Toxin-antitoxin systems could target invasive and resistant bacteria

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Each dot represents a plasmid, color-coded by its host bacteria. The plasmids are grouped into communities by their toxin-antitoxin systems. Credit: Jonathan Bethke

In a counterintuitive move, bacteria are known to produce self-destructive toxins. However, they also make antitoxins, and researchers at Lawrence Livermore National Laboratory (LLNL) have identified these toxin-antitoxin systems as a possible passkey to hack into bacteria

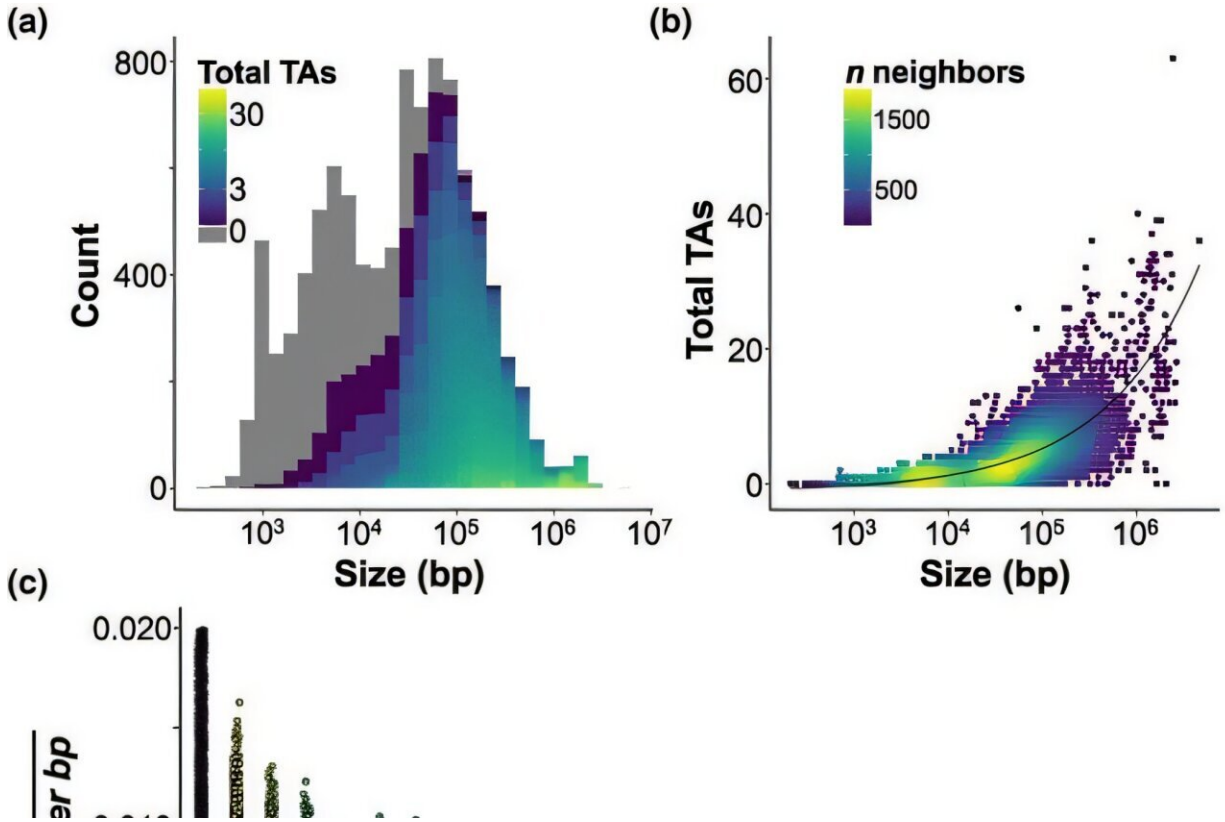
communities.

The study, recently published in *Molecular Biology and Evolution*, examines bacteria at a community level. A community of bacteria will interact and exchange DNA, which encourages having similar toxin-antitoxin systems. Any new or unusual invader, such as a Salmonella infection from contaminated food, will likely contain different systems.

"You might get an antibiotic from a doctor that wipes out everything, including the good stuff in your gut. That can lead to opportunistic infections like C. diff," said Jonathan Bethke, a postdoctoral scientist in LLNL's Biosciences and Biotechnology Division. "If we could selectively target the strangers, we could preserve the existing community."

Toxin-antitoxin systems were discovered in the 1980s in connection with plasmids, or genetic material that moves between bacteria. Bacteria exchange this DNA in all manner of ways. Pili, hair-like appendages that protrude from the surface, create bridges between cells. Free DNA floats around, just waiting to be scooped up. Even viruses transfer DNA between bacteria.

While the toxins important to plasmids do kill bacteria, their hosts can benefit from keeping them around. For example, the resistance genes that save bacteria from antibiotic treatment are often carried on plasmids. The toxin-antitoxin systems can also act like an innate immune system, inhibiting individual bacteria infected by viruses to save the population as a whole.



The distribution of toxins and antitoxins across plasmids. Credit: *Molecular Biology and Evolution* (2024). DOI: 10.1093/molbev/msae206

Using a computational approach, the team at LLNL investigated 10,000 plasmids and grouped them into communities based on their toxin-antitoxin systems. Surprisingly, this strategy recreated communities assembled from more resource-intensive, whole genome comparisons and suggested a more targeted method to manage infections.

"Say I asked you to selectively kill a particular kind of bacteria in a mixed community. If you're comparing all the genes in the whole community, you don't know what to focus on," said Bethke. "In this case, we show that toxin-antitoxin systems can help you narrow in."

Bacteria don't evolve in the same way as people. When they divide and create a clone, there is no genetic diversification. Instead, major changes critical to evolution happen via mobile genetic elements like plasmids.

"It's a very community-based evolution," said Bethke. "Because of that, by continuing to look at bacteria not through traditional species lenses but rather through a community lens, we may be able to understand them a lot better."

More information: Jonathan H Bethke et al, Toxin-Antitoxin Systems Reflect Community Interactions Through Horizontal Gene Transfer, *Molecular Biology and Evolution* (2024). DOI: 10.1093/molbev/msae206

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