Methods. PSA clinical isolates from Europe (n = 62), Asia-Pacific (n = 22), and Latin America (n = 25) in 2017 were susceptibility tested using reference methods and 109 were randomly selected for WGS and total mRNA-sequencing. Data were analyzed using custom software and logistic regression.

Results. Isolates carrying metallo-β-lactamases (MBLs) (n = 24) were resistant to all β-lactams, including CAZ-AVI and C-T. The only compound inhibiting >50% of the isolates was colistin. ESBL genes (blaCTX-M, or blaSHV), some oxacillinases, and PDC variants caused resistance to CAZ-AVI and C-T, but the presence of blaOXA-1, blaOXA-2, and PDC-97 led to resistance to C-T, but not to CAZ-AVI. Disruptions of ampR (PDC regulator) and ampC (RIF resistant PDC) were associated with resistance to CAZ-AVI and C-T, but armZ (anti-repressor of mexZ) disruption was only associated with C-T resistance. The combination of wild-type sequences of various genes was negatively associated with resistance to CAZ-AVI and C-T, but alterations in dfrA (chloramphenicol) and aac(3)-II (gentamicin) were only related to C-T resistance. mRNA-sequencing data did not show strong correlations with CAZ-AVI or C-T resistance or with expression of genes involved in β-lactam resistance, but further analyses will expand the genes analyzed. Interestingly, among 14 isolates overexpressing MexAB-OprM that exceed CAZ, only 6 had CAZ-AVI MICs >8 µg/mL.

Conclusion. Resistance mechanisms against CAZ-AVI and C-T remain poorly understood beyond MBL acquisition. In this study, resistance mechanisms statistically associated with CAZ-AVI resistance in PSA were noted among C-T-resistant isolates, but some mechanisms were only observed among C-T-resistant isolates. The richness of results employing these 2 methodologies requires further investigations that are being performed to evaluate sequences and expression alterations.

Disclosures. All authors: No reported disclosures.

603. Identification of a Carbapenemase-Producing, Extensively Drug-Resistant Klebsiella pneumoniae Isolate Carrying a blaNDM-1 Bearer, Hypervirulent Plasmid, United States 2017

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Abstract. Carbapenemase-producing Klebsiella pneumoniae (KP) isolates with the hypervirulent plasmid pKPNV2 have been isolated in the United States; however, very little is known about the genetic makeup of this plasmid. Isolate TP21, a hypervirulent K. pneumoniae (KPNV2) carrying a β-lactamase gene, a carbapenemase, and a KPNV2 plasmid, was isolated from a blood culture from a 61-year-old female with a peripherally inserted central catheter left arm line infection, who was admitted to a hospital in South Texas for treatment of septic shock. TP21 was positive for the carbapenemase metallo-β-lactamase-1 (blaNDM-1) and had an extended-spectrum β-lactamase (ESBL) (blaCTX-M-15). Whole genome sequencing (WGS) of TP21 demonstrated a hypothetical plasmid found in a KPNV2-NDM positive isolate from the United States.

Methods. Antimicrobial susceptibility testing (AST) was performed by reference broth microdilution against 23 agents. Whole-genome sequencing (WGS) was performed in Illumina MiSeq and PacBio RS II platforms. Bioinformatic analysis included showing the convergence of multidrug resistance and pathogenicity, with the potential for increased mortality. While previous studies of CP-HKP isolates revealed that most carried carbapenemase genes and hypervirulence elements on separate plasmids, a 2018 report from China confirmed that both could be harbored on a single, hybrid carbapenemase-hypervirulent plasmid. As part of a project sequencing isolates carrying multiple carbapenemase genes identified through CDC’s Antibiotic Resistance Laboratory Network (AR Lab Network), we further sequenced the TP21 plasmid in the United States.

Results. The AST indicated the isolate was extensively drug resistant, as it was non-susceptible to at least one agent in all but two drug classes; it was susceptible to only tigecycline and tetracycline. Analysis of WGS data showed the isolate was ST11, the same sequence type that caused a fatal outbreak of CP-HKP in China in 2016. The genome included two plasmids. The smaller one (129kbp) carried seven antibiotic resistance (AR) genes, including the carbapenemase gene blakPC-2. The larger plasmid (35kbp) harbored 11 AR genes, including the metallo-β-lactamase gene blakNDM-1, as well as virulence factors yscABC/D/ExsA, phe-sA, rmpA, and rmpA2, which comprised four of the five genes previously identified as predictors of hypervirulence in K. pneumoniae.

Conclusion. This is the first report of a hybrid carbapenemase-hypervirulent plasmid in the United States. The presence of both blakNDM-1 and hypervirulence