Serological profiling of human population and identification of epitopes in bacteriophage antigens most frequently recognized by specific antibodies of selected classes

Summary

As already known, bacteriophages are immunogenic agents and induce a specific immune response, including phage-specific antibodies. This applies both to phages present in the human body (phageome) and to phages delivered in various ways in phage therapy. In order to conduct phage therapy effectively and safely, it is necessary to understand the natural interactions of bacteriophages with the human immune system. So far, there is no data or known methodology to track the history of phage exposure in our lives, and in particular, the common phage epitopes that are most commonly recognized by the human immune system are not known. Phages are composed of multiple proteins displaying multiple epitopes, so phage-specific antibodies are actually the sum of responses to various phage proteins.

The aim of this study was to identify the most frequently recognized bacteriophage epitopes by IgG at the population level, using samples from healthy donors representing the population of Poland and the USA. In the performed studies, a high-throughput analysis method was used, combining many research techniques (cloning in the phage display system, immunoprecipitation, mass DNA sequencing using the NGS method).

The result of the completed project is the first database of identified bacteriophage epitopes (immunogenic phage groups and immunogenic bacteriophage proteins) in the context of entire phage pools (phageomes) found in human organisms. This made it possible to determine to which phages and proteins a specific immune response in humans is particularly common. Statistical analysis and identification of correlations between populations in terms of geography and gender allowed for the identification of epitopes more frequently recognized in the studied subpopulations and for the collective analysis of the population. The obtained data allow to outline the history of exposure to phages in the studied populations, to the extent to which these antibodies remain detectable, and provide key information for personalized phage therapy, e.g. selecting for therapy only those phages that are not neutralized by the patient's antibodies. This was made possible by identifying common bacteriophage epitopes, especially

those that are highly immunogenic and predispose the phage to be highly visible to cells of the immune system.