Results from the Reveal Rapid AST used with routine clinical samples at two hospitals in Paris

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CNR RÉSISTANCE AUX ANTIBIOTIQUES

Hôpital Bicêtre AP-HP

Hôpital Raymond-Poincaré AP-HP

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☑ Je n'ai pas de lien d'intérêt personnel à déclarer

Etude subventionnée par SPECIFIC

The Need for Rapid AST

- **Escalation** for septic patients when prophylactic treatment is not effective
- **De-escalation** to reduce cost, prevent development of resistance and safeguard the microbiome
- Choose the **optimal antibiotic**
- Choose **optimal dosage**

Rapid ID alone is "usually" not sufficient to guide appropriate therapy change

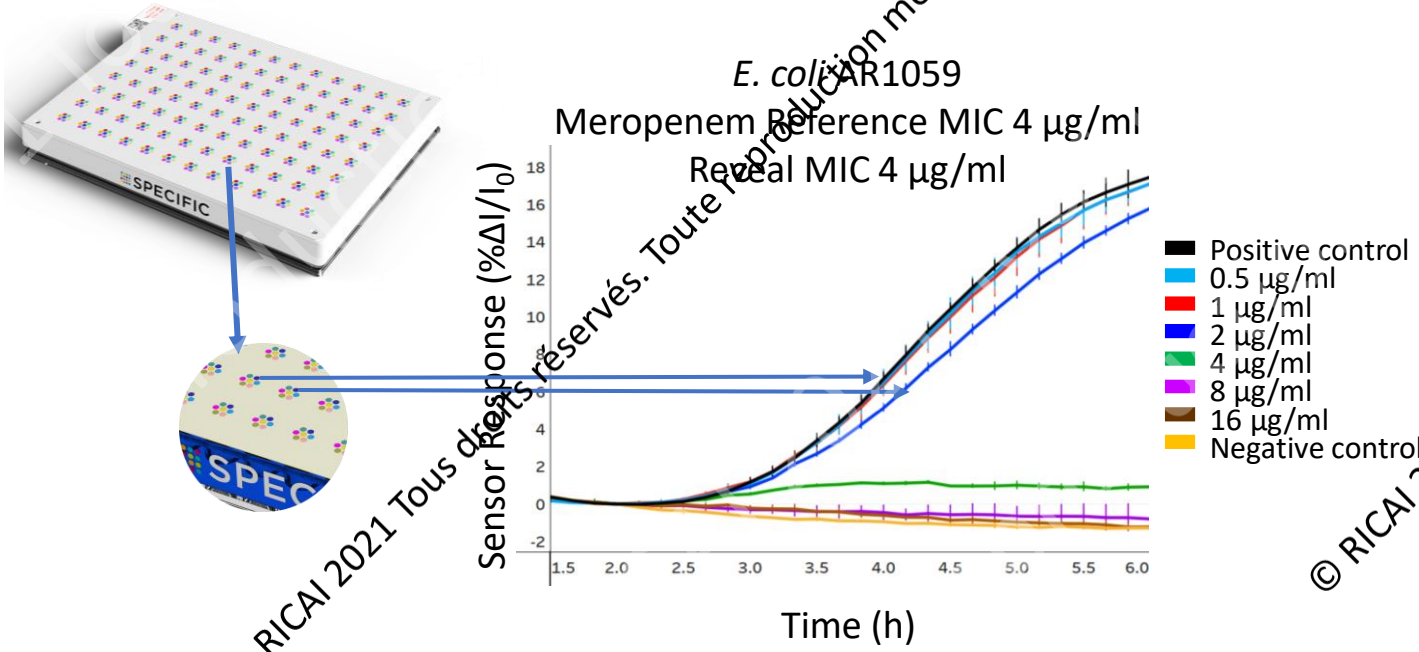
Principle of the Reveal instrument

- **Detection of Volatile Compounds Emission during bacterial growth** using small molecule sensors

  - **Printed volatile-responsive sensors rapidly respond to low concentrations** (10 parts per billion) of small volatile metabolites emitted during microorganism growth, on a well-by-well basis in a 96-well plate
  - Volatile emissions precede cell division, enabling a faster response than other measurements
  - Sampling of volatiles in the headspace **does not require removal of red blood cells** from sample, simplifying sample preparation

How is MIC determined

Sensor responses to the volatile emissions in wells with growing populations diverge from that in wells in which growth is suppressed; Green trace from well with 4 ug/mL, the MIC.

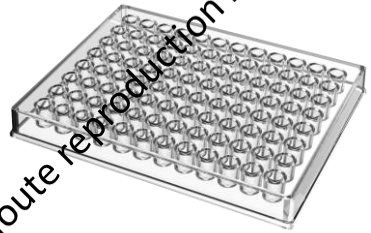


Reveal laboratory worflow

Positive blood culture

Dilute

Inoculate



96-well AST Panel

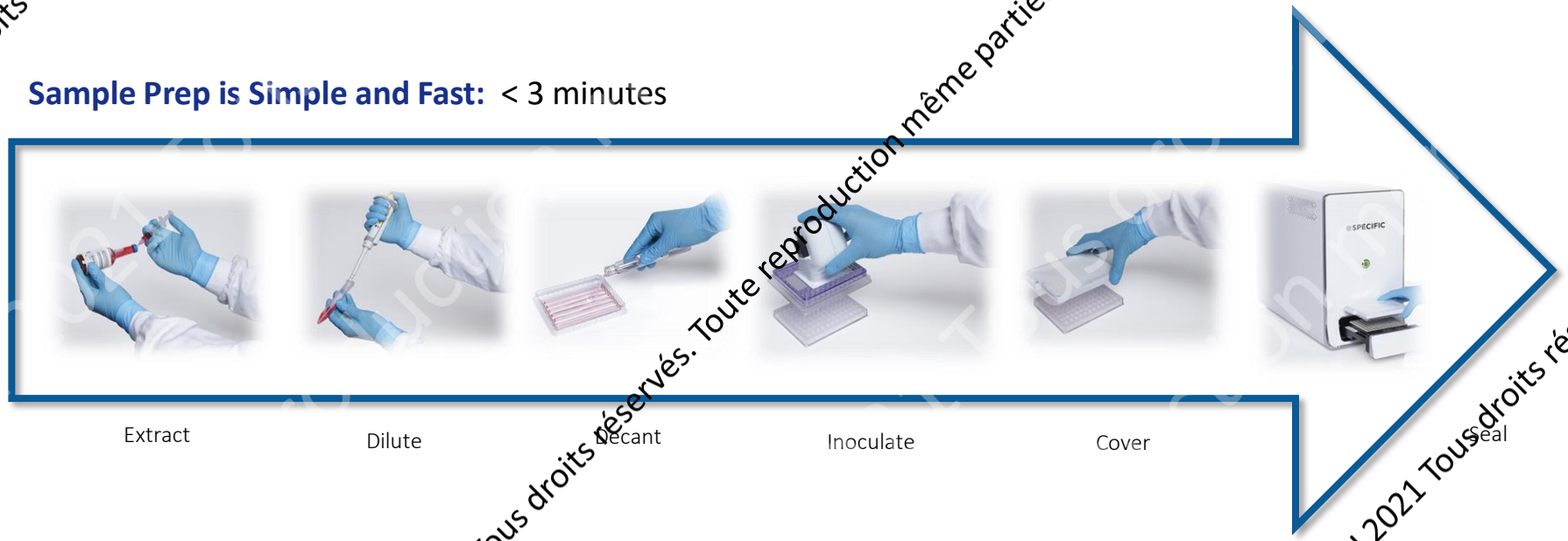
Sensor

Ready for sealing and loading on Reveal

< 3 minutes

Reveal laboratory worflow

Sample Prep is Simple and Fast: < 3 minutes



Study Plan

Clinical validation study of the CE-IVD marked Reveal rapid AST System on **positive Blood cultures with gram negatives**

- **Comparison of the Reveal results to Direct from Blood Disk Diffusion**
- Recording of the Reveal Time to Result
- Discords (note, only major and very major errors were settled) between Reveal result and DD settled with Sensititre to yield final categorical agreement

Rapid vs Conventional Workflow

Positive blood culture

Gram stain

AST results from Reveal 4-6 h

ID

Rapid MALDI ID

AST by direct disk diffusion on MH agar

Subculture on agar plates

Disk diffusion from isolates

Next Day Results from Direct Disk 20-24 h

Second Day Results, Disk from Isolate Dilution 40-48 h

Results with the Reveal System in 2 Independent Labs were very Concordant. Only 8 VME in 685 R tests.

	Pooled	Kremlin-Bicêtre	Raymond Poincaré
Categorical agreement	**95.6%**	**95.8%**	**95.4%**
Minor Error (I→R or I→S)	3.6%	3.5% (n=54)	3.7% (n=59)
Major Error (False R)	**0.8%**	**0.5% (n=6)**	**1.0% (n=12)**
Very Major Error (False S)	**1.2%**	**1.6% (n=5)**	**0.8% (n=3)**
Average Time to Result	**5h 32min**	**5h 29min**	**5h 35min**
Species		8	7
Antibiotics		17	18
Strains	204	100	104
R (%)	21.65%	19.79%	23.50%

Performance by species

Hôpital Bicêtre AP-HP

Species	strains	Average TTR	CA	mE	ME	VME
C. freundii	1	4h 42min	93.3%	1	0	0
C. koseri	2	5h 19min	100.0%	0	0	0
E. cloacae	13	5h 23min	90.8%	15	2	1
E. coli	46	5h 17min	97.0%	21	2	0
K. aerogenes	6	5h 23min	91.6%	6	1	0
K. oxytoca	4	5h 46min	96.9%	2	0	0
K. pneumoniae	18	5h 50min	96.5%	8	1	1
P. aeruginosa	10	**6h 21min**	96.5%	1	0	3
Overall	**100**		**95.8%**	**54**	**6**	**5**

Hôpital Raymond-Poincaré AP-HP

Species	strains	Average TTR	CA	mE	ME	VME
C. freundii	2	5h 04min	83.3%	5	0	0
C. koseri	3	5h 15min	95.8%	2	0	0
E. cloacae	11	5h 18min	94.4%	6	3	0
E. coli	43	5h 22min	96.4%	22	4	0
K. aerogenes	2	5h 32min	96.4%	1	0	0
K. pneumoniae	18	5h 30min	96.1%	10	1	1
P. aeruginosa	25	**6h 29min**	93.7%	13	4	2
Overall	**104**		**95.4%**	**59**	**12**	**3**

Performance by antimicrobial

Antimicrobial agent	Total	TTR	mE	ME	VME	CA
Amikacin	100	4h 37min	4	0	0	96.0%
Ampicillin	46	3h 39min	0	0	0	100.0%
Aztreonam	95	5h 36min	5	1	0	93.7%
Cefepime	100	6h 05min	4	1	1	94.1%
Cefotaxime	90	5h 56min	4	0	0	95.6%
Cefoxitin	69	4h 43min	0	1	0	98.6%
Ceftazidime	97	5h 58min	7	0	0	92.9%
Ceftazidime/Avibactam	98	6h 19min	0	0	1	99.0%
Ciprofloxacin	100	5h 05min	3	2	0	94.1%
Ertapenem	89	6h 31min	4	0	0	95.5%
Gentamicin	100	5h 59min	0	0	0	100.0%
Imipenem	99	6h 31min	1	0	0	99.0%
Levofloxacin	99	5h 12min	4	0	1	95.0%
Piperacillin	100	4h 15min	2	1	0	96.0%
Piperacillin/Tazobactam	**93**	**6h 35min**	**11**	**0**	**2**	**85.1%**
Tobramycin	99	4h 38min	5	0	0	95.0%
Trimethoprim/Sulfa	87	4h 38min	0	0	0	98.9%
	1561		**54**	**6**	**5**	**95.8%**

Antimicrobial agent	Total	TTR	mE	ME	VME	CA
Amikacin	104	4h 50min	5	0	0	95.2%
Aztreonam	86	5h 40min	5	0	0	94.2%
Cefepime	102	6h 01min	4	1	0	95.1%
Cefotaxime	79	5h 42min	2	1	0	96.2%
Cefoxitin	64	5h 12min	0	0	0	100.0%
Ceftazidime	102	6h 05min	2	0	0	98.0%
Ceftolozane/Tazobactam	25	6h 31min	0	0	0	100.0%
Cefuroxime	60	4h 26min	0	0	0	100.0%
Ciprofloxacin	**104**	**5h 22min**	**5**	**7**	**0**	**88.5%**
Ertapenem	76	6h 31min	0	0	0	100.0%
Gentamicin	104	6h 00min	0	1	0	99.0%
Imipenem	103	6h 31min	1	0	1	98.1%
Levofloxacin	104	5h 21min	5	0	0	95.2%
Meropenem	103	6h 31min	10	0	0	90.3%
Piperacillin	103	4h 24min	2	2	0	96.1%
Piperacillin/Tazobactam	**102**	**6h 32min**	**15**	**0**	**1**	**84.3%**
Tobramycin	104	4h 46min	1	0	0	99.0%
Trimethoprim/Sulfa	79	4h 17min	2	0	1	96.2%
	1604		**59**	**12**	**3**	**95.4%**

Several discords with direct disk diffusion were resolved in favor of Reveal

	VMEs with DD	VMEs after discord adjudication	MEs with DD	MEs after discord adjudication
Kremlin-Bicêtre	12	5	10	6
Raymond Poincaré	19	3	18	12

Of the initial VMEs, 15 were against Piperacillin/tazobactam, and discord resolution with broth microdilution resolved 10 of these in favor of Reveal, indicating direct disk diffusion may be problematic for Pip-Tazo.

Conclusions

- **Reveal performs in accordance with CE-IVD claims**
  - *Performance – **95.5% accuracy with just 1% VME**, at two hospitals in Paris, performed by different teams, different local epidemiologies*
  - ***Time to result** – approximately **5.5 hours**, averaged over all drugs and strains*
- Plausible, same-shift guidance for bacteremia therapy (in ICU ? or severe patients ?)
- **Easy to handle / quick workflow**

Perspectives

- Interesting results that to have to be confirmed for **gram positives**

- Bacterial **panel have to be enlarge** to other species (e.g. *S. marcescens*, *M. morganii* in Enterobacterales*)*

- Medico-economic impact *vs* Rapid ID + β-LACTA® test on antimicrobial stewardship ?

ACKNOWLEGMENTS

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