New resistance gene found in 'high risk' multidrug-resistant pathogen

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A team of Italian investigators has discovered a new variant of an emerging antibiotic resistance mechanism. The new variant, dubbed mcr-1.2, confers resistance to colistin, a last-resort antibiotic against multidrug-resistant Gram-negative pathogens. The research is published July 11, in *Antimicrobial Agents and Chemotherapy*, a journal of the American Society for Microbiology.

"This is a particularly worrisome development for the future of antimicrobial therapy," said corresponding author Gian Maria Rossolini, M.D., Director of the Clinical Microbiology and Virology Unit, Florence Careggi University Hospital, Florence. More worrying is that the new resistance mechanism was discovered on a multidrug-resistant strain of the pathogen Klebsiella pneumoniae, she added. That bacterium was isolated from a rectal swab of a child hospitalized with leukemia.

The investigators found the bacterium to be resistant to an unusual combination of antibiotics, said Rossolini. Noticing an odd resistance profile, first author Vincenzo Di Pilato, Ph.D., reanalyzed the genome data from the bacterium, and discovered the new gene, which is a variant on the colistin-resistant gene, mcr-1. Di Pilato is a senior research fellow at the University of Florence.

mcr-1 was first reported in China in late 2015. Since then it has been reported in several countries worldwide, mostly in Escherichia coli.

Like mcr-1, mcr-1.2 is carried on a plasmid. Plasmids are small pieces

of genetic material that exist independently of chromosomal DNA, but which are replicated every time the bacterium divides. They are pieces of genetic material that can be transferred from one bacterium to another, and even from one species of bacterium to another.

In this case, the patient from whom the bacterium was isolated had not been exposed to colistin. Rossolini said that it could have been transferred from E. coli, as unlike K. pneumoniae, that bacterium frequently carries mcr genes.

This is the first time an mcr-type gene has been found on a "high risk" clone of K. pneumoniae, said Rossolini. "Until now, only a few cases of human infections caused by carbapenemase-producing mcr-positive strains of E. coli and K. pneumoniae have been reported," the investigators write. Carbapenemase confers resistance to the critically important beta-lactam antibiotics. "Carbapenemase-producing strains are often resistant to many antibiotics except colistin and few others," said Rossolini, adding that the combination of the two forms of resistance is very concerning.

"'High risk' means that these multidrug-resistant clones retain a remarkable ability to disseminate in the clinical setting, and to cause infections," Rossolini explained. He added that multidrug resistant strains frequently are not high risk strains, as they are less able to spread than their drug-susceptible counterparts, making this discovery particularly concerning.

More information: Vincenzo Di Pilato et al, MCR-1.2: a new MCR variant encoded by a transferable plasmid from a colistin-resistant KPC carbapenemase-producingof sequence type 512, *Antimicrobial Agents and Chemotherapy* (2016). DOI: 10.1128/AAC.01075-16