Involvement of cell-surface vimentin in SARS-CoV-2 cell entry

Principal Investigator: prof. dr hab. Robert Bucki

In order to develop vaccine and effective treatment of SARS-CoV-2 (SARS-2) infections, it is crucial to understand the complex mechanism by which coronavirus enters human cells and further propagates. Due to the significant genetic similarity between the SARS-CoV-2 coronavirus and other viruses of this type (particularly SARS-1 virus), it is possible to predict potential virus target points, predict its sites of interaction with the human cell and thus, design drugs that inhibit its replication in human host. Entry and multiplying of SARS-CoV-2 virus inside human cells is initiated by its binding to receptors on the cell surface, particularly ACE2 receptor. Nevertheless, some studies indicate that ACE2 activation is not uniquely sufficient to allow host cells to become susceptible for coronavirus infection and this mechanism may involve also others factors such as cell-surface vimentin (VIM). VIM is mostly known from its building cellular skeleton function, assuring the proper architecture of cell and mechanical defense against extracellular stress, nevertheless, an ever-growing number of studies report its involvement in bacterial and viral infection. From this group, particularly important are the reports indicating VIM crucial role in the infection of host cells by the coronavirus SARS-1 and other viruses similar to SARS-CoV-2.

The guiding hypothesis of this project assumes that cell-surface vimentin on the host cell plasma membrane is an important factor facilitating coronavirus SARS-CoV-2 infection, This hypothesis will be tested by experiments aiming to identify the interaction sites of SARS-CoV-2 virus proteins with vimentin and establish existence and function of cell-surface vimentin on human lung cells during SARS-2 entry. It will be also tested whether blocking virus interaction with VIM protein will prevent virus entry and its further propagation.

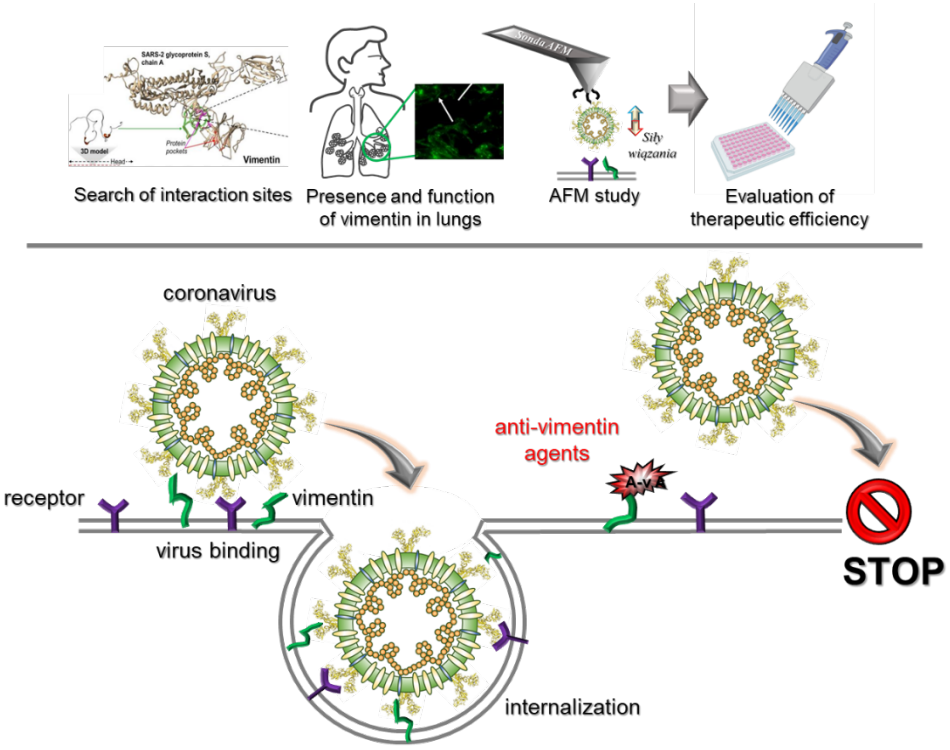

Figure 1. Schematic representation of the project

Overall, the implementation of this project will allow for comprehensive analysis of the origin, function and significance of cell surface vimentin in airway epithelia, which will expand the knowledge of pathophysiological mechanisms determining SARS-CoV-2 cellular entry and its infectivity. We propose that limiting the interaction between SARS-CoV-2 proteins and vimentin will translate into blocking of virus uptake and provide knowledge to develop new therapeutic option.