# Using phages to deliver CRISPR to resistant bacteria found to sensitize the microbes

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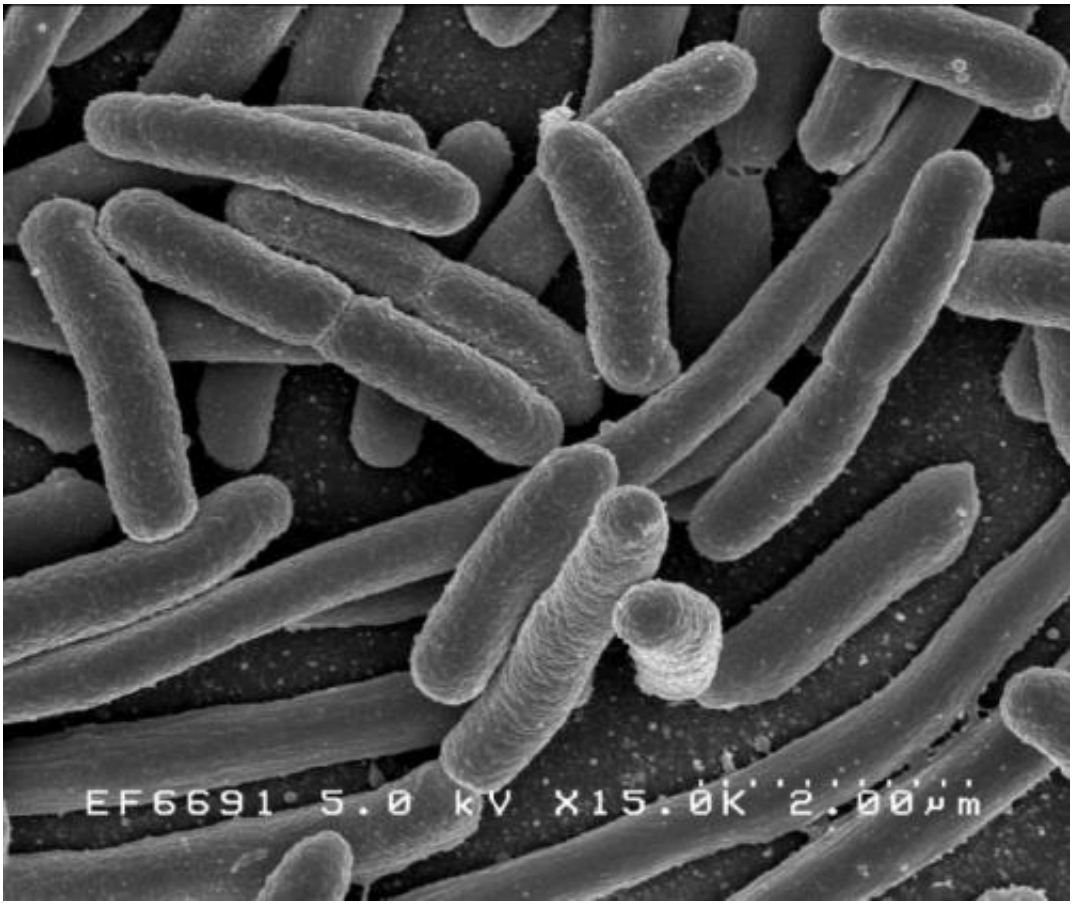


Escherichia coli. Credit: Rocky Mountain Laboratories, NIAID, NIH

(Phys.org)—A small team of researchers working at Tel Aviv University has found a way to deliver a CRISPR system to bacteria that have become resistant to drugs meant to kill them, using phages, to restore

sensitivity. In their paper published in *Proceedings of the National Academy of Sciences*, the team describes their approach and the applications they believe could benefit from it.

As bacteria grow ever more resistant to chemicals meant to kill them, scientists have turned to other avenues of attack, one of which is using bacteriophages, or phages for short—they are viruses that naturally take up residence inside of bacteria and sometimes kill them by causing them to burst, a process known as lysis—but using phages as a means to stop bacterial infections has been problematic, due to the difficulty in getting them to target specific tissue and because bacteria can develop a resistance to them as well. In this new effort, the researchers found a way to alter the part of specific bacteria (lactamase) that helps it become resistant, by using CRISPR, a gene editing system. Their technique involves using phages to carry a CRISPR system directly to a single type of bacteria, thus disabling its resistance. This method also has the advantage in that it does not have to target specific tissue, instead, it interacts only with a specified bacterium, thus, other non-harmful bacteria can be preserved.

The team tested their technique with *E. coli* by creating a CRISPR system designed specifically to target β lactamases in the bacteria, and delivered it via a lambda phage. They report that the targeted bacteria then became sensitive to antibacterial agents, which meant they had lost their resistance. The team also tried putting the same CRISPR system into phages that cause lysis and found that those bacteria that escaped modification were killed by the virus.

The researchers believe their efforts could lead to the development of treatments for surfaces and skin in places like hospitals which are hotbeds of antibiotic resistance development. They next plan to test their technique with *Pseudomonas aeruginosa*, a type of bacteria that causes a number of hospital infections and is notorious for its ability to develop

resistance to virtually any new drug used to kill it.

**More information:** Temperate and lytic bacteriophages programmed to sensitize and kill antibiotic-resistant bacteria, Ido Yosef, DOI: 10.1073/pnas.1500107112


## Abstract

The increasing threat of pathogen resistance to antibiotics requires the development of novel antimicrobial strategies. Here we present a proof of concept for a genetic strategy that aims to sensitize bacteria to antibiotics and selectively kill antibiotic-resistant bacteria. We use temperate phages to deliver a functional clustered regularly interspaced short palindromic repeats (CRISPR)–CRISPR-associated (Cas) system into the genome of antibiotic-resistant bacteria. The delivered CRISPR-Cas system destroys both antibiotic resistance-conferring plasmids and genetically modified lytic phages. This linkage between antibiotic sensitization and protection from lytic phages is a key feature of the strategy. It allows programming of lytic phages to kill only antibiotic-resistant bacteria while protecting antibiotic-sensitized bacteria. Phages designed according to this strategy may be used on hospital surfaces and hand sanitizers to facilitate replacement of antibiotic-resistant pathogens with sensitive ones.