Disclosures. **All Authors:** No reported Disclosures.

1826. Impact of Rapid Diagnostics and Ceftazidime–Avibactam on Mortality after Bacteremia Caused by Carbapenem-Resistant Enterobacteriaceae

Michael J. Satlin, MD, MS[1]; Liang Chen, PhD[2]; Gregory Weston, MD, MSCR[3]; Angela Gomez-Simmonds, MD[4]; Tanaya Bhowmick, MD[5]; Susan K. Seo, MD[6]; Steven Sperber, MD[7]; Angela Kim, MD[8]; Brandon Eilertson, MD[9]; Stephen Jenkins, PhD[1]; Michael Levi, ScD[10]; Anne-Catrin Uhlemann, MD, PhD[4]; Melvin P. Weinstein, MD[5]; Yi-Wei Tang, MD, PhD[6]; Tao Hong, PhD[7]; Stefan Juretschko, PhD[11]; Thomas J. Walsh, MD, PhD (Hon)[12]; Lars Westblade, PhD[1] and Barry Kreiswirth, PhD[2]; [1]Weill Cornell Medicine, New York, New York; [2]Center for Discovery and Innovation, Nutley, New Jersey; [3]Montefiore Medical Center and Albert Einstein College of Medicine, Bronx, New York; [4]Columbia University Irving Medical Center, New York, New York; [5]Rutgers Robert Wood Johnson Medical School, New Brunswick, New Jersey; [6]Memorial Sloan Kettering Cancer Center, New York, New York; [7]Hackensack University Medical Center, Hackensack, New Jersey; [8]Northwell Health, Manhasset, New York; [9]State University of New York Downstate, New York, New York; [10]Albert Einstein College of Medicine, Bronx, New York; [11]Northwell Health Laboratories, Lake Success, New York; [12]Weill Cornell Medicine of Cornell University, New York, New York

Session: 182. Emergent Mechanisms of Resistance and How to Prevent Them
Friday, October 4, 2019: 2:00 PM

Background. Patients with bloodstream infections (BSIs) due to carbapenem-resistant Enterobacteriaceae (CRE) have long delays until receipt of appropriate antimicrobial therapy and high mortality rates. Rapid molecular diagnostics and novel therapies, such as ceftazidime–avibactam (CAZ-AVI), offer promise to improve outcomes, but their clinical impact is unclear.

Methods. We conducted an observational study of patients with CRE BSI from January 2016 to June 2018 at 8 New York and New Jersey medical centers. Patient demographics, comorbidities, clinical presentations, diagnostic methods, and treatments were compared between patients who died within 30 days of BSI onset and survivors. Independent risk factors for mortality were identified using logistic regression. We then compared time to receipt of active antimicrobial therapy between patients whose positive blood culture bottles underwent testing for the Klebsiella pneumoniae carbapenemase gene (blaKPC PCR) and patients where this test was not used.

Results. We identified 178 patients with CRE BSI (K. pneumoniae: n = 104, 58%; Enterobacter cloacae: n = 26, 15%; Escherichia coli: n = 26, 15%). The 30-day mortality rate was 38%. An increasing Acute Physiology and Chronic Health Evaluation II score (adjusted odds ratio [aOR] 1.06, P = 0.005) was independently associated with increased 30-day mortality; whereas, use of blaKPC PCR (aOR 0.31, P = 0.005), urinary tract source (aOR 0.12, P = 0.001), and source control (aOR 0.25, P = 0.001) were independently associated with survival. Initial targeted therapy with CAZ-AVI was associated with a 28% 30-day mortality rate, compared with a 49% 30-day mortality rate among patients who received a polymyxin or aminoglycoside (P = 0.036). Patients whose blood culture underwent blaKPC PCR were more likely to receive active antimicrobial therapy within 24 hours of BSI onset (42% vs. 28%; P = 0.07) and had a decreased median time until receipt of active therapy (25 hours vs. 46 hours; P = 0.07), although these differences did not achieve statistical significance.

Conclusion. The use of PCR to rapidly identify blood cultures with blaKPC and definitive therapy with CAZ-AVI instead of polymyxins or aminoglycosides were associated with decreased mortality after CRE bacteremia.

Disclosures. **All Authors:** No reported Disclosures.

1827. Genetic Characterization of Methicillin-Resistant Staphylococcus aureus (MRSA) Isolates Associated with the Development of Reduced Susceptibility to Vancomycin from Latin America

Monica Liliana Vargas Ardila, DVM[1,2]; Betsy E. Castro-Cardozo, MSc[3]; Rafael Rios, MSc[4]; Angie K. Hernandez, BSc[3]; Lina V. Millan, MSc[3]; Lina P. Carvajal, PhD Student[5]; Carlos Seas, MD[6]; Carlos Seas, MD[6]; Jose M. Munita, MD[7]; Cesar A. Arias, MD, MSc, PhD[8]; Jinnethe Reyes, MSc, PhD[9] and Lorena Diaz, PhD[10]; [1]Universidad Nacional de Colombia, Distrito Capital de Bogota, Colombia, [2]Molecular Genetics and Antimicrobial Resistance Unit, Universidad El Bosque, Bogota, Distrito Capital de Bogota, Colombia; [2]Molecular Genetics and Antimicrobial Resistance Unit, Universidad El Bosque, Bogota, Distrito Capital de Bogota, Colombia; [3]Molecular Genetics and Antimicrobial Resistance Unit and International Center for Microbial Genomics, Universidad El Bosque, Bogota, Distrito Capital de Bogota, Colombia; [4]Molecular Genetics and Antimicrobial Resistance Unit and International Center for Microbial Genomics, Universidad El Bosque, Bogota, Distrito Capital de Bogota, Colombia; [5]Universidad Peruana Cayetano Heredia, Lima, Peru; [6]Genomics and Resistant Microbes (GeRM) Group, Millennium Initiative for Collaborative Research On Bacterial Resistance (MICROB-R), Santiago, Region Metropolitana, Chile; [7]University of Texas Health Science Center, Houston, Texas; [8]Molecular Genetics and Antimicrobial Resistance Unit and International Center for Microbial Genomics, Universidad El Bosque, Bogota, Distrito Capital de Bogota, Colombia; [9]Molecular Genetics and Antimicrobial Resistance Unit and International Center for Microbial Genomics, Universidad El Bosque, BOG, COL, Bogota, Distrito Capital de Bogota, Colombia; [10]MICROB-R, Bogota, Distrito Capital de Bogota, Colombia

Session: 182. Emergent Mechanisms of Resistance and How to Prevent Them
Friday, October 4, 2019: 2:15 PM

Background. Vancomycin (VAN) is a first-line therapeutic option for severe MRSA infections, especially in Latin America where other options are limited. However, reduced susceptibility to VAN may lead to therapeutic failures. The molecular mechanisms leading the development of VAN-intermediate *S. aureus* (VISA) and heterogeneous-VISA (hVISA) phenotypes are still unclear. We explored genetic signatures associated with hVISA phenotype in MRSA isolates recovered from bacteremic patients in 9 Latin American countries (2011–2014) in order to develop a genomic platform to identify these isolates.

Methods. From 538 VAN-susceptible MRSA (MIC_{90} = 1 μg/mL) we identified 30 hVISA isolates using GRD and macromethod *E*-tests; from these, 3 were confirmed by PAP-AUC. Whole-genome sequencing was performed in all 30 isolates using Illumina platform. Based on previous studies, we selected 46 genes involved in hVISA development. Multiple Blast alignments were performed using genomes of ATCC29213 and N315 (VAN-susceptible), Mu3 (hVISA) and Mu50 (VISA) as references.

Results. A total of 130 changes in 46 predicted proteins belonging to 8 functional categories were determined: 48 changes related to cell wall biogenesis, 22 to DNA/RNA processing, 17 to regulatory systems, 12 to cofactors and enzymes, 11 to membrane biosynthesis, 9 to virulence, 6 to amino acid metabolism, and 5 to transport of nitrogen and putrescine/spermidine. The most common changes identified in all the hVISA were: Y38H in Atl, N16S in PBP4, S160A in RpoB, L14I in WalK and E156G in YvqF, compared with VSSA strains. The proteins with the highest number of changes detected in the isolates confirmed by PAP-AUC were: CapP, DltA, Pbp4, TcaA, LytM (Cell wall biogenesis); MutL, RpoB (DNA/RNA processing); GraS (Regulatory systems); and PgsA (Membrane biosynthesis).

Conclusion. Changes in genes associated with cell wall biogenesis, DNA/RNA processing, regulatory systems, and membrane biosynthesis were the most prevalent in Latin American hVISA strains. Genetic signatures in genes encoding GraR (N197S), RpoB (H481Y, H481N), VraS (I5N), WalK (L14F, R222K) and MrsR (E146K) are potentially associated with this phenotype. These changes could be used to develop a platform for possible identification of hVISA isolates.

Disclosures. **All Authors:** No reported Disclosures.

1828. Bedaquiline Resistance in Mycobacterium intracellulare Is Mediated by the Transcriptional Repressor MmpT5

David Alexander, PhD[1]; Joshua Yoneda[2]; Supriya Bhat[2]; Teagan Oleksyn[3]; Jeffrey Chen, PhD[4] and Cameron Andrew, PhD[2]; [1]Cadham Provincial Laboratory, Winnipeg, MB, Canada; [2]University of Regina, Regina, SK, Canada; [3]University of Saskatchewan, Saskatoon, SK, Canada; [4]VIDO-InterVac, Saskatoon, SK, Canada

Session: 182. Emergent Mechanisms of Resistance and How to Prevent Them
Friday, October 4, 2019: 2:30 PM

Background. Bedaquiline (BDQ) is an FDA approved antibiotic with antimycobacterial activity. BDQ resistance has been observed in several *Mycobacterium* species. High-level resistance is due to mutations in ATP synthase. Low -level resistance is attributed to drug efflux. Previously, we suggested that the MmpSL5 efflux system mediates BDQ resistance in *M. intracellulare*. Here, we examine the role of MmpT5 in transcriptional regulation of *mmpSL5* and BDQ resistance.

Methods. In this study, *mmpSL5-mmpT5* genes were cloned from 2 pre-treatment (wild-type *mmpT5*) and 2 relapse (mutant *mmpT5*) isolates of *M. intracellulare* and transformed into *M. smegmatis*. BDQ MICs were determined as well as cell survival after 24 hours exposure to an inhibitory concentration (0.07 μg/mL) of BDQ. Transcription of the *M. intracellulare mmpT5* and *mmpSL5* promoters was monitored with luciferase reporter gene fusions in the presence of wild-type and mutant alleles of *mmpT5*. Single and multigene constructs were created using the MoClo system, and transformed into *E. coli* DH5α. Constructs containing the *M. tuberculosis rv0678* gene, which mediates low-level BDQ resistance in *M. tuberculosis*, were also examined.

Results. The BDQ MIC for the *M. smegmatis* control strain, and all strains containing *mmpSL5-mmpT5* constructs, was 0.007 μg/mL. Even so, strains containing mutant *mmpT5* alleles showed enhanced survival after 24 hours exposure to 0.007 μg/mL BDQ. Bacterial colonies associated with mutant *mmpT5* alleles exhibited altered morphology relative to wild-type strains. Transcription of *mmpSL5* was repressed by wild-type *mmpT5*, but neither mutant *mmpT5* nor *rv0678* repressed transcription. The *mmpT5* luciferase reporter was not active.

Conclusion. MmpT5 represses transcription of *mmpSL5* whereas the operon is dysregulated by *mmpT5* mutations. Although Rv0678 regulates *mmpSL* expression in *M. tuberculosis*, it cannot repress the *M. intracellulare mmpSL5* genes. The *mmpSL5-mmpT5* genes have no impact on the BDQ MIC for *M. smegmatis*, but constructs containing mutant *mmpT5* alleles do enhance bacterial survival. The altered morphology of these colonies suggests that BDQ resistance is mediated by cell wall changes in combination with drug efflux.

Disclosures. **All Authors:** No reported Disclosures.

1829. The Paradox of KPC Bearing Strains of Klebsiella pneumoniae with the D179Y Substitution: Resistance to Ceftazidine/Avibactam (CZA) and Susceptibility to Meropenem (MEM)

Melissa D. Barnes, PhD[1]; Magdalena A. Taracilla, MS[2]; Joseph D. Rutter, BS[3]; Minh-Hong Nguyen, MD[4]; Ryan K. Shields, PharmD, MS[4]; Cornelius J. Clancy, MD[4] and Robert A. Bonomo, MD[3]; [1]Case Western Reserve University, Cleveland, Ohio; [2]Research Service, Louis Stokes Veterans Affairs Medical Center, Cleveland, Ohio; [3]Louis Stokes Cleveland VA Medical Center, Cleveland, Ohio; [4]University of Pittsburgh, Pittsburgh, Pennsylvania

Session: 182. Emergent Mechanisms of Resistance and How to Prevent Them
Friday, October 4, 2019: 2:45 PM