USEFUL FOR

Characterizing the molecular mechanisms of antimicrobial resistance in Gram-negative bacilli to explain unusual phenotypic susceptibility profiles or for epidemiologic purposes. The panel detects the following beta-lactamase enzyme producing genes:

**Carbapenemase Genes:**
- GES (Carbapenemase)
- NDM
- OXA-58 like
- GIM
- OXA-23 like
- SPM
- IMP
- OXA-24 like
- VIM
- KPC
- OXA-48 like

**ESBL Genes:**
- BEL
- CTX-M/25 Group
- TEM
- GES (ESBL)
- CTX-M1 Group
- VEB
- CTX-M2 Group
- PER
- CTX-M9 Group
- SHV

**AmpC Genes:**
- ACC
- CMY MOX
- DHA
- ACT/MIR
- CMYII
- FOX

CLINICAL INFORMATION

The Check-MDR CT103XL panel, which is performed on bacterial isolates, detects 27 genes associated with antimicrobial resistance in Gram-negative bacilli.

Antibiotic resistance is evolving as a result of use and overuse of antibacterial agents. Characterizing the molecular mechanisms of antimicrobial resistance can be helpful to explain unusual phenotypic susceptibility profiles or for epidemiologic purposes. A myriad of beta-lactamase enzymes may be found in Gram-negative bacteria; these enzymes hydrolyze (break down) the beta-lactam ring of beta-lactam antibiotics, destroying their antibacterial activity. A single bacterial isolate may carry 1 or more genes that code for the production of a beta-lactamase enzyme. Beta-lactamases can be on the chromosome or on plasmids and may be classified as extended-spectrum beta-lactamases (ESBLs), AmpCs, and carbapenemases, among other types.

**ESBLs** are beta-lactamases with an expanded substrate profile and are typically plasmid-borne. They are capable of hydrolyzing first-, second-, third- and fourth-generation cephalosporins, penicillins, and monobactams. TEM, SHV, and CTX-M genes are the most clinically prevalent.
TEM and SHV subtypes are derived from the parental sequences by point mutations resulting in amino acid substitutions, which allow the enzymes to hydrolyze a wide range of beta-lactam antibiotics.

CTX-M genes originate from *Kluyvera* species and can be separated into 5 different groups based on their amino acid sequence: CTX-M-1, CTX-M-2, CTX-M-9, CTX-M-8, and CTX-M-25.

VEB, PER, BEL, and GES genes are less common.

**AmpC cephalosporinases** hydrolyze almost all beta-lactam antibiotics including penicillins, cephalosporins, and monobactams and may be chromosomally- or plasmid-encoded. Several *Enterobacteriaceae* carry a chromosomal copy of an AmpC gene.

<table>
<thead>
<tr>
<th>AMPC GENE</th>
<th>ORIGIN OF CHROMOSOMAL GENE</th>
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<tbody>
<tr>
<td>CMY II</td>
<td>Citrobacter freundii</td>
</tr>
<tr>
<td>DHA</td>
<td>Morganella morganii</td>
</tr>
<tr>
<td>FOX</td>
<td>Aeromonas caviae</td>
</tr>
<tr>
<td>ACC</td>
<td>Hafnia alvei</td>
</tr>
<tr>
<td>ACT/MIR</td>
<td>Enterobacter cloaceae and Enterobacter asburiae</td>
</tr>
<tr>
<td>CMY VMOX</td>
<td>Aeromonas hydrophila</td>
</tr>
</tbody>
</table>

Plasmid-encoded AmpC genes may be shared among bacteria. Plasmid-encoded AmpC genes may produce a higher amount of beta-lactamase as compared to chromosomally-encoded AmpC genes; knowing the mechanism may be useful in assessing treatment. An AmpC gene detected in a species that does not have a chromosomal AmpC (see table above) suggests that the gene is plasmid-encoded.

**Carbapenemases** show general resistance to all beta-lactam antibiotics including the beta-lactam-beta-lactamase inhibitor combinations and elevated or complete resistance against carbapenem antibiotics. In addition, isolates harboring carbapenemases often have additional beta-lactamase genes and genes for resistance to quinolones and aminoglycosides.

- *Klebsiella pneumoniae* Carbapenemase (KPC) is a plasmid-encoded carbapenemase first identified in *Klebsiella pneumoniae* isolates in North America. KPC has since spread to many parts of the world and can be found in several species of the *Enterobacteriaceae*.
- New Delhi Metallo-beta-lactamase (NDM) was first reported in 2009 from a patient of Indian origin in Sweden. It is prevalent in the Indian subcontinent, but has spread worldwide.
- The oxacillinase group consists of 10 members, of which OXA-48 and OXA-181 are the most prevalent variants. OXA-48 occurs predominantly in *Enterobacteriaceae*, originated from *Shewanella* species, and is most prevalent in Europe and the North African subcontinent. Another grouping of OXA-type carbapenemases are found in *Acinetobacter* species and consists of 3 type members, OXA-23, OXA-24, and OXA-58. Each type has several subtypes.
- VIM, a metallo-beta-lactamase, was first found in 1997 in a *Pseudomonas aeruginosa* isolate in Verona. It may be found in *Enterobacteriaceae* and includes at least 38 variants of which the DNA sequences may differ significantly.
- IMP, a metallo-beta-lactamase, was detected in Japan in 1990 (IMP-1) in *Pseudomonas aeruginosa*. It may be found worldwide in *Enterobacteriaceae* and includes at least 44 members with varying gene sequences.
- GIM-1 and SPM-1, also metallo-beta-lactamases, are less frequently found carbapenemases. GIM-1 originated in Germany and has been found in *Pseudomonas aeruginosa*, *Enterobacteriaceae*, and *Acinetobacter* spp. SPM-1 producing *Pseudomonas aeruginosa* is endemic in Brazilian hospitals where it has been associated with numerous outbreaks.
- *GES* gene family consists of both ESBL-types and carbapenemase types.