

One of the greatest challenges of medicine of the 21st century is the battle against civilization diseases, such as cardiovascular diseases, metabolic disorders, including obesity and diabetes, and cancer. The above group of the greatest medical challenges has recently been expanded by the COVID-19 pandemic, which has decimated humanity in an unexpected way. Since then, intensive work has been carried out to understand the mechanisms underlying the rapid development of this infection, which often leads to serious complications and even death. Despite intensive work in this area, the exact signaling pathways controlling these processes have not been fully understood. It seems particularly interesting to understand individual differences determining the different course of SARS-CoV-2 infection, from flu-like symptoms, to violent, difficult to stop infections. It is suspected that differences in the intensity of infection may be related to individual varieties in the expression profile of specific genes, and thus different levels of proteins conditioning the activation of specific signaling pathways. Interestingly, there are correlations between the occurrence of other diseases, so-called comorbidities, and the infection intensity and prognosis. It has been observed that some diseases, such as metabolic disorders, obesity or diabetes, predispose patients to a worse prognosis during COVID-19. This suggests that the mechanisms controlling all of these diseases may involve the same proteins and signaling pathways. One of the factors, which may be responsible for this has been identified recently. It is a protein that has been shown to be involved in the signaling pathways involved in the cancer progression, glucose metabolism and the antiviral response.

The aim of the project is to design novel nucleotide analogs with higher affinity towards one of the heat shock chaperon proteins, which has been recently shown to be involved in the SARS-COV-2 infection and cancer invasiveness. Due to the involvement in cancer progression and metastasis related processes, as well as in coronavirus infection, this protein is proposed as a novel drug target for these diseases. This protein has an ATPase activity and it is expected, that analogues of nucleotides through the structural similarities with natural substrate should exhibit a competitive mechanism of inhibition. To assess this, a series of nucleoside and nucleotide analogues will be tested for their binding affinity and inhibitory activity towards the target protein. Obtained results will be compared to the properties of other inhibitors. The aim of the research will be finding of non-toxic inhibitors which may be used as a lead compound for further drug development. After *in silico* screening and selection, new molecules (presumably nucleotide derivatives) will be chemically synthesized and after proper characterization tested in biological assays for the ability to bind to the target protein and the impact on the cells viability and cellular processes related to cancer progression and metastasis.