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Rapid detection of carbapenem and 3rd generation cephalosporin resistance directly from positive blood cultures

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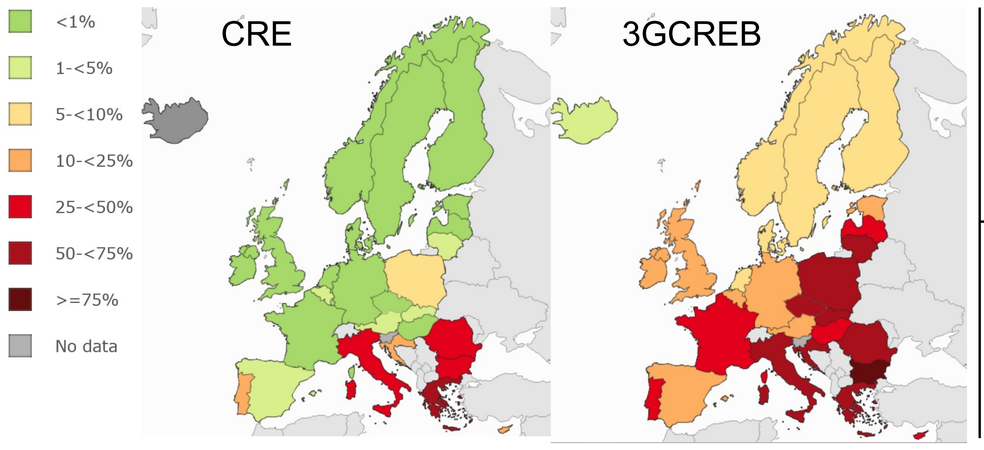
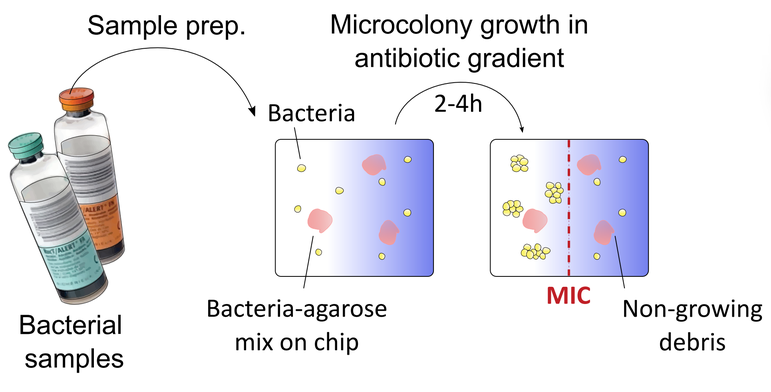
1 Carbapenem and cephalosporin resistance: global health threat

Carbapenem-resistant and 3rd generation cephalosporin resistant Enterobacterales (CRE and 3GCREB, respectively) have emerged as serious threats to global health in the last decade. The rapid dissemination due to plasmid-mediated horizontal transmission of these resistance genes highlights the need for accurate and timely detection methods, to allow interventions such as patient isolation and escalation of antibiotic therapy. Commonly used methods include specific phenotypic plate-based and genotypic PCR-based assays, with varying specificity and sensitivity. However, phenotypic detection of resistance according to MIC and clinical breakpoints remain the gold standard.



3rd generation cephalosporin resistance and carbapenem resistance in Europe, 2019. Data from EARS-Net

2 The QuickMIC system measures AST directly from blood culture



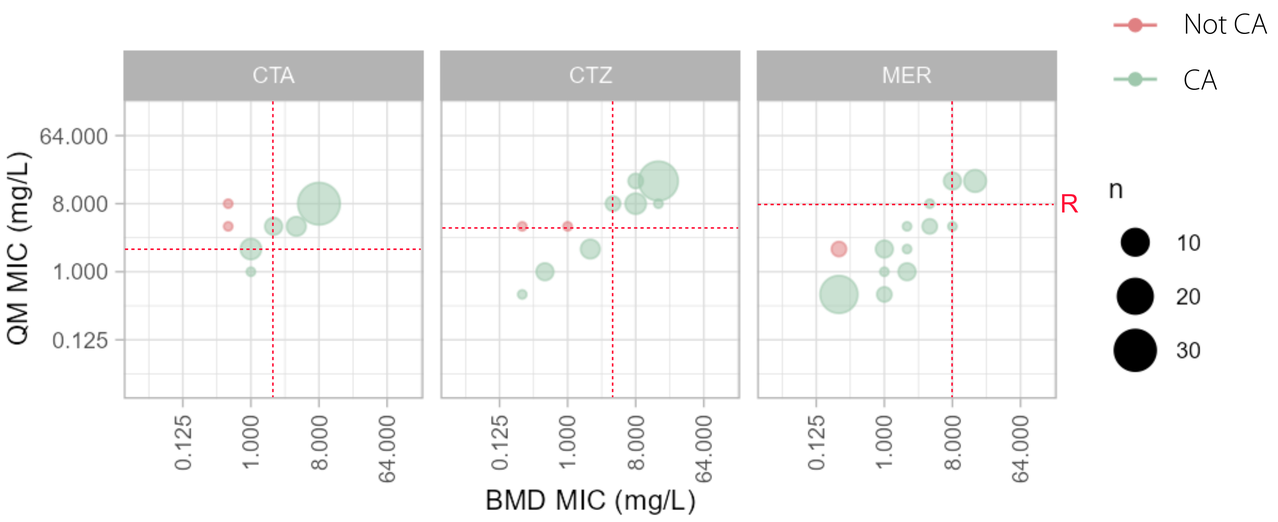
Gradientech AB has developed a new rapid AST system, QuickMIC. The QuickMIC system uses a microfluidic cartridge with 12 different antibiotics, forming gradients through each sample chamber. The QM Analyst read-out software can measure an exact linear MIC within 2-4 hours, directly from blood cultures. This allows rapid categorization of resistance, using EUCAST breakpoints.

Principle behind the QuickMIC rapid AST system, and example images of the instrument and microfluidic cassette.

3 Phenotypic detection of CRE and 3GCREB resistance in 2-4 hours

20 clinically derived and verified CRE (n=4) or 3GCREB (n = 20) *E.coli, K. pneumoniae* and *E. aerogenes* (n = 10, 9, 1, respectively) blood isolates as well as 15 wild-type controls (n = 8, 6, 1 for *E. coli, K. pneumoniae* and *E. aerogenes*, respectively) were tested with the QuickMIC system in duplicate for each strain. The results were classified as susceptible or resistant based on MIC and EUCAST breakpoints. Non-susceptibility was used to categorize resistance. Indicator antimicrobials for 3GCREB were ceftazidime and cefotaxime, and indicator for CRE was meropenem. Specificity and sensitivity of CRE and 3GCREB detection, as well as time to result were recorded. The QuickMIC system provided a categorical result on average within 3.6h from start (min: 2.3h, max 3.8h). CRE was correctly determined in 100% of tests, and 3GCREB was correctly determined in 100% of tests, using CTA and CTZ together.

	CRE (MER)	3GC (CTZ)	3GC (CTA)	3GC (combined)
Sensitivity	100%	94.6%	97.3%	100%
Specificity	97.3%	ND	ND	90.5%



Comparison of QuickMIC MIC and reference test (BMD) MIC. BMD was used for verifying CRE and 3GCREB in the tested isolates. Red: not in categorical agreement, green: in categorical agreement.

4 Conclusion:

The QuickMIC system can provide accurate detection of CRE and 3GCREB infections shortly after blood culture positivity, thereby enabling timely infection control and treatment interventions for patients with CRE and 3GCREB infections.

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