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Versatile antibiotic found with self-immunity gene on plasmid in staph strain

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A robust, broad spectrum antibiotic, and a gene that confers immunity to that antibiotic are both found in the bacterium *Staphylococcus epidermidis* Strain 115. The antibiotic, a member of the thiopeptide family of antibiotics, is not in widespread use, partly due to its complex structure, but the investigators, from Brigham Young University, Provo, Utah, now report that the mechanism of synthesis is surprisingly simple. "We hope to come up with innovative processes for large-scale production and derivitization so that new, and possibly more potent versions of the antibiotic can become available, says co-corresponding author Joel S. Griffitts. The research is published ahead of print in *Journal of Bacteriology*.

Strain 115 was originally discovered on turkeys that appeared to have enhanced immunity to bacterial infections. "The motivation behind our current work was a desire to understand the connection between Strain 115 and immunity to disease-causing bacteria," says Griffitts.

It quickly became clear to the investigators that Strain 115 could produce a potent antibiotic that targets a large number of medically relevant bacteria, including those that cause staph infections, strep throat, and severe gastrointestinal diseases. "We wanted to know the identity of this antibiotic and the means by which Strain 115 protects itself from its own antibiotic's deadly effects," says Griffitts.

"We found that the genes for both antibiotic synthesis and self protection in Strain 115 are conveniently clustered on a compact DNA molecule [a

plasmid] that replicates itself as a small circle within the cells of Strain 115," says Griffitts. Among experiments they conducted to prove this, they engineered a version of Strain 115 that was missing the plasmid. That version failed to produce both the antibiotic and the immunity to the antibiotic.

The investigators then analyzed the mechanism of immunity. "Thiopeptide antibiotics kill cells by blocking a part of the ribosome," Griffitts explains. Ribosomes, common to all living organisms, are the machines that read the genetic code, producing proteins based on the instructions therein. The plasmid, which directs the production of the thiopeptide antibiotic, also directs production of a spare part for the ribosome, a replacement for the part that is blocked by the antibiotic, which renders the ribosome insensitive to the antibiotic.

The investigation of Strain 115 began as an undergraduate project, after the bacteria had sat in a laboratory freezer for decades, says Griffitts. "It quickly grew into an effort involving two Ph.D. microbiologists, a talented graduate student, and several analytical biochemists." Hopefully, he says, the research will ultimately enable production of a valuable antibiotic, in quantities sufficient to make a dent in the antibiotic crisis.

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