AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy®

MECHANISMS OF RESISTANCE

Spread of NDM-5 and OXA-181 Carbapenemase-Producing *Escherichia coli* in Chad

Oumar Ouchar Mahamat,[a,b,c] Manon Lounnas,[a,b] Mallorie Hide,[b] Abelsalam Tidjani,[d] Julio Benavides,[e] Abibatou Diack,[b] Calèbe Somasse,[a,b] Kadidja Gamougam,[f] Christian Carrière,[a,b] Dominique Decré,[g,h] Anne-Laure Bañuls,[b,i] Hélène Jean-Pierre,[a,b] Yann Dumont,[a,b] Fabrice Compain,[j,k] Sylvain Godreuil[a,b,i]

[a]Laboratoire de Bactériologie, Centre Hospitalier Universitaire de Montpellier, Montpellier, France
[b]MIVEGEC, IRD, CNRS, Université de Montpellier, Montpellier, France
[c]Service de laboratoire Hôpital de la Mère et de l'Enfant, N'Djamena, Chad
[d]Faculté de Médecine, Université de N'Djaména, N'Djamena, Chad
[e]Departamento de Ecología y Biodiversidad, Facultad de Ciencias de la Vida, Universidad Andrés Bello, Santiago, Chile
[f]Service de laboratoire, Hôpital Général des Références Nationale, N'Djamena, Chad
[g]Assistance Publique des Hôpitaux de Paris, Hôpitaux Universitaires Est Parisiens, Paris, France
[h]Université Pierre et Marie Curie, Sorbonne Université, Paris, France
[i]Laboraoire Mixte International, DRISA, IRD, Montpellier, France
[j]Service de Microbiologie, Assistance Publique-Hôpitaux de Paris, Hôpital Européen Georges Pompidou, Paris, France
[k]Université Paris Descartes, Sorbonne Paris Cité, Paris, France

ABSTRACT We detected for the first time bla_{NDM-5} and $bla_{OXA-181}$ in *Escherichia coli* isolates from hospitalized patients and healthy volunteers in Chad. These resistance genes were located on IncX3 and IncF plasmids. Despite the large diversity of *E. coli* clones, the identified resistant intestinal isolates belonged mainly to the same sequence type.

KEYWORDS carbapenemases, *Escherichia coli*, clinical samples, fecal carriage prevalence, Chad

The rapid spread of carbapenemase-producing *Enterobacteriaceae* (CPE) represents a serious public health problem because carbapenems are the last antibiotics available to treat infections caused by multidrug-resistant (MDR) Gram-negative bacilli (1). To date, CPE emergence and dissemination have been described worldwide, but reports on CPE in Africa are rare, thus limiting our knowledge on the need of alternative strategies to treat patients infected by these bacteria (2). The few reports on CPE in Central Africa highlighted the presence of CPE isolates that produce NDM-4 in Cameroon, OXA-181 and NDM-1 in Angola, and NDM-7 in Gabon (2). Here, we determined the prevalence and genetic characteristics of CPE isolated from clinical and fecal carriage samples of hospitalized patients and healthy volunteers in Chad.

From January to the end of March 2017, 197 (inpatients, $n = 133$; outpatients, $n = 64$) nonduplicate *Enterobacteriaceae* and clinically significant bacteria were isolated from clinical samples processed in three main hospitals of N'Djamena, Chad. In the same period, 200 fecal samples (100 from patients hospitalized for more than 48 h and 100 from healthy volunteers in the community) were screened for CPE carriage using the selective medium ChromID Carba Smart plates (bioMérieux, Marcy-l'Etoile, France). Disk diffusion antimicrobial susceptibility testing (AST) of all clinical and fecal samples using the EUCAST guidelines and clinical breakpoints (http://www.eucast.org/) identified 18 potential CPE isolates (Table 1), and this finding was confirmed by PCR analysis. All 18 isolates were identified as *Escherichia coli* by matrix-assisted laser desorption ionization–time of flight (MALDI-TOF) mass spectrometry (Bruker Daltonics). The prev-

Citation Ouchar Mahamat O, Lounnas M, Hide M, Tidjani A, Benavides J, Diack A, Somasse C, Gamougam K, Carrière C, Decré D, Bañuls A-L, Jean-Pierre H, Dumont Y, Compain F, Godreuil S. 2019. Spread of NDM-5 and OXA-181 carbapenemase-producing *Escherichia coli* in Chad. Antimicrob Agents Chemother 63:e00646-19. https://doi.org/10.1128/AAC.00646-19.

Address correspondence to Oumar Ouchar Mahamat, ouchar10@yahoo.fr.

Y.D., F.C., and S.G. contributed equally to this article.

Received 27 March 2019
Returned for modification 23 April 2019
Accepted 19 July 2019

Accepted manuscript posted online 12 August 2019
Published 22 October 2019

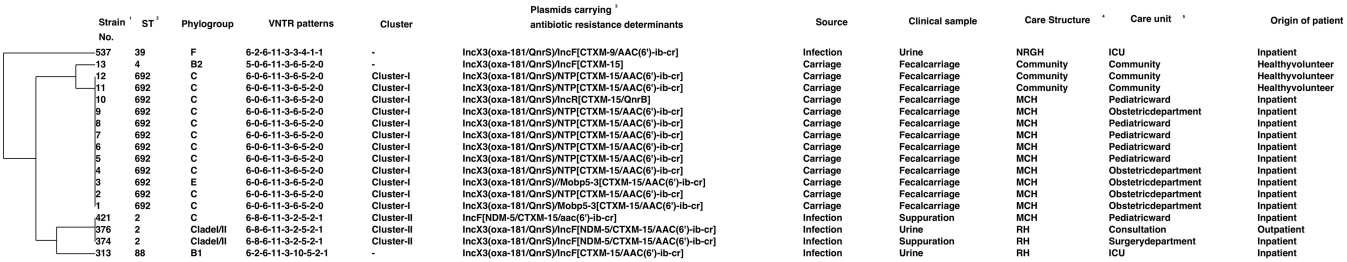
TABLE 1 Characteristics and resistance genes of carbapenemase-producing *E. coli* isolates recovered from clinical and fecal carriage samples

		Carbapenem MICs (mg/liter) for:[a]					PCR detection of antimicrobial resistance genes[b]					
Source	Isolate	ETP	IPM	MRM	DOR	ST	Carbapenemase	ESBL	PMQR genes	16S rRNA methylase	Other β-lactamases	Resistance to non-beta-lactams[c]
Clinical	313	32	4	32	4	88	OXA-181	CTXM-15	*qnrS*, *aac(6′)-Ib-cr*	*armA*	TEM-1/OXA-1	NA, OFX, CIP, LEV, CN, TOB, N, AK, TET, SXT
	374	32	4	32	6	2	OXA-181/NDM-5	CTXM-15	*aac(6′)-Ib-cr*		TEM-1/OXA-1	NA, OFX, CIP, LEV, CN, TOB, N, AK, TET, SXT
	376	32	4	32	4	2	OXA-181/NDM-5	CTXM-15	*aac(6′)-Ib-cr*		TEM-1/OXA-1	NA, OFX, CIP, LEV, CN, TOB, N, AK, TET, SXT
	421	32	3	32	2	2	NDM-5	CTXM-15	*aac(6′)-Ib-cr*		TEM-1/OXA-1	NA, OFX, CIP, LEV, CN, TOB, N, AK, TET, SXT
	537	0.5	0.5	0.19	4	39	OXA-181	CTXM9	*qnrS*			NA, OFX, CIP, LEV, TET, SXT
Carriage	1	2	0.25	0.38	0.19	692	OXA-181	CTXM-15	*qnrS*, *aac(6′)-Ib-cr*		TEM-1/OXA-1	NA, OFX, CIP, LEV, CN, TOB, TET, SXT
	2	2	0.38	0.25	0.25	692	OXA-181	CTXM-15	*qnrS*, *aac(6′)-Ib-cr*		TEM-1/OXA-1	NA, OFX, CIP, LEV, CN, TOB, TET, SXT
	3	1.25	0.25	0.25	0.25	692	OXA-181	CTXM-15	*qnrS*, *aac(6′)-Ib-cr*		TEM-1/OXA-1	NA, OFX, CIP, LEV, CN, TOB, TET, SXT
	4	1.25	0.25	0.38	0.91	692	OXA-181	CTXM-15	*qnrS*, *aac(6′)-Ib-cr*		TEM-1/OXA-1	NA, OFX, CIP, LEV, CN, TOB, TET, SXT
	5	3	0.38	0.5	0.25	692	OXA-181	CTXM-15	*qnrS*, *aac(6′)-Ib-cr*		TEM-1/OXA-1	NA, OFX, CIP, LEV, CN, TOB, N, TET, SXT
	6	0.12	0.25	0.03	0.03	692	OXA-181	CTXM-15	*qnrS*, *aac(6′)-Ib-cr*		TEM-1/OXA-1	NA, OFX, CIP, LEV, CN, TOB, N, TET, SXT
	7	0.01	2	0.12	0.19	692	OXA-181	CTXM-15	*qnrS*, *aac(6′)-Ib-cr*, *oqxAB*		TEM-1/OXA-1	NA, OFX, CIP, LEV, CN, TOB, TET, SXT
	8	0.01	1.5	0.12	0.19	692	OXA-181	CTXM-15	*qnrS*, *aac(6′)-Ib-cr*		TEM-1/OXA-1	NA, OFX, CIP, LEV, CN, TOB, TET, SXT
	9	1	0.38	0.38	0.12	692	OXA-181	CTXM-15	*qnrS*, *aac(6′)-Ib-cr*		TEM-1/OXA-1	NA, OFX, CIP, LEV, CN, TOB, N, TET, SXT
	10	0.06	0.19	0.03	0.03	692	OXA-181	CTXM-15	*qnrS*, *qnrB*, *aac(6′)-Ib-cr*		TEM-1/OXA-1	NA, OFX, CIP, LEV, CN, TOB, N, TET, SXT
	11	2	0.25	0.25	0.12	692	OXA-181	CTXM-15	*qnrS*, *aac(6′)-Ib-cr*		TEM-1/OXA-1	NA, OFX, CIP, LEV, CN, TOB, N, TET, SXT
	12	1	0.5	0.5	0.12	692	OXA-181	CTXM-15	*qnrS*, *aac(6′)-Ib-cr*		TEM-1/OXA-1	NA, OFX, CIP, LEV, CN, TOB, N, TET, SXT
	13	0.5	0.38	0.38	0.12	4	OXA-181	CTXM-15	*qnrS*		TEM-1/OXA-1	TET, SXT

[a]ETP, ertapenem; IPM, imipenem; MEM, meropenem; DOR, doripenem. The MICs of ertapenem, imipenem, meropenem, and doripenem were determined using the Etest method (bioMérieux), and the MIC of colistin was determined using the broth microdilution method.

[b]ESBL, extended-spectrum β-lactamase; PMQR, plasmid-mediated quinolone resistance.

[c]NA, nalidixic acid; OFX, ofloxacin; CIP, ciprofloxacin; LEV, levofloxacin; CN, gentamicin; TOB, tobramycin, N, netilmicin; AK, amikacin; TET, tetracycline; SXT, trimethoprim-sulfamethoxazole.



Strain No.	ST	Phylogroup	VNTR patterns	Cluster	Plasmids carrying antibiotic resistance determinants	Source	Clinical sample	Care Structure	Care unit	Origin of patient
537	39	F	6-2-6-11-3-3-4-1-1	-	IncX3(oxa-181/QnrS)/IncF[CTXM-9/AAC(6')-ib-cr]	Infection	Urine	NRGH	ICU	Inpatient
13	4	B2	5-0-6-11-3-6-5-2-0	-	IncX3(oxa-181/QnrS)/IncF[CTXM-15]	Carriage	Fecalcarriage	Community	Community	Healthyvolunteer
12	692	C	6-0-6-11-3-6-5-2-0	Cluster-I	IncX3(oxa-181/QnrS)/NTP[CTXM-15/AAC(6')-ib-cr]	Carriage	Fecalcarriage	Community	Community	Healthyvolunteer
11	692	C	6-0-6-11-3-6-5-2-0	Cluster-I	IncX3(oxa-181/QnrS)/NTP[CTXM-15/AAC(6')-ib-cr]	Carriage	Fecalcarriage	Community	Community	Healthyvolunteer
10	692	C	6-0-6-11-3-6-5-2-0	Cluster-I	IncX3(oxa-181/QnrS)/IncR[CTXM-15/QnrB]	Carriage	Fecalcarriage	MCH	Pediatricward	Inpatient
9	692	C	6-0-6-11-3-6-5-2-0	Cluster-I	IncX3(oxa-181/QnrS)/NTP[CTXM-15/AAC(6')-ib-cr]	Carriage	Fecalcarriage	MCH	Obstetricdepartment	Inpatient
8	692	C	6-0-6-11-3-6-5-2-0	Cluster-I	IncX3(oxa-181/QnrS)/NTP[CTXM-15/AAC(6')-ib-cr]	Carriage	Fecalcarriage	MCH	Pediatricward	Inpatient
7	692	C	6-0-6-11-3-6-5-2-0	Cluster-I	IncX3(oxa-181/QnrS)/NTP[CTXM-15/AAC(6')-ib-cr]	Carriage	Fecalcarriage	MCH	Pediatricward	Inpatient
6	692	C	6-0-6-11-3-6-5-2-0	Cluster-I	IncX3(oxa-181/QnrS)/NTP[CTXM-15/AAC(6')-ib-cr]	Carriage	Fecalcarriage	MCH	Pediatricward	Inpatient
5	692	C	6-0-6-11-3-6-5-2-0	Cluster-I	IncX3(oxa-181/QnrS)/NTP[CTXM-15/AAC(6')-ib-cr]	Carriage	Fecalcarriage	MCH	Pediatricward	Inpatient
4	692	C	6-0-6-11-3-6-5-2-0	Cluster-I	IncX3(oxa-181/QnrS)/NTP[CTXM-15/AAC(6')-ib-cr]	Carriage	Fecalcarriage	MCH	Obstetricdepartment	Inpatient
3	692	E	6-0-6-11-3-6-5-2-0	Cluster-I	IncX3(oxa-181/QnrS)//Mobp5-3[CTXM-15/AAC(6')-ib-cr]	Carriage	Fecalcarriage	MCH	Obstetricdepartment	Inpatient
2	692	C	6-0-6-11-3-6-5-2-0	Cluster-I	IncX3(oxa-181/QnrS)/NTP[CTXM-15/AAC(6')-ib-cr]	Carriage	Fecalcarriage	MCH	Obstetricdepartment	Inpatient
1	692	C	6-0-6-11-3-6-5-2-0	Cluster-I	IncX3(oxa-181/QnrS)/Mobp5-3[CTXM-15/AAC(6')-ib-cr]	Carriage	Fecalcarriage	MCH	Obstetricdepartment	Inpatient
421	2	C	6-8-6-11-3-2-5-2-1	Cluster-II	IncF[NDM-5/CTXM-15/aac(6')-ib-cr]	Infection	Suppuration	MCH	Pediatricward	Inpatient
376	2	Cladel/II	6-8-6-11-3-2-5-2-1	Cluster-II	IncX3(oxa-181/QnrS)/IncF[NDM-5/CTXM-15/AAC(6')-ib-cr]	Infection	Urine	RH	Consultation	Outpatient
374	2	Cladel/II	6-8-6-11-3-2-5-2-1	Cluster-II	IncX3(oxa-181/QnrS)/IncF[NDM-5/CTXM-15/AAC(6')-ib-cr]	Infection	Suppuration	RH	Surgerydepartment	Inpatient
313	88	B1	6-2-6-11-3-10-5-2-1	-	IncX3(oxa-181/QnrS)/IncF[CTXM-15/AAC(6')-ib-cr]	Infection	Urine	RH	ICU	Inpatient

FIG 1 UPGMA dendrogram based on the variable-number tandem-repeat (VNTR) (9 loci) and MLST data for the 18 CPEc isolates. The relationships between patterns were assessed using the UPGMA hierarchical clustering method. ST, sequence type; NTP, nontypeable plasmid; HGRN, National Reference General Hospital; RH, Renaissance Hospital; MCH, Mother and Child Hospital; ICU, Intensive Care Unit.

alence of carbapenemase-producing *E. coli* (CPEc) was 2.5% (5/197) in clinical samples, and 6.5% (13/200) in fecal carriage samples ($n = 3$ samples from healthy volunteers and $n = 10$ samples from patients; $P < 0.001$). These results are in agreement with previous literature data and confirm stronger selective antibiotic pressure and bacterial transmission in inpatients (3, 4). The presence of CPE in fecal samples from healthy volunteers is alarming, potentially increasing the risk of community-acquired CPE infections.

Besides resistance to broad-spectrum cephalosporins, all 18 CPE isolates were also frequently resistant to ciprofloxacin (94%), gentamicin (89%), amikacin (22%), and trimethoprim-sulfamethoxazole (100%) and remained susceptible to fosfomycin, chloramphenicol, and colistin.

The presence of genes encoding antibiotic resistance determinants was assessed using multiplex PCR followed by sequencing (see primers and references in Table S1 in the supplemental material). Among the five clinical CPEc isolates, two carried the $bla_{\text{OXA-181}}$ gene, one carried the $bla_{\text{NDM-5}}$ gene, and two carried both genes. All 13 CPEc isolates from fecal carriage samples harbored the $bla_{\text{OXA-181}}$ gene. Associated resistance determinants are reported in Table 1.

Genotyping data obtained by multilocus sequence typing (MLST) (http://bigsdb.web.pasteur.fr/), variable-number tandem-repeat typing (5), and the unweighted pair group method with arithmetic mean (UPGMA) hierarchical clustering allowed for the assessment of the genetic relationships among the 18 CPEc isolates. The dendrogram was elaborated based on the Nei's distance using the Phylip and Populations packages and visualized with TreeDyn (with annotations). The dendrogram highlighted the presence of two clusters (I and II) and three unique profiles (Fig. 1). Cluster I included 12 CPEc isolates from fecal carriage samples ($n = 10$ from inpatients and $n = 2$ from healthy volunteers) that belonged to sequence type 692 (ST692) and harbored the $bla_{\text{OXA-181}}$ gene. Cluster II was composed of three CPEc clinical isolates that belonged to ST2 and harbored the $bla_{\text{NDM-5}}$ gene alone or with the $bla_{\text{OXA-181}}$ gene. The CPEc isolates that belonged to ST4 (one fecal sample from a volunteer), ST39, and ST88 (one clinical sample each for ST39 and ST88) formed three unique profiles. The high number of CPEc isolates included in the two clusters (15/18; 83%) could reflect the importance of interhuman transmission of these multidrug-resistant bacteria in Chad. Analysis of the patients' medical records suggested a probable nosocomial outbreak among the ten patients (samples 1 to 10) from cluster I (Fig. 1) because they were in the same hospital at the same time. Phylogroups were also determined based on the PCR method developed by Clermont et al. (6), and most strains (14/18, 78%) belonged to commensal clones B1 and C (Fig. 1).

Mating experiments performed using the azide-resistant *E. coli* strain J53 as the recipient were successful for most of the isolates. In the case of transfer failure, plasmid DNA was extracted using the GeneJet plasmid miniprep kit (7) and transferred by electroporation into *E. coli* DH10B (Invitrogen, Cergy-Pontoise, France) (8). Plasmids were characterized by PCR-based replicon typing and plasmid relaxase gene typing (PRaseT) (9). PRaseT showed that $bla_{\text{OXA-181}}$ was located on IncX3 plasmids, and

bla_{NDM-5}, $bla_{CTX-M-9}$, and $bla_{CTX-M-15}$ were located on IncF plasmids in all clinical isolates. In most fecal isolates, the $bla_{CTX-M-15}$ gene was located on a nontypeable plasmid, except for four isolates where it was located on an IncF, IncR, or Mobp5-3 plasmid (Fig. 1).

Overall, our results revealed that most CPEc isolates (12/18; 67%) were *E. coli* ST692 harboring the $bla_{OXA-181}$ gene carried by the IncX3 plasmid, as already described in Burkina Faso (10). This suggests the circulation of this clone in sub-Saharan Africa; however, the factors that contribute to this success are still unknown.

We determined the complete sequences of all 17 IncX3 plasmids carrying $bla_{OXA-181}$ using the Oxford Nanopore MinION platform (Oxford Nanopore Technologies). We obtained 51-kb plasmids, which were highly similar (99% nucleotide identity) to pOXA181_EC14828 (GenBank accession no. KP400525), a $bla_{OXA-181}$-harboring plasmid first described in China in 2015 (11). The $bla_{OXA-181}$ gene was found in a 14,107-bp region flanked by two IS*26* elements in direct orientation, with duplicated nucleotides (GT) at both extremities. The PMQR gene *qnrS1* was found downstream of $bla_{OXA-181}$ and was the only other resistance gene found on these plasmids (apart from a truncated *ere* gene). Similar genetic environments were described in plasmids from other countries in Africa, in Europe, and in Asia (4, 10–16).

NDM-5, an NDM variant, was first identified in 2011 in an *E. coli* isolate from a patient in the United Kingdom who traveled to the Indian subcontinent (17) and, since then, has been increasingly detected worldwide. Interestingly, two *E. coli* clones recovered from clinical samples in this study were previously found to coharbor $bla_{OXA-181}$ and bla_{NDM-5} genes in Egypt and Myanmar (18, 19). The high frequency of population movements between Chad, Egypt, and China for medical treatment and economic relationships could promote the dissemination of carbapenemase-encoding genes.

This study shows the alarming CPE circulation in community and hospital environments in Chad. The transmission of MDR bacteria among inpatients could lead to therapeutic deadlocks associated with high mortality rates, especially in Chad where AST is expensive and limited. Our results call for urgent public health efforts to set up educational campaigns on strict infection prevention/control measures targeting the Chadian population and health care professionals and better surveillance to limit the spread of MDR bacteria.

SUPPLEMENTAL MATERIAL

Supplemental material for this article may be found at https://doi.org/10.1128/AAC.00646-19.

SUPPLEMENTAL FILE 1, PDF file, 0.1 MB.

ACKNOWLEDGMENTS

We thank the GenSeq technical facilities of ISEM, Institut des Sciences de l'Evolution de Montpellier and labex Centre Méditerranéen de l'Environnement et de la Biodiversité where some of the sample preparations were performed. We thank Elisabetta Andermarcher for assistance in preparing and editing the manuscript.

We declare no competing interests.

This work was supported by a grant from the Islamic Development Bank (IDB). The IDB was not involved in the study design, collection, analysis, interpretation of data, or in writing the manuscript.

O.O.M., C.C., M.H., H.J.-P., and S.G. conceived and designed the experiments. O.O.M., F.C., M.L., K.G., A.D., and C.S. performed the experiments. O.O.M., F.C., M.L., Y.D., A.T., J.B., D.D., C.C., A.-L.B., and S.G. contributed to the writing of the manuscript. All authors read and approved the final manuscript.

REFERENCES

1. Codjoe FS, Donkor ES. 2018. Carbapenem resistance: a review. Med Sci 6:1. https://doi.org/10.3390/medsci6010001.
2. Mitgang EA, Hartley DM, Malchione MD, Koch M, Goodman JL. 2018. Review and mapping of carbapenem-resistant *Enterobacteriaceae* in Africa: using diverse data to inform surveillance gaps. Int J Antimicrob Agents 52:372–384. https://doi.org/10.1016/j.ijantimicag.2018.05.019.

3. Dossim S, Bonnin RA, Salou M, Tanga K, Godonou V, Dagnra AY, Prince David M, Naas T, Dortet L. 2019. Occurrence of carbapenemase-producing *Enterobacteriaceae* in Togo, West Africa. Int J Antimicrob Agents 53:530–532. https://doi.org/10.1016/j.ijantimicag.2018.11.019.
4. Kieffer N, Nordmann P, Aires-de-Sousa M, Poirel L. 2016. High prevalence of carbapenemase-producing *Enterobacteriaceae* among hospitalized children in Luanda, Angola. Antimicrob Agents Chemother 60:6189–6192. https://doi.org/10.1128/AAC.01201-16.
5. Løbersli I, Haugum K, Lindstedt B-A. 2012. Rapid and high resolution genotyping of all *Escherichia coli* serotypes using 10 genomic repeat-containing loci. J Microbiol Methods 88:134–139. https://doi.org/10.1016/j.mimet.2011.11.003.
6. Clermont O, Christenson JK, Denamur E, Gordon DM. 2013. The Clermont *Escherichia coli* phylo-typing method revisited: improvement of specificity and detection of new phylo-groups. Environ Microbiol Rep 5:58–65. https://doi.org/10.1111/1758-2229.12019.
7. Kado CI, Liu ST. 1981. Rapid procedure for detection and isolation of large and small plasmids. J Bacteriol 145:1365–1373.
8. Folster JP, Pecic G, Stroika S, Rickert R, Whichard J. 2014. Changing plasmid types responsible for extended spectrum cephalosporin resistance in *Escherichia coli* O157:H7 in the United States, 1996–2009. J Glob Antimicrob Resist 2:87–91. https://doi.org/10.1016/j.jgar.2014.01.004.
9. Compain F, Poisson A, Le Hello S, Branger C, Weill F-X, Arlet G, Decré D. 2014. Targeting relaxase genes for classification of the predominant plasmids in *Enterobacteriaceae*. Int J Med Microbiol 304:236–242. https://doi.org/10.1016/j.ijmm.2013.09.009.
10. Ouédraogo A-S, Compain F, Sanou M, Aberkane S, Bouzinbi N, Hide M, Sangaré L, Ouédraogo-Traoré R, Jean-Pierre H, Vendrell J, Solassol J, Decré D, Godreuil S. 2016. First description of IncX3 plasmids carrying $bla_{OXA-181}$ in *Escherichia coli* clinical isolates in Burkina Faso. Antimicrob Agents Chemother 60:3240–3242. https://doi.org/10.1128/AAC.00147-16.
11. Liu Y, Feng Y, Wu W, Xie Y, Wang X, Zhang X, Chen X, Zong Z. 2015. First report of OXA-181-producing *Escherichia coli* in China and characterization of the isolate using whole-genome sequencing. Antimicrob Agents Chemother 59:5022–5025. https://doi.org/10.1128/AAC.00442-15.
12. Poirel L, Aires-de-Sousa M, Kudyba P, Kieffer N, Nordmann P. 2018. Screening and characterization of multidrug-resistant Gram-negative bacteria from a remote African area, São Tomé and Príncipe. Antimicrob Agents Chemother 62:e01021-18. https://doi.org/10.1128/AAC.01021-18.
13. Piazza A, Comandatore F, Romeri F, Pagani C, Floriano AM, Ridolfo A, Antona C, Brilli M, Mattioni Marchetti V, Bandi C, Gismondo MR, Rimoldi SG. 2018. First report of an ST410 OXA-181 and CTX-M-15 coproducing *Escherichia coli* clone in Italy: a whole-genome sequence characterization. Microb Drug Resist 24:1207–1209. https://doi.org/10.1089/mdr.2017.0366.
14. Baek JY, Cho SY, Kim SH, Kang C-I, Peck KR, Song J-H, Chung DR, Ko KS. 2019. Plasmid analysis of *Escherichia coli* isolates from South Korea co-producing NDM-5 and OXA-181 carbapenemases. Plasmid 104:102417. https://doi.org/10.1016/j.plasmid.2019.102417.
15. Zurfluh K, Poirel L, Nordmann P, Klumpp J, Stephan R. 2015. First detection of *Klebsiella variicola* producing OXA-181 carbapenemase in fresh vegetable imported from Asia to Switzerland. Antimicrob Resist Infect Control 4:38. https://doi.org/10.1186/s13756-015-0080-5.
16. Qin S, Cheng J, Wang P, Feng X, Liu H-M. 2018. Early emergence of OXA-181-producing *Escherichia coli* ST410 in China. J Glob Antimicrob Resist 15:215–218. https://doi.org/10.1016/j.jgar.2018.06.017.
17. Hornsey M, Phee L, Wareham DW. 2011. A novel variant, NDM-5, of the New Delhi metallo-β-lactamase in a multidrug-resistant *Escherichia coli* ST648 isolate recovered from a patient in the United Kingdom. Antimicrob Agents Chemother 55:5952–5954. https://doi.org/10.1128/AAC.05108-11.
18. Gamal D, Fernández-Martínez M, El-Defrawy I, Ocampo-Sosa AA, Martínez-Martínez L. 2016. First identification of NDM-5 associated with OXA-181 in *Escherichia coli* from Egypt. Emerg Microbes Infect 5:e30. https://doi.org/10.1038/emi.2016.24.
19. Aung MS, San N, Maw WW, San T, Urushibara N, Kawaguchiya M, Sumi A, Kobayashi N. 2018. Prevalence of extended-spectrum beta-lactamase and carbapenemase genes in clinical isolates of *Escherichia coli* in Myanmar: dominance of bla_{NDM-5} and emergence of $bla_{OXA-181}$. Microb Drug Resist 24:1333–1344. https://doi.org/10.1089/mdr.2017.0387.