Similarly to HSV-1 or varicella zoster virus, bacteriophages (shortly phages) are viruses however they attack bacterial not eukaryotic cells. Phages were discovered over 100 years ago and during this time they became known from both good and bad sides. They played a huge role in understanding the basics of many biological processes and in the development of genetic engineering and biotechnology. Unfortunately, bacteriophages also have "dark side", and in a result of their action, beneficial bacteria become harmful to humans. In this matter, temperate phages deserve special attention.

Bacteriophages described as temperate, have been called because of the way they treat their host - a bacterium. In contrast to virulent phages, the temperate phage infection does not always result in the death of a bacterial cell. This bacteriophage may reside in bacteria in the latent stage of prophage, during which its DNA multiplies with the bacterial DNA and is transferred to daughter cells. In this phase of the cycle, named lysogeny, the phage multiply as a result of divisions of the bacterial cell, without causing its destruction, while bacteria thanks to the presence of prophage gain resistance to such a type of phage. In this form, the bacteriophage can survive in bacteria for many generations. Under certain conditions, phage can switch from the stage of prophage to lytic development, during which intensively proliferates its DNA, independently of the bacterial DNA, triggers the expression of its own genes and production of proteins encoded in its genome. As a result, new offspring phages are formed and released from a bacterial cell, leading to its death and following infection of other bacteria. Unfortunately, in relation to the human, the term temperate phage is often misleading, because in reality these phages can be very dangerous for us. This happens when they carry harmful to humans toxins such as, for example, Shiga toxin that causes difficult to stop bloody diarrhea and complications associated with kidney failure, cholera toxin, or diphtheria toxin. Importantly, the production and release of these toxins occurs only as a result of the lytic phage development. During lysogeny toxins are not produced, but the genes coding for them are multiplied and transferred to daughter cells. In this light, it seems extremely important to understand in detail the mechanism of the phage switch from one state to another. The key in this aspect will be complete knowledge about the operation of the repression-antirepression system. The choice of the phage development path depends on the amount of repressors and antirepressors produced in the cell. The lytic cycle is activated if antirepressors dominate, while repressors are responsible for maintaining the phage in the state of lysogeny. Importantly, research on repressors has been conducted for years, but much less is known about antirepressors. There are only few reports indicating the involvement of small non-coding RNAs in the regulation of the expression of antirepressor genes.

Our team also managed to find a few small RNA molecules (derived from phages carrying Shiga toxins) that may have potential implications in this regulation. What is important, the molecules we found are much smaller than those described so far in the literature, and similar in size to microRNA molecules that function in viruses attacking eukaryotic cells. Although viral microRNAs play an important role in the regulation of the virus (e.g. herpesvirus) switch from latent to lytic state, this type molecules of phage origin were unknown until 2015, when we described the first such molecule. Before this date, prokaryotic RNAs similar in size to eukaryotic microRNAs have been poorly described only in the case of a few bacterial strains. In this project, we present six new, phage-encoded, microRNA-size molecules whose biological significance and mechanism of action we intend to explore as part of the planned work. The found molecules are located in the phage genome in the antirepressor regions and, as indicated by the bioinformatic analyzes, they may regulate the expression of antirepressor genes and thus the amount of the produced antirepressors. Essentially, the influence of one of these molecules on phage development in bacterial cells is very likely, thus it will be the first candidate for further analyzes that allow to characterize its regulatory network and thus to learn about its mechanism of action.

If this is indeed how we assume, and analogously to the viral microRNA molecules, the found by us small phage RNAs play an important role in regulation of the mechanism of phage transition from lysogeny to lytic cycle, such a discovery will significantly change current views on small RNA molecules functioning in prokaryotic systems and will shed new light on the regulation of the phage development in bacterial cells. In this light, the present project has enormous cognitive potential, and in the future, acquired knowledge may be used for development of an effective strategy to fight these bacteriophages. Perhaps it will be a method based on stopping the development of phage in the state of lysogeny. This method is currently not known, and the use of antibiotics often has the opposite effect, as they induce phage lytic mode and thereby increase the production of the encoded in phage genomes toxins.