



# Genome Analysis of the Carbapenem- and Colistin-Resistant *Escherichia coli* Isolate NRZ14408 Reveals Horizontal Gene Transfer Pathways towards Panresistance and Enhanced Virulence

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Colistin is used as a last-resort antibiotic for treating infections caused by multidrug-resistant members of the family *Enterobacteriaceae*, in particular for carbapenem-resistant isolates. Resistance to colistin in *Enterobacteriaceae* species has been attributed to chromosomal mutations (1), but recently a plasmid-encoded colistin resistance gene, *mcr-1*, was described in isolates from different sources and in many countries worldwide (2, 3). The emergence of plasmid-encoded colistin resistance is critical, as its transfer could render carbapenem-resistant bacteria pandrug resistant, resulting in virtually untreatable pathogens.

We recently reported the first *mcr-1/bla<sub>KPC-2</sub>*-encoding carbapenem-resistant *Escherichia coli* isolate (NRZ14408) from a patient with a wound infection (4). In order to characterize the isolate, we sequenced the whole genome to completion (see the supplemental material).

*E. coli* NRZ14408 harbored a chromosome of 5,344,876 bp with a GC content of 50.65%, four plasmids of about 12 to 238 kbp (p14408\_M, p14408\_1, p14408\_2, and p14408\_3; see Table S1 in the supplemental material), and two phages of 41 and 19 kbp (14408\_1, 14408\_2; see Table S1 in the supplemental material). *E. coli* NRZ14408 is an O7:H6 isolate of multilocus sequence type 362 (ST362) and phylogenetic group D, which is associated with extraintestinal infections (5).

Plasmid p14408\_3 harbored no antibiotic resistance genes but did have colicin R genes (*cra*, *cri*, and *crl*) and the *mobC* gene for mobilization of the plasmid. The *mcr-1* gene was flanked by two IS*ApI1* elements and located on an IncHI2 plasmid (p14408\_M) with high similarity to other *mcr-1*-encoding IncHI2 plasmids (pHNSHP45-2 [accession no. KU341381.1], pSA26-MCR-1 [KU743384.1], and pS38 [KX129782]). p14408\_M differed from these plasmids by the presence of five additional insertion sequences (IS*kpn11*, IS*kpn12*, IS*Aba14*, and two copies of IS629; Fig. 1) and a different set of antibiotic resistance genes (see Table S2 in the supplemental material). Plasmids p14408\_1 and p14408\_2 harbored the same 36,152-bp region, including nine antibiotic resistance genes (see Table S1 in the supplemental material) and a large portion of the

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#### SUPPLEMENTAL MATERIAL

Supplemental material for this article may be found at <https://doi.org/10.1128/AAC.02359-16>.

**TEXT S1**, PDF file, 0.5 MB.

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