



**HAL**  
open science

## **MCR-1 in ESBL-producing Escherichia coli responsible for human infections in New Caledonia**

Frederic Robin, Racha Beyrouthy, Julien Colot, Pierre Saint-Sardos, Anne Berger-Carbonne, Guillaume Dalmasso, Julien Delmas, Richard Bonnet

► **To cite this version:**

Frederic Robin, Racha Beyrouthy, Julien Colot, Pierre Saint-Sardos, Anne Berger-Carbonne, et al.. MCR-1 in ESBL-producing Escherichia coli responsible for human infections in New Caledonia. Journal of Antimicrobial Chemotherapy, 2017, 72 (3), pp.946-947. 10.1093/jac/dkw508 . hal-01604766

**HAL Id: hal-01604766**

**<https://hal.science/hal-01604766>**

Submitted on 16 Nov 2018

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Copyright

framework of the monitoring. We also thank the team of the Institute of Animal Hygiene and Environmental Health of the Free University of Berlin for providing reference strains R29 and R178 and Dr Jens Hammerl for scientific advice.

## Funding

This work was supported by the Federal Institute for Risk Assessment (BfR) (BfR-43-001) and the RESET II Project (FKZ01KI1313B; German Federal Ministry for Education and Research).

## Transparency declarations

None to declare.

## Supplementary data

Figures S1 and S2 are available as Supplementary data at JAC Online (<http://jac.oxfordjournals.org/>).

## References

- 1 WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance. *Critically Important Antimicrobials for Human Medicine, 3rd Revision 2011*. Geneva, Switzerland: WHO, 2012. [http://apps.who.int/iris/bitstream/10665/77376/1/9789241504485\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/77376/1/9789241504485_eng.pdf).
- 2 Tangden T, Giske CG. Global dissemination of extensively drug-resistant carbapenemase-producing Enterobacteriaceae: clinical perspectives on detection, treatment and infection control. *J Intern Med* 2015; **277**: 501–12.
- 3 Guerra B, Fischer J, Helmuth R. An emerging public health problem: acquired carbapenemase-producing microorganisms are present in food-producing animals, their environment, companion animals and wild birds. *Vet Microbiol* 2014; **171**: 290–7.
- 4 Fischer J, San Jose M, Roschanski N *et al*. Spread and persistence of VIM-1 carbapenemase-producing Enterobacteriaceae in three German swine farms in 2011 and 2012. *Vet Microbiol* 2016; doi: 10.1016/j.vetmic.2016.04.026.
- 5 Fischer J, Rodríguez I, Schmoger S *et al*. *Escherichia coli* producing VIM-1 carbapenemase isolated on a pig farm. *J Antimicrob Chemother* 2012; **67**: 1793–5.
- 6 Kaesbohrer A, Schroeter A, Tenhagen B-A *et al*. Emerging antimicrobial resistance in commensal *Escherichia coli* with public health relevance. *Zoonoses Public Health* 2012; **59** Suppl 2: 158–65.
- 7 Rodriguez I, Barownick W, Helmuth R *et al*. Extended-spectrum  $\beta$ -lactamases and AmpC  $\beta$ -lactamases in ceftiofur-resistant *Salmonella enterica* isolates from food and livestock obtained in Germany during 2003–07. *J Antimicrob Chemother* 2009; **64**: 301–9.

*J Antimicrob Chemother* 2017

doi:10.1093/jac/dkw508

Advance Access publication 24 December 2016

## MCR-1 in ESBL-producing *Escherichia coli* responsible for human infections in New Caledonia

Frederic Robin<sup>1,2†</sup>, Racha Beyrouthy<sup>1,2†</sup>, Julien Colot<sup>3</sup>, Pierre Saint-Sardos<sup>1</sup>, Anne Berger-Carbonne<sup>4</sup>, Guillaume Dalmasso<sup>1</sup>, Julien Delmas<sup>1</sup> and Richard Bonnet<sup>1,2\*</sup>

<sup>1</sup>Clermont Université, Université d'Auvergne, Inserm U1071, INRA USC2018, Clermont-Ferrand, France; <sup>2</sup>French National Reference Centre for Antibiotic Resistance, Bacteriology Laboratory, University Hospital of Clermont-Ferrand, Clermont-Ferrand, France; <sup>3</sup>Institut Pasteur in New Caledonia, Nouméa, New Caledonia; <sup>4</sup>Santé Public, Saint-Maurice, France

\*Corresponding author. Tel: +33-(0)4-73-754-920; Fax: +33-(0)4-73-754-921; E-mail: rbonnet@chu-clermontferrand.fr  
†These authors contributed equally.

Sir,

Following the report on the plasmid-mediated colistin resistance gene *mcr-1* in Enterobacteriaceae in China from multiple sources,<sup>1</sup> this gene has been observed in *Escherichia coli*, *Klebsiella* spp., *Salmonella* spp. and *Shigella* spp. isolates, mostly of animal origin.<sup>1–6</sup> It has also been detected in humans in Asia, South-East Asia, Europe, the Middle East, North Africa and North and South America.<sup>6</sup>

In order to study the plasmid-mediated colistin resistance gene *mcr-1* in Enterobacteriaceae isolated from clinical specimens in France, we performed retrospective screening in a database of 610 whole-genome sequences of ESBL-producing Enterobacteriaceae isolates collected in French hospitals.

The bacterial collection included consecutive and non-repetitive strains representative of ESBL-producing Enterobacteriaceae observed in clinical samples collected in French hospitals in different geographic areas (Metropolitan France  $n = 210$ , Guadeloupe  $n = 100$ , Guyana  $n = 100$ , Reunion Island  $n = 100$  and New Caledonia  $n = 100$ ). The whole-genome sequences were assembled *de novo* at a  $\geq 60\times$  coverage level from  $2 \times 150$  bp paired-end reads produced by the NextSeq facility (Illumina, San Diego, CA, USA). WGS data were used to characterize the isolates according to antibiotic resistance genes and plasmid incompatibility with the CARD resistance gene database and the website of the Center for Genomic Epidemiology, respectively. The strains were genotyped by MLST using the Warwick University scheme.

We detected gene *mcr-1* in only two *E. coli* isolates, designated NC68 and NC101. These isolates were further tested for

susceptibility to colistin by the broth microdilution method. The MIC of colistin was 4 mg/L for both isolates, as usually observed for *mcr-1*-encoding *E. coli* (all other *E. coli* had MICs  $\leq$  0.25 mg/L).

NC68 belonged to ST617 and contained the plasmid replicons *IncFII*, *IncX1* and *IncI2*. NC101 belonged to ST773 and contained different replicon plasmids (*IncFII*, *IncFIA*, *IncFIB* and *IncI2*). The isolates harboured different resistance genes, in addition to *mcr-1* [*bla*<sub>CTX-M-55</sub>, *aph*(3')-IIa, *catA2*, *folP* and *mcr-1* for NC68 and *bla*<sub>CTX-M-27</sub>, *strA*, *strB*, *aadA5*, *tetAR*, *sulI*, *sulII*, *dfrA17*, *folP*, *mphA*, *ermB* and *mcr-1* for NC101]. The isolates were therefore not related and harboured different plasmids, except plasmids of incompatibility group *IncI2*, which have already been observed in association with gene *mcr-1*.

However, the *IncI2* replicon sequences only shared 98% identity, suggesting the presence of two different *mcr-1*-encoding plasmids, designated pNC68 for strain NC68 and pNC101 for strain NC101. *De novo* assembly of reads and their alignment against the *mcr-1*-encoding plasmids submitted to GenBank revealed that the most closely related plasmid of pNC68 is the *mcr-1*-encoding reference plasmid pHNSHP45.<sup>1</sup> The pNC68 sequence covered 99% of the pHNSHP45 sequence (absence of ORF45) and the shared sequences (63.2 kb) only differed by five single-nucleotide variants (SNVs) (the minimum coverage of SNVs was 60 $\times$  and a 2 kb region containing 27 SNVs located in a transposase-encoding gene was removed). pNC101 differed significantly from pNC68 and pHNSHP45, covering only 86% of their sequences. The shared sequences (54.9 kb) differed by 219 SNVs (the minimum coverage of SNVs was 60 $\times$  and a 1 kb putative recombinant region containing 58 SNVs was removed).

To our knowledge, these data show the first two human infection cases mediated by *mcr-1*-encoding *E. coli* in Oceania. The two isolates came from a Pasteur Institute subcollection of 48 ESBL-producing *E. coli* isolated in the hospital of Noum ea (New Caledonia) in 2014. No clear epidemiological relationships could be traced among these *mcr-1*-positive isolates. NC68 was isolated in April 2014 from ascitic fluid collected from a 42-year-old male hospitalized in an ICU and NC101 was isolated on June 2014 in the maternity department from gastric fluid of a newborn. The patients had no apparent direct contact with animals, had not been treated with colistin and had not recently travelled to other countries.

The two strains were not related and the gene was encoded by two different *IncI2* plasmids, suggesting that these cases are not linked to a clonal diffusion of an *mcr-1*-encoding strain or to a plasmid outbreak. The resulting frequency (4.2% of *mcr-1* producers among ESBL-producing *E. coli*) is unusually high for a human source. Although this frequency needs to be confirmed with a broad and recent collection, the situation we describe is different from those observed in other French hospitals, where no case has been detected using a similar collection comprising 236 ESBL-producing *E. coli* ( $\chi^2$  test,  $P = 0.0016$ ). The analysis of *mcr-1* genetic support in strain NC68 showed a high genetic relatedness with plasmid pHNSHP45, initially reported in China.<sup>1</sup> Although no

direct link was identified, this result suggests that the origin of the specificity could be due to the relative geographical closeness of this area of high *mcr-1* prevalence.

In the context of increasing problems posed by MDR Enterobacteriaceae, particularly those producing carbapenemases, for which colistin is one of the last active antibiotics, national and international recommendations for detection and control of the spread of this new, emerging resistance are necessary.

## Acknowledgements

We are grateful to Alexis Pontvianne and Laurent Guillouard for their technical assistance.

## Funding

This work was supported by the National Institute of Agronomic Research (USC-2018), the Universit  d'Auvergne, France and the Centre Hospitalier Regional Universitaire de Clermont-Ferrand, France and Sant  Publique France.

## Transparency declarations

None to declare.

## References

- 1 Liu Y-Y, Wang Y, Walsh TR *et al.* Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study. *Lancet Infect Dis* 2016; **16**: 161–8.
- 2 Hasman H, Hammerum AM, Hansen F *et al.* Detection of *mcr-1* encoding plasmid-mediated colistin-resistant *Escherichia coli* isolates from human bloodstream infection and imported chicken meat, Denmark 2015. *Euro Surveill* 2015; **20**: pii=30085.
- 3 Falgenhauer L, Waezsada S-E, Yao Y *et al.* Colistin resistance gene *mcr-1* in extended-spectrum  $\beta$ -lactamase-producing and carbapenemase-producing Gram-negative bacteria in Germany. *Lancet Infect Dis* 2016; **16**: 282–3.
- 4 Doumith M, Godbole G, Ashton P *et al.* Detection of the plasmid-mediated *mcr-1* gene conferring colistin resistance in human and food isolates of *Salmonella enterica* and *Escherichia coli* in England and Wales. *J Antimicrob Chemother* 2016; **71**: 2300–5.
- 5 Haenni M, Poirel L, Kieffer N *et al.* Co-occurrence of extended spectrum  $\beta$  lactamase and MCR-1 encoding genes on plasmids. *Lancet Infect Dis* 2016; **16**: 281–2.
- 6 Baron S, Hadjadj L, Rolain J-M *et al.* Molecular mechanisms of polymyxin resistance: knowns and unknowns. *Int J Antimicrob Agents* 2016; **48**: 30193–5.