Polyclonal Dissemination of OXA-232 Carbapenemase–Producing *Klebsiella pneumoniae*, France, 2013–2021

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During 2013–2021, increased prevalence of oxacillinase 232–producing Enterobacterales was observed in France, mostly driven by its emergence in *Klebsiella pneumoniae*. Whole-genome sequencing identified that oxacillinase 232–producing *K. pneumoniae* belonged to 14 sequence types (STs), among which 2 polyclonal high-risk clones, ST-231 and ST-2096, were overrepresented.

The massive dissemination of carbapenemase-producing Enterobacterales poses a global threat to public health. Carbapenem antibiotics remain the last line of defense against highly resistant Enterobacterales. Carbapenemases have been identified in 3 of the 4 classes of the Ambler classification: class A carbapenemases (mostly *Klebsiella pneumoniae* carbapenemase types) (*1*), class B carbapenemases or metallo-β-lactamases (mostly New Delhi metallo-β-lactamase [NDM], Verona integron-mediated metallo-β-lactamase [VIM], or imipenemase types) (*2*), and class D carbapenemases (mostly oxacillinases [OXAs] of OXA-48 types) (*3*). In France, the most prevalent carbapenemases are of OXA-48 type (*4*). According to the Beta-Lactamase Database (http://www.bldb.eu), >50 OXA-48–like carbapenemase variants have been identified. OXA-48, OXA-162, OXA-181, OXA-232, OXA-204, and OXA-244 are the most common enzymes identified among these carbapenemases (*4*).

OXA-232 differs from OXA-181 by a single amino acid substitution (Arg214Ser), differing itself from OXA-48 by 4 substitutions (Thr104Ala, Asn110Asp, Glu168Gln, and Ser171Ala). OXA-232 has been demonstrated to possess a weaker hydrolytic activity toward carbapenems but a stronger ability to hydrolyze penicillins compared with OXA-48 and OXA-181 (*5*,*6*). The $bla_{\text{OXA-232}}$ gene usually is located on a 6-kb nonconjugative ColE-type plasmid within a truncated Tn*2013*-like transposon (*5*). Furthermore, the genetic environment surrounding the $bla_{\text{OXA-232}}$ gene is comparable to that of the $bla_{\text{OXA-181}}$ gene, suggesting that OXA-232 is derived directly from OXA-181 (*4*).

Previous research has mainly identified OXA-232 in *Escherichia coli* and *K. pneumoniae* isolates and has found that this variant is endemic in China, India, South Korea, and Thailand (*4*,*7*,*8*). For *K. pneumoniae,* several outbreaks have been reported with different sequence types (STs), including ST-14, ST-15, ST-16, ST-23, ST-231, and ST-437 (*4*,*9*–*11*). Moreover, to the best of our knowledge, there are no data from France regarding OXA-232 outbreaks and epidemiology since the first description of 1 *E. coli* ST-2968 and 2 *K. pneumoniae* ST-14 isolates from patients returning to France from India in 2012 (*5*).

In addition, strains coproducing NDM and OXA-232 have been reported in several countries (*12*–*14*). In these strains, bla_{NDM} and $bla_{\text{OXA-232}}$ are carried by 2 different plasmids (*13*). The $bla_{\text{OXA-232}}$ gene is located on a ColE-type plasmid, whereas the bla_{NDM} gene usually is carried by an incF-type plasmid (*8*).

Given the increasing prevalence of OXA-232–producing Enterobacterales in Europe, it is crucial to better understand the driving forces of such

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dissemination. In this study, we used whole-genome sequencing to decipher the epidemiology of OXA-232–producing *K. pneumoniae* in France during 2013–2021.

The Study

During 2013–2021, France's National Reference Centre received 122 nonduplicate OXA-232–producing Enterobacterales, including 99 *K. pneumoniae*, 13 *Citrobacter freundii*, 7 *E. coli*, 2 *K. aerogenes*, and 1 *K. oxytoca* (Figure 1, panel A; Appendix Table 1, https://wwwnc.cdc.gov/EID/article/28/11/20-1040-App1.pdf). These clinical isolates were cultured from rectal swabs (n = 92), urine samples (n = 18), blood cultures (n = 2), respiratory tracts samples (n = 1), and other or unknown origins (n = 9) (Appendix Table 1).

Among these strains, 16 coproduced NDM-1 and 9 coproduced NDM-5 (Figure 1, panel A). Overall, the prevalence of OXA-232 among OXA-48–like producers was significantly higher during 2019–2021 (1.33% among OXA-48–like) compared to 2013–2018 (0.70% among OXA-48–like) (χ^2 test, $p<0.05$) (Figure 1, panel A; Table 2). The prevalence of NDM and OXA-232–coproducing isolates also slightly increased (0.15% among NDM and 0.27% among OXA-48–like from 2013–2018 to 2019–2021) (Figure 1, panel A; Appendix Table 2).

We performed short-read next-generation sequencing on all *K. pneumoniae* strains producing OXA-232 during 2015–2021 (n = 95) using a HiSeq system (Illumina, https://www.illumina.com) and submitted them to GenBank (Appendix Table 1). We assembled Illumina reads using shovill 1.1.0 (https://github.com/tseemann/shovill) and SPAdes 3.14.0 (http://bioinf.spbau.ru/spades) multilocus sequence typing programs, and we performed resistome analysis using pubMLST (https://pubmlst.org) and Resfinder (https://cge.cbs.dtu.dk/services/ResFinder). For phylogenetic analysis, we mapped next-generation sequencing reads to the reference genome (K. pneumoniae HS11286 [GenBank accession no. NC_016845.1]) using SNIppy 4.6.0 (https://software.cqls.oregonstate.edu/updates/snippy-4.6.0). We visualized metadata and phylogenetic trees using iTOL 6.5.2 (https://itol.embl.de).

Among the 95 patients colonized or infected with OXA-232–producing *K. pneumoniae*, 19 had recently returned from Asia (including 15 from India) and 12 from the Middle East. Among *K. pneumoniae* isolates, we identified 14 different STs, 5 of which were

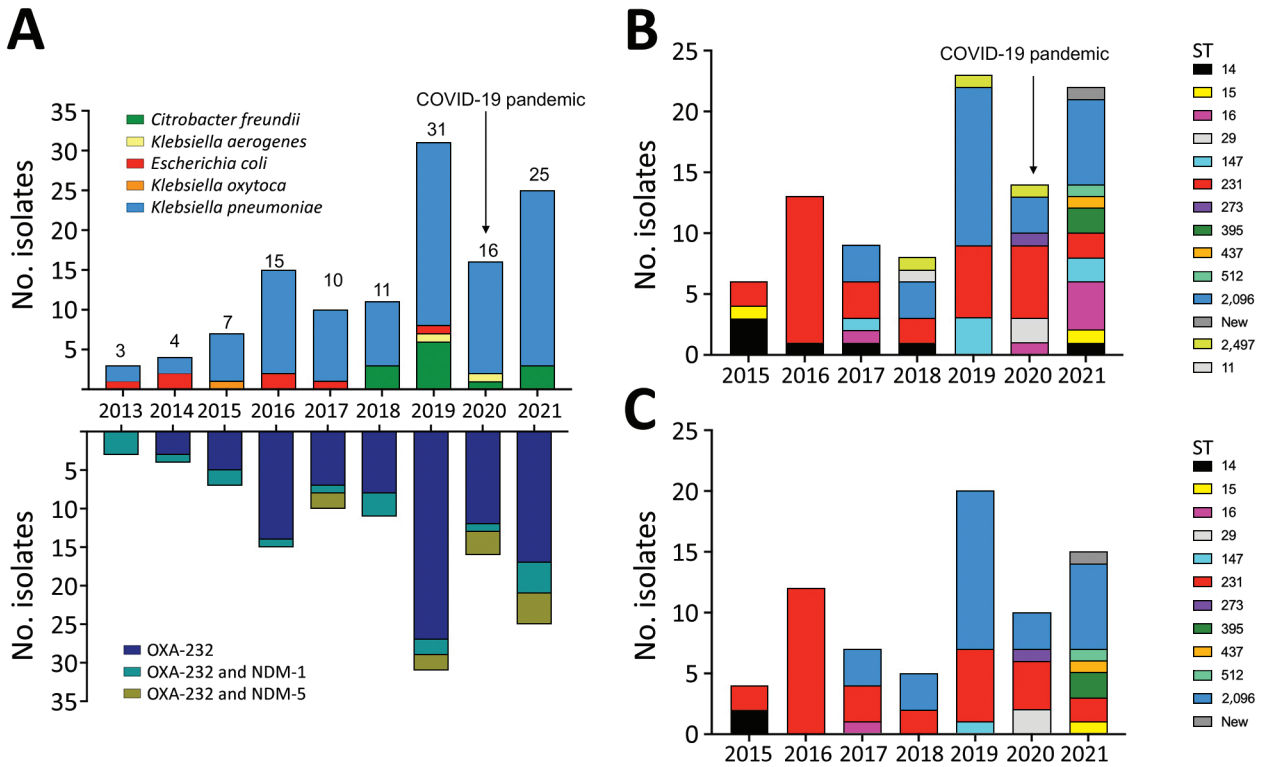

Figure 1. OXA-232–producing Enterobacterales received at the National Reference Center for Carbapenem-Resistant Enterobacterales, France 2013–2021. A) Evolution of several OXA-232–producing Enterobacterales, by species (top of panel) and carbapenemase variant (bottom). B) Evolution of distribution of ST among all OXA-232–producing *K. pneumoniae*. C) Evolution of distribution of ST among NDM and OXA-232–coproducing *K. pneumoniae*. NDM, New Delhi metallo-β-lactamase; OXA, oxacillinase; ST, sequence type.

represented by >5 strains: ST-231 (n = 33), ST-2096 (n = 29), ST-14 (n = 7), ST-16 (n = 6), and ST-147 (n = 6). We observed a diversification in OXA-232–producing *K. pneumoniae* STs over the last 2 years of the study period. In addition, the number of *K. pneumoniae* ST-231 isolates decreased, whereas the number of *K. pneumoniae* ST-2096 isolates increased (Figure 1, panel B). We built single nucleotide polymorphism (SNP) matrices and phylogenetic trees for the 2 main STs (ST-231 and ST-2096) and compared them to epidemiologic data. We considered 2 isolates to be clonally related (probably by cross-transmission) if they differed by <21 SNPs, as previously reported for *K. pneumoniae* clonal complex 258 (*15*). For both STs, we identified many subclones (20 for ST-231 and 21 for ST-2096) (Figure 2), suggesting polyclonal dissemination including within these 2 high-risk clones.

K. pneumoniae coproducing OXA-232 and NDM (NDM-1 or NDM-5) belonged to several STs (ST-14, ST-16, ST-147, ST-231, and ST-2497) but not to ST-2096 (Figure 1, panel C; Figure 2; Appendix Figure). Among the 95 OXA-232–producing *K. pneumoniae*, we identified additional β-lactamases in all strains except 1 (309B8). Eighty-two coproduced Temoniera β-lactamase 1 (32/33 for ST-231 and 25/29 for ST-2096), 86 coproduced the cefotaximase–Munich extended-spectrum β-lactamase 15 (31/33 for ST-231 and 26/29 for ST-2096), and 42 coproduced OXA-1 (0/33 for ST-231 and 25/29 for ST-2096) (Appendix Figure). Furthermore, 3 non–clonally related isolates coproduced the acquired *C. freundii* intrinsic cephalosporinase 6 (ST-231, ST-11, and ST-15) (Appendix Figure). Analysis of the genetic environment revealed that the $bla_{OXA-232}$ was carried by the 6-kb in size ColE-type plasmid as previously described (*5*).

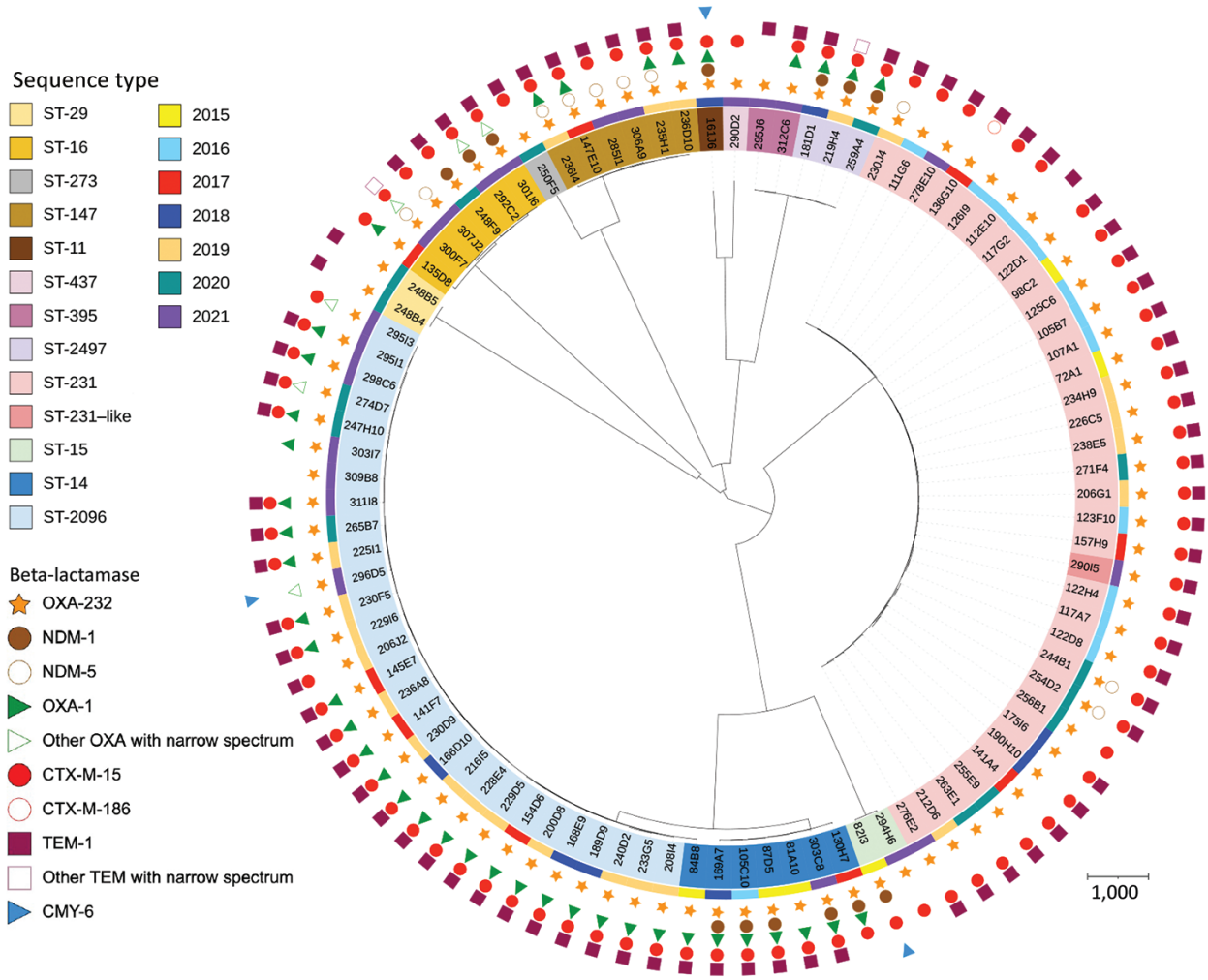

Figure 2. Phylogenetic relationship of OXA-232–producing *K. pneumoniae* ST-231 (A) and ST-2096 (B) analyzed at the National Reference Center for Carbapenem-Resistant Enterobacterales, France 2013–2021.The phylogenetic trees were built with an SNP analysis approach. Scale bars under trees indicate the number of SNPs per position of common sequences. OXA, oxacillinase; SNP, single nucleotide polymorphism; ST, sequence type.

Conclusions

Recent data suggested that the dissemination of OXA-232–producing *K. pneumoniae* is increasing rapidly, especially in Asia and the Middle East (*7*,*11*). In our study, about a third of patients had recently visited 1 of these regions. Furthermore, we observed an increasing number of OXA-232 and NDM coproducers. These isolates are of high concern because of their lack of susceptibility to all antimicrobials, including last-resort combinations such as ceftazidime/avibactam, meropenem/vaborbactam, and imipenem/relebactam.

The OXA-232–producing *K. pneumoniae* isolates that are reported to be responsible for outbreaks usually belonged to ST-231, ST-15, ST-16 and ST-147 (*4*,*9*). In our study, a wide diversity of STs was found, but the 2 main types were ST-231 and ST-2096. ST-231 was widely reported with OXA-232–producing *K. pneumoniae*, but ST-2096 was first reported only recently in India in 2019 (*7*,*9*). ST-2096 in India was also reported to be hypervirulent because it produced characteristic virulence genes such as *rmpA2*, *iutA*, and *iuc* operon (*9*). Our results suggest that the ST-2096 appeared very recently in France (2017). SNPs analysis demonstrated that the emergence and rapid dissemination of ST-2096 OXA-232–producing *K. pneumoniae* is not linked to a single or a few outbreaks. In our collection, 29 of the 30 ST-2096 *K. pneumoniae* isolates produced OXA-232, whereas the remaining isolate did not produce any carbapenemase, suggesting a recent acquisition of $bla_{\text{OXA-232}}$ in this clone.

A recent publication reported an association between ST-2096 and a higher risk for bacteriemia and death (*7*). In our study, the unique isolate responsible for bacteriemia belonged to ST-231. In contrast, 25 of the 29 ST-2096 isolates were cultured from rectal swabs.

As expected, $bla_{\text{OXA-232}}$ was located on a ColE plasmid in all isolates. The close genetic environment of $bla_{\text{OXA-232}}$ involved IS*Ecp1* upstream of the $bla_{\text{OXA-232}}$ gene as previously described (*5*).

About the Author

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References

1. Naas T, Dortet L, Iorga BI. Structural and functional aspects of class a carbapenemases. Curr Drug Targets. 2016;17:1006–28. https://doi.org/10.2174/1389450117666160310144501
2. Mojica MF, Bonomo RA, Fast W. B1-metallo-β-lactamases: where do we stand? Curr Drug Targets. 2016;17:1029–50. https://doi.org/10.2174/1389450116666151001105622
3. Poirel L, Potron A, Nordmann P. OXA-48-like carbapenemases: the phantom menace. J Antimicrob Chemother. 2012;67:1597–606. https://doi.org/10.1093/jac/dks121
4. Pitout JDD, Peirano G, Kock MM, Strydom KA, Matsumura Y. The global ascendency of OXA-48-type carbapenemases. Clin Microbiol Rev. 2019;33:33. https://doi.org/10.1128/CMR.00102-19
5. Potron A, Rondinaud E, Poirel L, Belmonte O, Boyer S, Camiade S, et al. Genetic and biochemical characterisation of OXA-232, a carbapenem-hydrolysing class D β-lactamase from Enterobacteriaceae. Int J Antimicrob Agents. 2013;41:325–9. https://doi.org/10.1016/j.ijantimicag.2012.11.007
6. Oueslati S, Retailleau P, Marchini L, Berthault C, Dortet L, Bonnin RA, et al. Role of arginine 214 in the substrate specificity of OXA-48. Antimicrob Agents Chemother. 2020;64:64. https://doi.org/10.1128/AAC.02329-19
7. Isler B, Özer B, Çınar G, Aslan AT, Vatansever C, Falconer C, et al. Characteristics and outcomes of carbapenemase harbouring carbapenem-resistant *Klebsiella* spp. bloodstream infections: a multicentre prospective cohort study in an OXA-48 endemic setting. Eur J Clin Microbiol Infect Dis. 2022;41:841–7. https://doi.org/10.1007/s10096-022-04425-4
8. Naha S, Sands K, Mukherjee S, Saha B, Dutta S, Basu S. OXA-181-like carbapenemases in *Klebsiella pneumoniae* ST14, ST15, ST23, ST48, and ST231 from septicemic neonates: coexistence with NDM-5, resistome, transmissibility, and genome diversity. MSphere. 2021;6:6. https://doi.org/10.1128/mSphere.01156-20
9. Shankar C, Mathur P, Venkatesan M, Pragasam AK, Anandan S, Khurana S, et al. Rapidly disseminating $bla_{\text{OXA-232}}$ carrying *Klebsiella pneumoniae* belonging to ST231 in India: multiple and varied mobile genetic elements. BMC Microbiol. 2019;19:137. https://doi.org/10.1186/s12866-019-1513-8
10. Weng X, Shi Q, Wang S, Shi Y, Sun D, Yu Y. The characterization of OXA-232 carbapenemase–producing ST437 *Klebsiella pneumoniae* in China. Can J Infect Dis Med Microbiol. 2020; 2020:5626503. https://doi.org/10.1155/2020/5626503
11. Zhu Z, Huang H, Xu Y, Wang M, Lv J, Xu L, et al. Emergence and genomics of OXA-232–producing *Klebsiella pneumoniae* in a hospital in Yancheng, China. J Glob Antimicrob Resist. 2021;26:194–8. https://doi.org/10.1016/j.jgar.2021.05.015
12. Avolio M, Vignaroli C, Crapis M, Camporese A. Co-production of NDM-1 and OXA-232 by ST16 *Klebsiella pneumoniae*, Italy, 2016. Future Microbiol. 2017;12:1119–22. https://doi.org/10.2217/fmb-2017-0041
13. Doi Y, Hazen TH, Boitano M, Tsai YC, Clark TA, Korlach J, et al. Whole-genome assembly of *Klebsiella pneumoniae* coproducing NDM-1 and OXA-232 carbapenemases using single-molecule, real-time sequencing. Antimicrob Agents Chemother. 2014;58:5947–53. https://doi.org/10.1128/AAC.03180-14
14. Kesarimangalam Kalyanavenkatramanan S, Sewunet T, Wangchinda W, Tangkoskul T, Thamlikitkul V, Giske CG, et al. Optical DNA mapping of plasmids reveals clonal spread of carbapenem-resistant *Klebsiella pneumoniae* in a large Thai hospital. Antibiotics (Basel). 2021;10:10. https://doi.org/10.3390/antibiotics10091029
15. David S, Reuter S, Harris SR, Glasner C, Feltwell T, Argimon S, et al.; EuSCAPE Working Group; ESGEM Study Group. Epidemic of carbapenem-resistant *Klebsiella pneumoniae* in Europe is driven by nosocomial spread. Nat Microbiol. 2019;4:1919–29. https://doi.org/10.1038/s41564-019-0492-8

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Appendix

Appendix Table 1. OXA-232-producing isolates included in the study

Strain	Species	Year	Origin	Carbapenemase	ST	Genome Accession Number
72A1	*K. pneumoniae*	2015	Rectal swab	OXA-232	231	JALXFX000000000
81A10	*K. pneumoniae*	2015	Rectal swab	OXA-232	14	JALXFY000000000
82I3	*K. pneumoniae*	2015	Rectal swab	OXA-232 + NDM-1	15	JALXFZ000000000
84B8	*K. pneumoniae*	2015	Rectal swab	OXA-232	14	JALXGA000000000
87D5	*K. pneumoniae*	2015	Rectal swab	OXA-232 + NDM-1	14	JALXGB000000000
98C2	*K. pneumoniae*	2015	Rectal swab	OXA-232	231	JALXFW000000000
105B7	*K. pneumoniae*	2016	Blood culture	OXA-232	231	JALXGC000000000
105C10	*K. pneumoniae*	2016	Rectal swab	OXA-232 + NDM-1	14	JALXGD000000000
107A1	*K. pneumoniae*	2016	Rectal swab	OXA-232	231	JALXGE000000000
111G6	*K. pneumoniae*	2016	Other or unknown origin	OXA-232	231	JALXGF000000000
112E10	*K. pneumoniae*	2016	Rectal swab	OXA-232	231	JALXGG000000000
117A7	*K. pneumoniae*	2016	Respiratory tract	OXA-232	231	JALXGH000000000
117G2	*K. pneumoniae*	2016	Rectal swab	OXA-232	231	JALXGI000000000
122D1	*K. pneumoniae*	2016	Rectal swab	OXA-232	231	JALXGJ000000000
122D8	*K. pneumoniae*	2016	Rectal swab	OXA-232	231	JALXGK000000000
122H4	*K. pneumoniae*	2016	Rectal swab	OXA-232	231	JALXGL000000000
123F10	*K. pneumoniae*	2016	Rectal swab	OXA-232	231	JALXGM000000000
125C6	*K. pneumoniae*	2016	Rectal swab	OXA-232	231	JALXGN000000000
126I9	*K. pneumoniae*	2016	Rectal swab	OXA-232	231	JALXGO000000000
130H7	*K. pneumoniae*	2017	Rectal swab	OXA-232 + NDM-1	14	JALXGP000000000
135D8	*K. pneumoniae*	2017	Rectal swab	OXA-232	16	JALXGQ000000000
136G10	*K. pneumoniae*	2017	Rectal swab	OXA-232	231	JALXGR000000000
141A4	*K. pneumoniae*	2017	Other or unknown origin	OXA-232	231	JALXGS000000000
141F7	*K. pneumoniae*	2017	Rectal swab	OXA-232	2096	JALXGT000000000
145E7	*K. pneumoniae*	2017	Other or unknown origin	OXA-232	2096	JANJFV000000000
147E10	*K. pneumoniae*	2017	Rectal swab	OXA-232 + NDM-5	147	JALXGU000000000
154D6	*K. pneumoniae*	2017	Rectal swab	OXA-232	2096	JALXGV000000000
157H9	*K. pneumoniae*	2017	Urines	OXA-232	231	JALXGW000000000
161J6	*K. pneumoniae*	2018	Rectal swab	OXA-232 + NDM-1	11	JALXGX000000000
166D10	*K. pneumoniae*	2018	Urines	OXA-232	2096	JALXGY000000000
168E9	*K. pneumoniae*	2018	Rectal swab	OXA-232	2096	JALXGZ000000000
169A7	*K. pneumoniae*	2018	Rectal swab	OXA-232 + NDM-1	14	JALXHA000000000

Strain	Species	Year	Origin	Carbapenemase	ST	Genome Accession Number
175I6	*K. pneumoniae*	2018	Rectal swab	OXA-232	231	JALXHB000000000
181D1	*K. pneumoniae*	2018	Urines	OXA-232 + NDM-1	2497	JALXHC000000000
189D9	*K. pneumoniae*	2018	Rectal swab	OXA-232	2096	JANJFW000000000
190H10	*K. pneumoniae*	2018	Rectal swab	OXA-232	231	JALXHD000000000
200D8	*K. pneumoniae*	2019	Rectal swab	OXA-232	2096	JALXHE000000000
206G1	*K. pneumoniae*	2019	Rectal swab	OXA-232	231	JALXHF000000000
206J2	*K. pneumoniae*	2019	Rectal swab	OXA-232	2096	JALXHG000000000
208I4	*K. pneumoniae*	2019	Rectal swab	OXA-232	2096	JALXHH000000000
212D6	*K. pneumoniae*	2019	Rectal swab	OXA-232	231	JALXHI000000000
216I5	*K. pneumoniae*	2019	Rectal swab	OXA-232	2096	JALXHJ000000000
219H4	*K. pneumoniae*	2019	Urines	OXA-232 + NDM-1	2497	JALXHK000000000
225I1	*K. pneumoniae*	2019	Rectal swab	OXA-232	2096	JALXHL000000000
226C5	*K. pneumoniae*	2019	Rectal swab	OXA-232	231	JALXHM000000000
228E4	*K. pneumoniae*	2019	Rectal swab	OXA-232	2096	JALXHN000000000
229D5	*K. pneumoniae*	2019	Rectal swab	OXA-232	2096	JALXHO000000000
229I6	*K. pneumoniae*	2019	Urines	OXA-232	2096	JALXHP000000000
230D9	*K. pneumoniae*	2019	Rectal swab	OXA-232	2096	JANJFX000000000
230F5	*K. pneumoniae*	2019	Rectal swab	OXA-232	2096	JALXHQ000000000
230J4	*K. pneumoniae*	2019	Rectal swab	OXA-232	231	JALXHR000000000
233G5	*K. pneumoniae*	2019	Rectal swab	OXA-232	2096	JANJFY000000000
234H9	*K. pneumoniae*	2019	Rectal swab	OXA-232	231	JALXHS000000000
235H1	*K. pneumoniae*	2019	Urines	OXA-232	147	JALXHT000000000
236A8	*K. pneumoniae*	2019	Rectal swab	OXA-232	2096	JALXHU000000000
236D10	*K. pneumoniae*	2019	Urines	OXA-232 + NDM-5	147	JALXHV000000000
236I4	*K. pneumoniae*	2019	Urines	OXA-232 + NDM-5	147	JALXHW000000000
238E5	*K. pneumoniae*	2019	Rectal swab	OXA-232	231	JALXHX000000000
240D2	*K. pneumoniae*	2019	Rectal swab	OXA-232	2096	JALXHY000000000
244B1	*K. pneumoniae*	2020	Rectal swab	OXA-232 + NDM-5	231	JALXHZ000000000
247H10	*K. pneumoniae*	2020	Urines	OXA-232	2096	JANJFZ000000000
248B4	*K. pneumoniae*	2020	Rectal swab	OXA-232	29	JALXIA000000000
248B5	*K. pneumoniae*	2020	Rectal swab	OXA-232	29	JALXIB000000000
248F9	*K. pneumoniae*	2020	Urines	OXA-232 + NDM-1	16	JALXIC000000000
250F5	*K. pneumoniae*	2020	Rectal swab	OXA-232	273	JALXID000000000
254D2	*K. pneumoniae*	2020	Rectal swab	OXA-232 + NDM-5	231	JALXIE000000000
255E9	*K. pneumoniae*	2020	Other or unknown origin	OXA-232	231	JALXIF000000000
256B1	*K. pneumoniae*	2020	Rectal swab	OXA-232	231	JALXIG000000000
259A4	*K. pneumoniae*	2020	Urines	OXA-232 + NDM-1	2497	JALXIH000000000
263E1	*K. pneumoniae*	2020	Rectal swab	OXA-232	231	JALXII000000000
265B7	*K. pneumoniae*	2020	Rectal swab	OXA-232	2096	JALXIJ000000000
271F4	*K. pneumoniae*	2020	Other or unknown origin	OXA-232	231	JALXIK000000000
274D7	*K. pneumoniae*	2020	Rectal swab	OXA-232	2096	JALXIL000000000
276E2	*K. pneumoniae*	2021	Urines	OXA-232	231	JALXIM000000000
278E10	*K. pneumoniae*	2021	Urines	OXA-232	231	JALXIN000000000
285I1	*K. pneumoniae*	2021	Rectal swab	OXA-232 + NDM-5	147	JALXIO000000000
290D2	*K. pneumoniae*	2021	Rectal swab	OXA-232	437	JALXIP000000000
290I5	*K. pneumoniae*	2021	Rectal swab	OXA-232	New	JALXIQ000000000
292C2	*K. pneumoniae*	2021	Rectal swab	OXA-232 + NDM-1	16	JALXIR000000000

Strain	Species	Year	Origin	Carbapenemase	ST	Genome Accession Number
294H6	*K. pneumoniae*	2021	Other or unknown origin	OXA-232	15	JALXIS000000000
295I1	*K. pneumoniae*	2021	Rectal swab	OXA-232	2096	JALXIT000000000
295I3	*K. pneumoniae*	2021	Rectal swab	OXA-232	2096	JALXIU000000000
295J6	*K. pneumoniae*	2021	Rectal swab	OXA-232	395	JALXIV000000000
296D5	*K. pneumoniae*	2021	Rectal swab	OXA-232	2096	JALXIW000000000
298C6	*K. pneumoniae*	2021	Rectal swab	OXA-232	2096	JALXIX000000000
300F7	*K. pneumoniae*	2021	Rectal swab	OXA-232 + NDM-5	16	JALXIY000000000
301I6	*K. pneumoniae*	2021	Rectal swab	OXA-232 + NDM-1	16	JALXIZ000000000
303C8	*K. pneumoniae*	2021	Urines	OXA-232 + NDM-1	14	JALXJA000000000
303I7	*K. pneumoniae*	2021	Rectal swab	OXA-232	2096	JALXJB000000000
304B3	*K. pneumoniae*	2021	Rectal swab	OXA-232	512	JALXJC000000000
306A9	*K. pneumoniae*	2021	Rectal swab	OXA-232 + NDM-5	147	JALXJD000000000
307J2	*K. pneumoniae*	2021	Rectal swab	OXA-232 + NDM-5	16	JALXJE000000000
309B8	*K. pneumoniae*	2021	Rectal swab	OXA-232	2096	JALXJF000000000
311I8	*K. pneumoniae*	2021	Rectal swab	OXA-232	2096	JALXJG000000000
312C6	*K. pneumoniae*	2021	Urines	OXA-232	395	JALXJH000000000
ND	*E. coli*	2013	Rectal swab	OXA-232 + NDM-1	ND	
ND	*K. pneumoniae*	2013	Rectal swab	OXA-232 + NDM-1	ND	
ND	*K. pneumoniae*	2013	Rectal swab	OXA-232 + NDM-1	ND	
43B6	*K. pneumoniae*	2014	Rectal swab	OXA-232	ND	
44C5	*K. pneumoniae*	2014	Rectal swab	OXA-232	ND	
46A8	*E. coli*	2014	Other or unknown origin	OXA-232 + NDM-1	ND	
68B2	*E. coli*	2014	Other or unknown origin	OXA-232	ND	
111C6	*E. coli*	2016	Rectal swab	OXA-232	ND	
117C6	*E. coli*	2016	Rectal swab	OXA-232	ND	
148H7	*E. coli*	2017	Rectal swab	OXA-232 + NDM-5	ND	
227H1	*E. coli*	2019	Rectal swab	OXA-232	ND	
165B3	*C. freundii*	2018	Rectal swab	OXA-232	ND	
170F5	*C. freundii*	2018	Urines	OXA-232	ND	
188H3	*C. freundii*	2018	Urines	OXA-232	ND	
203I10	*C. freundii*	2019	Rectal swab	OXA-232	ND	
207F9	*C. freundii*	2019	Rectal swab	OXA-232 + NDM-1	ND	
213I9	*C. freundii*	2019	Rectal swab	OXA-232	ND	
229I3	*C. freundii*	2019	Rectal swab	OXA-232	ND	
230B3	*C. freundii*	2019	Rectal swab	OXA-232	ND	
236A9	*C. freundii*	2019	Rectal swab	OXA-232	ND	
263J3	*C. freundii*	2020	Rectal swab	OXA-232 + NDM-5	ND	
285D4	*C. freundii*	2021	Urines	OXA-232 + NDM-1	ND	
292G1	*C. freundii*	2021	Rectal swab	OXA-232	ND	
299H2	*C. freundii*	2021	Other or unknown origin	OXA-232	ND	
214J10	*K. aerogenes*	2019	Rectal swab	OXA-232	ND	
255E10	*K. aerogenes*	2020	Blood culture	OXA-232	ND	
85F5	*K. oxytoca*	2015	Rectal swab	OXA-232	ND	

ST, sequence type obtained by MLST; ND, not determined.

Appendix Table 2. Percentage of OXA-232 producing isolates received at the French National Reference Center for carbapenem-resistant Enterobacterales among all carbapenemase-producing Enterobacterales (CPE) or among OXA-48-like from 2013 to 2021.

Year	OXA-232 and OXA-232 +NDM (n)	% among CPE	% among OXA-48 like	OXA-232 (n)	% among CPE	% among OXA-48 like	OXA-232 + NDM (n)	% among CPE	% among OXA-48 like
2013	3	0.47%	0.59%	0	0.00%	0.00%	3	0.47%	0.59%
2014	4	0.37%	0.43%	3	0.28%	0.33%	1	0.09%	0.11%
2015	7	0.55%	0.71%	5	0.39%	0.51%	2	0.16%	0.20%
2016	15	0.97%	1.26%	14	0.90%	1.18%	1	0.06%	0.08%
2017	10	0.52%	0.69%	8	0.42%	0.56%	2	0.10%	0.14%
2018	10	0.37%	0.52%	8	0.30%	0.42%	2	0.07%	0.10%
2019	30	0.99%	1.40%	26	0.86%	1.22%	4	0.13%	0.19%
2020	16	0.73%	1.14%	12	0.54%	0.86%	4	0.18%	0.29%
2021	23	0.94%	1.40%	17	0.69%	1.03%	6	0.25%	0.36%
2013–2018	49	0.54%	0.70%	38	0.42%	0.55%	11	0.12%	0.16%
2019–2021	69	0.91%	1.33%	55	0.72%	1.06%	14	0.18%	0.27%

Appendix Figure. Global characterization (sequence type, year of isolation, β-lactamase content) of nonduplicate 95 OXA-232–producing *Klebsiella pneumoniae* analyzed at the National Reference Center for Carbapenem-Resistant Enterobacterales, France, 2013–2021. Scale bar indicates the number of SNP per position of common sequences. CMY-6, variant of *C. freundii* intrinsic cephalosporinase; CTX-M, cefotaximase–Munich extended-spectrum β-lactamase; OXA, oxacillinase; NDM, New Delhi metallo-β-lactamase; ST, sequence type, TEM, Temoniera β-lactamase.