Natural sniper kills hospital bacterium

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Bacteria produce proteins to take out specific competitors. One of these proteins can kill the hospital bacterium pseudomonas aeruginosa. Microbial geneticists at KU Leuven, Belgium, have unraveled how this protein launches its attack and ensures that the bacteria die very quickly. In the long term, these proteins hold potential for new antibiotic cocktails.

In the fight against antibiotic-resistant bacteria, scientists are constantly searching for new antibiotics. One promising avenue of research involves protein antibiotics. These proteins are produced by bacteria and are only toxic to their direct enemies.

One type of these proteins, LIpA bacteriocins, is highly effective in eliminating the hospital bacterium Pseudomonas aeruginosa. This hospital bacterium can be life-threatening for patients with burn wound or cystic fibrosis. The infections it causes are often hard to fight because Pseudomonas bacteria are resistant to many of the antibiotics used today.

Protein antibiotics can be part of the solution in this case. But, until recently, it wasn't clear how the LIpA protein kills the Pseudomonas hospital bacterium.

Professor René De Mot's team at the KU Leuven Centre of Microbial and Plant Genetics has now shown how the protein operates. "The LIpA protein has a specific target in the outer wall of the bacterial cells," postdoctoral researcher Maarten Ghequire explains. "That target is a protein as well: the BamA protein, which is involved in maintaining the

bacterial cell wall. Without the BamA protein, bacteria cannot survive. LlpA binds to that BamA protein and, by doing so, shuts it down."

These protein antibiotics are effective as well as very specific in how they operate. "They're similar to snipers, whereas traditional antibiotics are more like cluster bombs," says Maarten Ghequire. "Traditional antibiotics are effective against many bacteria but they also kill a lot of harmless organisms. That may lead to other infections. Unlike standard antibiotics, LIpA proteins don't even need to get inside the bacteria; they recognise their target and then sabotage it from the outside."

The study opens up new long-term perspectives for antibiotic cocktails that can fight all types of pathogenic Pseudomonas, for instance. "But before we can even consider using these antibiotics in patients, we need to find out more about the precise effects of the LIpA protein. That will be part of our follow-up research."

More information: Maarten G. K. Ghequire et al, Hitting with a BAM: Selective Killing by Lectin-Like Bacteriocins, *mBio* (2018). DOI: 10.1128/mBio.02138-17

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