

Proteins are the basic building blocks of all living organisms. They undergo modifications, such as the attachment of various molecules. Proteins participate in almost all reactions taking place in the body, because enzymes – catalysts, or "accelerators" of the reactions taking place – are most often proteins. The increase in the efficiency of the occurrence of chemical transformations assisted by enzymes is often enormous – natural catalysts can reduce the reaction time from several years to several seconds. Most enzymes are very "picky" – they are responsible for only one type of chemical reaction involving specific elements – substrates.

One of the most interesting families of enzymes are ADP-ribosyltransferases (ARTs). They attach ADP-ribose to nucleic acids (DNA, RNA), other proteins, and various small molecules. In this way, they modify their function or affect the processes in which they participate. ARTs participate in both physiological processes of the cell and organism, as well as in the development of pathological conditions. A very interesting feature of ADP-ribosyltransferases is the great diversity of their amino acid sequence while keeping the structure (shape) of the protein constant. This can be compared to travel postcards – they all look the same, but carry different greetings. However, this is the main reason for the problems of correctly identifying new ARTs on the basis of sequence similarity alone.

ARTs are involved in both physiological processes of the cell and organism, as well as in the development of pathological conditions. ADP-ribosylation in bacteria acts as a defense mechanism against viruses, other bacterial species and antimicrobial molecules such as antibiotics. In pathogenic bacteria (e.g., cholera, pertussis, anthrax), ADP-ribosylation allows the host's signaling pathways to be modified so that its environment becomes as favorable as possible for the bacteria. ARTs are also involved in the development of many human diseases including diabetes and gastrointestinal cancers.

Up to now, I have discovered by bioinformatics methods two new families of viral ART enzymes. In doing so, I have used exclusively methods that examine amino acid sequence similarity. These new families are very interesting – one of them is found almost exclusively in a group of viruses characterized by huge genomes and sizes comparable to bacteria. The other is often found in viruses that attack arthropods. These preliminary results, obtained with other studies, suggest that there are probably still many undiscovered ART families that could prove crucial in the pathogenesis of viral diseases, for example.

The project envisages the search for new ARTs in viruses using the latest and most efficient methods for modeling protein structures, working on the basis of artificial intelligence (AI) methods. The obtained structure models will be compared with a database containing experimentally verified protein structures. Subsequently, detailed studies of the sequence and structure of the new ARTs will be carried out, and their functions will be proposed. An additional goal of the project is to describe and catalog the viral ADP-ribosyltransferases and make the results available in the form of a publicly accessible database, which will undoubtedly stimulate and facilitate research into still unknown pathways and mechanisms involving ADP-ribosylation in viruses.