Project goal

This research project aims to develop inhibitors for specific proteins in the SARS-CoV-2 virus responsible for viral RNA capping. Vaccination alone is not enough to control the pandemic due to virus mutations. The project involves screening chemical compounds and studying their interactions with the proteins to design more effective treatments for coronaviruses in future. The goal is to incapacitate the virus and reduce the severity of the disease.

Description of research

This research project focuses on finding ways to stop the coronavirus from multiplying by understanding the mode of action of specific proteins in the virus that are responsible for a process called viral RNA capping. Designing of specific inhibitors that can interact with viral proteins we aim to develop a new strategy to control the early stage of the infection.

The first stage of the project will involve screening of small-molecular compounds libraries for their activity against selected viral proteins. The selected inhibitors will be further tested to confirm their efficacy. Structural studies are also planned to understand inhibitor-viral protein interactions at the molecular level. The crystallographic structure of the critical nsp14 methyltransferase, which we obtained during our research on coronavirus during the pandemic, provides an excellent basis for developing libraries of inhibitors both by SAR and using modern artificial intelligence (AI) methods. This is possible thanks to numerous foreign and domestic collaborations and within our research unit.

Reasons for attempting a particular research topic

The COVID-19 pandemic was a global health crisis that required urgent solutions. While vaccinations had been crucial in fighting the virus, they were not enough due to the emergence of new variants for future outbreaks. That's why the alternative strategies to combat the virus are of highest demand. One promising approach is to develop inhibitors that target specific proteins in the virus called methyltransferases. These proteins are responsible for viral RNA capping, which is essential for the virus to function and protect itself. By developing inhibitors that can block the activity of these proteins, the ability of virus replication and spread could be affected. Precisely, targeting the viral RNA capping process with inhibitors could provide an extra layer of defense against the virus. Through ongoing research and development, I aim to contribute to the development of more effective treatments and interventions to control the spread of the virus, minimizing its impact on public health.

Substantial results expected

The research on developing inhibitors targeting SARS-CoV-2 methyltransferases, which are important for viral RNA capping, holds great promise in the fight against COVID-19, such as:

1. Identification of novel inhibitors: By screening a unique compound library and conducting experiments to study how the inhibitors interact with the target proteins, I am likely to discover new inhibitors. These inhibitors have the potential to block the activity of viral methyltransferases and disrupt the process of viral RNA capping, hindering the virus's ability to function.

2. Understanding how the inhibitors work: Through techniques like co-crystallization – an insight into the precise mechanisms by which the identified inhibitors act on the target proteins.

3. Developing highly specific inhibitors: During the project, inhibitors with different mechanisms of action, such as allosteric, covalent, or competitive inhibitors that interact with different fragments of the viral protein molecule, will be analyzed. The strategy is to create highly specific inhibitors for the methyltransferase while minimizing their potential effects on host proteins.

4. Advancing antiviral drug development: The ultimate goal of this research is to contribute to the development of specific and targeted antiviral drugs for treating future coronavirus disease. By blocking the activity of methyltransferases, particularly nsp14 and nsp16, the research aims to block the virus's ability to replicate, opening up potential therapeutic options for combating the disease.

5. Expanding scientific knowledge: The research will expand our understanding of SARS-CoV-2 methyltransferases and their role in viral RNA capping. These findings will contribute to the collective knowledge in the scientific community, serving as a foundation for future studies on antiviral drug discovery and deepening our understanding of how the virus replicates.

Overall, this research holds significant potential in the development of effective treatments against coronaviruses. By identifying new inhibitors, understanding their mechanisms of action, enhancing specificity, and contributing to scientific knowledge, I aim to make meaningful strides in our battle against the pandemic.