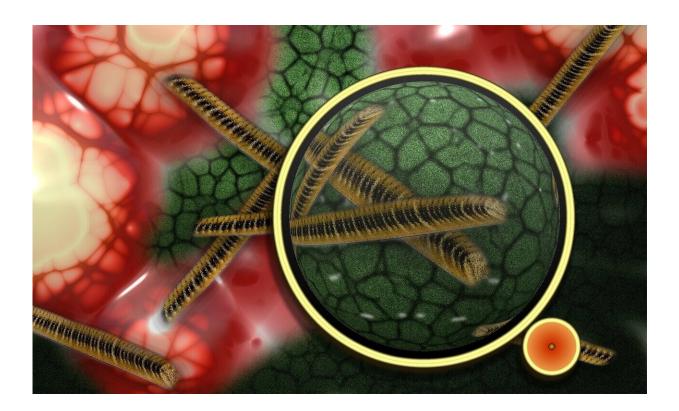


Machine learning predicts antibiotic resistance spread

October 22 2021



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Genes aren't only inherited through birth. Bacteria have the ability to pass genes to each other, or pick them up from their environment, through a process called horizonal gene transfer, which is a major culprit in the spread of antibiotic resistance.



Cornell researchers used machine learning to sort <u>organisms</u> by their functions and use this information to predict with near-perfect accuracy how genes are transferred between them, an approach that could potentially be used to stop the spread of antibiotic resistance.

The team's paper, "Functions Predict Horizontal Gene Transfer and the Emergence of Antibiotic Resistance," published Oct. 22 in *Science Advances*. The lead author is doctoral student Hao Zhou.

"Organisms basically can acquire resistance genes from other organisms. And so it would help if we knew which organisms <u>bacteria</u> were exchanging with, and not only that, but we could figure out what are the driving factors that implicate organisms in this transfer," said Ilana Brito, assistant professor and the Mong Family Sesquicentennial Faculty Fellow in Biomedical Engineering in the College of Engineering, and the paper's senior author. "If we can figure out who is exchanging genes with who, then maybe it would give insight into how this actually happens and possibly even control these processes."

Many novel traits are shared through gene transfer. But scientists haven't been able to determine why some bacteria engage in gene transfer while others do not.

Instead of testing individual hypotheses, Brito's team looked to bacteria genomes and their various functions—which can range from DNA replication to metabolizing carbohydrates—in order to identify signatures that indicate "who" were swapping genes and what was driving these networks of exchange.

Brito's team used several <u>machine-learning models</u>, each of which teased out different phenomena embedded in the data. This enabled them to identify multiple networks of different antibiotic resistance genes, and across strains of the same organism.



For the study, the researchers focused on organisms associated with soil, plants and oceans, but their model is also well-suited to look at human-associated organisms and pathogens, such as *Acinetobacter baumannii* and *E. coli*, and within localized environments, such as an individual's gut microbiome.

They found the machine-learning models were particularly effective when applied to antibiotic resistance genes.

"I think one of the big takeaways here is that the network of bacterial gene exchange—specifically for antibiotic resistance—is predictable," Brito said. "We can understand it by looking at the data, and we can do better if we actually look at each organism's genome. It's not a <u>random process</u>."

One of the most surprising findings was that the modeling predicted many possible antibiotic resistance transfers between human-associated bacteria and pathogens that haven't yet been observed. These probable, yet undetected, transfer events were almost exclusive to humanassociated bacteria in the <u>gut microbiome</u> or oral microbiome.

The research is emblematic of Cornell's recently launched Center for Antimicrobial Resistance, according Brito, who serves on the center's steering committee.

"One can imagine that if we can predict how these genes spread, we might be able to either intervene or choose a specific antibiotic, depending what we see in a patient's gut," Brito said. "More broadly, we may see where certain types of organisms are predicted to transfer with others in a certain environment. And we think there might be novel antibiotic targets in the data. For example, genes that could cripple these organisms, potentially, in terms of their ability to persist in certain environments or acquire these genes."



Juan Felipe Beltrán, Ph.D. '19, contributed to the research.

More information: Hao Zhou et al, Functions predict horizontal gene transfer and the emergence of antibiotic resistance, *Science Advances* (2021). <u>DOI: 10.1126/sciadv.abj5056</u>. www.science.org/doi/10.1126/sciadv.abj5056

Provided by Cornell University

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