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Project title: Determination of the 3D structure of key regulatory regions at the 5' and 3' termini of SARS-CoV-2 RNA and identification of small molecule compounds that prevent the formation of these structures

The pandemic of COVID-19, a severe acute respiratory syndrome caused by the coronavirus SARS-CoV-2, is a great challenge for humanity and science. It is necessary to develop new ways of diagnosing, treating and preventing infections in order to stop the spread of COVID-19 disease, which attacks the whole world. Developing new vaccines, diagnostic approaches and antiviral drugs requires understanding how the SARS-CoV-2 coronavirus works on a molecular level.

The coronavirus genetic material consists of a ribonucleic acid (RNA), which encodes viral proteins, and also contains various regulatory elements that control the virus's actions, from creating new virus copies in cells to suppressing the body's immune responses. The attention of researchers has so far focused mainly on viral proteins, which have been considered as primary antiviral targets. However noncoding elements in viral RNAs offer new opportunities to expand the repertoire of drug targets for the development of antiviral therapy.

While working on a better understanding of the SARS-CoV-2 virus and developing strategies for action against it, it is important to remember that SARS-CoV-2 has many related viruses, which function in a similar, but not identical way. Coronaviruses include SARS and MERS, and other viruses that infect humans and many various animals. For example, there are many different coronaviruses that infect bats. The fight against SARS-CoV-2 requires us to have a better understanding not only of this single virus, but also of other related viruses, which may also help prevent pandemics in the future that could be caused by other coronaviruses.

As part of our research we propose to achieve two main goals:

Firstly, we will determine the three-dimensional structures of important regions of coronavirus RNA that are necessary for the virus functions. Knowledge of these structures will allow us to understand how does it function at the molecular level, and how the structure of the viral RNA can be disrupted at the molecular level. We will use a combination of various experimental techniques together with computational modeling. Our research will focus not on one coronavirus, but on the whole group, including SARS-CoV-2, SARS and MERS viruses attacking humans, as well as other coronaviruses infecting animals, to understand their similarities and differences. This knowledge can help scientists develop more universal antiviral drugs.

Secondly, we will carry out a computational virtual search to identify chemical molecules that are likely to bind to structures common to the RNAs of all coronaviruses, blocking their functioning. We will use computational analyses to search databases of millions of molecules to select a small number of the most promising candidates to be experimentally tested.

In our research project we will use a combination of proven tools and experimental techniques as well as prototypes of innovative tools recently developed in our laboratory in IIMCB in Warsaw. The results of our research will significantly contribute to understanding the relationship between coronavirus RNA structure and its functioning. This knowledge will be useful for the global effort to understand the mechanisms of coronaviruses. It will also have great potential for practical applications in the future, including the development of new therapies and drugs targeting coronavirus RNA molecules.