699. Relationship Between *Klebsiella pneumoniae* Antimicrobial Resistance and Biofilm Formation

Jaclyn Cusumano
Kathryn Daffinee
Megan Luther
Vrishali Lopes
Aisling R. Caffrey

*See next page for additional authors*

Follow this and additional works at: https://digitalcommons.uri.edu/php_facpubs
Authors
Jaclyn Cusumano, Kathryn Daffinee, Megan Luther, Vrishali Lopes, Aisling R. Caffrey, and Kerry L. LaPlante
combinations based on the breakpoint of MERO. The strains harboring K73R, S130G, and K234R had slightly elevated MERO-nucabactin MICs relative to wild type but did not have significant increases in MERO MICs. Strains with pBCK-KPC2, K73R or S130G had 0.015 mg/L MERO MICs. The pBR322-K234R strain had a twofold lower MERO MIC than pBR322-KPC2 (Figure 1C). The IC₅₀ of cell extracts containing the K234R variant is 781 µM, which is 12-fold higher than that for KPC-2 (66 µM) (Figure 1C). Extracts containing the S130G variant were not inhibited by nacubactam (IC₅₀ > 2.6 mM).

Conclusion. Meropenem-nucabactin is an effective β-lactam β-lactamase inhibitor combination for Enterobacteriaceae with KPC or OXA-48 β-lactamases. The single amino acid substitutions K73R, S130G, and K234R in KPC-2 affect the inactivation mechanism.

Disclosures. M. J. Jacobs, F. Hoffmann-La Roche Ltd.: Grant Investigator, Research grant. J. A. Papp-Walent, F. Hoffmann-La Roche Ltd.: Grant Investigator, Research grant. R. A. Bonomo, F. Hoffmann-La Roche Ltd.: Grant Investigator, Research grant.

699. Relationship Between Klebsiella pneumoniae Antimicrobial Resistance and Biofilm Formation

Jaclyn Casusano, PharmD1,2; Kathryn Daffinee, BS3; Megan Luther, Pharm.D.1,2; Vrishi Lopes, MSc; Aisling Caffrey, PhD, MS3; and Kerry LaPlante, Pharm.D., FCCP.1,2,3

Background. Klebsiella pneumoniae is a frequently multidrug-resistant organism with a high propensity to form biofilm. K. pneumoniae is the most common carbapenem-resistant Enterobacteriaceae (CRE), and labeled an urgent threat by the CDC. The relationship between K. pneumoniae biofilm formation and specific antimicrobial resistance patterns has not been well defined.

Methods. K. pneumoniae isolates (n = 139) were evaluated for antimicrobial resistance and biofilm formation (CDC, Providence VA Med. Ctr., Rhode Island Hosp., BEL and ATCC). Susceptibility was based predominantly on 2017 CLSI (Clinical and Laboratory Standards Institute) breakpoints. Isolates were categorized as multidrug-resistant (MDR; resistant to ≥ 2 antimicrobials in ≥ 3 out of 16 antimicrobial categories) or extensively drug-resistant (XDR; resistant to ≥ 2 antimicrobials in all but ≥ 2 out of 16 antimicrobial categories) based on expert consensus criteria for Enterobacteriaceae (European CDC (ECDC)/CDC, 2012). We collapsed antimicrobial categories described by the ECDC/CDC consensus group into nine categories: penicillins, cephalosporins, monobactams, carbapenems, protein synthesis inhibitors, fluoroquinolones, folate pathway inhibitors, fosfomycin, and colistin. Biofilm formation was assessed using a modified crystal violet method (OD₅₇₀) and defined by titer cut points. Antimicrobial resistance was compared between groups (n = 12/47 vs. strong = 46) biofilm former by chi-square or Fisher’s exact test. Predictors of strong biofilm formation were identified using logistic regression.

Results. MDR isolates were more common among weak (n = 46/47, 97.9%) vs. strong biofilm formers (n = 55/46, 76.1%; P = 0.002), whereas XDR was similar between groups (n = 12/47, 25.5% vs. n = 13/46, 28.3%; P = 0.77). Resistance to penicillins, cephalosporins, monobactams, carbapenems, protein synthesis, or fluoroquinolones was more common among weak biofilm formers (P < 0.05). Carbapenem resistance was inversely associated with strong biofilm formation (odds ratio 0.09; 95% confidence interval 0.02–0.33).

Conclusion. Carbapenem-resistant K. pneumoniae was 91% less likely to form strong biofilm. Potential trade-off mechanisms between antimicrobial resistance and biofilm formation require further exploration.


700. Identification and Whole-Genome Sequencing (WGS) of Meropenem-Vaborbactam (MV) Resistant Klebsiella pneumoniae (MV/KP) Among Patients Without Prior Exposure to MV, Colistin, or Ceftazidime

Mohammad Yasmine, MD,1; Liang Chen, PhD,2; Steven H. Marshall, MS,3; Barry N. Kreiswirth, PhD,3; Federico Perez, MD, MS,3; and Robert A. Bonomo, MD,3

Background. Klebsiella pneumoniae is the most common carbapenem-resistant Enterobacteriaceae. Among isolates resistant to KPC and other Ambler class A β-lactamases, vaborbactam is inactive against metallo-β-lactamases (MBL) and certain Class D enzymes (e.g. OXA-2 and OXA-48). We encountered a case of MV-resistant Klebsiella pneumoniae (MV/KP) and sought to explore the various mechanisms of MV resistance within KP. Methods. A 65-year-old nursing home resident with multiple prior hospitalizations and recent exposure to antibiotics (Timeline) developed sepsis secondary to carbapenem-resistant Klebsiella pneumoniae (CRKP) cUTI. WGS of the patient’s isolate was performed. This was followed by random screening for MV resistance and WGS of others from a historical database. Results. Results of WGS are seen in the table below. Sequencing of our patient’s isolate revealed strain ST258 with a premature stop in aa89 of OmpK35 as well as insertions at Gly134 and Asp135 (i.e., the GD repeat) of OmpK36. Furthermore, the KPC plasmid’s copy number was approximately five times higher than the chromosome. No mutations encoding efflux system AcrAB-ToIC were found.

Conclusion. Resistance to MV in KP was found in isolates that predate the drug’s availability. Notably, resistance occurred in the absence of MBLs and OXAs. The mechanism seems to involve outer membrane porin mutations in OmpK35 and/or OmpK36. WGS is a useful tool in identifying the mechanism of resistance especially for newer agents.

Table: Characterization of MV/KP by WGS

<table>
<thead>
<tr>
<th>Strain</th>
<th>Date</th>
<th>MIC (mg/mL)</th>
<th>MLST</th>
<th>β-Lactamase</th>
<th>Multidrug Transporters and Regulators</th>
<th>OmpK35</th>
<th>OmpK36</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2-12</td>
<td>16</td>
<td>ST258</td>
<td>KPC-2, SHV-160</td>
<td>Emr, Mex, ampC, OmpK35, OmpK36</td>
<td>S to CZA and TGC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>4-3-12</td>
<td>16</td>
<td>ST258</td>
<td>KPC-2, SHV-160</td>
<td>Emr, Mex, ampC, OmpK35, OmpK36</td>
<td>S to CZA and TGC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2013</td>
<td>16</td>
<td>ST258</td>
<td>KPC-2, SHV-160</td>
<td>Emr, Mex, ampC, OmpK35, OmpK36</td>
<td>S to CZA and TGC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>2014</td>
<td>4</td>
<td>ST258</td>
<td>KPC-2, SHV-160</td>
<td>Emr, Mex, ampC, OmpK35, OmpK36</td>
<td>S to CZA and TGC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>2017</td>
<td>32</td>
<td>ST258</td>
<td>KPC-2, SHV-160</td>
<td>N/A</td>
<td>STOP ade8</td>
<td>134-135</td>
<td></td>
</tr>
</tbody>
</table>

Disclosures. All authors: No reported disclosures.

701. Rapid Detection of Antimicrobial Resistance Determinants with the BioFire System

Stefanie Marxreiter, MSc1; Eric Lo, BS2; Cody Oswald, BS2; Aubrie Hopper, MLS, ASCP; Becky Barr, MLS, ASCP3; Judy A. Daly, PhD,4; Kimberly E. Hansen, MD, MHS,1 Christine C. Ginocchio, PhD MT5;6; Robert Crisp, PhD7; and Andrew Hemmett, PhD8;9;10;11 BioFire Diagnostics, LLC, Salt Lake City, Utah, 1Primary Children’s Hospital, Salt Lake City, Utah, 2University of Utah, Salt Lake City, Utah, 3AstraZeneca, North Carolina, 4Hofstra Northwell School of Medicine, Hempstead, New York

Session: 67. Resistance Mechanisms: Gram-Negative

Thursday, October 4, 2018: 12:30 PM

Background. MV is a newly approved β-lactam/β-lactamase inhibitor combination (BLIC) for the treatment of complicated urinary tract infections (cUTI). Vaborbactam is a cyclic boronic acid BI1 that was mainly developed as a potent inhibitor of KPC carbapenemases and other Ambler class A β-lactamases. Vaborbactam is inactive against metallo-β-lactamases (MBL) and certain Class D enzymes (e.g. OXA-2 and OXA-48). We encountered a case of MV-resistant Klebsiella pneumoniae (MV/KP) and sought to explore the various mechanisms of MV resistance within KP. Methods. A 65-year-old nursing home resident with multiple prior hospitalizations and recent exposure to antibiotics (Timeline) developed sepsis secondary to carbapenem-resistant Klebsiella pneumoniae (CRKP) cUTI. WGS of the patient’s isolate was performed. This was followed by random screening for MV resistance and WGS of others from a historical database. Results. Results of WGS are seen in the table below. Sequencing of our patient’s isolate revealed strain ST258 with a premature stop in aa89 of OmpK35 as well as insertions at Gly134 and Asp135 (i.e., the GD repeat) of OmpK36. Furthermore, the KPC plasmid’s copy number was approximately five times higher than the chromosome. No mutations encoding efflux system AcrAB-ToIC were found.

Conclusion. Resistance to MV in KP was found in isolates that predate the drug’s availability. Notably, resistance occurred in the absence of MBLs and OXAs. The mechanism seems to involve outer membrane porin mutations in OmpK35 and/or OmpK36. WGS is a useful tool in identifying the mechanism of resistance especially for newer agents.

Table: Characterization of MV/KP by WGS

Typing Enzymes Efflux Outer Membrane Porin Variant

<table>
<thead>
<tr>
<th>Strain</th>
<th>Date</th>
<th>MIC (mg/mL)</th>
<th>MLST</th>
<th>β-Lactamase</th>
<th>Multidrug Transporters and Regulators</th>
<th>OmpK35</th>
<th>OmpK36</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2-12</td>
<td>16</td>
<td>ST258</td>
<td>KPC-2, SHV-160</td>
<td>Emr, Mex, ampC, OmpK35, OmpK36</td>
<td>S to CZA and TGC</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>