Viral pandemics pose an imminent threat to humanity. The ongoing **COVID-19** pandemic, caused by the **SARS-CoV-2** coronavirus, requires the urgent development of anti-viral therapies, including effective vaccines. Viruses have evolved numerous **immunomodulatory mechanisms** that can not only shape the pathogenesis but also affect the elicitation of responses to other infections or vaccines. Therefore, to contain an infection or efficiently prevent it with vaccines – **we must know specific features of the antiviral response and the immune evasion strategies of a virus**. Because of the recent emergence of SARS-CoV-2 in a human population, and despite an increased effort of scientists all over the world, we have still limited data on its immune evasion properties. Especially, little is known on adaptive immune evasion by coronaviruses. Although there is a high degree of similarity between SARS-CoV-2 and its related, better-characterized coronavirus "cousins", SARS-CoV and MERS-CoV, there are also unique genomic features and that of COVID-19 pathogenesis, especially in the early phase of infection. Therefore, it would be only speculative that SARS-CoV-2 utilizes similar strategies to modulate the host immune response, especially of the type I interferons, and additional novel mechanisms may be uncovered. **This justifies a need for projects on the interactions of SARSCoV-2 with the immune system**.

We are a virus immunology group, specializing in immune evasion of herpesviruses, masters of immunomodulation. To contribute to the huge need for basic research on SARS-CoV-2, we can use our knowledge and methodology developed during years of studies on herpesviruses, **to screen all SARSCoV-2 proteins for immunomodulatory properties**. Basic potential modulatory mechanisms, both inhibition of innate immune responses, especially **type I interferon recognition and signaling**, and inhibition of **MHC class I/II-mediated antigen presentation** will be studied. The change of a host to humans, either from horseshoe bats or pangolins, must have required interference with human cell-present **restriction factors**. We plan to study the effect of SARS-CoV-2 proteins on **tetherin (BST-2)**, a protein that can "glue" the viruses to the cell membrane. It has been identified as a restriction factor for coronaviruses and we study it in the context of herpesviruses. Finally, there is a medical concern about the crossroads between two respiratory pathogens – SARS-CoV-2 and **influenza**. Therefore, we plan to address the molecular interaction of the two viruses experimentally, in infection studies.

To address immunomodulatory properties of SARS-CoV-2 proteins, we will use a similar approach that we applied several years ago in a search for bovine herpesvirus 1-encoded TAP inhibitors. The idea is to use the already established methodology and majority of the reagents already present or commercially available, optimized at our Department during studies on herpesviruses, to perform the tasks of the Project and fulfill its aims. We are sufficiently equipped and trained to perform extensive molecular cloning, generation of stable cell lines and their analysis, including culture and experiments with viral pathogens at our Laboratory of Cell Culture and Virus Propagation. Our screen can identify immunomodulatory properties of SARS-CoV-2 proteins for the next, most detailed studies, e.g., with the application of chemical inhibitors, and will contribute to a better understanding of COVID-19 immunopathogenesis.