## Complete Genome Sequence of the Epidemic and Highly Virulent CTX-M-15-Producing H30-Rx Subclone of *Escherichia coli* ST131

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We report the complete genome sequence, including five complete plasmid sequences, of *Escherichia coli* ST131 isolate JJ1886. The isolate was obtained in 2007 in the United States from a patient with fatal urosepsis and belongs to the virulent, CTX-M-15-producing H30-Rx sublineage.

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**E** scherichia coli sequence type 131 (ST131) has emerged as one of the most prevalent extraintestinal pathogenic *E. coli* lineages in circulation today (1). The ST131 *H30* lineage dominates among fluoroquinolone-resistant and extended-spectrum  $\beta$ -lactamase (ESBL)-producing *E. coli* strains and is associated with recurrent urinary tract infections, pyelonephritis, and sepsis (1, 2, 3, 4, 5). Phylogenomic analysis indicated that the dominant ST131 ESBL gene,  $bla_{CTX-M-15}$ , is associated with an *H30* sublineage, designated *H30*-Rx (6). Here, we present the complete genome sequence of J1886, an ST131 *H30*-Rx isolate recovered from a patient with fatal urosepsis (7).

The genome sequence was assembled using 320 Mb of pairedend 100-bp HiSeq reads (Illumina, Hayward, CA), 225 Mb of 500-bp reads from the Roche Genome Sequencer FLX (Roche Diagnostics, Switzerland), and 187,000 reads (296 Mb) from the PacBio RS platform (Pacific Biosciences, Menlo Park, CA). The PacBio sequence reads were error corrected using HiSeq data (8). Sequences were assembled using multiple de novo assemblers, including MIRA (9), ABySS (10), and CLCbio (CLCbio, Denmark). Initial assembly of the Roche and HiSeq data yielded 52 chromosomal contigs after extension using PBJelly and PAGIT (11, 12). PacBio reads further reduced the number of chromosomal contigs to 18. Gaps were closed in silico using Genomics workbench 6.0.4 (CLCbio) by a combination of comparisons to E. coli reference genome sequences, with manual curation using HiSeq and PacBio data and verification using an optical map (OpGen, MD). Five complete plasmids were identified based on BLAST analysis and were verified using Illumina MiSeq sequencing (250-bp paired end) on isolated plasmids. The genome sequence was annotated using RAST (13).

The complete genome of JJ1886 comprises a 5,129,938-bp chromosome with a GC content of 50.8%, with 5,086 coding sequences, 88 tRNAs, and 22 rRNA features, plus five plasmids, pJJ1886-1 through pJJ1886-5, of sizes 1.6, 5.2, 5.6, 56, and 110 kb, respectively. According to ResFinder 1.4 (14), only pJJ1886-5 car-

ries genes for resistance, including resistance to aminoglycosides and fluoroquinolones [aac(6')-Ib, aac(6')-Ib-cr, aac(6')-31(~85% sequence homology)], beta-lactams ( $bla_{OXA-30}$ ,  $bla_{TEM-1}$ ), and chloramphenicols (catB3). However, the ESBL gene  $bla_{CTX-M-15}$ was integrated into the JJ1886 chromosome via an incomplete Tn3 transposable element embedded within a lambda-like 58-kb prophage (identified by PHAST analysis [15]). This is in contrast with the only other complete, published ST131-H30 genome sequence, that of NA114 (isolated from a patient with prostatitis [16]), which likely has  $bla_{CTX-M-15}$  integrated into a previously described plasmid (17).

JJ1886 is the first complete genome sequence for a urosepsis ST131 isolate that includes all plasmids and has a chromosomal  $bla_{CTX-M-15}$  integration site. The genome sequence will serve as a valuable resource for studies on the epidemiology and pathogenicity of the highly virulent ST131 lineage.

**Nucleotide sequence accession numbers.** The complete sequences of the chromosome of *E. coli* JJ1886 and its five plasmids, pJJ1886-1 through pJJ1886-5, have been deposited in GenBank (accession numbers CP006784, CP006785, CP006786, CP006787, CP006788, and CP006789, respectively).

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## REFERENCES

- Johnson JR, Johnston B, Clabots C, Kuskowski MA, Castanheira M. 2010. *Escherichia coli* sequence type ST131 as the major cause of serious multidrug-resistant *E. coli* infections in the United States. Clin. Infect. Dis. 51:286–294.
- Johnson JR, Tchesnokova V, Johnston B, Clabots C, Roberts PL, Billig M, Riddell K, Rogers P, Qin X, Butler-Wu S, Price LB, Aziz M, Nicolas-Chanoine MH, Debroy C, Robicsek A, Hansen G, Urban C, Platell J, Trott DJ, Zhanel G, Weissman SJ, Cookson BT, Fang FC, Limaye AP, Scholes D, Chattopadhyay S, Hooper DC, Sokurenko EV. 2013. Abrupt emergence of a single dominant multidrug-resistant strain of *Escherichia coli*. J. Infect. Dis. 207:919–928.
- Coque TM, Novais A, Carattoli A, Poirel L, Pitout J, Peixe L, Baquero F, Cantón R, Nordmann P. 2008. Dissemination of clonally related *Escherichia coli* strains expressing extended-spectrum beta-lactamase CTX-M-15. Emerg. Infect. Dis. 14:195–200.
- Nicolas-Chanoine MH, Blanco J, Leflon-Guibout V, Demarty R, Alonso MP, Caniça MM, Park YJ, Lavigne JP, Pitout J, Johnson JR. 2008. Intercontinental emergence of *Escherichia coli* clone O25:H4-ST131 producing CTX-M-15. J. Antimicrob. Chemother. 61:273–281.
- Peirano G, Pitout JD. 2010. Molecular epidemiology of *Escherichia coli* producing CTX-M beta-lactamases: the worldwide emergence of clone ST131 O25:H4. Int. J. Antimicrob. Agents 35:316–321.
- Price LB, Aziz M, Clabots C, Johnston B, Tchesnokova V, Nordstrom L, Pearson T, Stegger M, Andersen PS, Keim P, Sokurenko EV, Johnson JR. Epidemic clonal expansion of CTX-M-15-producing *Escherichia coli* ST131. mBio, in press.
- Owens RC, Jr, Johnson JR, Stogsdill P, Yarmus L, Lolans K, Quinn J. 2011. Community transmission in the United States of a CTX-M-15producing sequence type ST131 *Escherichia coli* strain resulting in death. J. Clin. Microbiol. 49:3406–3408.
- Koren S, Schatz MC, Walenz BP, Martin J, Howard JT, Ganapathy G, Wang Z, Rasko DA, McCombie WR, Jarvis ED, Phillippy AM. 2012.

Hybrid error correction and *de novo* assembly of single-molecule sequencing reads. Nat. Biotechnol. **30**:693–700.

- Chevreux B, Wetter T, Suhai S. 1999. Genome sequence assembly using trace signals and additional sequence information, p 45–56. *In* Computer science and biology: proceedings of the German Conference on Bioinformatics (GCB). Hannover, Germany.
- Simpson JT, Wong K, Jackman SD, Schein JE, Jones SJ, Birol I. 2009. ABySS: a parallel assembler for short read sequence data. Genome Res. 19: 1117–1123.
- English AC, Richards S, Han Y, Wang M, Vee V, Qu J, Qin X, Muzny DM, Reid JG, Worley KC, Gibbs RA. 2012. Mind the gap: upgrading genomes with Pacific Biosciences RS long-read sequencing technology. PLoS One 7:e47768. doi:10.1371/journal.pone.0047768.
- Swain MT, Tsai IJ, Assefa SA, Newbold C, Berriman M, Otto TD. 2012. A post-assembly genome-improvement toolkit (PAGIT) to obtain annotated genomes from contigs. Nat. Protoc. 7:1260–1284.
- 13. Aziz RK, Bartels D, Best AA, DeJongh M, Disz T, Edwards RA, Formsma K, Gerdes S, Glass EM, Kubal M, Meyer F, Olsen GJ, Olson R, Osterman AL, Overbeek RA, McNeil LK, Paarmann D, Paczian T, Parrello B, Pusch GD, Reich C, Stevens R, Vassieva O, Vonstein V, Wilke A, Zagnitko O. 2008. The RAST server: rapid annotations using Subsystems Technology. BMC Genomics 9:75.
- Zankari E, Hasman H, Cosentino S, Vestergaard M, Rasmussen S, Lund O, Aarestrup FM, Larsen MV. 2012. Identification of acquired antimicrobial resistance genes. J. Antimicrob. Chemother. 67:2640–2644.
- Zhou Y, Liang Y, Lynch KH, Dennis JJ, Wishart DS. 2011. PHAST: a fast phage search tool. Nucleic Acids Res. 39:W347–W352.
- Avasthi TS, Kumar N, Baddam R, Hussain A, Nandanwar N, Jadhav S, Ahmed N. 2011. Genome of multidrug-resistant uropathogenic *Escherichia coli* strain NA114 from India. J. Bacteriol. 193:4272–4273.
- Smet A, Van Nieuwerburgh F, Vandekerckhove TT, Martel A, Deforce D, Butaye P, Haesebrouck F. 2010. Complete nucleotide sequence of CTX-M-15-plasmids from clinical *Escherichia coli* isolates: insertional events of transposons and insertion sequences. PLoS One 5:e11202. doi:1 0.1371/journal.pone.0011202.