Reg. No: 2021/43/B/NZ6/00461; Principal Investigator: dr hab. Krzysztof Hinc

Bacteriophages (phages) or viruses infecting bacteria are present in almost all ecosystems. The number of bacteriophages in biosphere is estimated to exceed 10-fold the number of bacteria and it has been calculated that there are about 1023 cases of infection per second in the world. Therefore, these viruses are thought to be an important factor driving bacterial evolution.

Within last decade relatively little bacteriophages infecting an important human pathogen *Clostridioides difficile* have been described. The clinical picture of *C. difficile* infection (CDI) is complex and most often it manifests as a mild, moderate, or severe diarrhea. The infection can develop into the life-threatening pseudomembranous colitis or toxic megacolon. The largest percentage of patients (70-80%) with *C. difficile* infection are people above 65 years of age. Elderly people are more prone to *C. difficile* infection and such severe effects of CDI as internal organ failure, recurrent infections and high mortality rate. In the CDC's latest report on the risk of drug resistance, *C. difficile* was classified as the leading cause of nosocomial infections. Not so long ago, there was information about the discovery of a new virulent strain of C. difficile that causes infections in the population of young people, also outside the hospital environment.

The genomes of the phages infecting *C. difficile* described so far contain many regulatory genes and genes, which can influence the host phenotype, in particular its virulence.

In this project, we plan to study phage-host interactions *in vitro* to understand how prophages can influence the host virulence and the *in vivo* course of infection in a mouse model of *C. dificile* infection.

This research is in line with the current interests of science. There is now a tendency to understand phage-host and bacteria-host interactions in the environment of the intestinal microbiome which is considered a key element of human health. Our research approach should show whether the tested phages, by influencing the host virulence, pose a real threat to patients in the hospital. This is of great diagnostic importance. Knowledge acquired, together with the possibility of detecting such prophages in strains infecting patients, may be a reason for the clinicians and epidemiologists that we are dealing with a lysogenic strain of *C. difficile* with greater virulence and should be implementation of CDI surveillance.