

Researchers analyze genome of deadly, drug-resistant pathogen

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Infections by microbes like bacteria and fungi that don't respond to available antimicrobial treatments pose an increasingly dangerous public health threat around the world. In the United States alone, such infections kill 23,000 people annually. To better understand the molecular drivers behind resistance, researchers at the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, recently conducted a whole-genome analysis of an unusual bacterial strain cultured from a patient in the United States. Their results are published this week in *mBio*, an open-access journal of the American Society for Microbiology.

That strain, an isolate of *Klebsiella pneumoniae*, was cultured from a hip infection of a patient in Nevada who did not respond to treatment by antibiotics and died in 2016. The microbe is one of the first *K. pneumoniae* [strains](#) reported to the CDC that was resistant to all 26 antibiotics available for treatment, says Tom de Man, a bioinformatics expert at the CDC who led the study. Bacteria and other pathogens can develop resistance to drugs after repeated exposure, which means that increasing use of these treatments can actually make surviving strains stronger.

"The right drug at the right dose, taken for the right duration, is life-saving," says Alison Halpin, a molecular epidemiologist at the CDC whose lab produced the study. "But overuse can lead to adverse events including the development of resistance."

De Man and his collaborators identified four genes known to confer resistance to beta-lactams, a family of [broad spectrum antibiotics](#) often used to treat gram-positive and gram-negative infections. Penicillin-derived drugs, for example, are beta-lactams. Two of those genes were found on the chromosome, which means they were in the inheritable genetic material of the microbe. Two were found on plasmids, which are round bits of DNA that easily transfer from germ to germ and are often responsible for resistance. Other genes identified in the analysis are associated with resistance to fosfomycin, tetracyclines, and other antibiotics.

The isolate at the center of the new study belongs to a strain type that has spread around the world. Plasmids identified in the study also suggested this microbe may be related to resistant bacteria that have been reported in other countries including China, Nepal, India, and Kenya—clues that give the researcher a sense of where the isolate may have originated.

The genomic analysis will provide [public health](#) workers with better information about resistant infections, says de Man. Knowledge about which strains have which genes can help guide the development of more precise tests that can be used at hospitals and health centers. "We can find new resistance mechanisms," he says. Tests informed by genome-wide analyses may help epidemiologists recognize and contain [resistant strains](#) before they spread to other patients. Though it's not possible now, in the future genomic information might help guide treatment decisions and strategies.

"We will likely know from this information which drugs work and which do not work," de Man says.

In the last two years, the CDC has established a network of laboratories across the United States that track the emergence and spread of resistant pathogens like *K. pneumoniae*. Those centers are designed to quickly

identify dangerous microbes with the goal of stopping transmission as quickly as possible, says Halpin. However, the threat of [antimicrobial resistance](#) isn't going away, and responding to it will require a global effort.

"Bacteria are going to continue to evolve," says Halpin. "We cannot stop [resistance](#) because it's part of biology. But we do want to slow it."

Provided by American Society for Microbiology

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