699. Relationship Between Klebsiella pneumoniae Antimicrobial Resistance and Biofilm Formation

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Available at: https://doi.org/10.1093/ofid/ofy210.706

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combinations based on the breakpoint of MERO. The strains harboring K73R, S130G, and K234R had slightly elevated MERO-nacubactam MICs relative to wild type but did not have corresponding increases in MERO MICs. Strains with pBKS-KPC2, K73R or S130G had 0.015 mg/L MERO MICs. The pRBS2-K234R strain had a twofold lower MER0 MIC than pRBS22-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-nacubactam 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. R. Jacobs, F. Hoffmann-La Roche Ltd.: Grant Investigator, Research grant.
Papp-Wallace K. M., F. Hoffmann-La Roche Ltd.: Grant Investigator, Research grant.
Bonomo R. A., F. Hoffmann-La Roche Ltd.: Grant Investigator, Research grant.

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

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 ≥ 1 antimicrobial in ≥ 3 out of 16 antimicrobial categories) or extensively drug-resistant (XDR: resistant to ≥ 2 antimicrobial 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, antipseudomonal β-lactams, and carbapenem-resistant Enterobacteriaceae (CRE). Results were compared using χ² or Fisher's exact test. Biofilm formation was assessed using a modified crystal violet method (OD₅⁷⁰).

Results. MDR isolates were more common among weak (n = 46/47, 97.9%) vs. strong biofilm formers (n = 35/46, 76.1%; P = 0.002), whereas XDR was similar between groups (n = 12/47, 25.5% vs. n = 13/46, 28.3% vs. 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. Integration and Whole-Genome Sequencing (WGS) of Meropenem-Vaborbactam (MV) Resistant Klebsiella pneumoniae (MVLRKP) Among Patients Without Prior Exposure to MV: Collabora Damazi, Mohamed Yasin, MD1; Liang Chen, PhD2; Steven H. Marshall, MS3; Barry N. Kreiswhirz, PhD4; Federico Perez, MD, MS5,6 and Robert A. Bonomo, MD3, 1Infectious Diseases, Case Western Reserve University, Cleveland, Cleveland, Ohio; 2Public Health Research Institute, New Jersey Medical School, Newark, New Jersey; 3Research Service, Louis Stokes Cleveland VA Medical Center, Cleveland, Ohio; 4Division of Infectious Diseases, Case Western Reserve University School of Medicine, Cleveland, Cleveland, Ohio; 5Department of Pharmacology, Biochemistry, Proteomics and Bioinformatics, Case Western Reserve University School of Medicine, Cleveland, Ohio

Session: 67. Resistance Mechanisms: Gram-Negative
Friday, October 5, 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 BLI that was mainly developed as a potent inhibitor of KPC β-lactamases and other Ambler class A & C enzymes. 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 (MVLRKP) 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 other isolates 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 at 89 in OmpK35 as well as insertions at Gly34 and Asp123 (i.e., the deletion) of OmpK36. The single amino acid substitutions K73R, S130G and K234R in KPC-2 affect the inactivation mechanism.

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 MVLRKP 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</th>
<th>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 &amp; SHV-15</td>
<td>Emr, makr, oqxAB, smeD</td>
<td>OqxAB, TGC</td>
<td>SD</td>
<td>SD</td>
<td>CZA</td>
</tr>
<tr>
<td>2</td>
<td>4-3-12</td>
<td>16</td>
<td>ST258</td>
<td>KPC-2 &amp; SHV-15</td>
<td>Emr, makr, oqxAB, smeD</td>
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<td>SD</td>
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<td>CZA</td>
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<tr>
<td>3</td>
<td>2013</td>
<td>4</td>
<td>ST258</td>
<td>KPC-2 &amp; SHV-15</td>
<td>Emr, makr, oqxAB, smeD</td>
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<td>SD</td>
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<tr>
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<td>KPC-2 &amp; SHV-15</td>
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<td>SD</td>
<td>SD</td>
<td>CZA</td>
</tr>
</tbody>
</table>

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

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

Disclosures. All authors: No reported disclosures.