

Detection of carbapenem resistance by the Reveal rapid phenotypic AST assay in strains from the CDC and FDA antimicrobial resistant isolate bank

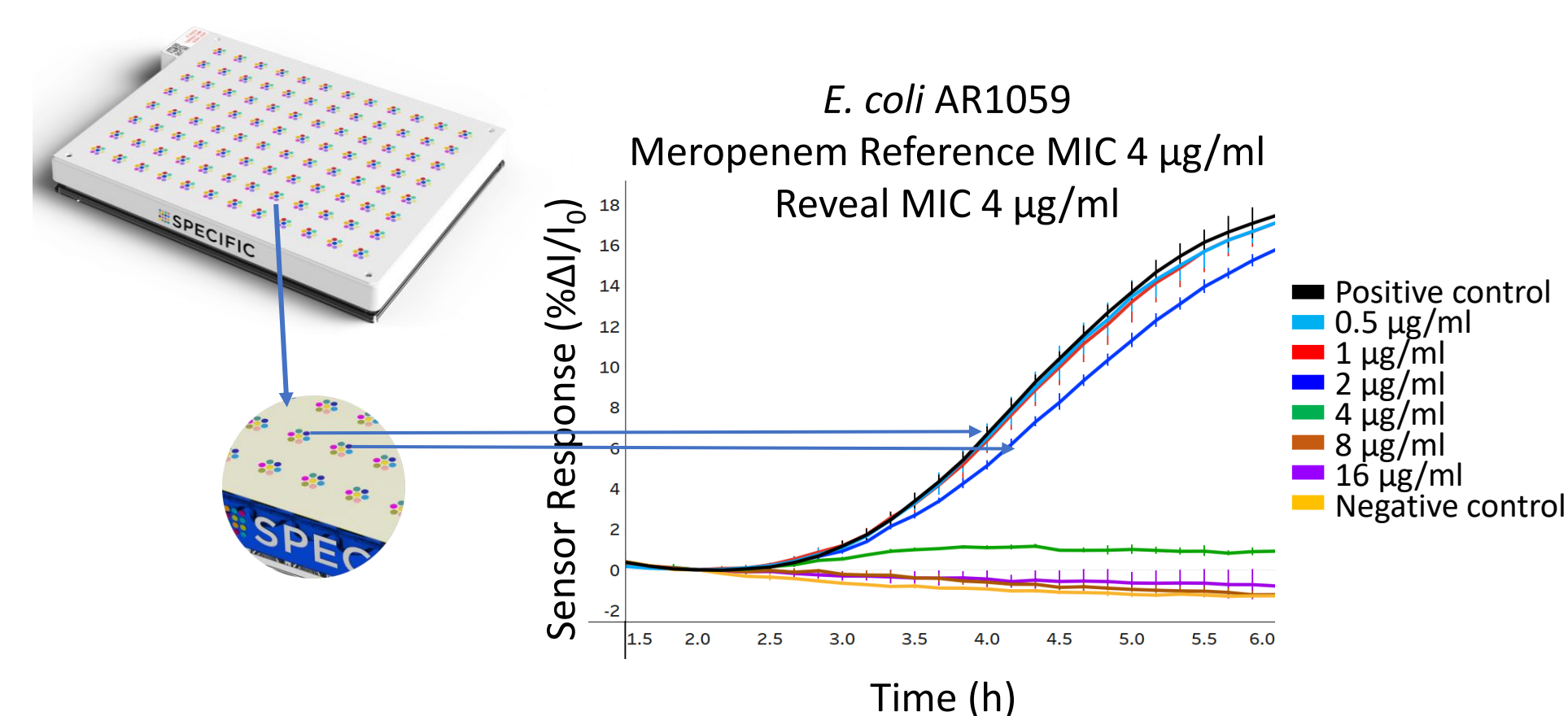
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Background

Carbapenem-resistant Gram-negative bacteria, “superbugs”, are one of the world’s great healthcare threats. The CDC has partnered with the FDA to compile a unique library of these organisms and made them available to foster the development of diagnostic assays and therapeutics suited to address this threat. Here, we evaluated the performance of the Reveal rapid AST with 317 carbapenem-resistant organisms from the CDC AR isolate bank, and compared the results to the sensitivity with which carbapenem resistance could be predicted by the 5 carbapenemase targets (KPC, NDM, IMP, VIM and Oxa-48-like) present on widely available PCR panels.

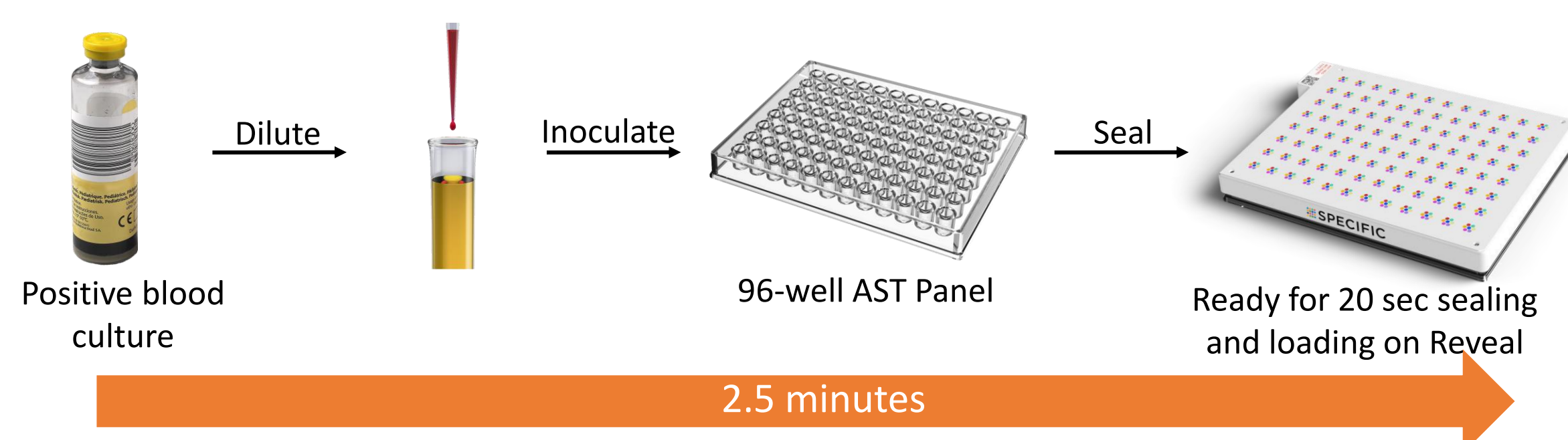
The Reveal technology

An array of 96 7-indicator nanoporous printed volatile sensor arrays are positioned above each well of a 96-well antibiotic plate. Changes in sensor color produced by the volatile emissions associated with by microbial growth are used to assay population growth and hence antimicrobial effectiveness in each well. Sensor color is monitored every 10 minutes by line scan, producing 21 (7 sensors x R, G and B color channels), with one such plot in the figure below.

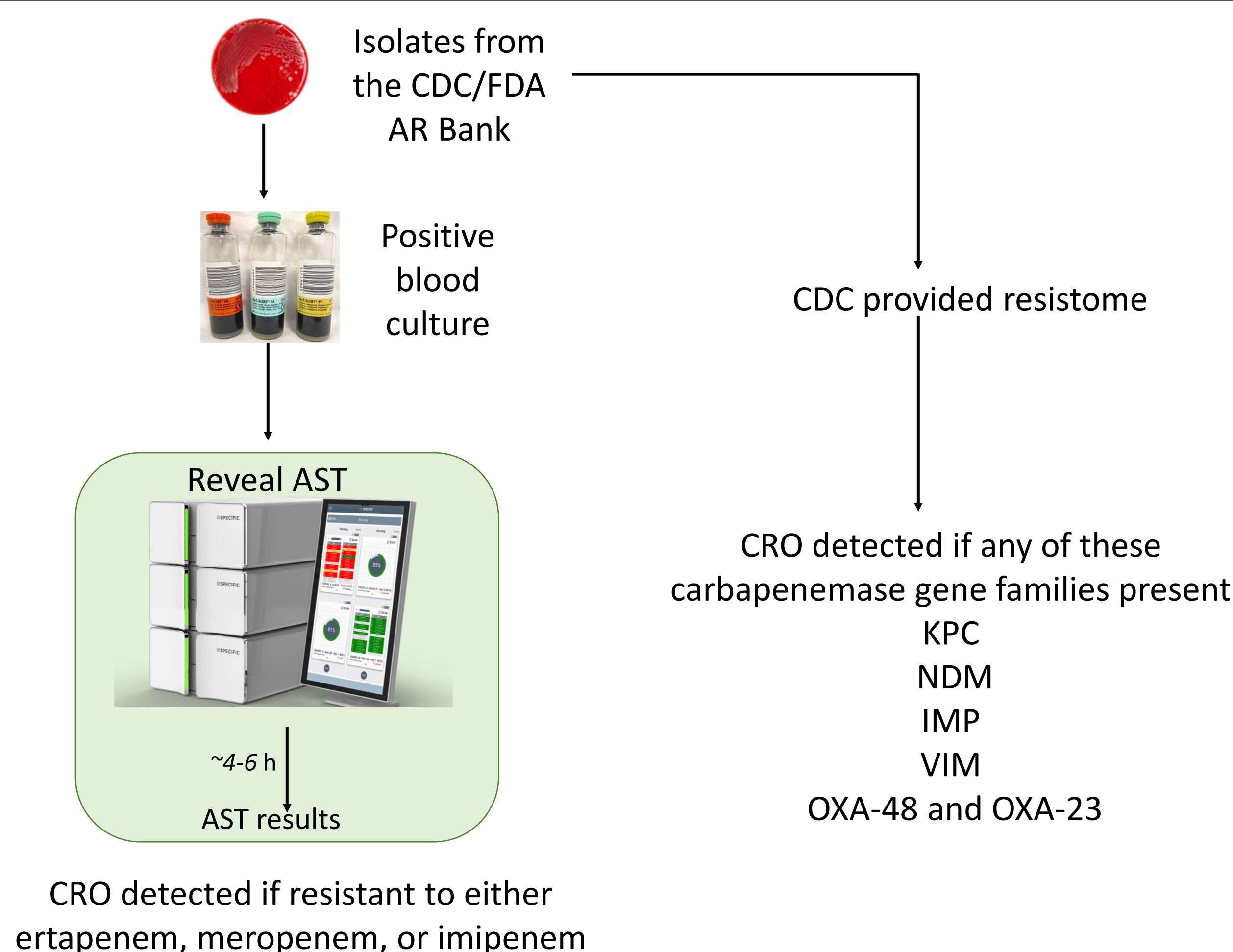


Sensor responses to the positive (no drug) control (black trace) and negative control (no growth medium) (flat yellow trace) are compared to those of wells with a range of meropenem concentrations to determine the MIC. Note growth (divergence between positive and negative control) of this MDR strain is clear at 3 hours. The lowest concentration effective at suppressing the color change indicating growth was 4 µg/mL (green trace), matching the reference MIC.

< 3-minute low-skill sample prep workflow



Methods



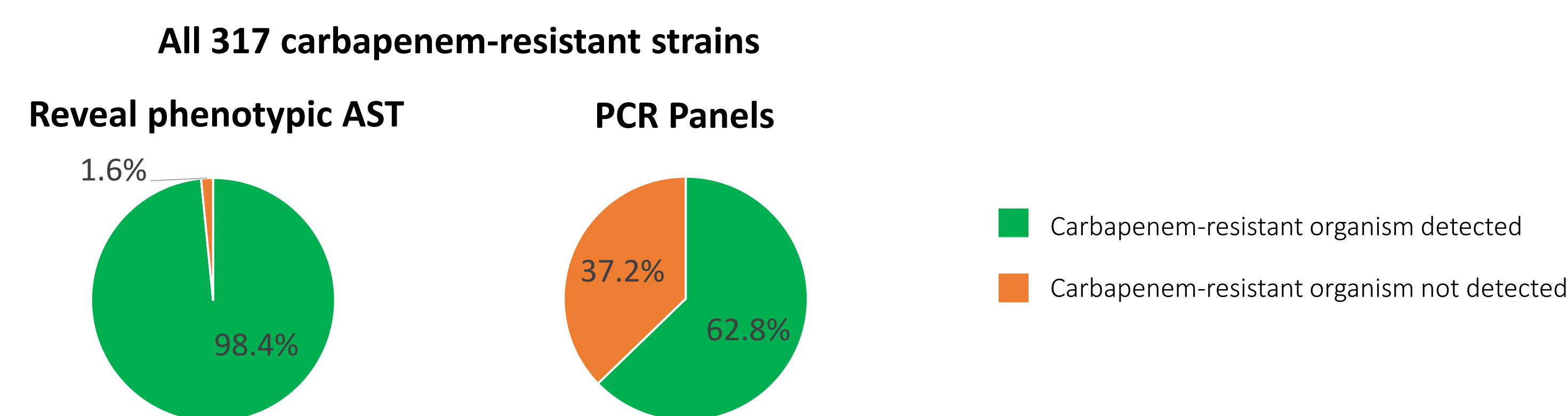
Results

Carbapenem resistance detection by mechanism and species

Group/Species	# Carbapenem resistant strains	% CRO detected by Reveal	% CPO* detected by Reveal	% non-CPO detected by Reveal
All	317	98.4% (312/317)	99.5% (204/205)	96.4% (108/112)
<i>K. pneumoniae</i>	101	100% (101/101)	100% (90/90)	100% (11/11)
<i>E. coli</i>	37	100% (37/37)	100% (29/29)	100% (8/8)
Other Enterobacterales	61	95.1% (58/61)	97.1% (33/34)	92.6% (25/27)
<i>P. aeruginosa</i>	66	98.5% (65/66)	100% (23/23)	97.7% (42/43)
<i>A. baumannii</i>	52	98.1% (51/52)	100% (29/29)	95.7% (22/23)

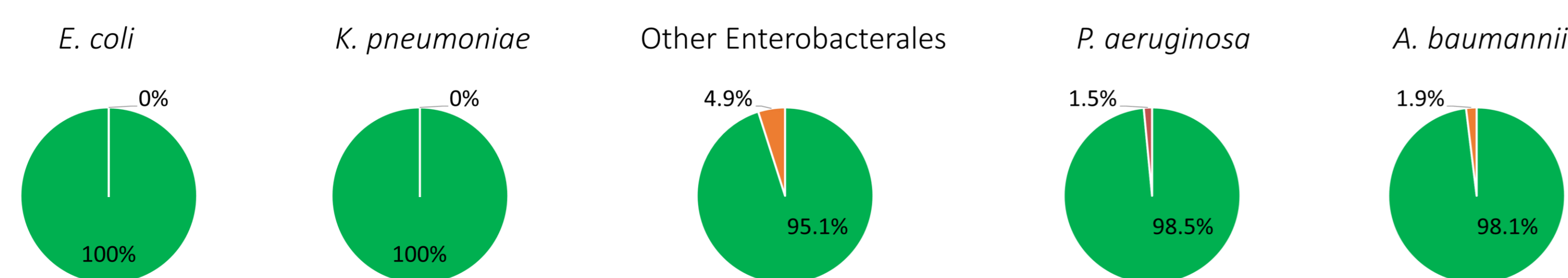
* Carbapenemase-producing organisms, includes those producing enzymes from the following carbapenemase families: NDM, KPC, IMP, VIM, OXA-48-like or OXA-23

Results

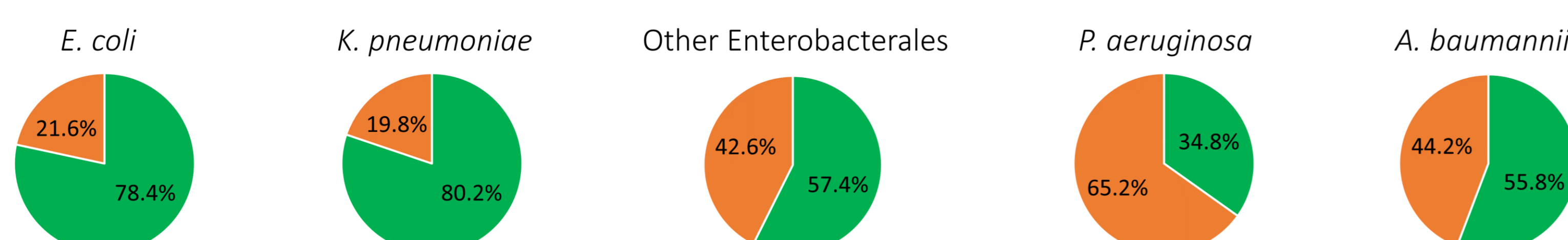


Carbapenem resistance detection by species

Reveal Phenotypic AST



PCR Panels



Results

Reveal performance by carbapenem

Antibiotic	# S	# I	# R	EA	CA	# mE	# ME	# VME
Meropenem	29	24	264	95.3%	90.9%	23	2	4
Ertapenem	10	3	184	95.4%	94.5%	8	0	3
Imipenem	19	23	275	93.7%	91.5%	23	1	3

#S, I, R – the number of susceptible, intermediate, and resistant strains tested.

EA – Essential agreement between CDC reference MIC and Reveal MIC calls

CA – Categorical agreement between CDC reference S/I/R categories and Reveal categories

mE – minor errors; ME – major errors; VME – very major errors

Conclusions

Reveal detected carbapenem resistance in 98.4% of the CDC AR bank carbapenem-resistant isolates tested, with 99.5% sensitivity in carbapenemase-producing isolates and 96.4% in the non-carbapenemase producing isolates. The PCR panels would, assuming 100% sensitivity, detect only 62.8% of the carbapenem-resistant strains. We conclude that the diversity of genomic mechanisms responsible for resistance to carbapenems requires a rapid phenotypic test, and that Reveal is highly effective at detecting this clinically important phenotype.