



Media Release

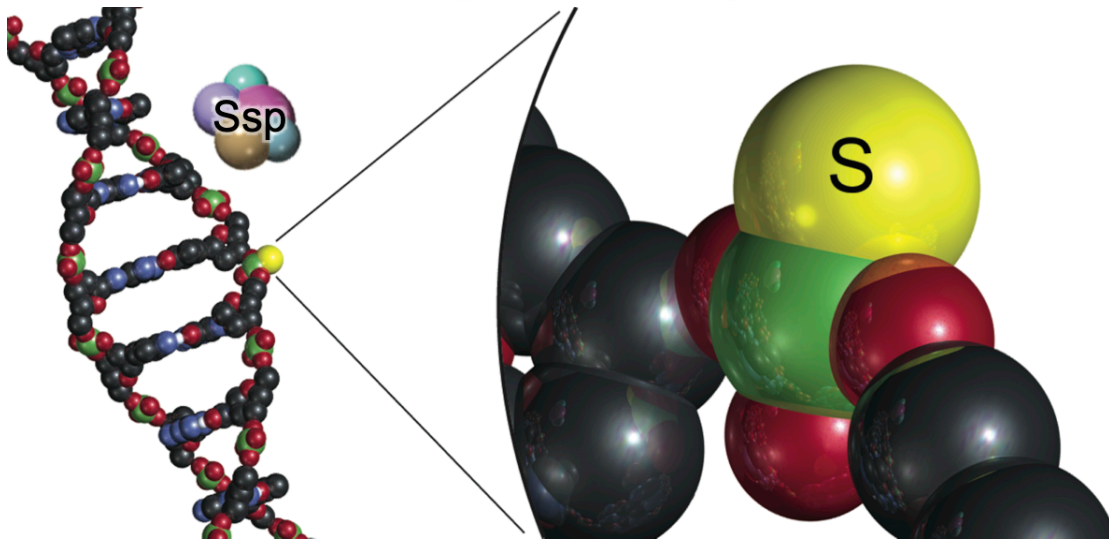
SMART Researchers Uncover New Anti-Phage Defence Mechanisms in Bacteria

Groundbreaking discovery explains why some bacteria have been able to defend against phage therapy, and opens new ways for the medical community to overcome existing challenges

- Previously unknown defence system allows bacteria to fight against phages in unique ways with single-stranded phosphorothioate modifications of DNA
- New protection mechanism also nicks the DNA to inhibit phage replication, rather than cutting the phage DNA in pieces as with previously identified PT-based defences
- Discovery will allow the medical community to formulate new ways to overcome existing bacterial defences against phages - natural killers of bacteria and the next-generation way of combating drug-resistant bacterial infections

Singapore, 6 May 2020 - Researchers from [Singapore-MIT Alliance for Research and Technology](#) (SMART), MIT's research enterprise in Singapore, have discovered a new anti-phage defence mechanism found in some bacteria, which 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 defence system with broad anti-phage activities](#)" published in the prestigious journal *Nature Microbiology*, the research team describes a brand new defence system found in many bacteria that work in unique ways to protect themselves against bacteriophages.

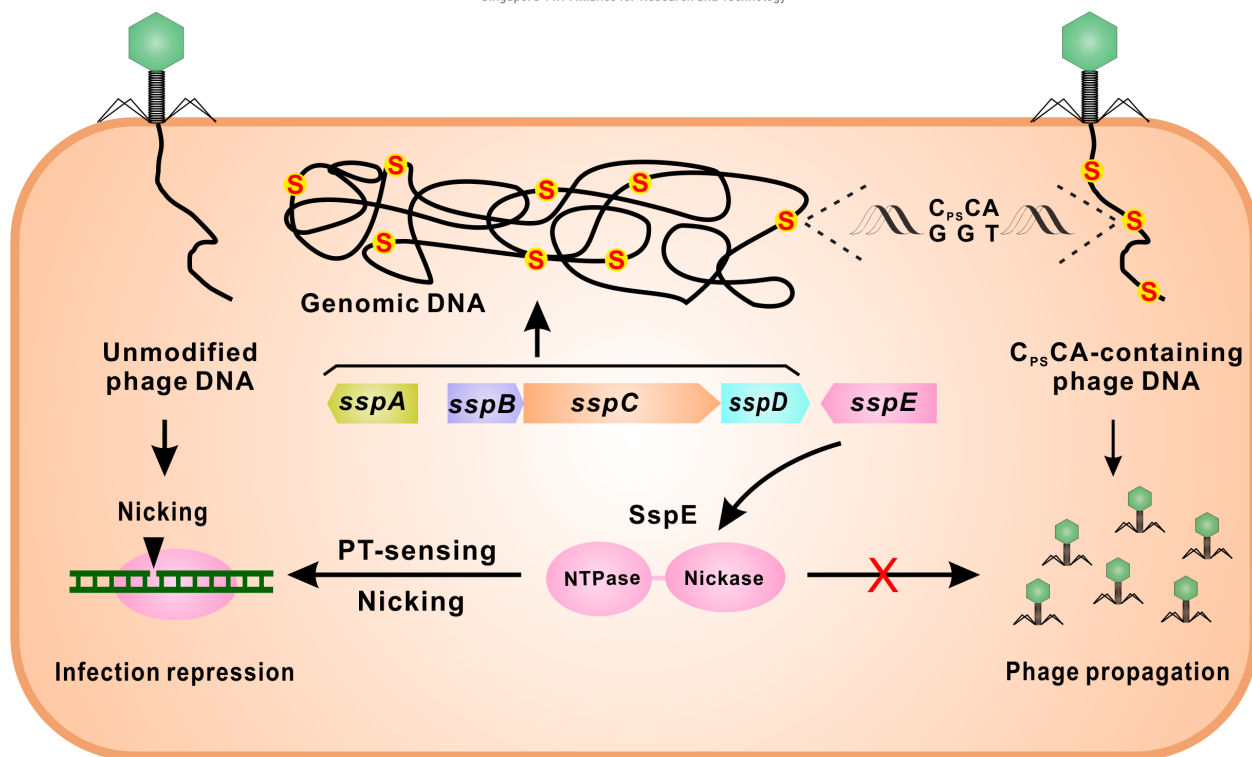


By replacing oxygen with sulfur in the DNA backbone to make a phosphorothioate modification, bacteria protect their DNA from invading viruses without changing the genetic code in the DNA

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 defence 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 defence 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

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 defences 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 defences 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.

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About Antimicrobial Resistance Interdisciplinary Research Group (AMR IRG)

The AMR IRG is a translational research and entrepreneurship program that tackles the growing threat of antimicrobial resistance. By leveraging talent and convergent technologies across Singapore and MIT, we aim to tackle AMR head-on by developing multiple innovative and



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disruptive approaches to identify, respond to, and treat drug-resistant microbial infections. Through strong scientific and clinical collaborations, our goal is to provide transformative, holistic solutions for Singapore and the world.

For more information, please log on to: <http://amr.smart.mit.edu/#home>

**About Singapore-MIT Alliance for Research and Technology (SMART) [新加坡-麻省理工学院
院研究中心]**

Singapore-MIT Alliance for Research and Technology (**SMART**) is MIT's Research Enterprise in Singapore, established by the Massachusetts Institute of Technology (MIT) in partnership with the National Research Foundation of Singapore (NRF) since 2007. SMART is the first entity in the Campus for Research Excellence and Technological Enterprise (**CREATE**) developed by NRF. SMART serves as an intellectual and innovation hub for research interactions between MIT and Singapore. Cutting-edge research projects in areas of interest to both Singapore and MIT are undertaken at SMART. SMART currently comprises an Innovation Centre and five Interdisciplinary Research Groups (IRGs): Antimicrobial Resistance (AMR), Critical Analytics for Manufacturing Personalized-Medicine (CAMP), Disruptive & Sustainable Technologies for Agricultural Precision (DiSTAP), Future Urban Mobility (FM) and Low Energy Electronic Systems (LEES).

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For more information, please visit - <http://smart.mit.edu>

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