

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*_{OXA-232} gene usually is located on a 6-kb nonconjugative ColE-type plasmid within a truncated Tn2013-like transposon (5). Furthermore, the genetic environment surrounding the *bla*_{OXA-232} gene is comparable to that of the *bla*_{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*_{OXA-232} are carried by 2 different plasmids (13). The *bla*_{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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DOI: <https://doi.org/10.3201/eid2811.221040>

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 Enterobacteriales, 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

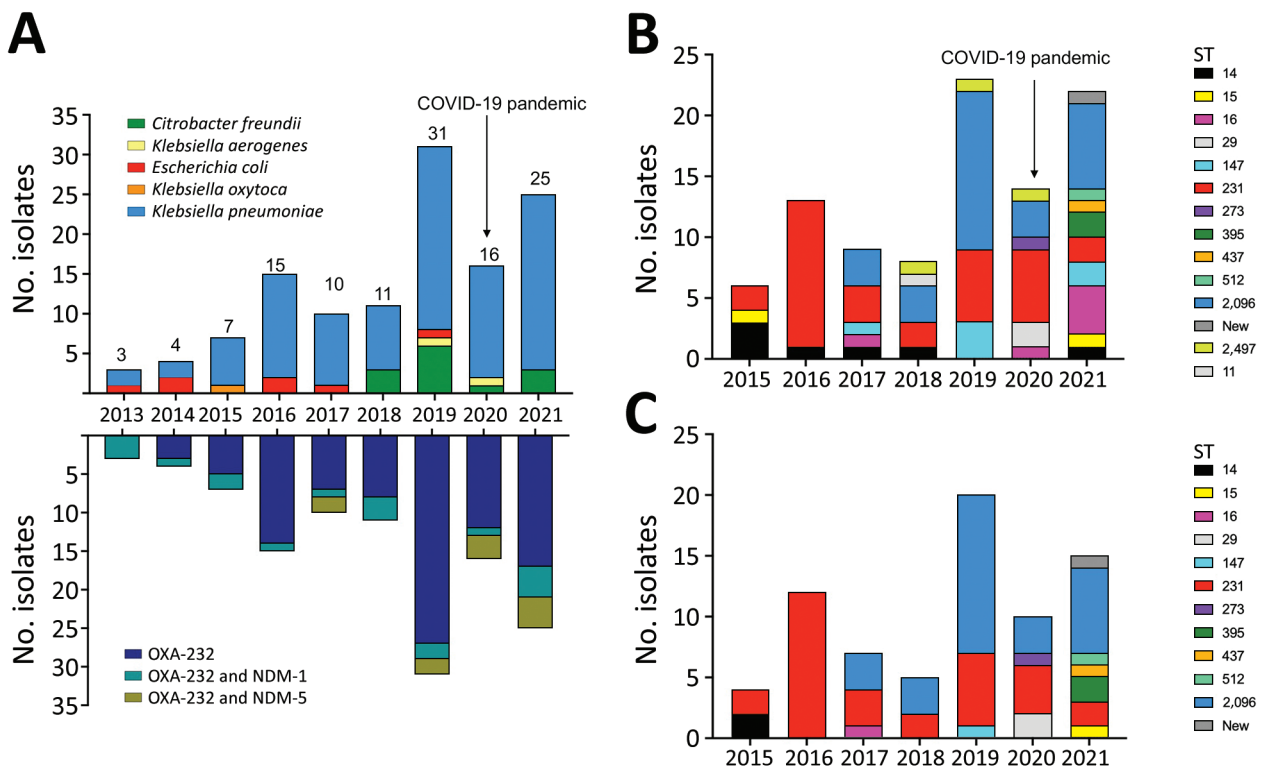


Figure 1. OXA-232–producing Enterobacteriales received at the National Reference Center for Carbapenem-Resistant Enterobacteriales, France 2013–2021. A) Evolution of several OXA-232–producing Enterobacteriales, by species (top of panel) and carbapenemase variant (bottom). B) Evolution of distribution 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).

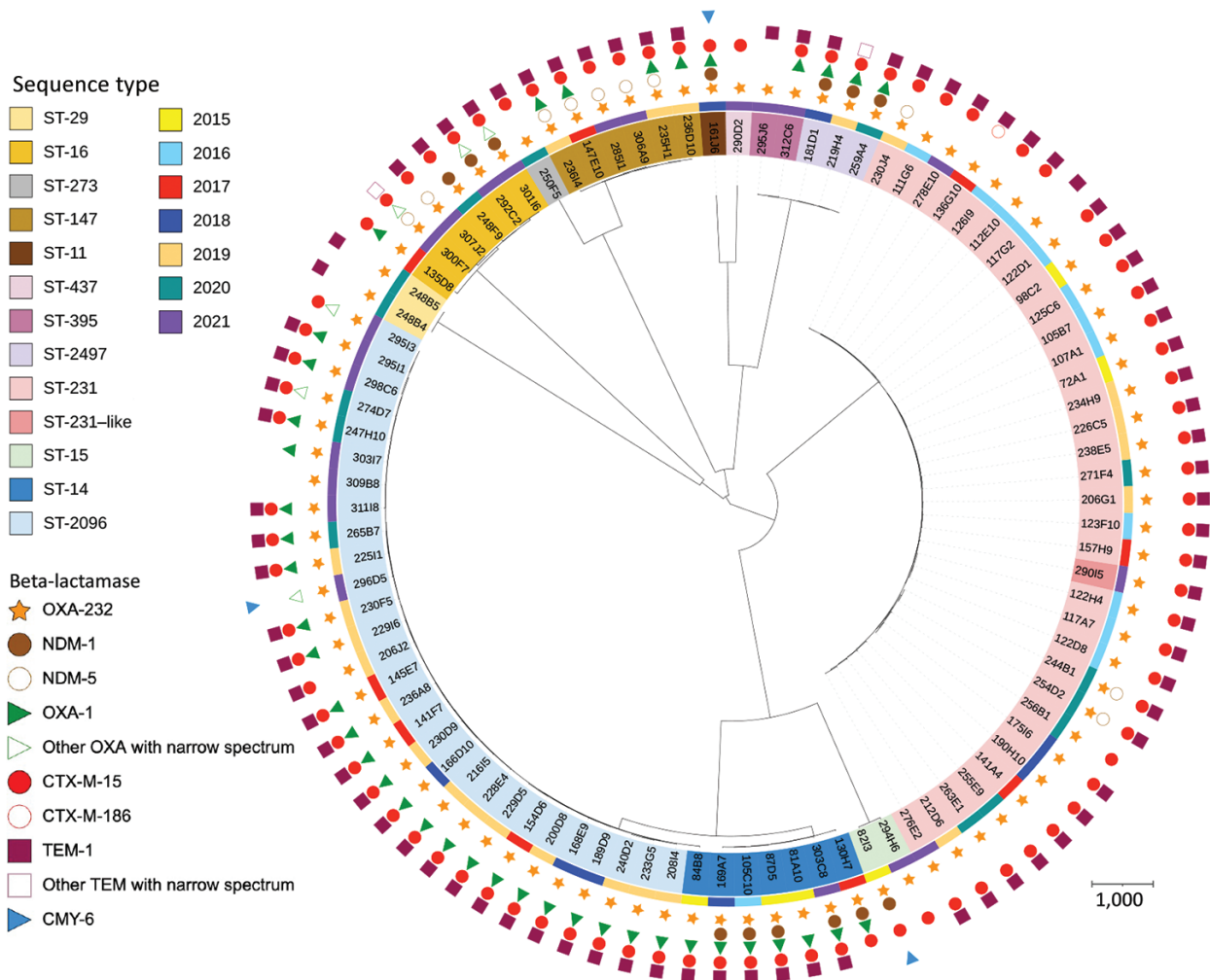


Figure 2. Phylogenetic relationship of OXA-232-producing *K. pneumoniae* ST-231 (A) and ST-2096 (B) analyzed at the National Reference Center for Carbapenem-Resistant Enterobacteriales, France 2013–2021. The phylogenetic trees were built with an SNP analysis approach. Scale bars under trees indicate 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*_{OXA-232} in this clone.

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

As expected, *bla*_{OXA-232} was located on a ColE plasmid in all isolates. The close genetic environment of *bla*_{OXA-232} involved *ISEcp1* upstream of the *bla*_{OXA-232} gene as previously described (5).

About the Author

Dr. Emeraud is an assistant professor at the Institut National de la Santé et de la Recherche Médicale. Her primary research interests include epidemiology, genetics, and biochemistry of β -lactamases in gram-negative bacteria.

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

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

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