Background. *Klebsiella pneumoniae* carbapenemase (KPC) and Verona integron-encoded metallo-β-lactamase (VIM) have been the most commonly identified carbapenemases among carbapenemase-producing carbapenem-resistant Enterobacteriaceae (CP-CRE) in Kentucky since 2013. Understanding the frequency and epidemiology of these CP-CRE can help inform prevention strategies.

Methods. We reviewed reports of KPC- and VIM-producing CRE from January 2013 through December 2017. CRE became reportable in Kentucky in February 2015 and statewide request to laboratories and healthcare facilities for isolate submission for mechanism testing was made in September 2017. Prior to that time, mechanism testing for CRE was conducted at a limited number of laboratories or during outbreak investigations. Demographic data included age, sex, and inpatient or outpatient status. Descriptive analyses were performed.

Results. As of December 31, 2017, a total of 156 CP-CRE isolates had been identified (124 KPC, 31 VIM, 1 NDM), with an increase from 2013 ($n = 13$) to 2017 ($n = 48$). KPC was identified in isolates from 124 patients; VIM was identified in isolates from 26 patients, with 4 patients (15%) having multiple organisms with the mechanism. KPC was identified most commonly from *Klebsiella pneumoniae* (57/124, 46%); VIM was identified most commonly from *Enterobacter cloacae* (14/31, 45%). KPC was found in 6 different Enterobacteriaceae genera; VIM in 4. KPC-producing CRE were identified in 22 acute-care and long-term acute-care facilities in 14 counties, with nine reporting >2 isolates. Fifteen percent (19/124) of KPC-producing CRE were isolated from outpatients. VIM-producing CRE were identified in two acute-care facilities located in two urban areas; one was from an outpatient. Patients with VIM were younger than those with KPC (43 vs. 60 years, $P < 0.001$).

Conclusion. KPC is the predominant carbapenemase in Kentucky and is more widely disseminated than VIM, which has been limited to two facilities. CRE reporting and mechanism testing have yielded a greater understanding of regional CRE epidemiology and has the potential to facilitate response efforts to slow further spread.

Disclosures. **All authors:** No reported disclosures.

705. Four Superbugs Isolated From a Single Patient in the United States: *E. coli* (*EC)* and *K. pneumoniae (KP)* Harboring NDM-5, *P. aeruginosa (PA)* Harboring NDM-1 and *Candida auris*

Ayesha Khan, BSc[1]; Blake Hanson, PhD[2]; An Dinh, BS[3]; Audrey Wanger, PhD[4]; Luis Ostrosky-Zeichner, MD, FIDSA, FSHEA[5]; William Miller, MD[6] and Cesar Arias, MD, PhD, FIDSA[7]; [1]Microbiology and Infectious Diseases, University of Texas Health Science Center at Houston, Houston, Texas, [2]Center for Antimicrobial Resistance and Microbial Genomics (CARMiG), UTHealth McGovern Medical School, Houston, Texas, [3]Department of Internal Medicine, University of Texas McGovern Medical School at Houston, Houston, Texas, [4]Department of Pathology and Lab Medicine, Department of Pathology and Laboratory Medicine, McGovern Medical School, Houston, Texas, [5]Division of Infectious Diseases, Department of Internal Medicine, McGovern Medical School, Houston, Texas, [6]Department of Internal Medicine, Division of Infectious Diseases, UTHealth McGovern Medical School, Houston, Texas, [7]Microbiology and Molecular Genetics, University of Texas McGovern Medical School, Houston, Texas

Session: 67. Resistance Mechanisms: Gram-Negative
Thursday, October 4, 2018: 12:30 PM

Background. The spread of carbapenem resistance in *Enterobacteriacae* (CRE) and *PA* is an urgent public health concern. *Candida auris* (*CA)* is also an emerging threat, with the epicenter of US cases on the East Coast. Transcontinental spread of multi-drug-resistant (MDR) organisms has the potential to change local susceptibility patterns via dissemination of resistance determinants or high-risk clones. Here, we report and characterize MDR-isolates of *EC, KP, PA* and *CA,* all isolated from a single patient admitted to an ICU in Houston, Texas after complications from plastic surgery in India.

Methods. CRE were isolated from the urine, *PA* from respiratory cultures and *CA* from wound cultures. Antimicrobial susceptibility testing was performed on Vitek 2 or by Etest. Synergy testing was done by Aztreonam (ATM) E-test on Mueller-Hinton agar supplemented with 2.2 μg/mL avibactam. Bacterial isolates underwent whole genome sequencing on an Illumina MiSeq, and resistance determinants (Abricate using CARD), plasmid replicon types (PlasmidFinder 1.3) and sequence type (Tseemann MLSTtool) were identified. Genes were verified by PCR.

Results. The CRE were resistant to all β-lactams, including ceftazidime/avibactam (CZA) and ceftolozane/tazobactam. Synergy testing with CZA+ATM reduced the ATM MICs of the *EC* from >256 to 0.5 μg/mL and the *KP* from >256 to .094 μg/mL, while the *PA* ATM MIC was 4 μg/mL irrespective of the presence of avibactam. WGS indicated that the *EC* and *KP* shared the bla_{NDM-5}, bla_{TEM-4}, and $bla_{CTX-M-15}$ β-lactamase genes, as well as IncFII and IncX3 plasmid replicon types. In addition, the *EC* harbored bla_{CMY-59}, $bla_{OXA-181}$, *qnrS1* and two additional IncB and IncY plasmid replicon types. The *PA* isolate harbored bla_{NDM-1}, *qnrVC1*, several aminoglycoside resistance genes and a type 1 integrase. The *CA* isolate had a fluconazole MIC of >256 μg/mL and a micafungin MIC of 0.125 μg/mL.

Conclusion. Here we report the identification of 4 MDR organisms, including the first reported isolate of *CA* in Houston, in one patient. The pattern of resistance determinants suggests horizontal transmission of bla_{NDM-5} between the CRE isolates. Prompt recognition of MDR organisms is imperative to prevent healthcare-associated spread.

Disclosures. **W. Miller**, Merck: Investigator, Research support. **C. Arias**, Merck & Co., Inc.: Grant Investigator, Research support. MeMed: Grant Investigator, Research support. Allergan: Grant Investigator, Research support.

706. Ceftazidime-Avibactam (CZA) and Meropenem (MER) Are Synergistic and Bactericidal Against Genetically Diverse KPC-Producing *Klebsiella pneumoniae* (Kp)

Chelsea Jones, BA[1]; Ellen Kline, MS[1]; Kristin Morder, BA[1]; Cornelius J. Clancy, MD[2]; M. Hong Nguyen, MD[2] and Ryan K. Shields, PharmD[3]; [1]University of Pittsburgh, Pittsburgh, Pennsylvania, [2]Infectious Diseases, University of Pittsburgh, Pittsburgh, Pennsylvania, [3]University of Pittsburgh, School of Medicine, Pittsburgh, Pennsylvania

Session: 67. Resistance Mechanisms: Gram-Negative
Thursday, October 4, 2018: 12:30 PM

Background. We previously showed that CZA MICs are higher among KPC-3 Kp and KPC-2 Kp with porin mutations. Clinical resistance has emerged among KPC-3 Kp. Here, we tested various agents in combination with CZA for synergistic and bactericidal activity.

Methods. We tested isolates for responses to CZA alone (1 and 4× MIC; avibactam fixed at 4 μg/mL), and in combination with colistin (COL; 2 μg/mL), fosfomycin (FOS; 100 μg/mL + 25 μg/mL G6P), gentamicin (GEN; 2 μg/mL), MER (8 μg/mL), and tigecycline (TGC; 2 μg/mL) by time-kill using a starting inoculum of 1×10^8 cFu/mL. Log-kills were calculated as log cFu/mL decrease from time 0; 24 hours was the primary endpoint.

Results. Thirty KPC-Kp isolates were studied (22 KPC-2 and 8 KPC-3); all isolates were CZA-susceptible (MIC range: 0.125–4 μg/mL). Fifty-three percent harbored *ompK36* mutations (eight each with IS*5* and 134–135 DG insertions). Mean log-kills by CZA at 1× and 4× MIC were 2.00 and 2.35, respectively; CZA was bactericidal (≥3-log kill) at 24 hours against 33% and 50%, respectively. CZA mean log-kills at 4× MIC were greater for KPC-3 (3.81) than KPC-2 (1.82) isolates ($P = 0.03$), but did not vary by porin genotype ($P = 0.44$). GEN was the most active single agent and was bactericidal against 57%; the mean log-kill was 3.06. In combination with CZA, rates of synergy (>2-log kill in combo) with COL, FOS, GEN, MER, and TGC were 83%, 60%, 40%, 87%, and 7%, respectively. The corresponding rates of bactericidal activity were 87%, 77%, 80%, 100%, and 30%, respectively. Antagonism (>1-log kill by most active single agent) was identified in 7%, 23%, 20%, 0%, and 27% with CZA + COL, FOS, GEN, MER, and TGC, respectively. Mean log-kills by CZA + MER were greater among isolates with wild-type (6.58) vs. mutant (5.48) *ompK36* ($P = 0.0006$), and isolates harboring KPC-3 (7.02) vs. KPC-2 (5.63; $P = 0.0004$). CZA + COL responses were attenuated among isolates with COL MICs ≥2 (log-kills 2.88 vs. 7.94; $P = 0.0009$), but not affected by *ompK36* genotype ($P = 0.53$). Among isolates with COL MICs <2; log-kills were greater for CZA + COL (7.94) than CZA + MER (6.44; $P < 0.0001$).

Conclusion. A two-drug combination of CZA + MEM results in high rates of synergy and bactericidal activity against genetically diverse KPC-Kp. Mean log-kills were less among isolates with mutations in *ompK36.* CZA + COL was highly active against isolates *ompK36* mutations, but contingent on COL susceptibility.

Disclosures. **M. H. Nguyen**, Merck: Grant Investigator, Research grant. Astellas: Grant Investigator, Research grant. **R. K. Shields**, Allergan: Grant Investigator, Research grant. Pfizer: Consultant and Scientific Advisor, Speaker honorarium. Shionogi: Scientific Advisor, Consulting fee. Roche: Grant Investigator, Research grant. Venatorx: Grant Investigator, Research grant. Medicines Company: Grant Investigator and Scientific Advisor, Consulting fee and Research grant. Accelerate Diagnostics: Scientific Advisor, Consulting fee.

707. Clarifying the Role of CrrB in Polymxyin-resistant *Klebsiella pneumoniae* Clinical Isolates Utilizing a Novel CRISPR-Cas9 System

Thomas McConville, MD; Marla Giddins, BA; Nenad Macesic, MBBS and Anne-Catrin Uhlemann, MD, PhD; Columbia University Medical Center, New York, New York

Session: 67. Resistance Mechanisms: Gram-Negative
Thursday, October 4, 2018: 12:30 PM

Background. Polymyxin resistance (PR) threatens the mainstay of therapy for carbapenem-resistant Enterobacteriaceae (CRE) infections. While *mgrB* disruption accounts for most cases of PR, missense mutations in *crrB* have been proposed as an alternative pathway for PR through PmrA/B/C upregulation of the *pmrHFIJKLM* operon. It remains unknown if CrrB acts as a positive or negative regulator on its downstream targets.

Methods. We assembled a CRISPR-Cas9 system for gene knockouts (KO) in CRE *K. pneumoniae* (CRKP) using zeocin as a selectable marker. We chose a polymyxin susceptible (PS) and a PR isolate with a missense mutation in *crrB* (L87V) (NR5337 and NR5083, respectively) for KO. Isolates were transformed with a *crrB* KO plasmid, grown with zeocin selection, induced with arabinose, and plated on low-salt LB-zeocin/arabinose. KOs were confirmed via PCR and Sanger sequencing. Polymyxin susceptibility was performed with broth-microdilution. Gene expression was determined by qRT-PCR of cDNA extracts.

Results. Colistin MIC following *crrB* KO of NR5337 (PS) remained unchanged. In contrast, *crrB* KO of NR5083 (PR), decreased polymyxin MIC (MIC >128 to 1.0 μg/mL). qRT-PCR of NR5083 did not show increased expression of *pmrA/C*, nor *pmrK*. NR5083 ^*crrB* showed a small decrease in *pho*Q expression, compared with NR5083, but similar expression of *phoP*, *pmrA/C* and *pmrK* (Table 1).

Conclusion. Polymyxin MIC decreased >128 fold after *crrB* KO in a PR isolate, but colistin MIC remained unchanged after KO in a PS isolate. *CrrB* mutations in PR isolates may confer a gain of function with CrrB acting as a positive regulator on its downstream targets. Contrary to previous literature, no upregulation of *pmrA/C* and *pmrHFIJKLM* was detected. Differences in *crrB* mutations or clonal background may explain this finding. CRISPR-Cas9 may serve as a reliable system for genetic manipulation of CRKP. Further data on the impact of individual *crrB* missense mutations are needed.