underscores the important role WGS plays in identifying new mechanisms of antimicrobial resistance.

Disclosures. All authors: No reported disclosures.

607. Scope and Predictive Genetic/Phenotypic Signatures of “Bicarbonate [NaHCO₃]-Responsiveness” and β-Lactam Sensitization among Methicillin-Resistant Staphylococcus aureus (MRSA) Selvi Caren, Ersoy, BS, MA, PhD1; Brenda Zapata-Davila, BS, MS2; Mariam Otomshi, BS1; Vanessa Milan, BS1; Liang Li, PhD1; Henry Chambers, BA, MD1; Henry Chambers, BA, MD2; Yan Xiong, MD, PhD3 and Arnold Bayer, MD1; 1Los Angeles Biomedical Research Institute, Los Angeles, CA; 2SNU Dominic Hills, Torrance, California; 3LA BioMed at Harbor-UCLA Medical Center, Torrance, California; 4UC San Francisco School of Medicine, San Francisco, California

Session: 65. Mechanisms of Antimicrobial Resistance
Thursday, October 3, 2019: 12:15 PM

Background. Selected MRSA strains become susceptible to β-lactams (e.g., oxacillin [OX]; cefazolin [CFZ]) in vitro when tested in a standard medium (cat.-adjusted Mueller-Tintop Broth; CA-MHB) supplemented with NaHCO₃ (“NaHCO₃, responsiveness”). In vivo activity of β-lactams was demonstrated for MRSA strains with this phenotype in a rabbit endocarditis model (Ersoy et al Antimicrobial Agents Chemotherapy 2019). The current study was designed to: (i) determine the prevalence of the NaHCO₃-responsive phenotype in a large collection of clinical MRSA isolates; and (ii) identify genetic and phenotypic predictors of this phenotype. Methods. 58 recent MRSA bloodstream isolates representing contemporary clonal complex (CC) genotypes were screened for the NaHCO₃-responsive phenotype by broth microdilution methods in CA-MHB, with or without NaHCO₃ supplementation (25–44 mM). MRSA bloodstream isolates representing contemporary clonal complex (CC) genotypes were screened for the NaHCO₃-responsive phenotype by broth microdilution methods in CA-MHB, with or without NaHCO₃ supplementation (25–44 mM).

Results. 43/58 (74.1%) and 21/58 (36.2%) were rendered susceptible to CFZ and OX, respectively, in the presence of NaHCO₃. 20 of 21 OX susceptible CFZ resistant clones were also susceptible to CFZ in the presence of NaHCO₃. High baseline β-lactam MICs (i.e., MICs in CA-MHB alone 2644 μg/mL) was not predictive of NaHCO₃ responsiveness. The CC8 genotype was correlated with NaHCO₃ responsiveness for OX, but not CFZ (P = 0.05). Conclusion. The NaHCO₃-responsive phenotype is relatively common for both OX and especially CFZ against clinical MRSA isolates. Identification of specific genetic factors linked to this phenotype remains ongoing. Confirmation in relevant animal models that this phenotype is predictive of β-lactam efficacy in vivo could provide a solid foundation for a paradigm shift in antimicrobial susceptibility testing of MRSA.

Disclosures. All authors: No reported disclosures.

608. Emerging Methicillin Resistance Mechanism in mec Gene-Negative Staphylococcus lugdunensis Not Detected by Reference Methods Geraldine Durand, PharmD, PhD1; Celine Dupieux-Chabert, PharmD2; Claude-Alexandre Gustave, MD1; Michele Bes, PhD3; Berangere Frasnique, MS4; Corine Fulchiron, MS5; Lorette Munoz, Tech1; Sarah Rivat, Tech1; Anne-gaëlle Ranc, Pharm D2; Francois Vandenbes, MD, Pr1; Frederic Laurent, Pharm, D Pr2; Anne Tristan, Pharm D, PhD3 and Patricia Martins-Simeo, PhD2; 1bioMérieux, Lab Balme Les Grottes, Rhone-Alpes, France; 2French National Reference Center for Staphylococci, Lyon, Rhone-Alpes, France

Session: 65. Mechanisms of Antimicrobial Resistance
Thursday, October 3, 2019: 12:15 PM

Background. B-lactamase resistant in Staphylococci is mediated by mec genes usually diagnosed by disc diffusion Cefoxitin test (DDFOX) and PCR testing. Here, we report methicillin-resistant Staphylococcus lugdunensis and Staphylococcus aureus strains lacking mec gene misdiagnosed by reference methods. Since the strains are not B-lactamase hyperproducers we investigated the molecular basis of the methicillin resistance.

Methods. We tested 2 S. lugdunensis isolates (SL1, SL2) collected from distinct blood cultures of the same patient and 2 S. aureus isolates (SA1, SA2): (i) by DDFOX, (ii) isolates displayed variable results for V2 OXA MIC (0.5 to 24 mg/mL) and for V2 OXSF (POSITIVE, NEGATIVE). For SL1 and SL2 isolates, the V2 OXSF growth curve atypical pattern has led to investigating the OXSF wells. The plates inoculated with the broth extracted from the OXSF well showed 2 colony morphotypes (small “P” and regular “G”) for both isolates. The small colonies (SL1P, SL2P) were Oxacillin resistant (V2 OXA MIC ≥ 4; AD MIC = 4) and V2 OXSF POSITIVE whereas the regular colonies (SL1G, SL2G) were Oxacillin susceptible (V2 OXA MIC = 2; AD MIC = 0.5) and V2 OXSF NEGATIVE. The 4 morphotypes were cefoxitin susceptible by DDFOX and mec negative. Interestingly, WGS revealed a GdpP truncation in the N-terminal domain only found in S. lugdunensis small colonies (SL1P, SL2P) phenotypically resistant to Oxacillin. GdpP is a cyclic diadenosine monophosphate phosphodiesterase enzyme which function is the hydrolysis of a signaling nucleotide.

Conclusion. We described mec negative S. lugdunensis and S. aureus strains expressing heterogeneous methicillin resistance detected by the VITEK2 OXSF test.

S. lugdunensis subpopulation of small colonies resistant to oxacillin is associated with a truncation of GdpP protein previously described in S. aureus. Interestingly GdpP loss of function in Staphylococci is associated with a reduced growth and may arise as a result of the selective pressure of exposure to β Lactams.

Disclosures. All authors: No reported disclosures.

609. Differing Genotypic Contexts Between E. coli and A. baumannii Modulate the Role of blaADC-7 in the Development of Antibiotic Collateral Sensitivity Erin McClure, BS1; Julia Newman1; Nikolish Kshnash, BS1; Joseph Rutter2; Andrea M. Hujer, BS1; Mark D. Adams, PhD3; Jacob Scott, MD, DPSP1 and Robert A. Bonomo, MD1; 1Cleveland Clinic Foundation, Cleveland Heights, Ohio; 2Hawken School, Gates Mills, Ohio; 3Case Western Reserve University School of Medicine, Cleveland, Ohio

Session: 65. Mechanisms of Antimicrobial Resistance
Thursday, October 3, 2019: 12:15 PM

Background. Antibiotic resistance is a global health crisis. While persistent drug discovery of novel antibiotics has previously been relied upon to thwart resistance, evolution inevitably perseveres. While genes conferring an antibiotic resistance have previously been characterized, it is unclear how varying genetic contexts can change the antibiotic resistance phenotype a given gene confers.

Methods. The DH1108 strain of E. coli was transformed with a blaADC-7 plasmid. In 12 evolutionary replicates, the modified E. coli strain and a clinical strain of A. baumannii containing the same resistance gene were passaged daily for 10 days on cefepime gradient agar plates with gradually increasing concentrations of cefepime. MICs of cefepime and a diverse set of 15 other drugs were determined for the parental strains and after the final passage. MICof cefepime after intermediary passages were determined for select replicates. Lastly, the blaADC-7 gene after the final passage was sequenced.

Results. At the end of 10 passages, collateral sensitivity in A. baumannii was observed to tigecycline and fosfomycin in 5 and 6 replicates respectively, out of 10 total. 4 out of 12 evolved replicates of E. coli retained collateral sensitivity to minocycline (Figure 1). In the third E. coli replicate, Sanger sequencing revealed a novel S286R mutation in blaADC-7, appearing in passage seven which preceded a several log fold increase in the MIC of cefepime (Figures 2 and 3). No additional mutations were found in the other evolutionary replicates.

The MIC of cefepime varied among antibiotics of the same class, (e.g., tetracyclines, fourth-generation cephalosporins) in both E. coli and A. baumannii; however, A. baumannii expressed less widespread collateral resistance than E. coli. A previously undiscovered S286R mutation in blaADC-7 coincided with a pronounced increase in resistance to cefepime. Further studies are required to determine whether this mutation gives rise to a structural change in the protein product. Given that no other mutations were found, resistance to cefepime and subsequent collateral resistance to other antibiotics may have developed due to epigenetic changes or mutations outside the blaADC-7 genes. Indeed, future experiments with whole-genome sequencing may reveal such changes.
Disclosures. All authors: No reported disclosures.

610. Meropenem-vaborbactam (MV) In Vitro Activity Against Carbapenem-Resistant Klebsiella pneumoniae (CRKP) Isolates with Outer Membrane Porin Gene Mutations
Mohamad Yasmin, MD1; Steven Marshall, MSc2; Michael Jacobs, MBBS2; Daniel D. Rhoads, MD3; Laura J. Rojas, PhD4; Federico Perez, MD, MSc3 and Robert A. Bonomo, MD1; 1Case Western Reserve University, Cleveland, Ohio; 2University of Colorado School of Medicine, Aurora, Colorado; 3University of Texas Health Science Center, Dallas, Texas; 4University of Nebraska Medical Center, Omaha, Nebraska.

Background. Klebsiella pneumoniae (KP) is a major cause of nosocomial infections, and the emergence of CRKP strains has been increasing over the past years. MV is an attractive option for the treatment of KP complicated infections. It has been shown that porin variants are associated with decreased susceptibility to MV.

Methods. WGS of CRKP clinical isolates was performed and those harboring mutations in Ompk35 and -36 were selected for testing. Meropenem-vaborbactam (MV) was recently approved for the treatment of carbapenem-resistant Enterobacteriaceae complicated urinary tract infections. This study aimed to determine whether MV is active against CRKP isolates with either partial or complete mutations in Ompk35 or Ompk36.

Results. A total of 283 clinical isolates from patients with Escherichia coli species during the period of January 2018 to June 2018, in three tertiary hospitals of Republic of Korea. In vitro antimicrobial susceptibility tests were performed in all E. coli isolates using the broth microdilution method according to the Clinical and Laboratory Standard Institute (CLSI). Multilocus sequence typing (MLST) of the Oxford scheme was conducted to determine the genotypes of E. coli.

Conclusion. The resistant rate of fosfomycin to E. coli is still low. Fosfomycin was active against E. coli including ESBL producing strains.

Disclosures. All authors: No reported disclosures.