respiration, which leads to production of energy, required for the life processes. For that reason, mitochondria are known as the “powerhouses” of cells. Recent studies have shown that they also play an important role in the nonspecific, innate immunity, responsible for fighting the viruses. Immune function of mitochondria is related to the presence of MAVS protein on their surface, which is a key element in the cascade of events, leading to production of type I interferons (IFN) and proinflammatory cytokines. These substances inform the immune cells of danger and stimulate them into action. The mitochondrial morphology is an important factor for success of the mitochondrial dependent immune mechanisms. It has long been known that these are very dynamic organelles. They can change their shape, connect and disconnect, and so they communicate with each other and with other organelles, ensuring the proper functioning of the cell. According to recent studies, strongly elongated mitochondria enhance the production of type I IFN and proinflammatory cytokines in the MAVS-dependent pathway in the presence of viruses, while short, fragmented mitochondria inhibit this process. This is due to the influence of changes in the interaction between mitochondria and endoplasmic reticulum, where is located yet another protein involved in the immunity - STING. The binding of a virus-derived nucleic acid to specific intracellular receptors, RIG-I and MDA-5, which then interact to the MAVS protein, starts the way to production of previously mentioned cytokines. The efficiency of this process is significantly increased when the STING protein, present in the endoplasmic reticulum, interacts with MAVS protein on mitochondria. This is possible only in the case of elongated mitochondria, which then they have an opportunity to connect with the endoplasmic reticulum and multiply chances of cell success in the fight against viruses.

In the evolutionary path, viruses have developed the ability to "escape" from the host immune system, especially mechanisms associated with mitochondria. Recent studies have indicated that hepatitis B and C virus (HBV and HCV) and influenza A virus (IAV) cause the mitochondrial fragmentation, in order to avoid the effects given by type I IFN and the proinflammatory cytokines. However, the influence of orthopoxvirus, such as ectromelia virus, on MAVS-dependent immunity mechanisms in context of changes in the mitochondrial morphology has not yet been revealed; therefore, it is the aim of this study.

Mouse cells will be treated with substances, which affect mitochondrial morphology, i.e. mdvi1 which induces mitochondrial elongation, and CCCP which leads to mitochondrial fragmentation. Moreover, cells will be treated with poly(I:C), which will activate MAVS-dependent pathway, by imitation of the viral-derived genetic material. Subsequently, cells will be infected with ectromelia virus and then they will undergo the next few steps of experiment. **(I)** In the first step MAVS protein distribution within cells and its presence in the mitochondria will be determined. **(II)** Then, the amount of this protein will be measured, as well as the level of RIG-I and MDA-5 receptors, and STING protein. **(III)** The next step will be performed to examine the MAVS interaction with proteins involved in the modulation of the mitochondrial morphology, which is responsible for their extension and fragmentation, and also with RIG-I and MDA-5 receptors, and STING protein. **(IV)** Then, the expression of IFN type I genes will be measured. **(V)** In the last step the level of type I IFN and the proinflammatory cytokines will be determined. Procedures described above will be designed to determine the influence of ectromelia virus infection on MAVS-dependent mechanisms of antiviral immunity in the context of changes in the mitochondrial morphology.

Orthopoksviruses played an important role in the human history. Except for ectromelia virus, this group of viruses includes notorious smallpox virus (VARV) and vaccinia virus (VACV), which was used as a vaccine against VARV. Due to effective vaccination system, no further cases of smallpox have been reported. To the best of our knowledge, the smallpox virus stocks are still stored in two laboratories in the world (USA and Russia). Accidental escape of VARV to the environment or the bioterrorist attack with this virus, poses a real threat to the human population that has not been vaccinated since 1980. Furthermore, in recent years an increasing number of zoonotic infections (zoonoses), caused by other orthopoksviruses – cowpox virus (CPXV) and monkeypox virus (MPXV) is observed on the African continent and in the United States. The lack of vaccination, the risk of a terrorist attack and zoonoses present strong arguments for the legitimacy of studies on orthopoxvirus immunobiology, which in the future could lead to the emergence of new antiviral therapies.