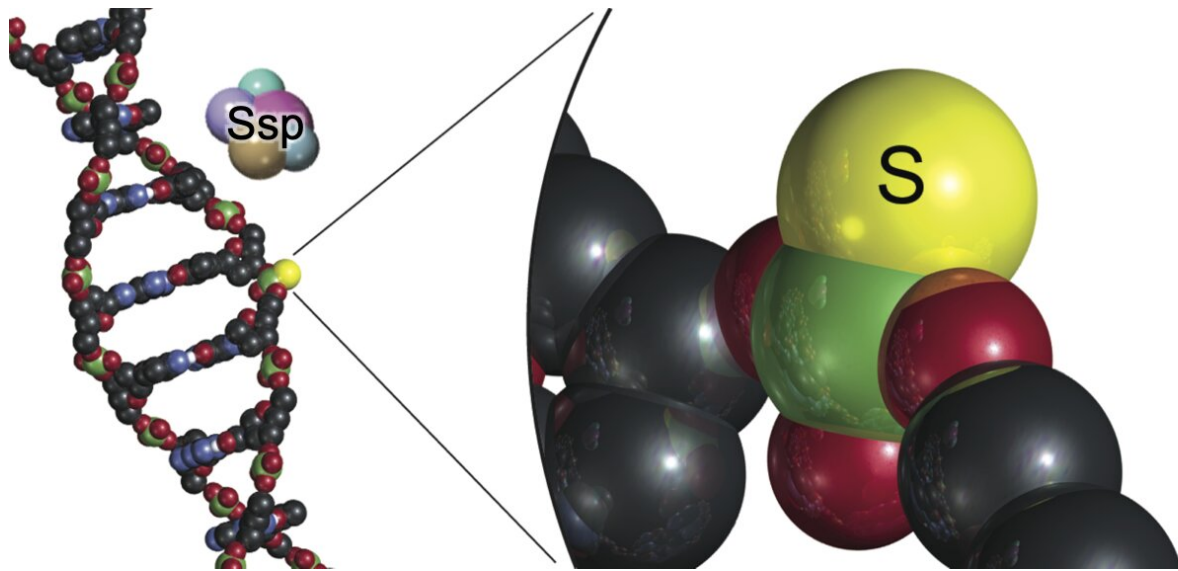


Researchers uncover new anti-phage defense mechanisms in bacteria

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By replacing oxygen with sulfur in the DNA backbone to make a phosphorothioate modification, bacteria protect their DNA from invading viruses without changing the genetic code in the DNA. Credit: Singapore-MIT Alliance for Research and Technology (SMART)

Researchers from Singapore-MIT Alliance for Research and Technology (SMART), MIT's research enterprise in Singapore, have discovered a new anti-phage defense mechanism in some bacteria that uses previously unknown features to protect their DNA. The groundbreaking discovery enables scientists to overcome existing challenges in bacterial resistance

to antibiotics. The growing antimicrobial resistance is a major concern for the global health community, and phage therapy is an important pillar in combating bacterial infections.

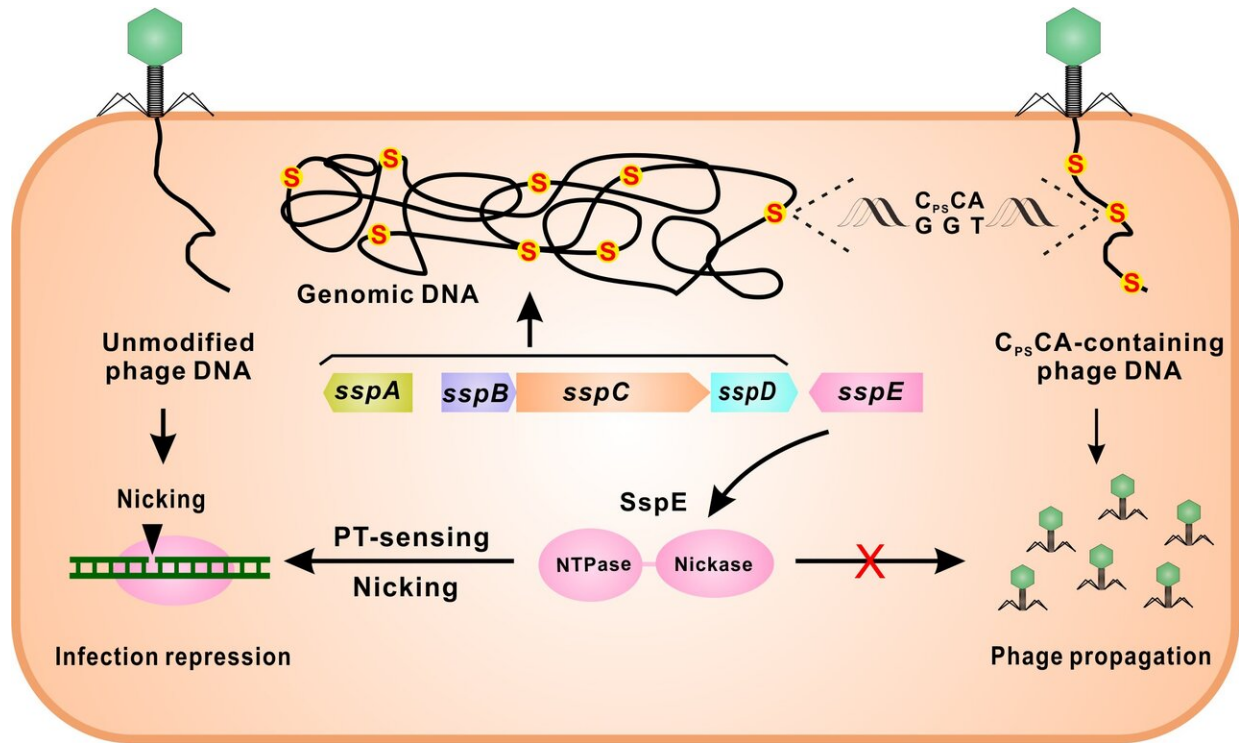
Bacteriophages, an effective alternative to fight [bacteria](#) that are resistant to commonly used antibiotics, work by injecting their own DNA into the bacteria where it can replicate to the point that it destroys the bacteria. In a paper titled "SspABCD–SspE is a phosphorothioation-sensing bacterial defense system with broad anti-phage activities" published in the prestigious journal *Nature Microbiology*, the research team describes a brand new defense system found in many bacteria that work in unique ways to protect themselves against bacteriophages.

Led by Professor Lianrong Wang at Wuhan University the paper was jointly written by a group of scientists at SMART's Antimicrobial Resistance (AMR) Interdisciplinary Research Group (IRG), Shanghai Jiao Tong University, and Tsinghua University. SMART's AMR IRG is a translational research and entrepreneurship program that aims to solve the growing threat of resistance to antimicrobial drugs.

"We previously discovered a new type of defense mechanism that bacteria use against phages, where sulfur is inserted into the DNA backbone as a phosphorothioate modification on each strand of the DNA," says Professor Peter C Dedon, co-author of the paper and lead Principal Investigator at SMART AMR. "If the attacking phage DNA didn't have the modifications, host enzymes would chop the DNA into pieces to destroy it. This restriction-modification mechanism is like a bacterial immune system to protect against invaders."

"What the team discovered now is an entirely new and different mechanism in which phosphorothioates are located on only one strand of DNA at very high-frequency. The host defense enzymes then nick one strand of the invader DNA to stop the virus from making copies of

itself. Like a surgeon's knife compared to a meat cleaver."



The newly discovered Ssp system prevents viral replication by nicking unmodified viral DNA. If the virus already possesses the phosphorothioate modification, then the Ssp system does not sense the invading DNA and the virus is allowed to replicate Credit: Singapore-MIT Alliance for Research and Technology (SMART)

The newly identified SspABCD-SspE PT system is unique from the previously known PT modification system which uses multiple proteins and enzymes to attack phage DNA by chopping it into pieces. The discovery will help researchers understand how to tackle the ever-growing arsenal of bacterial defenses against phages and can have huge implications for [phage](#) therapy.

"We keep pushing to discover DNA modification systems in phages as well as in bacteria. There are likely to be many more waiting to be found. We're finding some bizarre new ones that can be exploited to engineer phages to thwart bacterial defenses in common pathogens," adds Professor Dedon, who is also a professor at Massachusetts Institute of Technology (MIT) and helped create the university's Department of Biological Engineering.

More information: Xiaolin Xiong et al. SspABCD–SspE is a phosphorothioation-sensing bacterial defence system with broad anti-phage activities, *Nature Microbiology* (2020). [DOI: 10.1038/s41564-020-0700-6](https://doi.org/10.1038/s41564-020-0700-6)

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