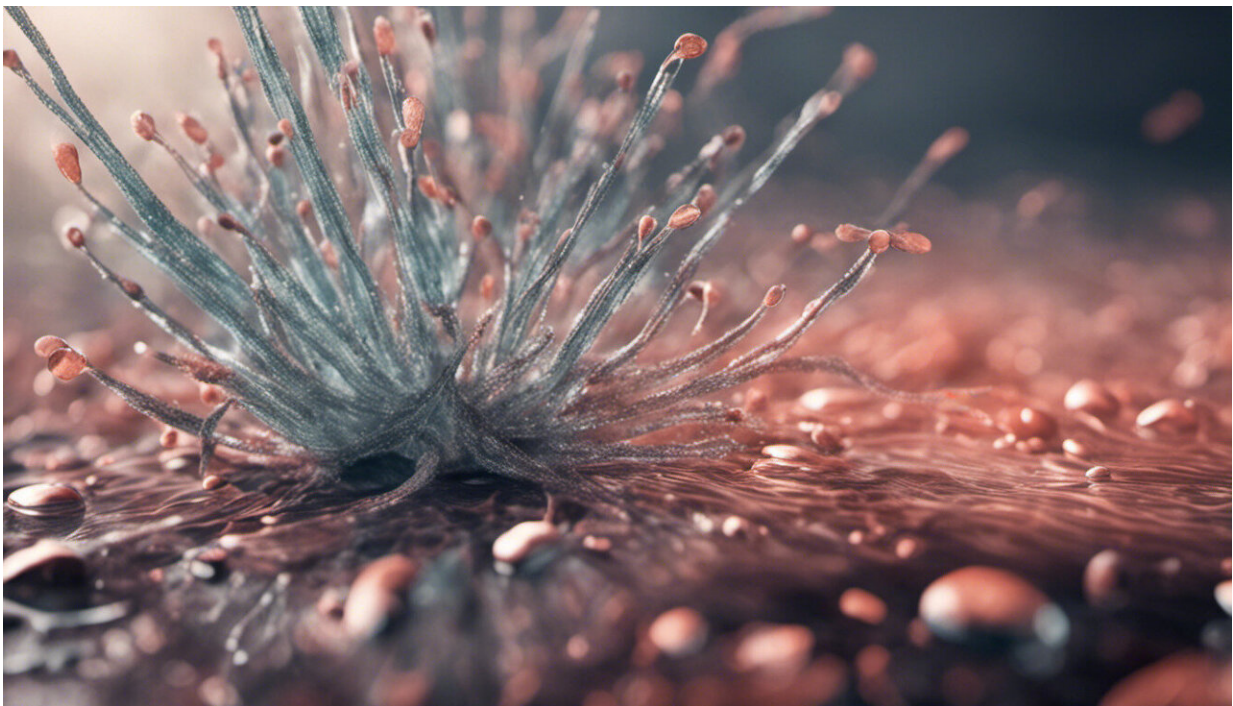


Teams identifies protein characteristics in three bacteria that convey antibiotic resistance

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Antibiotic resistance (ARE) is a threat to human health worldwide, as diverse proteins allow pathogenic bacteria to develop increasing levels of resistance to antibiotic medicines. Now, a team from the University of Tsukuba have discovered the characteristics of certain proteins known as

ARE-ABCs from three different bacteria, providing insights into their function and role that, with other resistance mechanisms, convey very powerful combined resistance.

The work is published in the journal *Nucleic Acids Research*.

Antibiotics often target the bacterial ribosome, the machinery within a cell that produces proteins. Bacteria therefore develop ways to protect the ribosome as ways to resist antibiotics. The ARE-ABC proteins are associated with ribosomal antibiotic resistance in various bacteria. The expression of the ARE-ABCs is induced by an antibiotic challenge—when the bacteria encounter an antibiotic and the ribosome "stalls" the process of translation that makes proteins, the ARE-ABCs are activated and the resistance mechanisms work to protect the bacteria.

A class of bacteria called "Clostridia" contains some important human pathogens, such as *Clostridium perfringens* that causes [food poisoning](#), and *Clostridioides difficile* that has a high level of antibiotic resistance and can cause [chronic infections](#), diarrhea, and dangerous "nosocomial" infections that patients acquire after admission to hospital or other healthcare facilities.

"The risk of infection with *C. difficile* is known to increase after treatment with an antibiotic called clindamycin, but the reason for this was unknown," says lead author Assistant Professor Nozomu Obana. "Our research showed that the ARE-ABC found in Clostridia bacteria, called CplR, conveys resistance to the class of antibiotics to which clindamycin belongs."

The research team also showed that CplR can work in synergy with another method of antibiotic resistance mediated by a protein called "Erm." Erm adds a molecule called a [methyl group](#) onto the ribosomal RNA, the primary component of the ribosome. This methylation

conveys resistance to other classes of antibiotic.

"These two mechanisms working in synergy results in extremely high levels of [antibiotic resistance](#), even to a synthetic antibiotic that is usually effective against resistant bacteria," explains lead author Professor Obana. This provides a reason for why treatment with clindamycin, inducing expression of CplR, can lead to an increased risk of *C. difficile* infection.

This study provides insights into [resistance mechanisms](#) in human pathogens that have direct clinical importance. These findings will assist in the development of new antibiotics that could stall the ribosome in novel ways that do not induce the expression of ARE-ABCF resistance proteins.

More information: Nozomu Obana et al, Genome-encoded ABCF factors implicated in intrinsic antibiotic resistance in Gram-positive bacteria: VmlR2, Ard1 and CplR, *Nucleic Acids Research* (2023). [DOI: 10.1093/nar/gkad193](https://doi.org/10.1093/nar/gkad193)

Provided by University of Tsukuba

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