

Performance Characteristics of an FDA Cleared Multiplex Panel for the Rapid Identification of Fungal Pathogens from Positive Blood Culture

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Background

- Routine identification of fungal pathogens from positive blood cultures by conventional culture-based methods can be time consuming, delaying effective treatment of appropriate antifungal agents.
- The GenMark Dx ePlex[®] Investigational Use Only Blood Culture Identification Fungal Pathogen Panel (BCID-FP) is able to detect 15 fungal targets simultaneously using electrowetting and eSensor[®] technology (Figure 1) direct from positive blood culture samples positive for fungi by gram stain in approximately 100 minutes.
- We aim to determine the performance of the BCID-FP in a multi-center clinical study.

Methods

- Ten sites across the United States collected samples that were tested at 4 clinical sites comparing the BCID-FP to traditional culture, MALDI-TOF MS, microbiological and biochemical techniques.
- Discrepant results were analyzed by a bi-directional PCR/sequencing directly in residual blood culture samples.
- Sensitivity and specificity were determined for each fungal target.

Table 1. Clinical Performance ePlex BCID-FP Panel With Comparator Methods

ePlex BCID-FP Target	Sensitivity/PPA		Specificity/NPA	
	TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Candida albicans</i>	66/68	97.1 (89.9-99.2)	797/798	99.9 (99.3-100)
<i>Candida auris</i>	49/49	100 (92.7-100)	817/817	100 (99.5-100)
<i>Candida dubliniensis</i>	52/52	100 (93.1-100)	814/814	100 (99.5-100)
<i>Candida famata</i>	51/51	100 (93.0-100)	815/815	100 (99.5-100)
<i>Candida glabrata</i>	59/60	98.3 (91.1-99.7)	804/806	99.8 (99.1-99.9)
<i>Candida guilliermondii</i>	49/50	98.0 (89.5-99.6)	816/816	100 (99.5-100)
<i>Candida kefyr</i>	51/51	100 (93.0-100)	813/815	99.8 (99.1-99.9)
<i>Candida krusei</i>	50/50	100 (92.9-100)	816/816	100 (99.5-100)
<i>Candida lusitanae</i>	48/49	98.0 (89.3-99.6)	816/817	99.9 (99.3-100)
<i>Candida parapsilosis</i>	59/60	98.3 (91.1-99.7)	805/806	99.9 (99.3-100)
<i>Candida tropicalis</i>	50/50	100 (92.9-100)	815/816	99.9 (99.3-100)
<i>Cryptococcus gattii</i>	50/50	100 (92.9-100)	816/816	100 (99.5-100)
<i>Cryptococcus neoformans</i>	57/57	100 (93.7-100)	809/809	100 (99.5-100)
<i>Fusarium</i> ^a	69/70	98.6 (92.3-99.7)	796/796	100 (99.5-100)
<i>Rhodotorula</i> ^b	50/52	96.2 (87.0-98.9)	813/814	99.9 (99.3-100)

^a *F. dimerum*, *F. oxysporum*, *F. sacchari*, *F. solani*, *F. verticillioides*; ^b *R. glutinis*, *R. mucilaginosa*

ePlex BCID-FP Target	Sensitivity/PPA with Discordant Resolution		Specificity/NPA with Discordant Resolution	
	TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Candida glabrata</i>	61/62	98.4 (91.4-99.7)	804/804	100 (99.5-100)
<i>Candida parapsilosis</i>	60/61	98.4 (91.3-99.7)	805/805	100 (99.5-100)
<i>Candida tropicalis</i>	51/51	100 (93.0-100)	815/815	100 (99.5-100)

Results

- A total of 866 samples including 120 retrospectively- and 21 prospectively- collected clinical samples along with 725 contrived samples were tested with the BCID-FP Panel.
- Of the 11 *Candida* species on the panel (*C. albicans*, *C. auris*, *C. dubliniensis*, *C. famata*, *C. glabrata*, *C. guilliermondii*, *C. kefyr*, *C. krusei*, *C. lusitanae*, *C. parapsilosis*, *C. tropicalis*), sensitivity and specificity ranged from 97.1-100% and 99.8-100%, respectively (Table 1).
- For the other organisms detected on the panel, sensitivity and specificity was 100% for both *Cryptococcus neoformans* and *C. gattii*. Sensitivity and specificity for *Fusarium* sp. were 98.6% and 100% and for *Rhodotorula* sp. were 96.2% and 99.9%, respectively (Table 1).
- In 4 of the 141 clinical samples, the ePlex BCID-FP Panel correctly identified an additional *Candida* species that was undetected by standard-of-care methods (Table 2 and 3).

Table 2. Discrepant Results Between Standard-of-Care (SOC) Testing and the ePlex BCID-FP Panel

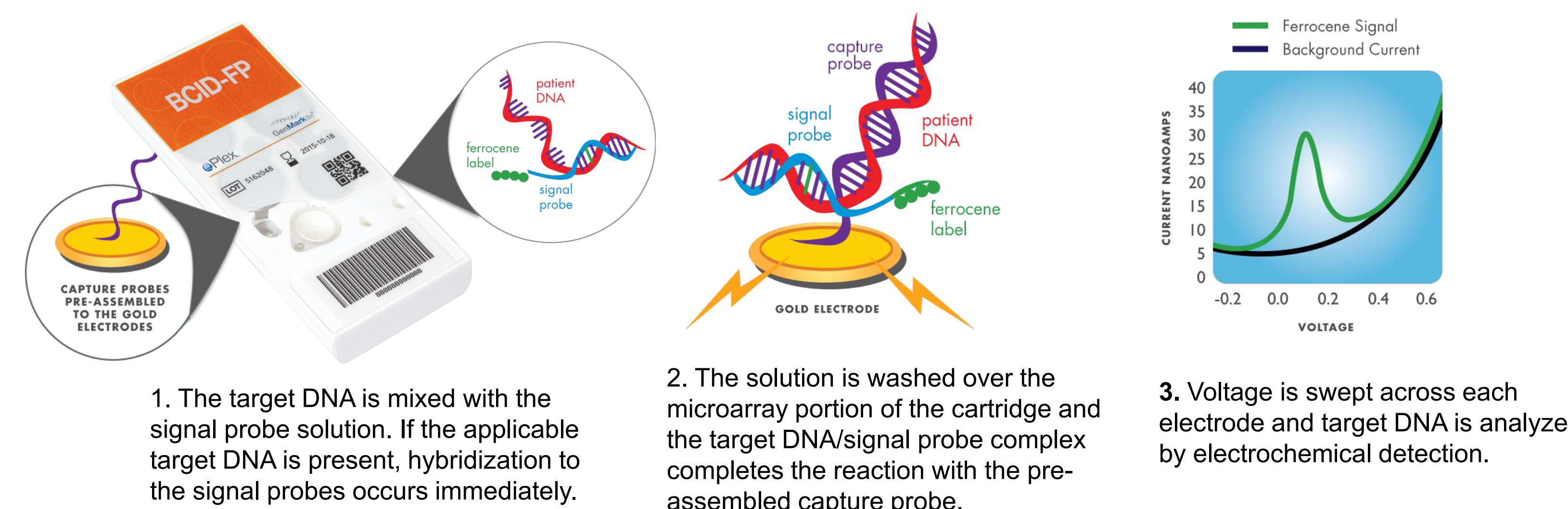
Target	# SOC+ BCID-FP-	PCR/ Sequencing Result	Interpretation	# SOC- BCID-FP+	PCR/ Sequencing Result	Interpretation
<i>C. albicans</i>						
Clinical sample	1	<i>C. albicans</i>	False negative			
Contrived sample	1	N/A	False negative			
Contrived sample				1	N/A	False positive
<i>C. glabrata</i>						
Clinical sample	1	Not Detected	Inconclusive			
Clinical sample				2	<i>C. glabrata</i>	True positive
<i>C. guilliermondii</i>						
Contrived sample	1	N/A	False negative			
<i>C. kefyr</i>						
Contrived sample				2	N/A	False positive
<i>C. lusitanae</i>						
Clinical sample	1	<i>C. lusitanae</i>	False negative			
Contrived sample				1	N/A	False positive
<i>C. parapsilosis</i>						
Clinical sample	1	<i>C. parapsilosis</i>	False negative			
Clinical sample				1	<i>C. parapsilosis</i>	True positive
<i>C. tropicalis</i>						
Clinical sample				1	<i>C. tropicalis</i>	True positive
<i>Fusarium</i>						
Contrived sample	1	N/A	False negative			
<i>Rhodotorula</i>						
Contrived sample	2	N/A	False negative			
Contrived sample				1	N/A	False positive
Total	9			9		

Note: For the contrived discordant samples, PCR/sequencing was not performed indicated by a result of N/A.

Table 3. Detection of Mixed Fungal Organisms by the ePlex BCID-FP Panel in Positive Blood Cultures (prospective/retrospective clinical samples)

Case	SOC Testing	BCID-FP	PCR /Sequencing	Interpretation
1	<i>C. albicans</i>	<i>C. albicans</i>	Not detected	Inconclusive
	<i>C. glabrata</i>	-		
	<i>C. dubliniensis</i>	<i>C. dubliniensis</i>		
2	<i>C. albicans</i>	<i>C. albicans</i>	<i>C. parapsilosis</i>	BCID-FP true positive
	<i>C. parapsilosis</i>	<i>C. parapsilosis</i>		
3	<i>C. albicans</i>	<i>C. albicans</i>	<i>C. parapsilosis</i>	BCID-FP false negative
	<i>C. parapsilosis</i>	-		
4	<i>C. dubliniensis</i>	<i>C. dubliniensis</i>	<i>C. parapsilosis</i>	BCID-FP true positive
	<i>C. parapsilosis</i>	<i>C. parapsilosis</i>		
5	<i>C. dubliniensis</i>	<i>C. dubliniensis</i>	<i>C. tropicalis</i>	BCID-FP true positive
6	<i>C. lusitanae</i>	<i>C. lusitanae</i>	<i>C. glabrata</i>	BCID-FP true positive
7	<i>C. lusitanae</i>	<i>C. lusitanae</i>	<i>C. glabrata</i>	BCID-FP true positive
8	<i>C. metapsilosis</i>	No targets detected		Off-panel
	<i>Trichosporon asahii</i>	No targets detected		Off-panel

Figure 1: eSensor Technology



Conclusions

- The ePlex BCID-FP panel is a sample to answer multiplex molecular diagnostic that tests for the largest breadth of fungal targets and proved to be an accurate, fast, easy-to-use tool to detect common fungal pathogens in positive blood cultures.
- The BCID-FP Panel has a short hands-on time < 2 minutes to load each sample into the cartridge and a run time of 100 minutes.
- The BCID-FP Panel also is the only rapid fungal detection panel available to date containing multi-drug resistant *C. auris* target.