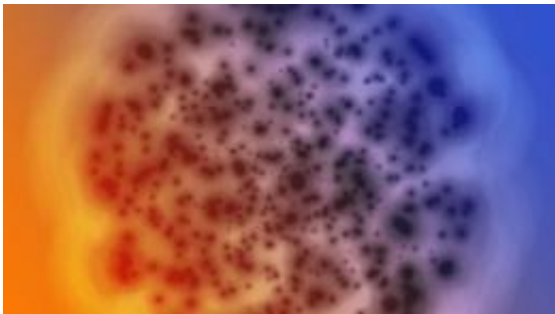


# Bacterial protein called UmuD may prevent antibiotic resistance

March 27 2015, by Marlene Cimon

---



Bacteria

The widespread and indiscriminate use of antibiotics has prompted many bacteria to mutate, an adaptation that often renders the drugs useless. The increasing threat of resistance worries infectious disease experts who fear that the era of public health successes brought by the introduction of antibiotics in the 1940s is seriously eroding, or soon even may be at an end.

But what if science could improve existing antibiotics in such a way as to not only destroy [bacteria](#), but prevent them from mutating?

At least one research team, in seeking to better understand bacterial mutation, may provide scientific answers that ultimately could lead to thwarting the organisms' ability to mutate, thus blunting the increasing threat of [antibiotic resistance](#).

"The idea would be a one-two punch," says Penny Beuning, an associate professor of chemistry and chemical biology at Northeastern University's college of science. "We need a good therapeutic target that will both kill the bacteria and prevent mutagenesis."

To be sure, the approach almost certainly is years away. Still, the National Science Foundation (NSF)-funded scientist thinks it may be possible. She and her colleagues are studying an important bacterial protein known as UmuD that regulates mutagenesis and may provide important clues about how to stop the process that eventually results in antimicrobial resistance.

Using the bacterium *E. coli* as a model, she has learned that UmuD interacts with the machinery that replicates DNA, and, when altered, may provide the switch that triggers mutation. UmuD exists in two forms, a full length version when first expressed, and later, if DNA is damaged, a much shorter form. It is this shorter version that allows bacteria to mutate.

Once there is DNA damage, "there is an SOS response, and the levels of some specific proteins go up," she says. "There is a massive stress response, and UmuD responds by cutting its arms off."

In cells where only the full-length version of the protein is present, the bacteria cannot mutate. "But when it forms its shorter self, the cells are mutable," she says.

The fact that UmuD is not present outside bacteria makes it a viable antibiotic target.

"The hope would be to find something that targets UmuD together with an existing antibiotic to prevent bacteria from mutating and developing a resistance to that particular drug," she says. "Among the things we have

been looking at: how does UmuD work, and what controls the cleavage of the arms?"

Beuning is conducting her research under an NSF Faculty Early Career Development (CAREER) grant awarded in 2009 under the American Recovery and Reinvestment Act. The award supports junior faculty who exemplify the role of teacher-scholars through outstanding research, excellent education and the integration of education and research within the context of the mission of their organization. NSF is funding her work with \$994,655 over five years.

Beuning specifically is looking at the cleavage process of UmuD using gel electrophoresis, which separates proteins according to size.

"UmuD is a small protein—139 amino acids—which loses 24 amino acids from the arm. So it goes from 139 to 115," she says. "We can observe this difference with electrophoresis, allowing us to determine how different conditions or other proteins might affect UmuD cleavage."

The team is studying different UmuD protein interactions in the lab, using biochemistry to see when and how different proteins bind to one another. Essentially "we light up the proteins and measure how they change when other proteins bind, using a method called FRET, which stands for fluorescence resonance [energy transfer](#)," she says.

"This measures energy transfer between two proteins using light emission," she adds. "The proteins have to be close to each other for energy transfer to occur, so it's a way of detecting whether two things bind to each other. People often call the technique a molecular ruler, because it can be used to measure precise distances, but we use it simply to measure proximity."

Using FRET, they discovered that UmuD prevents specific protein interactions in the replication process. That is, it stops or slows down replication by keeping two proteins that need to interact for replication from binding to each other. "Protein-protein interactions are generally hard to target with drugs, but the approach has some potential," she says.

They also use another technique that measures how floppy or flexible proteins are by putting them in heavy water and measuring how much heavier the [protein](#) gets as it trades its regular hydrogens with heavy hydrogens from the heavy water. "The floppier parts swap out the hydrogens faster than the less floppy parts," she says.

As part of the grant's education component, she has up to ten undergraduates—as well as local high school students and teachers—working in her research lab. Several students have worked in her lab as part of Northeastern's signature co-op program, in which students work full-time for six months in positions related to their career goals.

Also, she teaches an upper level [chemical biology](#) class to undergraduates, and created a lab research project for the students that takes place during half of the semester that actually involves them directly in her mutagenesis research.

"A lot of these students had not yet conducted any research, so they were really motivated by the idea of doing something that someone would use as part of a bigger project," she says. "Particularly at Northeastern, where co-op is such a large part of the culture, it is fun to take advantage of the laboratory as the ultimate in experiential education."

Provided by National Science Foundation

Citation: Bacterial protein called UmuD may prevent antibiotic resistance (2015, March 27)  
retrieved 30 April 2024 from  
<https://phys.org/news/2015-03-bacterial-protein-umud-antibiotic-resistance.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.