Popular science abstract

Peptide foldamer-based inhibitors of human ACE2 – SARS-CoV-2 S protein interaction

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Covid-19 disease is caused by the SARS-CoV-2 virus, which belongs to coronaviruses. The surface of the SARS-CoV-2 virus is covered with the S protein. Recently, it has been proven that the interaction of the receptor binding domain of S protein with the human angiotensin converting enzyme 2 (ACE2) is necessary for the virus to enter the cell. For this reason, the interaction of the ACE2 and SARS-Cov-2 S proteins is a new, very promising target for potential Covid-19 drugs.

Foldamers are oligomers with a high tendency to form well-defined three-dimensional structures in solution. In particular, peptide foldamers are a class of compounds with unique properties that include the adoption of predictable and extensive three-dimensional structures, the ability to include any functional groups in any spatial distribution, synthetic availability, and the possibility of using a number of effective methods for determining structure. The significant potential of peptide foldamers has already been proven by obtaining a series of compounds with high biological activity.

The main goal of the project is to develop new compounds from the group of peptide foldamers that would be able to inhibit the interaction of human ACE2 and SARS-Cov-2 virus S protein. Peptides containing rigid fragments will be used to construct planned inhibitors of protein-protein interactions. This approach will allow to effectively optimize the required biological activity by placing appropriate functional groups on the surface of the foldamer and simultaneously controlling its three-dimensional structure. Two groups of foldamer structures are planned as scaffolds for molecules: helix and mini-proteins. The compounds will be designed using computer methods and obtained and analyzed using modern methods of peptide chemistry. The whole process will be repeated iteratively to obtain molecules with the desired inhibitory activity.

Project results can have a significant impact on various fields of science. The general methodology for developing protein-protein interaction inhibitors based on peptide foldamers will be verified and improved. ACE2 and SARS-CoV-2 S protein interaction inhibitors could be used as research tools to better understand the process of virus entrance into human cells, and may also be candidates for drugs against Covid-19. In addition, the methodology for inhibiting coronavirus entry into the cell may be useful in the treatment of other diseases caused by similar infections that may appear in the future.