P1150a
Poster Session IV
MDR Gram-negatives - molecular biology of resistance genes

Can rapid molecular diagnostics assist in the choice of beta-lactam antibiotics? An analysis of data from Primers-1

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Objectives
The goal of the Antibiotic Resistance Leadership Group (ARLG) is to advance clinical research on antibiotic resistance. An immediate objective of the ARLG is to also evaluate rapid molecular diagnostics, including novel platforms. We evaluated the ability of four platforms - PCR/ESI-MS (Ibis Biosciences); Molecular Beacons (MB); Ion Torrent DNA sequencing (IT), and DNA microarrays (CheckPoints CT103 microarray kit) to predict resistance to beta-lactam antibiotics in a collection of multidrug-resistant (MDR) Escherichia coli and Klebsiella pneumoniae.

Methods
79 previously characterized clinical isolates of E. coli and K. pneumoniae known to express a wide variety of extended-spectrum beta-lactamase (bla) genes (ESBLs) and carbapenemases were chosen. Susceptibility and resistance to 12 beta-lactams and 2 beta-lactam beta-lactamase inhibitor combinations was determined using CLSI standards. Platforms were used to identify the genetic determinants of bla mediated resistance. The probabilities of correctly predicting susceptibility/non-susceptibility based on the presence of certain bla genes (vs. MIC phenotype) were estimated using 95% confidence intervals (CIs), for each antibiotic for each platform. Platform performance was compared.

Results
Select estimated probabilities of correctly predicting non-susceptibility and susceptibility are summarized (Table 1). In a community that has a prevalence of 15% ceftazidime resistance and 5% carbapenem resistance, the ability of each platform to correctly predict phenotype susceptibility is 100%, 98%, 99%, and 99% for ceftazidime; and 100%, 100%, 100%, and 99% for imipenem. The ability of each platform to correctly predict phenotype non-susceptibility is 18%, 20%, 21%, and 16% for ceftazidime; and 22%, 38%, 31%, and 22% for imipenem.

Conclusion
Performances of the platforms were similar with regard to correctly predicting susceptibility and non-susceptibility for most beta-lactams and for identifying a complex background of 3-4 bla genes. The false non-susceptibility rate for carbapenems may be less than for cephalosporins. Use of molecular diagnostic platforms in clinical trials can identify bla genotypes that confer beta-lactam resistance and can lead to informed choices of precisely targeted antibiotic therapy.

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Estimated probabilities (95% CIs) of correctly predicting non-susceptibility</th>
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<tbody>
<tr>
<td></td>
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<tr>
<td>Ceftriaxone</td>
<td>1.00 (0.95, 1.00)</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>1.00 (0.95, 1.00)</td>
</tr>
<tr>
<td>Cefepime</td>
<td>1.00 (0.95, 1.00)</td>
</tr>
<tr>
<td>Piperacillin/tazobactam</td>
<td>0.77 (0.65, 0.87)</td>
</tr>
<tr>
<td>Imipenem</td>
<td>0.93 (0.81, 0.99)</td>
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</tbody>
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All authors are members of the Antibiotic Resistance Leadership Group (ARLG)