Comparison of Yeasts Identification by Biofire, Culture and ePlex for Quality Assurance Purpose

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Introduction:

Rapid Molecular diagnosis of blood stream infections (BSI) caused by bacteria and yeast for pathogen identification have given healthcare providers additional tools in the treatment of patients. The BioFire FilmArray® Blood Culture Identification Panel (BCID) (Biomerieux, L'Etoile, France) is a CE-marked 2-stage nested multiplex PCR with melting temperature confirmation of all positives. It allows for the identification of 5 fungal targets with results reported in approximately 75 minutes. The GenMark ePlex® Fungal BCID Panel (Carlsbad, CA) is a multiplex PCR assay using electrowetting technology followed by the detection of Ferrorcyanin-labled signal probe-DNA hybrid that is captured on a microarray target for specific eSensorTM detection of fungal organisms in about 90 minutes of culture bottle positivity. Both systems provide rapid diagnostic blood culture results that can be delivered directly to a provider to optimize antimicrobial coverage for the patient. Both systems may play a critical role in antimicrobial stewardship. At University of Kentucky Medical Center (UKMC), positive fungal blood cultures were concurrently cultured and also run through the Biofire BCID panel following manufacturer's protocols. This study compares the performance of the Biofire BCID panel to standard culture methods and examines whether the GenMarkDx ePlex® BCID-FP panel would provide greater benefit for UKMC providers based on 1 year of data collected with the Biofire/Culture system.

Table 1: Comparison of Film Array® and ePlex® BCID Blood Culture Fungal Panels

Film Array®	ePlex®
Candida albicans	*Candida albicans*
Candida glabrata	*Candida auris*
Candida krusei	*Candida glabrata*
Candida parapsilosis	*Candida krusei*
Candida tropicalis	*Candida parapsilosis*
	Candida tropicalis
	Cryptococcus neoformans
	Cryptococcus gattii
	Candida famata
	Candida guilliermondii
	Candida kyfr
	Fusarium species
	Rhodotorula species
5 Total Analytes	13 Total Analytes

Methods:

- During the study period July 1 2018 to until June 31, 2019, blood cultures positive for yeast were automatically tested using the Biofire® FilmArray® BCID panel (BioMerieux, L'Etoile, France), following the manufacturer's instructions.
- All positive cultures were backed up with culture on solid medium with full organism identification using Bruker Biotyper CA MALDI-tof (Bruker Daltonics inc, Billerica, MA) or the API 20C AUX Sugar Assimilation Assay (BioMerieux, L'Etoile, France).
- Historical data were collected in an a SUNQUEST Epi report for correlation of the molecular data with the culture results.
- Biofire results were categorized as true or false positive or negative (TP,FP,FN,TN) as compared to culture. Cultures whose organisms identified an organism that was not listed on Biofire panel was classified as "Analyte Not In Panel" (ANIP).
- Anticipated performance of the ePlex Panel was compared to the actual performance of the Biofire to support the change in technology for UK Healthcare.

Results:

Table 2. Samples With Discrepancies Between Biofire and Culture Results

Acc #	Specimen CDate	Culture Result (BLC or ARBLC)	Biofire Result	Classification of Biofire Result (TP, FP, ANIP)	Anticipated ePlex Result	Classification of ePlex Result (Detectable, ANIP)
W11413	06122019	*Candida tropicalis* (detected)	*Candida albicans*	FP *C. albicans*	*Candida tropicalis*	Detectable
S57021	03092019	*Candida albicans* (detected), *Pichia ohermera, T. ashai*	*Candida parapsilosis*	FP *C. parapsilosis*	*Candida albicans*	Detectable
S28307	05042019	*Candida albicans, C. glabrata, C. tropicalis* (all detected)	*Candida parapsilosis*	FP *C. parapsilosis*	*Candida albicans, C. glabrata, C. tropicalis*	Detectable
X60312	05122019	*Candida tropicalis*	Negative for all analytes	FN *C. tropicalis*	*Candida tropicalis*	Detectable
H13267	11152018	*Candida parapsilosis*	Negative for all analytes	FN *C. parapsilosis*	*Candida parapsilosis*	Detectable
H61683	12202018	*Candida glabrata*	Negative for all analytes	FN *C. glabrata*	*Candida glabrata*	Detectable
W12960	04172019	*Candia dubliniensis*	Negative for all analytes	ANIP	*Candia dubliniensis*	Detectable
X21054	06302019	*Candia dubliniensis*	Negative for all analytes	ANIP	*Candia dubliniensis*	Detectable
T77840	10302018	*Candida kefyr* (formerly *Candida pseudotropicalis*)	Negative for all analytes	ANIP	*Candida kefyr*	Detectable
H15099	03142019	*Candida lusitaniae*	Negative for all analytes	ANIP	*Candida lusitaniae*	Detectable
H68529	06202019	*Candida lusitaniae*	Negative for all analytes	ANIP	*Candida lusitaniae*	Detectable
T19560	03052019	*Candida lusitaniae*	Negative for all analytes	ANIP	*Candida lusitaniae*	Detectable
F26565	03082019	*Candida lusitaniae*	Negative for all analytes	ANIP	*Candida lusitaniae*	Detectable
F13271	03022019	*Candida lusitaniae*	Negative for all analytes	ANIP	*Candida lusitaniae*	Detectable
F26566	03082019	*Candida lusitaniae*	Negative for all analytes	ANIP	*Candida lusitaniae*	Detectable
W12446	10312018	*Cryptococcus neoformans*	Negative for all analytes	ANIP	*Crypto. neoformans*	Detectable
T48060	10022018	*Cryptococcus neoformans* var *grubii*	Negative for all analytes	ANIP	*Crypto.neoformans*	Detectable
W26461	06192019	*Cryptococcus neoformans* var *grubii*	Negative for all analytes	ANIP	*Crypto. neoformans*	Detectable
H44058	10112018	*Candida nivariensis*	Negative for all analytes	ANIP	Negative for all analytes	ANIP
T41095	01222019	*Candida nivariensis*	Negative for all analytes	ANIP	Negative for all analytes	ANIP
S57021	03092019	*Pichia ohermera, [Candida albicans* (detected), *T. ashai]*	*Pichia* is not in panel	ANIP	*Pichia* is not in panel	ANIP
S57021	03092019	*Trichosporon ashai, [Candida albicans* (detected), *P. ohermera]*	*Trichosporon* is not in panel	ANIP	*Trichosporon* not in panel	ANIP
S18853	04202019	*Trichosporon faecale*	Negative for all analytes	ANIP	Negative for all analytes	ANIP

Table 3. Classification of Results and Statistical Analysis for the Biofire BCID Panel

Organism Name	True Positives	True Negatives	False Positives	False Negatives	Sensitivity	Specificity	NPV	PPV	Efficiency
Candida albicans	31	101	1	0	100	99	96.9	100	99.2
Candida glabratta	46	86	0	1	97.9	100	100	97.9	99.2
Candida krusei	1	132	0	0	*	*	*	*	100
Candida parapsilosis	21	109	2	1	95.5	98.2	99.1	91.3	97.7
Candida tropicalis	19	113	0	1	95	100	99.1	100	99.2
Total (n=133 panels)	118	541	3	3	97.5	99.4	97.5	99.4	99.1

- A total of 133 specimens [141 isolates] were tested via the Biofire BCID panel.
- 123 isolates (87%) yielded Biofire results in concordance with culture.
- Eighteen isolates (13%) would have test positive on the GenMarkDx ePlex BCID-FP panel and not the Biofire BCID panel. These organisms were *Candida lusitaniae* (6), *Cryptococcus neoformans* (3), *C. dublinensis* (2), and *C. keyfr* (1).
- Organisms that were found on culture that were not detectable by either GenMarkDx ePlex BCID-FP panel and Biofire BCID panel included *Candida nivariensis* (2), *Pichia ohm*eri (1), *Trichospon* spp (2).
- Overall, there would have been unanticipated 4 panels [5 isolates] that would have yielded ANIP results by ePlex (3% of all ePlex Panels) compared to 16 of Biofire panels [17 isolates] for a rate of 12% ANIP using the Biofire panel.
- The overall predicted efficiency of the Eplex FP BCID was 99.1% for the year.

Conclusions:

- Although the BioFire FilmArray® BCID Panel demonstrated an overall efficiency of 99.1% for the detection of the 5 yeast contained in its panel, when "Negative for all analytes" panels were considered, the efficiency falls to 87%.
- *Candida lusitaniae* and *Cryptococcus neoformans,* NOT detected by the panel, were seen in significant numbers during this study year.
- Since *Cryptococcus neoformans* is intrinsically resistant to echinocandins and *Candida lusitaniae* has shown intrinsic and acquired resistance to amphotericin, having a more comprehensive panel like the GenMark ePlex® BCID FP would have had a significant impact on guiding antifungal therapy for these cultures.
- Since the ePlex panel has the ability to detect 13 fungal pathogens, 99.1% overall testing efficiency could have been achieved for this year's isolates. As a result of this study, UKMC implemented the GenMarkDx ePlex® BCID-FP panel in June, 2020. Studies are currently ongoing measuring its ongoing performance.