

INHIBITION OF A BACTERIAL ANTIVIRAL BREX DEFENSE SYSTEM

Justė Adomaitytė¹, Tomas Šinkūnas¹

¹Department of Protein - DNA Interactions, Institute of Biotechnology, Life Sciences Center, Vilnius
juste.adomaityte@chgf.stud.vu.lt

Bacteriophages are viruses with the ability to infect and replicate in bacterial cells. Numerous bacteriophage species are virulent and therefore kill the infected cell. However, these organisms have a long history of coexistence. During their evolution, bacteria have been able to adapt by developing defense mechanisms that protect cells from the entry of bacteriophages and foreign nucleic acids. Although more than a hundred bacterial defense systems are currently known, bacteriophages can inhibit them by various mechanisms¹. Research of defense systems and their inhibitors is crucial not only for a better understanding of microbial evolution, but also as a resource for the development of various tools for biotechnology and biomedicine.

One of the bacterial antiviral defense systems is BREX (Bacteriophage Exclusion). It is present in about 10% of prokaryotic genomes. However, the mechanism of action is still undefined. BREX systems are divided into 6 types, with our research focusing on the predominant type 1 BREX system (BREX1), which consists of 6 genes: *brxA*, *brxB*, *brxC*, *pglZ*, *brxL*, *pglX*. The *pglX* gene encodes the m6A DNA methyltransferase, which methylates specific sequences in the host genomic DNA to distinguish itself from foreign DNA². Bacteriophages can evade the BREX1 system by two different mechanisms: (i) by epigenetically modifying (either by methylation or glycosylation) BREX1 recognition sequences in their genomes³, or (ii) by blocking the BREX1 system with their encoded protein inhibitors⁴. In this study, we analyse some phage-encoded proteins as potential inhibitors of the *Escherichia coli* HS BREX1 system in cells.

[1] Mayo-Munoz et al., (2023). A host of armor: Prokaryotic immune strategies against mobile genetic elements. *Cell reports*, 42(7), 112672.

[2] Goldfarb et al., (2015). BREX is a novel phage resistance system widespread in microbial genomes. *The EMBO journal*, 34(2), 169-183.

[3] Gordeeva et al., (2019). BREX system of *Escherichia coli* distinguishes self from non-self by methylation of a specific DNA site. *Nucleic acids research*, 47(1), 253-265.

[4] Isaev et al., (2020). Phage T7 DNA mimic protein Ocr is a potent inhibitor of BREX defence. *Nucleic acids research*, 48(10), 5397-5406.