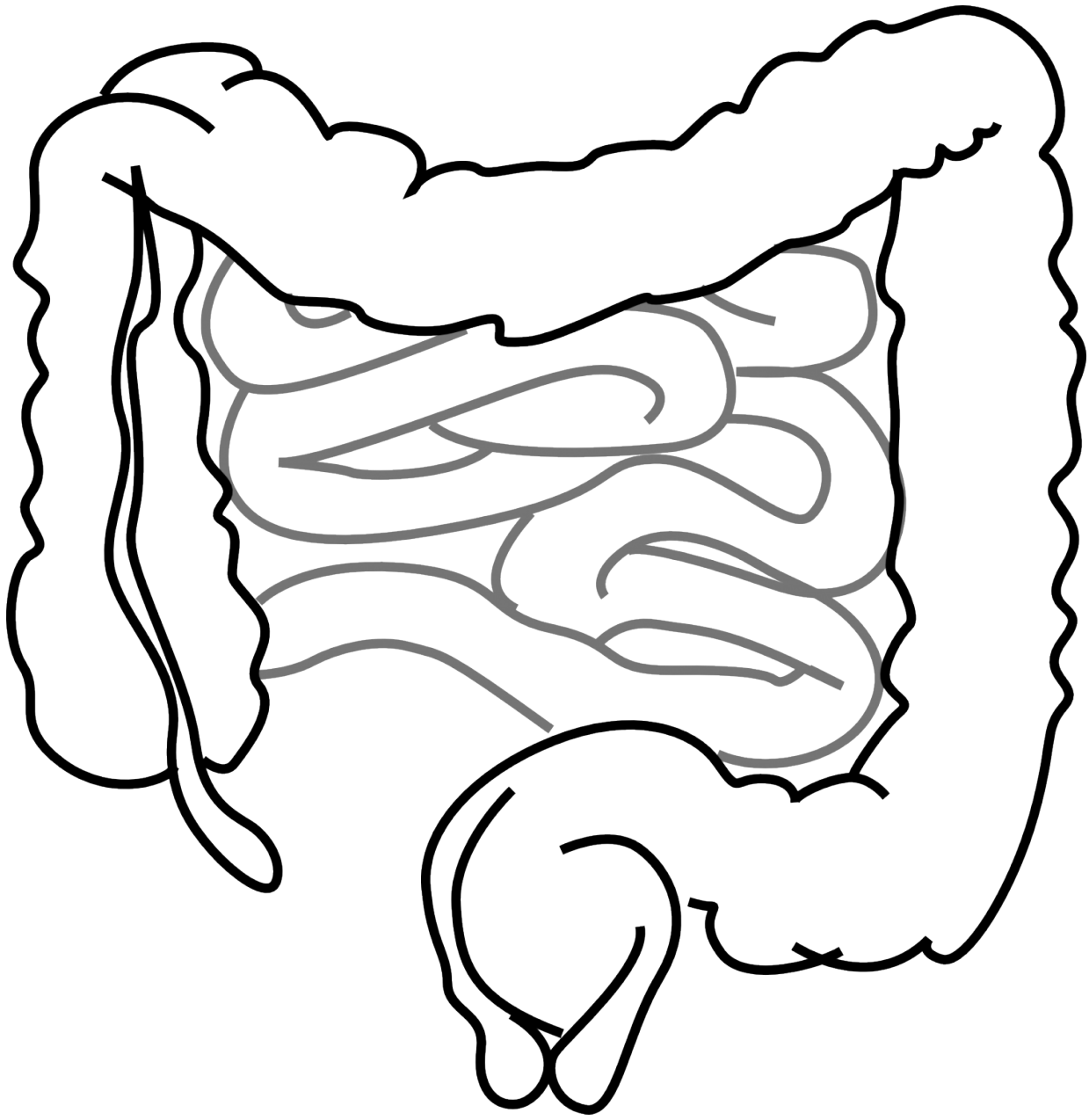
A host's genes likely influence the spread of antibiotic resistance

January 29 2020



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In the gastrointestinal tract of host animals, bacteria can exchange the genes responsible for antibiotic resistance (AR) via small, circular chunks of DNA called plasmids. However, the process in this complex environment isn't completely understood, and AR has become a public health menace. Every year, according to the CDC, more than 2.8 million people are diagnosed with infections resistant to antibiotic treatment, and 35,000 people die.

"The human gut has millions of bacteria," said microbiologist Melha Mellata, Ph.D., at Iowa State University in Ames, Iowa. "If an AR plasmid is introduced into our gut through contaminated food or by another means, it will quickly spread to other gut bacteria, which will generate bacteria resistant to treatments with antibiotics." To stop that from happening, she said, researchers need to know what factors trigger or reduce the transfer of plasmids.

This week in *mSphere*, an open-access journal of the American Society for Microbiology, Mellata and her colleagues published findings that suggest the genetic background of the host organism itself may play an underappreciated role in the sharing of resistance between bacteria, at least in mice. The researchers analyzed how AR-associated plasmids were transferred from one microbe to another in two genetically different groups of mice. Both groups started with the same population of gut microbes and were fed the same diet in the same environment.

The researchers found that the plasmids transferred successfully in some mice but not in others, which meant that AR didn't spread in the same way in all groups. That observation led the researchers to run further

analyses, which suggested that the microbial transactions could be attributed to genetic factors in the mice themselves, as well as the complexity of the gut microbiota.

"There is something in the host's genes that can amplify this transfer," said Mellata, who led the study.

Mellata and her colleagues used a strain of Salmonella known to harbor large plasmids that make the bacterium resistant to treatment with streptomycin and tetracycline, two common antibiotics. Previous studies by other researchers have confirmed that these plasmids can transfer to Escherichia coli.

But those previous experiments were conducted in bacterial cultures. For the new study, Mellata's group studied how the plasmids spread to E. coli in the animals themselves. A better understanding of how resistance spreads requires examining what's going on in the host gastrointestinal tract, she said. "We need to study this issue through the lens of the host's complex environment, since in reality this is how this phenomenon happens."

Mellata's research at Iowa State focuses on understanding large plasmids—which may contain many AR-related genes—and developing vaccines for strains of E. coli that are resistant to antibiotic treatment. Previous work by her group showed that mouse strains with a limited set of known gut microbes are more susceptible to infections than conventional mice. That observation led them to investigate how the genetic background of the animal itself—and not just the microbial community—might have some influence on the transfer of plasmids.

Mellata's group is now following up on the experiment by trying to identify the specific genetic host factors that can trigger the plasmid transfer. She hopes those findings can lead to a new way to stop the

spread of antibiotic resistance. "If we can target those specific host factors, we can reduce the plasmid transfer, which will prevent the emergence of new antibiotic-resistant strains," she said.

"People are dying from bacterial infections," she said. "They should not be dying from bacteria like E. coli. The emergence of bacteria resistant to last-resort antibiotics is happening really fast, and we want to discover what's making that happen."

Provided by American Society for Microbiology