Acuitas® CR Elite and Acuitas Lighthouse™ - A Genetic, Phenotypic and Bioinformatics Solution for Typing and Tracking Multidrug-Resistant Organisms (MDROs)
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Abstract
Multidrug resistant organisms (MDROs) pose a threat to patients and place an economic burden on healthcare systems. Carbapenem-resistant bacilli and extended spectrum beta-lactamase (ESBL) producers have accelerated the need for faster and better typing and tracking to prevent outbreaks, lower infection rates, and decrease patient length of stay.

The Acuitas CR Elite Test and Acuitas Lighthouse (OpGen Inc., Gaithersburg, MD) integrate molecular and phenotypic analysis with bioinformatics to track pathogen prevalence, incidence, and transmission trends on local, regional, and global levels for infection control and patient/population management. Multiplex PCR detection across hundreds of gene subtypes of the KPC, NDM, VIM, IMP, OXA-23, OXA-48, OXA-51, CTX-M-1, CTX-M-2 and vanA resistance genes is combined with simultaneous culture plate screening for carbapenem-resistant Enterobacteriaceae (CREs) with confirmatory antibiotic susceptibility testing. Results are integrated with patient demographics and clinical data to construct patient antibiotic resistance profiles (Lighthouse Profiles) using a bacterial typing algorithm and bioinformatic analytics.

A total of 518 clinical samples, including 318 collected peri-anal swabs and 264 submitted clinical isolates from seven hospitals in the United States were tested with Acuitas CR Elite. The targeted gene prevalence among swabs was 55 (18%) vanA, 15 (5%) CTX-M-1, 5 (2%) OXA-51, 4 (1%) KPC, 3 (1%) CTX-M-2, 1 (<1%) IMP, and 1 (<1%) OXA-23. The targeted gene prevalence among clinical isolates was 126 (48%) KPC, 33 (13%) OXA-51, 28 (11%) CTX-M-1, 21 (8%) OXA-23, and 3 (1%) NDM, and 1 (<1%) VIM. The majority of the 147 CRE identified were Klebsiella pneumoniae with KPC. Carbapenem-resistant Gram negative bacilli and CRE were differentiated into Lighthouse profiles allowing for higher resolution tracking at the hospital and regional levels. KPC-containing K. pneumoniae at one site was differentiated into multiple profiles.

Acuitas CR Elite Test and Lighthouse provide an early warning resource for hospital acquired infection (HAI) prevention and control. Potential benefits include better antibiotic stewardship, decreased infection rates, improved patient outcomes, and reduced patient length of stay.

Clinical Samples
A total of 518 clinical samples were submitted to OpGen’s clinical services laboratory (OpGen, Inc., Gaithersburg, MD) in 2014 for testing from seven institutions. Institution names were blinded to protect identity. Of the total samples, 318 samples were peri-anal swabs collected using the Copen eSwab™ and 264 were clinical culture isolates submitted on agar growth medium.

Acuitas MDRO Gene Test
The Acuitas Multi Drug Resistant Organism (MDRO) Gene Test is a PCR-based, microwell array assay that detects high-risk antibiotic resistant genes (Table 1) for better informed infection control decisions in a single swab test provided through the OpGen clinical service laboratory.

Table 1. Acuitas MDRO Gene Test targets 9 high-risk gene groups associated with CRE, carbapenemase producers, ESBL, and VRE.

<table>
<thead>
<tr>
<th>Acuitas MDRO Genes Detected per Swab</th>
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<tbody>
<tr>
<td>Carbenpenem Resistant Enterobacteriaceae (CRE)</td>
</tr>
<tr>
<td>KPC</td>
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<tr>
<td>NDM</td>
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<tr>
<td>VIM</td>
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<tr>
<td>IMP</td>
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<tr>
<td>OXA-48</td>
</tr>
<tr>
<td>Carbapenemase Producer Associated</td>
</tr>
<tr>
<td>OXA-23</td>
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<tr>
<td>OXA-51</td>
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<tr>
<td>ESBL Associated</td>
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<tr>
<td>CTX-M</td>
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<tr>
<td>VRE Associated</td>
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Results
Figure 3. Detection of high-risk antimicrobial resistance genes among swabs (left) and clinical isolates (right) allowed for surveillance and epidemiological characterization.

Figure 4. The prevalence of high-risk antimicrobial resistance genes were determined for all hospitals. Hospital F showed the highest number of submitted isolates for KPC.

Figure 5. Lighthouse profiles for each sample were determined and used to differentiate cephalexin-resistant Gram negative bacilli and CRE in the hospitals in region 1. C1, Citrobacter freundii; E1, Escherichia coli; E10, Enterobacter cloacae complex; E9, Enterobacter aerogenes; E3, Enterobacter gergoviae, K1, Klebsiella pneumoniae; K5, K. oxytoca; Ceph-RGN, cephalexin-resistant Gram negative bacilli, C1, CTX-M-1; C2, CTX-M-2.

Figure 6. Lighthouse profiles are able to further differentiate organisms and indicated that Hospital F had two major types of KPC-containing K. pneumoniae with profiles (red circles). Lighthouse profiles include gene targets in addition to Acuitas MDRO Gene Test targets.

Conclusions
1. Acuitas CR Elite Test is a useful test for hospital Infection Prevention (IP) and Control (IC) to provide genotypic and phenotypic data together with ID/AST.
2. Lighthouse can track and trend genotypic and phenotypic data.
3. Acuitas CR Elite Test and Lighthouse can provide an early warning to IP and IC to decrease infection rates, improve patient outcomes, and reduce patient length of stay.

Figure 2. The Acuitas Lighthouse profiles is a novel typing methodology that combines identity, phenotype, genotype, and how often the specific combination of characteristics have been observed into a single nomenclature. Lighthouse profiles can be combined with additional patient information (e.g., location, date) within the Lighthouse MDRO Management System to track and trend MDROs within a hospital proactively. Acuitas Lighthouse is for research use only and not for use in diagnostic procedures.

Figure 1. The Acuitas CR Elite Test combines the MDRO Gene Test with parallel phenotypic testing with CRE selective culture on chromogenic agar medium and reflex Identification (ID) and Antimicrobial Susceptibility Testing (AST) for confirmation of CRE.

Figure 6. Lighthouse profiles are able to further differentiate organisms and indicated that Hospital F had two major types of KPC-containing K. pneumoniae with profiles (red circles). Lighthouse profiles include gene targets in addition to Acuitas MDRO Gene Test targets.