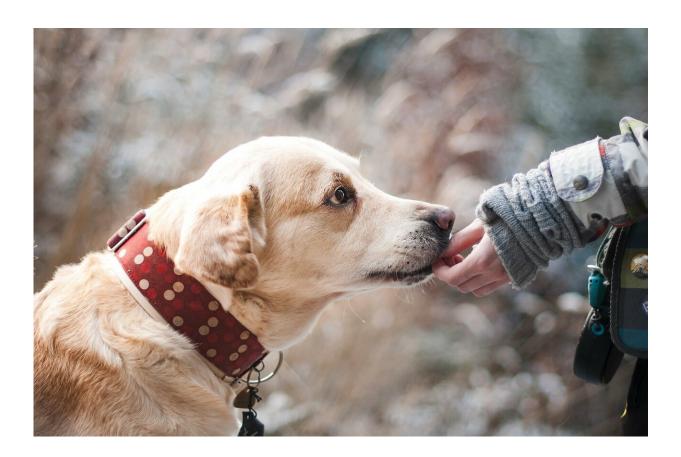


E. coli variant may cause antimicrobial resistance in dogs, humans

July 16 2024



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Researchers studying antimicrobial-resistant E. coli—the leading cause of human death due to antimicrobial resistance worldwide—have identified a mechanism in dogs that may render multiple antibiotic



classes ineffective.

The <u>paper</u>, which was published July 16 in the journal *Applied and Environmental Microbiology*, opens up new avenues for therapies to treat both animals and humans—and establishes clinical infections in dogs as a surveillance approach for public health.

The research team analyzed more than 1,000 genomes of the resistant E. coli pathogen isolated from sick dogs and identified a set of genes that evolutionary selection tests revealed were becoming obsolete in the genome and were losing function. But in an unusual twist, the loss of function may have repurposed this set of genes to create conditions that trap antibiotics in E. coli's cell membrane, preventing them from entering the bacteria.

"I like to think of it as a serendipitous event of evolution, because it appears that these capsule proteins have been repurposed to trap antibiotics," said Laura Goodman, assistant professor at Cornell University and the paper's senior author.

"What appears to be happening is that we're looking at a loss of function mutation that is potentially conferring a new phenotype unrelated to its original purpose," she said.

This study may not only help improve canine health but is also an example of how dogs serve as an important model for <u>human health</u>.

Dogs tend to share similar E. coli strains as their owners and are treated with similar antibiotics. Two particular classes of antibiotics—third generation cephalosporins and quinolones—are considered critically important by the World Health Organization.

Clinicians and <u>public health</u> experts are particularly concerned about



overuse of these drugs in <u>veterinary medicine</u>; although there are no <u>legal restrictions</u> on using these drugs in dogs, big efforts have been made to promote good stewardship of these treatments.

The researchers hypothesized that mechanisms affecting those classes of drugs identified in dogs would also be important for humans, Goodman said. "When we looked for this genetic variant in human infections, we found many of them in hospital and public surveillance data of E. coli and Klebsiella infections in people," she said.

Researchers may now explore potential new <u>drug</u> targets that would prevent the pore in the E. coli membrane channel from closing, allowing antibiotics to freely move inside the cell.

The study is unique in that it provides a mechanistic understanding of antibiotic resistance and fills important gaps in surveillance for human E. coli infections using leftover clinical samples from <u>dogs</u> that were collected as part of routine care, Goodman said.

The study was performed in collaboration with the U.S. Food and Drug Administration's Veterinary Laboratory and Response Network.

More information: Evolutionary genomic analyses of canine E. coli infections identify a relic capsular locus associated with resistance to multiple classes of antimicrobials, *Applied and Environmental Microbiology* (2024). DOI: 10.1128/aem.00354-24

Provided by Cornell University

Citation: E. coli variant may cause antimicrobial resistance in dogs, humans (2024, July 16) retrieved 16 July 2024 from <u>https://phys.org/news/2024-07-coli-variant-antimicrobial-resistance-</u>



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