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consequences from mutations in F-protein antigenic sites. Although the G protein is under greater selective pressure and has higher mutation rates (3), observing its evolutionary trajectory in context with the F protein will be critical. Our study demonstrates the value of using whole-genome sequencing to identify genetic mutations in respiratory pathogens, including RSV, to ensure ongoing effectiveness of RSV vaccines.

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References

1. Tin Tin Htar M, Yerramalla MS, Moisi JC, Swerdlow DL. The burden of respiratory syncytial virus in adults: a systematic review and meta-analysis. *Epidemiol Infect.* 2020;148:e48. <https://doi.org/10.1017/S0950268820000400>
2. Centers for Disease Control and Prevention. Increased respiratory virus activity, especially among children, early in the 2022–2023 fall and winter [cited 2023 Jun 16]. <https://emergency.cdc.gov/han/2022/han00479.asp#print>
3. Muñoz-Escalante JC, Comas-García A, Bernal-Silva S, Robles-Espinoza CD, Gómez-Leal G, Noyola DE. Respiratory syncytial virus A genotype classification based on systematic intergenotypic and intragenotypic sequence analysis. *Sci Rep.* 2019;9:20097. <https://doi.org/10.1038/s41598-019-56552-2>
4. Khare S, Gurry C, Freitas L, Schultz MB, Bach G, Diallo A, et al. GISAID's role in pandemic response. *China CDC Wkly.* 2021;3:1049–51. <https://doi.org/10.46234/ccdcw2021.255>
5. Wang L, Piedra PA, Avadhanula V, Durigon EL, Machabishvili A, López MR, et al. Duplex real-time RT-PCR assay for detection and subgroup-specific identification of human respiratory syncytial virus. *J Virol Methods.* 2019; 271:113676. <https://doi.org/10.1016/j.jviromet.2019.113676>
6. Adams G, Moreno GK, Petros BA, Uddin R, Levine Z, Kotzen B, et al. Viral lineages in the 2022 RSV surge in the United States. *N Engl J Med.* 2023;388:1335–7. <https://doi.org/10.1056/NEJMc2216153>
7. Goya S, Sereewit J, Pfalmer D, Nguyen TV, Bakhsh SAKM, Sobolik EB, et al. Genomic characterization of respiratory syncytial virus during 2022–23 outbreak, Washington, USA. *Emerg Infect Dis.* 2023;29:865–8. <https://doi.org/10.3201/eid2904.221834>
8. Papi A, Ison MG, Langley JM, Lee D-G, Leroux-Roels I, Martinon-Torres F, et al.; AReSVi-006 Study Group. Respiratory syncytial virus prefusion F protein vaccine in older adults. *N Engl J Med.* 2023;388:595–608. <https://doi.org/10.1056/NEJMoa2209604>
9. Kampmann B, Madhi SA, Munjal I, Simões EAF, Pahud BA, Llapur C, et al.; MATISSE Study Group. Bivalent prefusion F vaccine in pregnancy to prevent RSV illness in infants. *N Engl J Med.* 2023;388:1451–64. <https://doi.org/10.1056/NEJMoa2216480>
10. Gilman MS, Castellanos CA, Chen M, Ngwuta JO, Goodwin E, Moin SM, et al. Rapid profiling of RSV antibody repertoires from the memory B cells of naturally infected adult donors. *Sci Immunol.* 2016;1:eaaj1879.

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Domestically Acquired NDM-1–Producing *Pseudomonas aeruginosa*, Southern California, USA, 2023

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We describe a case of New Delhi metallo- β -lactamase 1–producing carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) in a transplant patient with multiple hospitalizations in California, USA. Whole-genome sequencing revealed the isolate was genetically distinctive, despite $\approx 95\%$ similarity to other global strains. The patient's lack of international travel suggests this CRPA was acquired domestically.

Carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) is increasing worldwide and has up to 30% prevalence in US *P. aeruginosa* isolates (1). The Antimicrobial Resistance Laboratory Network reported 280 carbapenemase-producing CRPA in 2021, most commonly Verona integron metallo- β -lactamase (Centers for Disease Control and Prevention, <https://arpsp.cdc.gov/profile/arln/crpa>). New Delhi metallo- β -lactamase (NDM)–producing CRPA is prevalent in Eurasia and the Middle East. Sporadic NDM CRPA cases linked to international travel have been reported in the United States, the earliest of which was identified in Delaware in 2014 (2). We describe a case of NDM CRPA in southern California.

A previously healthy patient in his 50s was admitted to a hospital in Riverside County, California, in 2023 with cardiogenic shock secondary to new onset nonischemic cardiomyopathy. He was briefly admitted to the same hospital a few weeks earlier because of chest pain and dyspnea. He had no other healthcare exposures and had only traveled briefly to Hawaii earlier that year.

Shortly after the second admission, the patient experienced cardiac arrest, was cannulated for extracorporeal life support, and was transferred to Ronald Reagan UCLA Medical Center for heart transplant evaluation. Admission blood cultures grew *Bacillus cereus*, attributed to gastrointestinal translocation. The patient received vancomycin, resulting in bacteremia clearance, and empiric piperacillin/tazobactam for gram-negative bacteria coverage. Four days pretransplant, hypotension and leukocytosis worsened, and antimicrobial therapy was empirically changed to meropenem and amikacin. A urine culture sent during sepsis evaluation grew *P. aeruginosa*. On the basis of susceptibility testing results, cefiderocol was initiated; the patient received heart and kidney transplants the next day. Cefiderocol was continued for 6 days posttransplant; subsequent urine cultures were negative. *P. aeruginosa* was not isolated from other blood or respiratory cultures.

Initial susceptibility testing of the urine isolate revealed extensive resistance to carbapenems,

aminoglycosides, fluoroquinolones, and cephalosporins, except cefiderocol (Appendix, <https://wwwnc.cdc.gov/EID/article/29/11/23-0646-App1.xlsx>). Rapid Carba-5 (Hardy Diagnostics, <https://hardydiagnostics.com>) testing detected NDM. We performed whole-genome sequencing by using MiSeq (Illumina, <https://www.illumina.com>) and assembled reads de novo by using CLC Genomics Workbench (QIAGEN, <https://www.qiagen.com>). We submitted tentative assemblies to the Comprehensive Antibiotic Resistance Database Resistance Gene Identifier tool (<https://card.mcmaster.ca/analyze/rgi>) for resistance gene detection and verified results by using ResFinder (Center for Genomic Epidemiology, <https://genomicepidemiology.org>) (Table). The isolate contained 5 β -lactamase genes: class A extended-spectrum β -lactamase *bla*_{PME-1}, class B carbapenemase *bla*_{NDM-1}, class D oxacillinase *bla*_{OXA-50}-type *bla*_{OXA-488} and *bla*_{OXA-10}, and class C cephalosporinase *bla*_{PDC-35}.

Multilocus sequence typing designated the isolate as sequence type (ST) 235, frequently associated with *bla*_{NDM-1}, including in isolates from Serbia, France, and Italy (3,4). ST235 is considered a high-risk clone, notable for harboring multiple β -lactamases, causing invasive infections and high mortality rates (5). Although most metallo- β -lactamases detected in ST235 are imipenemase variants, NDM CRPA are globally disseminated and have been reported in Asia, Europe, the Middle East, and Africa (5). We also detected other resistance genes reported in ST235 strains, including aminoglycoside-modifying enzyme *aac(6')-Ib9* and chloramphenicol resistance genes *cmlA* and *catB7* (6). In an outbreak of NDM CRPA in Iran, 86.2% of isolates coharbored *bla*_{OXA-10} (7), which we also detected in the isolate in this case.

Table. Antimicrobial genetic markers detected in a case of domestically acquired NDM-1–producing *Pseudomonas aeruginosa*, southern California, USA, 2023

Resistance mechanism	Genes
Aminoglycoside modifying enzymes	<i>aac(6')-Ib9</i> , <i>ant(3')-IIa</i> , <i>aph(3')-IIb</i> , <i>aph(3')-VIa</i>
β -lactamases	<i>bla</i> _{NDM-1} , <i>bla</i> _{OXA-10} , <i>bla</i> _{OXA-488} , <i>bla</i> _{PDC-35} , <i>bla</i> _{PME-1}
Fluoroquinolone resistance determinant	<i>gyrA</i> (T831), <i>parE</i> (S457R)
Chloramphenicol resistance determinant	<i>catB3</i> , <i>catB7</i> , <i>cmlA9</i>
Fosfomycin resistance determinant	<i>fosA</i>
Tetracycline resistance determinant	<i>tet(D)</i>
Sulfonamide resistance determinant	<i>sul1</i>

*NDM, New Delhi metallo- β -lactamase.

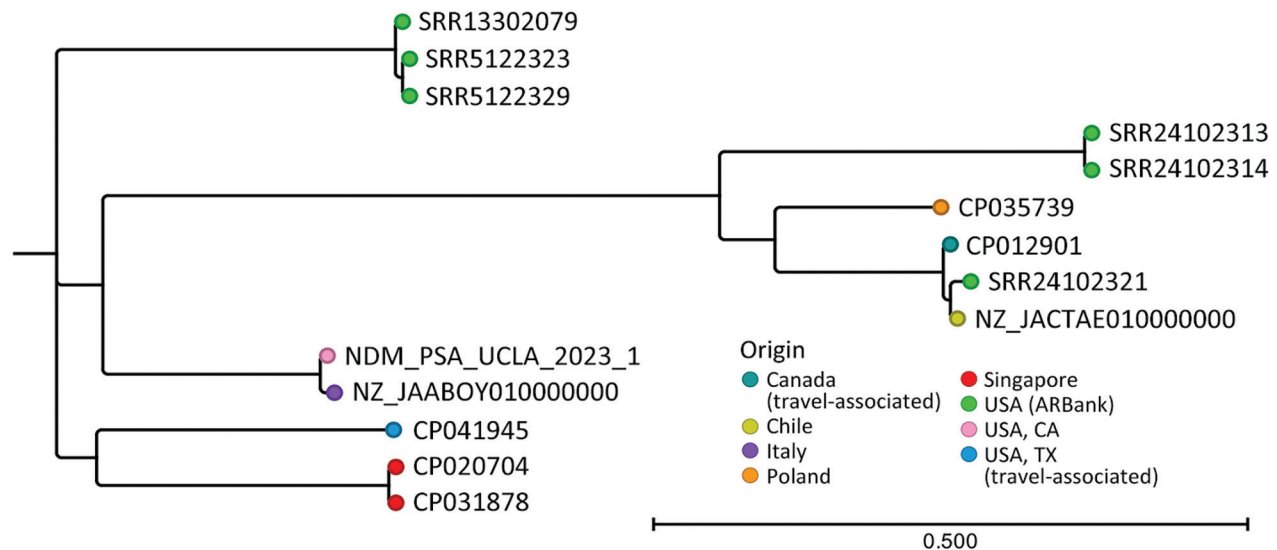


Figure. Phylogenetic tree for domestically acquired NDM-1–producing *Pseudomonas aeruginosa*, southern California, USA, 2023. Node colors indicate geographic location of organism isolation; the isolate described in this case report is designated as NDM_PSA_UCLA_2023_1. Accession numbers are provided for reference sequences. Scale bar indicates nucleotide substitutions per site. ARBank, CDC & FDA Antimicrobial Resistance (AR) Isolate Bank (<https://www.cdc.gov/drugresistance/resistance-bank/>); NDM, New Delhi metallo- β -lactamase; UCLA, University of California Los Angeles.

Consistent with other bla_{NDM-1} -positive isolates, bla_{NDM-1} in this isolate was flanked by IS91-type insertion sequences, indicating mobilizability (8). The isolate also exhibited intermediate susceptibility to colistin, sometimes used to treat carbapenemase-producing CRPA. The isolate lacked an *mcr* gene, indicating mutations in *pmrAB* could be responsible for this phenotype, consistent with other ST235 carbapenemase-producing CRPA (9).

We used CSIPhylogeny (Center for Genomic Epidemiology) to perform single-nucleotide polymorphism (SNP) analysis against other NDM-1-producing ST235 isolates, then CLC Bioinformatics Workbench (QIAGEN) to generate a phylogenetic tree. The isolate from this study exhibited highest homology (≈ 30 SNPs difference) with 2 non-NDM-producing ST235 isolates from Malaysia (Appendix). Among NDM-producing carbapenemase-producing CRPA, the isolate clustered with an NDM CRPA from Italy (147 SNPs distance), suggesting origin in Europe (Figure). Among US strains, the isolate was genetically distinct from all NDM CRPA strains in isolate banks (Appendix Table 3) and a travel-associated strain from Texas ($>20,000$ SNPs distance) (10). That finding, and our patient's lack of international travel, suggest that a domestic NDM CRPA strain is circulating in southern California. The patient received care at multiple institutions, making the precise origin of this strain unknown. Before this isolate, the rate of NDM-pro-

ducing organisms at our institution remained low, <3 carbapenem-resistant Enterobacterales isolated annually, with no NDM CRPA.

The NDM CRPA isolate we report exhibited susceptibility to cefiderocol, which was used to clear the urinary tract infection. Upon phenotypic carbapenem resistance identification, cefiderocol susceptibility testing indicated sensitivity. The rapid availability of susceptibility testing results and preliminary testing performed within 24 hours after isolation were crucial for appropriate clinical management and antimicrobial drug choice, leading to safe heart transplantation and receipt of immunosuppression. Carbapenemase-producing bacteria should not disqualify a patient from transplantation.

In conclusion, high mortality rates of ST235 NDM CRPA in invasive infection and a potential community spread in southern California warrant concern. The mobilization potential of bla_{NDM-1} remains unknown. Infection control measures and expanded surveillance efforts, including routine laboratory screening of all CRPA isolates via carbapenemase tests, could curb the spread of this high-risk genotype.

About the Author

Dr. Gray is a clinical microbiologist at the University of California Los Angeles Medical School, USA. Her research interests include antimicrobial resistance, genomic epidemiology, and healthcare acquired infections.

References

1. Tenover FC, Nicolau DP, Gill CM. Carbapenemase-producing *Pseudomonas aeruginosa* – an emerging challenge. *Emerg Microbes Infect.* 2022;11:811–4. <https://doi.org/10.1080/22221751.2022.2048972>
2. Delaware Health and Social Services. Health alert: first confirmed US case of NDM-producing carbapenem-resistant *Pseudomonas aeruginosa* [cited 2023 Jul 22]. <http://dhss.delaware.gov/dph/php/alerts/dhan324.html>
3. Kocsis B, Gulyás D, Szabó D. Diversity and distribution of resistance markers in *Pseudomonas aeruginosa* international high-risk clones. *Microorganisms.* 2021;9:359. <https://doi.org/10.3390/microorganisms9020359>
4. Hong DJ, Bae IK, Jang IH, Jeong SH, Kang HK, Lee K. Epidemiology and characteristics of metallo- β -lactamase-producing *Pseudomonas aeruginosa*. *Infect Chemother.* 2015;47:81–97. <https://doi.org/10.3947/ic.2015.47.2.81>
5. Recio R, Villa J, Viedma E, Orellana MA, Lora-Tamayo J, Chaves F. Bacteraemia due to extensively drug-resistant *Pseudomonas aeruginosa* sequence type 235 high-risk clone: facing the perfect storm. *Int J Antimicrob Agents.* 2018; 52:172–9. <https://doi.org/10.1016/j.ijantimicag.2018.03.018>
6. Loconsole D, Accogli M, Monaco M, Del Grosso M, De Robertis AL, Morea A, et al. First detection of autochthonous extensively drug-resistant NDM-1 *Pseudomonas aeruginosa* ST235 from a patient with bloodstream infection in Italy, October 2019. *Antimicrob Resist Infect Control.* 2020;9:73. <https://doi.org/10.1186/s13756-020-00734-5>
7. Shahin M, Ahmadi A. Molecular characterization of NDM-1-producing *Pseudomonas aeruginosa* isolates from hospitalized patients in Iran. *Ann Clin Microbiol Antimicrob.* 2021;20:76. <https://doi.org/10.1186/s12941-021-00482-3>
8. Fortunato G, Vaz-Moreira I, Gajic I, Manaia CM. Insight into phylogenomic bias of *bla*_{VIM-2} or *bla*_{NDM-1} dissemination amongst carbapenem-resistant *Pseudomonas aeruginosa*. *Int J Antimicrob Agents.* 2023;61:106788. <https://doi.org/10.1016/j.ijantimicag.2023.106788>
9. Vatansever C, Menekse S, Dogan O, Gucer LS, Ozer B, Ergonul O, et al. Co-existence of OXA-48 and NDM-1 in colistin resistant *Pseudomonas aeruginosa* ST235. *Emerg Microbes Infect.* 2020;9:152–4. <https://doi.org/10.1080/22221751.2020.1713025>
10. Khan A, Shropshire WC, Hanson B, Dinh AQ, Wanger A, Ostrosky-Zeichner L, et al. Simultaneous infection with *Enterobacteriaceae* and *Pseudomonas aeruginosa* harboring multiple carbapenemases in a returning traveler colonized with *Candida auris*. *Antimicrob Agents Chemother.* 2020;64:64. <https://doi.org/10.1128/AAC.01466-19>

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Plasmodium vivax Prevalence in Semiarid Region of Northern Kenya, 2019

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In urban and rural areas of Turkana County, Kenya, we found that 2% of household members of patients with *Plasmodium falciparum* infections were infected with *P. vivax*. Enhanced surveillance of *P. vivax* and increased clinical resources are needed to inform control measures and identify and manage *P. vivax* infections.

Until recently, little or no endemic transmission of *Plasmodium vivax* has been reported in sub-Saharan Africa outside of the Horn of Africa (1). *P. vivax* was presumed to be largely absent because the Duffy blood group antigen was rare in persons living in the region. However, accumulating evidence of endemic *P. vivax* has indicated that this parasite might be present in many areas of sub-Saharan Africa, albeit at low levels, and Duffy antigen-negative persons can be infected and contribute to transmission (2).

Turkana County is in northwestern Kenya and shares a border with Uganda, South Sudan, and Ethiopia. Turkana county's harsh climate is characterized by an average rainfall of <215 mm/year and daytime temperatures of 40°C. Malaria transmission in this region was predicted to occur in isolated pockets with epidemic potential only after unusual rainfall. However, reactive case detection conducted across central Turkana County documented year-round symptomatic and asymptomatic *P. falciparum* infections and confirmed perennial endemic transmission of malaria (3).

We hypothesized that *P. vivax* might also be circulating in Turkana County because of stable malaria transmission and proximity to Ethiopia, where *P.*