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Prospective assessment of FilmArray® technology for the rapid identification of yeast isolated from blood cultures



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ABSTRACT

We prospectively assessed the ability of FilmArray® device to identify fungal species involved in bloodstream infections. It succeeded in identifying 85.7% of isolates. The automated readout of results enabled the rapid initiation of appropriate antifungal therapy. Thus, FilmArray® appeared as a reliable alternative diagnostic method for the most common yeast-like species.

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Fungemia is a severe bloodstream infection caused by miscellaneous fungal organisms (Pfaller and Diekema, 2007). Yeast of the *Candida* genus is mostly isolated, representing the fourth most common cause of sepsis (Pfaller et al., 2001). New lab tools have been developed recently to overcome the limitations of current methods of diagnosis, which usually require several days to identify correctly the species responsible for FBI. For instance, MALDI-TOF MS can be used directly in positive blood cultures, but its lack of standardisation for the extraction method limits its widespread use (Ferreira et al., 2011; Spanu et al., 2012). Likewise, DNA sequencing can reliably identify

species, but only once the considered strain has been isolated in subculture (Leaw et al., 2006). Consequently, there is room for the development of additional diagnostic tests, especially those which would be easy-to-use, without requiring additional expensive equipment. The FilmArray® Blood Culture ID Panel (BioFire Diagnostics, Salt Lake City, UT, U.S.) is a user-friendly system based on a PCR method which tests for a comprehensive panel of 24 pathogens (Poritz et al., 2011), including five *Candida* species: *Candida albicans*, *Candida glabrata*, *Candida krusei*, *Candida parapsilosis* and *Candida tropicalis*. It has been already assessed in a few laboratories, but mostly for the identification of bacteria (Blaschke et al., 2012; Poritz et al., 2011). We specifically tested the fidelity of this novel diagnostic method to identify yeast-shaped fungi isolated from blood cultures in routine practice.

This study was carried out prospectively in a hospital of 1217 inpatient beds, over a 14-month period. Blood samples were collected in BD Bactec® bottles (Becton Dickinson & Company, Le Pont-De-Claix, France), and incubated into a Bactec® automated system (Becton Dickinson & Company, Le Pont-De-Claix, France). Each bottle flagged as positive was removed. If yeast were visualised at direct examination, the specimen was subjected to the identification processes described below.

Abbreviations: ATCC, American Type Culture Collection; BLAST, basic local alignment search tool; CE, Conformité Européenne; DNA, deoxyribonucleic acid; F, female; FBI, fungal bloodstream infections; FDA, Food and Drug Administration; h, hour; IDSA, Infectious Diseases Society of America; M, male; MALDI-TOF, matrix assisted laser desorption ionisation time of flight; MIC, minimal inhibitory concentration; min, minute; mL, millilitre; MS, mass spectrometry; PBS, phosphate buffered saline; PCR, polymerase chain reaction; Tm, melting temperature; U.S., United States of America.

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Table 1
Description of the cases of fungal bloodstream infections. All the patients with proven fungemia were prospectively included in the present study, which aimed to assess the diagnostic performance of the FilmArray® device in comparison with conventional methods of yeast identification. DNA sequencing of the D1/D2 region was considered as the standard method.

Case no.	Demographics (gender/age)	Underlying disease	Risk factors	Inpatient department	Blood culture bottle	TTD (for positive blood culture)	FilmArray®	Yeast identification				Clinical outcome
								Rapid tests	API20C® strip (score ^a)	MALDI-TOF MS (score ^b)	DNA sequencing (% query cover; % ident ^c)	
1	M/44	Metastatic colorectal adenocarcinoma	Anticancer chemotherapy, portacath	Department of Infectious Diseases	Plus + Aerobic/F	2 days 20 h 50 min	<i>C. glabrata</i>	RTT +	<i>C. glabrata</i> (20000400, 99.4%)	<i>C. glabrata</i> (99.9%)	<i>C. glabrata</i> (100%; 100%)	Survival
2	F/85	Stroke	Diabetes, gastrostomy, urinary catheter	Post-acute care & rehabilitation	Plus + Aerobic/F	1 day 16 h 21 min	<i>C. parapsilosis</i>	NA	<i>C. parapsilosis</i> (6747175, 99.9%)	<i>C. parapsilosis</i> ^d (99.9%)	<i>C. parapsilosis</i> (100%; 100%)	Survival
3	M/0.1	Extreme premature birth	Central catheter	NICU	Mycosis IC/F	5 days 18 h 48 min	<i>C. albicans</i>	BichroLatex –	<i>C. albicans</i> (2576174, 97.4%)	<i>C. albicans</i> (99.9%)	<i>C. albicans</i> (100%; 99%)	Survival
4	M/77	Idiopathic thrombocytopenic purpura	Corticosteroids, digestive surgery	MICU	Mycosis IC/F	3 days 17 h 39 min	<i>C. albicans</i>	BichroLatex +	<i>C. albicans</i> (2576174, 97.1%)	<i>C. albicans</i> (99.9%)	<i>C. albicans</i> (100%; 100%)	Survival
5	M/6	Polymalformative syndrome	Portacath, hypo-γ-globulinemia	PICU	Plus + Aerobic/F	0 day 13 h 03 min	<i>C. tropicalis</i>	NA	<i>C. tropicalis</i> (2556075, 93.7%)	<i>C. tropicalis</i> ^d (99.9%)	<i>C. tropicalis</i> (100%; 100%)	Survival
6	F/53	Liver transplant	Diabetes, kidney failure, central catheter	SICU	Mycosis IC/F	1 day 3 h 15 min	<i>C. albicans</i> <i>C. glabrata</i>	BichroLatex – RTT +	<i>C. albicans</i> (2566174, 99.3%) <i>C. glabrata</i> (2000040, 99.4%)	<i>C. albicans</i> (99.9%) <i>C. glabrata</i> (99.9%)	<i>C. albicans</i> (100%; 100%) <i>C. glabrata</i> (100%; 99%)	Death (d + 104)
7	F/54	Sarcoma of the pubic symphysis	Abdominal surgery, central catheter, urinary catheter	Urology	Plus + Aerobic/F	1 day 1 h 28 min	<i>C. albicans</i>	BichroLatex –	<i>C. albicans</i> (2576174, 97.4%)	<i>C. albicans</i> (99.9%)	<i>C. albicans</i> (100%; 100%)	Survival
8	F/53	B-cell lymphoma	Abdominal surgery, kidney failure, corticosteroids, central catheter, urinary catheter	MICU	Plus + Aerobic/F	1 day 5 h 44 min	<i>C. albicans</i>	BichroLatex +	<i>C. albicans</i> (2566174, 99.3%)	<i>C. albicans</i> ^d (84.8%)	<i>C. albicans</i> (100%; 100%)	Death (d0)
9	M/60	Large B-cell lymphoma	Anticancer chemotherapy, uncontrolled AIDS, catheter	Haematology	Plus + Aerobic/F	2 days 2 h 12 min	No detection	NA	<i>C. dubliniensis</i> (6172134, 99.9%)	<i>C. dubliniensis</i> (86.4%)	<i>C. dubliniensis</i> (100%; 100%)	Death (d + 1)
10	M/61	Liver transplant	Central catheter, digestive surgery	SICU	Plus + Aerobic/F	1 day 9 h 51 min	<i>C. glabrata</i>	RTT +	<i>C. glabrata</i> (2000040, 99.4%)	<i>C. glabrata</i> (99.9%)	<i>C. glabrata</i> (100%; 99%)	Survival
11	M/63	Gastric adenocarcinoma	Total gastrectomy, central catheter	MICU	Mycosis IC/F	2 days 16 h 03 min	<i>C. albicans</i>	BichroLatex +	<i>C. albicans</i> (2576174, 97.4%)	<i>C. albicans</i> ^d (99.9%)	<i>C. albicans</i> (100%; 100%)	Death (d + 74)
12	F/67	Multiple sclerosis	Urinary catheter, recurrent pyelonephritis	Urology	Plus + Aerobic/F	1 day 10 h 32 min	<i>C. albicans</i>	BichroLatex +	<i>C. albicans</i> (2542134, 97.4%)	<i>C. albicans</i> ^d (99.9%)	<i>C. albicans</i> (100%; 99%)	Survival
13	F/70	T-cell lymphoma	Portacath, anticancer chemotherapy, corticosteroids	Haematology	Plus + Aerobic/F	3 days 12 h 01 min	no detection	NA	<i>C. neoformans</i> (2147133, 99.9%)	<i>C. neoformans</i> - ^d (99.9%)	<i>C. neoformans</i> (100%; 100%)	Death (d + 85)

Abbreviations:

TTD—time to detection; NA—not applicable; RTT—rapid trehalose test; M—male; F—female.

SICU—surgical intensive care unit; MICU—medical intensive care unit; NICU—neonatal intensive care unit; PICU—paediatric intensive care unit.

d—day(s); h—hour(s); min—minute(s).

^a An API20C® score of ≥98% was defined as the threshold for accurate identification.

^b The species was identified with confidence if at least one spot gave a rating of ≥99% with no conflicting result on the duplicate spot of analysis. The quality control was an *Escherichia coli* strain (ATCC 8739) provided by the manufacturer (LyfoCults® Plus, BioMérieux, Marcy L'Etoile, France).

^c A matching score of ≥99% between the unknown sequence and the closest sequence from the reference database was defined as a reliable criterion to identify accurately an isolate. The positive quality control was a *C. glabrata* strain (no. CLIB-891; CIRM-levures).

^d MALDI-TOF MS run failed at least one time for the control process or the identification step.

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