Bacteriophages (phages) are viruses that can kill bacteria, including those bacteria that infect and endanger humans. We know phage biology, however exact functions of phage genes have not been discovered yet in many cases. These genes are so-called “phage dark matter” and they probably mediate many important functions of phage. These functions are often difficult to identify since they are not self-evident: they may relate to how phage interacts with animal and human organisms, even though phage is a bacterial virus, not able to infect animal or humans. However, not able to infect does not necessary mean not able to interact with. The goal of this project is to find out how and why our immune system responds to proteins produced by bacteriophages, with special regard to the proteins that belong to the phage-derived dark matter.

Significance of this problem results directly from the problem of drug-resistant infections. In the EU alone, more than 25 000 patients die from infections by multidrug-resistant bacteria every year. This problem has even been called the threat of a return to the pre-antibiotic era. Antibiotic-resistant bacteria can be sensitive to phage-derived products since cross-resistance is not observed. Phage-derived products are proposed as an alternative to the insufficient antibacterial drugs arsenal. Moreover, phages belong to microorganisms that are omnipresent in our environment and inside our bodies together with beneficial bacteria. It means that we all are constantly exposed to various phages and our bodies are exposed to interactions with these viruses.

This project starts with a high-throughput assay that allows for complete screening of all proteins, including the “dark matter” of representative bacteriophages of various types. Responses of mammalian cell lines to these proteins will be investigated. This will allow for selection for the active proteins. Also, typical complexes of phage proteins with bacterial products (as produced when a phage lyses a bacterium) will be investigated. Further, identified active phage products, either those stimulating mammalian immune system or those attenuating ones, will be studied in complex assays allowing for understanding how and why they are able to exert their effects on the cells.

As a result, new functions of bacterial viruses (phages) in mammals will be discovered and described. This will explain yet unknown effects of phages on our health (as natural the part of natural microflora) and will enhance safety and efficacy of phages when used as antibacterials in treatment of difficult bacterial infections.