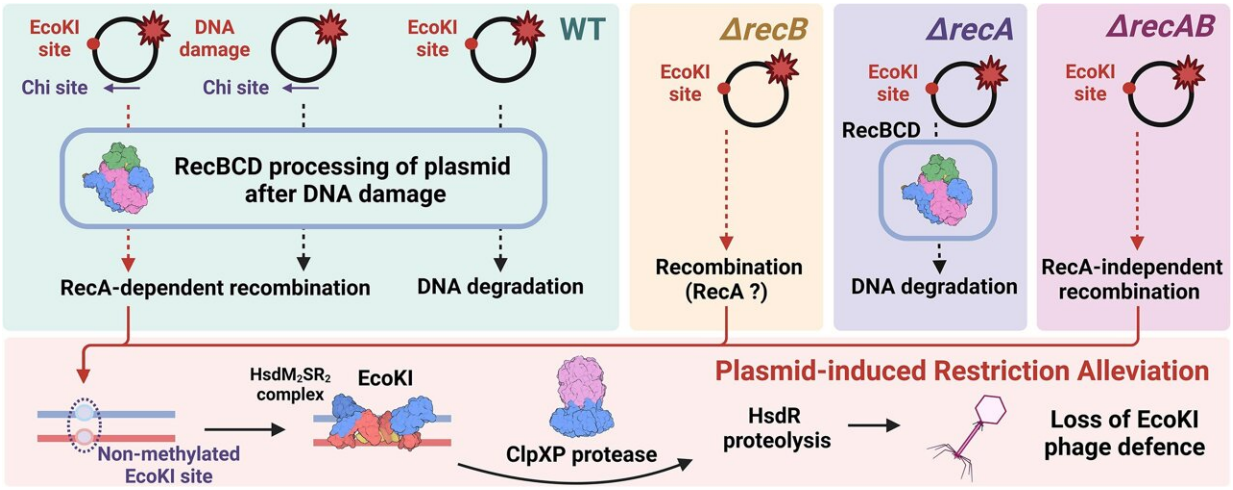
Mobile genetic elements can inadvertently suppress bacterial immune systems, research reveals

April 18 2024, by Oleg Sherbakov



Graphical abstract of the study. Credit: RecA-dependent or independent recombination of plasmid DNA generates a conflict with the host EcoKI immunity by launching restriction alleviation.

Bacterial restriction-modification systems are responsible for protecting cells from foreign genetic material, for example, bacteriophages and plasmids. Immune systems require strict regulation, as bacteria, like humans, can have autoimmune reactions—an attack on their own DNA.

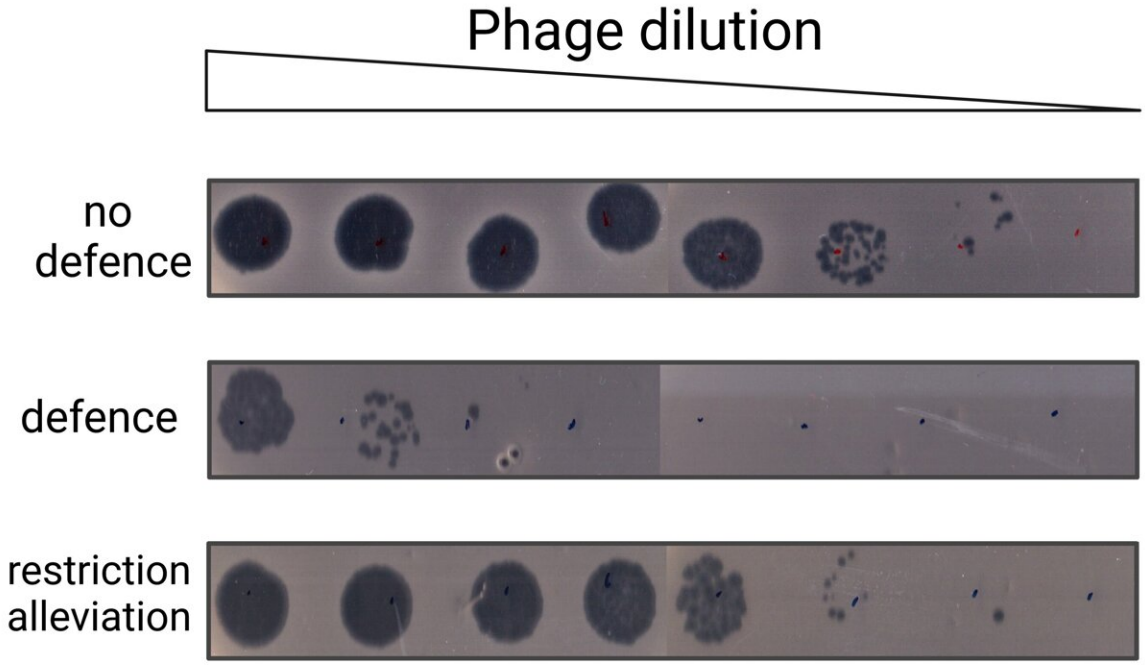
A research group led by Artem Isaev, the head of the Metagenome

Analysis Laboratory at Skoltech, studied one of the first discovered bacterial immune systems, EcoKI, and found that the presence of plasmid DNA in a cell leads to the activation of restriction alleviation, a built-in immune suppression program. This effect has been called plasmid-induced restriction alleviation. It occurs when plasmids with special properties enter the cell, which launches a conflict with intracellular immunity. The results are presented in the *Nucleic Acids Research* journal.

Plasmids are a form of mobile genetic elements, circular DNA molecules that bacteria actively exchange with each other, which leads to their rapid spread throughout the population.

"The discovery turned out to be completely unexpected for us. We studied a protein that was supposed to inhibit the EcoKI system, but were unable to explain the data. Then we guessed: Could the plasmid DNA itself be responsible for suppressing bacterial immunity? It turned out that the presence of a plasmid, which has special elements (EcoKI recognition sites) attracted EcoKI nuclease to plasmid DNA, which enabled degradation of this protein.

"This program is required to safeguard the cell against an unintended nuclease attack on the bacterial chromosome, but it turned out that plasmid DNA can also serve as a 'sponge' that attracts EcoKI nuclease and channels it to proteolysis, which completely turns off bacterial immunity. This is also detrimental for the plasmid itself, since the cell becomes sensitive to phage infection. Thus we suppose that this conflict occurs unintentionally and is simply a reflection of the complexity of different biological mechanisms that could sometimes interfere with each other," said Artem Isaev, the leader of the project.



Dark plaques are zones of phage lysis. Phage is able to infect cells without immunity even in the eighth dilution (first line). However, phages infect cells with the immune system only in the second dilution (second line). The bacterial immunity is suppressed in cells with a defense system and a plasmid causing restriction alleviation, so phages infect cells in a higher dilution (third line). Credit: Daria Yanovskaya

The findings helped gain a better understanding of bacterial recombination processes, which allows a single DNA molecule to exchange fragments with its copy within a cell. The cell repairs DNA breaks in the bacterial genome through a process of homologous recombination. This process also requires a special sequence called a Chi site. If this site is removed, a double-stranded break can lead to complete

degradation of the damaged DNA plasmid.

"We have established that in order to trigger restriction alleviation, the plasmid needs a Chi site, that is, the ability to actively recombine. However, under special conditions, if we remove the cell components responsible for the major recombination pathway (RecBCD and RecA proteins), we can still observe restriction alleviation.

"This suggests that there are hidden or alternative recombination pathways in the bacterial cell that don't manifest themselves in the presence of RecBCD and RecA. Our new model system will help explore these mechanisms," explained Mikhail Skutel and Daria Yanovskaya, the leading authors of the study, graduate students at Skoltech's Life Sciences program.

More information: Mikhail Skutel et al, RecA-dependent or independent recombination of plasmid DNA generates a conflict with the host EcoKI immunity by launching restriction alleviation, *Nucleic Acids Research* (2024). DOI: 10.1093/nar/gkae243

Provided by Skolkovo Institute of Science and Technology

Citation: Mobile genetic elements can inadvertently suppress bacterial immune systems, research reveals (2024, April 18) retrieved 2 May 2024 from https://phys.org/news/2024-04-mobile-genetic-elements-inadvertently-suppress.html

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.