

# We have you covered when it comes to bacterial resistance mechanisms

Rising rates of antimicrobial resistance are a clinical dilemma for the management of patients with bacteremia. The presence of a resistance gene, as detected by one of several commercially available molecular test panels, can assist clinicians in ruling out options for antibiotic therapy. For example, the presence of KPC in an isolate of *Klebsiella pneumoniae* typically rules out beta-lactam therapy. Conversely, the absence of these resistance genes does not indicate which antibiotics will be active.

Molecular genotypic testing only detects the most common bacterial resistance genes, and cannot detect other methods of resistance including new and emerging resistance genes, genetic mutations, porin mutations and efflux pumps.

The Accelerate PhenoTest® BC kit decreases the time to direct antimicrobial susceptibility results by approximately 40 hours over conventional methods. The Accelerate PhenoTest BC kit provides minimum inhibitory concentrations (MICs) to specific antimicrobials along with interpretation as susceptible (S), intermediate (I), or resistant (R), allowing for clinically actionable results.

## Superior Resistance Coverage

Resistance Phenotype	Resistance Mechanism	Accelerate Pheno® system (MIC result) <sup>a</sup>	Luminex Verigene®	Genmark ePlex®	BioFire® BCID 2
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### Gram-Positives

MRSA	<i>mecA</i>	●	●	●	●
	<i>mecC</i>	●		●	●
	MREJ	●			●
VRE	<i>vanA</i>	●	●	●	●
	<i>vanB</i>	●	●	●	●
VRSA	<i>vanA</i>	●			
VISA	combination of mutations	●			

### Gram-Negatives

Extended-Spectrum Cephalosporin Resistance <sup>b</sup>	TEM (select variants)	●			
	SHV (select variants)	●			
	CTX-M (select variants)	●	●	●	●
	AmpC	●			
	100's of others <sup>c</sup> ...	●			
Carbapenem Resistance	KPC (select variants)	●	●	●	●
	IMP (select variants)	●	●	●	●
	OXA (select variants)	●	●	●	●
	NDM (select variants)	●	●	●	●
	VIM (select variants)	●	●	●	●
	AmpC overexpression	●			
	AmpC + porin loss / efflux pump	●			
	ESBL + porin loss / efflux pump	●			
Colistin Resistance	<b>100's of others<sup>d</sup>...</b>	●			
	mcr-1	●			●
	other mcr variants	●			
	LPS modification	●			

<sup>a</sup> Detects resistance agnostic of mechanism. The Accelerate Pheno system does not detect genotypic resistance markers.

<sup>b</sup> Includes third- and fourth-generation cephalosporins such as ceftriaxone, ceftazidime and cefepime

<sup>c</sup> Other CTX-M variants, TEM variants, SHV variants, etc.

<sup>d</sup> Other KPC variants, IMP variants, OXA variants, NDM variants, VIM variants, etc.

## Addendum

- **AmpC:** chromosomal beta-lactamases that confer resistance to penicillins, cefazolin, cephamycins (including ceftiofur and cefotetan) and beta-lactam/beta lactamase inhibitor combinations. AmpC enzymes are inducible and can be expressed at high levels by mutation.
- **CTX-M:** ESBL enzyme, confers resistance to 3rd generation cephalosporins and monobactams
- **Efflux pumps:** protein-based active transport systems located in the bacterial cell membrane which allow bacteria to export or “pump” antibiotics out of the bacterial cell.
- **ESBL:** extended spectrum beta-lactamase enzymes produced by many Enterobacterales. ESBLs confer resistance to most penicillins, cephalosporins and the monobactam aztreonam.
- **IMP:** plasmid-encoded class B metallo-beta-lactamase. Confers resistance to all beta lactams including carbapenems
- **KPC:** *Klebsiella pneumoniae* carbapenemases produced by many Enterobacterales and have been found in isolates of *Pseudomonas* and *Acinetobacter* spp. They confer resistance to all beta lactams including carbapenems.
- **LPS modification:** gram-negative bacterial lipopolysaccharide (LPS) is a major component of the outer membrane. Lipopolysaccharide modifications are thought to facilitate bacterial evasion of innate immunity, enhancing pathogenicity.
- **mcr-1:** mobilized colistin resistance gene. Confers plasmid mediated resistance to colistin
- **mecA gene:** encodes for PBP2a, which confers resistance to beta-lactams in MRSA. Note: *mecA* can be detected by resistance to both oxacillin and ceftiofur (Accelerate uses a ceftiofur screen for methicillin-resistance, which is more reproducible and accurate than oxacillin, according to the CDC<sup>1</sup>).
- **mecC gene:** homologue of *mecA* gene. Note: *mecC* can be detected by resistance to ceftiofur, but cannot be detected using oxacillin because it tests susceptible (Accelerate uses a ceftiofur screen for methicillin-resistance).
- **MREJ:** MREJ refers to the SCC*mec* right extremity junction, which is located between the *mecA* cassette and the *orfX* gene. It is an alternative target for detecting methicillin-resistance in *Staphylococcus aureus*.
- **MRSA:** methicillin-resistant *Staphylococcus aureus*
- **NDM:** class B metallo-beta-lactamase. Confers resistance to all beta lactams including carbapenems
- **OXA:** plasmid-encoded class D beta-lactamase. Commonly found on isolates of *Acinetobacter baumannii*
- **PBP:** penicillin binding protein is a component of the bacterial cell wall. Beta-lactam antibiotics (i.e. penicillin and related antibiotics) work by irreversibly binding to PBP, which impedes bacterial cell wall synthesis and kills the bacteria.
- **PBP2a:** mutation of PBP with a lower affinity for beta-lactam antibiotics. Because the binding of beta-lactam antibiotics to PBP2A is reversible, this allows bacterial cell wall synthesis to continue and confers resistance to beta-lactam antibiotics.
- **Porin:** barrel-shaped membrane transport proteins that act as a pore through which molecules, such as antibiotics can diffuse into a bacterial cell.
- **Porin loss:** mutation to the porin gene that results in antibiotics having a lower permeability or being completely excluded from transport. Porin mutations are more likely to occur in gram-negative bacteria.
- **SHV:** ESBL enzyme, confers resistance to 3rd generation cephalosporins and monobactams
- **SCC*mec*:** staphylococcal cassette chromosome *mec* element
- **TEM:** ESBL enzyme, confers resistance to 3rd generation cephalosporins and monobactams
- **vanA gene:** confers resistance to vancomycin and teicoplanin in enterococci
- **vanB gene:** confers resistance to only vancomycin in enterococci
- **VIM:** class B metallo-beta-lactamase. Confers resistance to all beta lactams including carbapenems
- **VISA:** vancomycin-intermediate *Staphylococcus aureus*
- **VRE:** vancomycin-resistant enterococci
- **VRSA:** vancomycin-resistant *Staphylococcus aureus*

<sup>1</sup>CDC website: <https://www.cdc.gov/mrsa/lab/index.html>. Published February 6, 2019. Accessed May 15, 2020.