

06. Fungal infection & disease

6b. Diagnostic mycology (incl molecular)

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Background Cryptococcal infection is a global invasive fungal disease with significant morbidity and mortality. Cryptococcal glucuronoxylomannan (GXM) antigen test in CSF or blood could confirm cryptococcosis according to the 2019 revised EORTC/MSG consensus criteria. Point-of-care (POC) Cryptococcal GXM antigen lateral flow assay (LFA) has revolutionized the diagnosis of cryptococcosis in human patients. Taking into account the fact uneven quality of the detection kits from different manufacturers, we compared of four available Cryptococcal antigen kits using well-defined strains for evaluation.

Methods Comparison of the performance of four cryptococcal antigen kits: 1. Cryptococcal antigen LFA (Dynamiker Biotechnology (Tianjin) Co., Ltd.). 2. Cryptococcal antigen LFA (KONT Biology&Technology (Wenzhou) Co., Ltd). 3. Cryptococcal antigen LFA (Bio-Products (Nanjing) Co., Ltd). 4. Cryptococcal antigen LFA (Immuno-Mycologics, Inc., USA). 83 well-defined strains were tested by the four kits in parallel (Table 1). The specificity was evaluated using strain suspensions of a concentration of 0.5 McFland (0.5 M), of which 0.5 M positive strain suspensions were prepared as a series of 10-fold dilutions to evaluate sensitivity.

Results The results of the four kits were completely consistent with each other. 25 Cryptococcus strains and 13 Trichosporon strains could be detected by the four kits (Table 1). The detection limit of the four kits was 1.0×10^2 CFU/ml in 31 Cryptococcus strains (Table 2). There were 6 Cryptococcus strains with inconsistent sensitivity results between the four kits at the lowest dilution. Dynamiker test showed the highest sensitivity (6 Cryptococcus strains were all positive) (Table 3).

Conclusions We confirmed that the four Cryptococcal antigen kits showed highly consistent sensitivity, the specific detection results showed that there are some intra-genus and extra-genus cross-reaction results, and no hook effect was observed.

Table 1 The specificity of four manufacturer kits

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	Strains (n)	Positive rate %
1	<i>Cryptococcus</i> species(31): <i>C.neoformans</i> (15), <i>C.neoformans var.grubii</i> (3), <i>C.gattii</i> (3), <i>C.humicola</i> (1), <i>C.albidus</i> (1), <i>C.laurentii</i> (1), <i>C.uzbekistanensis</i> (1), <i>C.victoriae</i> (4), <i>C.dimennae</i> (1), <i>C.magnum</i> (1)	80.65% (25/31)
2	<i>Trichosporon</i> species (17): <i>T.asahii</i> (2), <i>T.mucooides</i> (1), <i>T.jirovecii</i> (3), <i>T.dermatitis</i> (1), <i>T.montevideense</i> (1), <i>T.guehoae</i> (1), <i>T.inkin</i> (1), <i>T.montevideense</i> (3), <i>T.dohaense</i> (2), <i>T.coremiiforme</i> (1), <i>Cutaneotrichosporon curvatum</i> (1)	76.47% (13/17)
3	<i>Candida</i> species(11): <i>C.albicans</i> (3), <i>C.parapsilosis</i> (1), <i>C.krusei</i> (1), <i>C.rugosa</i> (1), <i>C.lusitaniae</i> (1), <i>C.auris</i> (1), <i>C.dubliniensis</i> (1), <i>C.haemulonis</i> (1), <i>C.guilliermondii</i> (1)	0%(0/11)
4	Other Yeast species(24): <i>S.cerevisiae</i> (2), <i>H.zeeae</i> (1), <i>R.minuta</i> (1), <i>M.capitatus</i> (3), <i>R.mucilaginoso</i> (4), <i>M.pollinis</i> (1), <i>K.marxianus</i> (1), <i>M.faoirosa</i> (1), <i>P.kudriavzevii</i> (1), <i>W.anomalus</i> (2), <i>L.elongisporus</i> (1), <i>C.fabianii</i> (2), <i>S.salmonicolor</i> (2), <i>Y.keelungensis</i> (1), <i>K.blattae</i> (1)	0%(0/24)

Table 2 The sensitivity of four manufacturer kits

Name (n)	Detection limit range (CFU/mL)			
	Dynamiker	Kangtai	Liming	IMMY
<i>C.neoformans</i> (8)	4.0×10 ² -2.0×10 ⁴	4.0×10 ² -2.0×10 ⁴	4.0×10 ² -1.0×10 ⁵	1.0×10 ³ -2.0×10 ⁴
<i>C.neoformans var.grubii</i> (3)	1.8×10 ³ -6.0×10 ³	1.8×10 ³ -3.0×10 ⁴	1.8×10 ³ -3.0×10 ⁴	6.0×10 ³ -3.0×10 ⁴
<i>C.gattii</i> (2)	1.0×10 ¹ -1.3×10 ²	1.0×10 ¹ -1.3×10 ³	1.0×10 ² -1.3×10 ³	1.0×10 ² -1.3×10 ³
<i>C.albidus</i> (1)	1.0×10 ³	1.0×10 ⁴	1.0×10 ⁴	1.0×10 ⁴
<i>C.laurentii</i> (1)	1.0×10 ³	1.0×10 ³	1.0×10 ³	1.0×10 ³
<i>C.uzbekistanensis</i> (1)	3.0×10 ⁴	3.0×10 ⁵	3.0×10 ⁵	3.0×10 ⁵
<i>T.dermatitis</i> (1)	2.0×10 ³	2.0×10 ⁴	2.0×10 ⁴	2.0×10 ⁴
<i>Trichosporon mucooides</i> (1)	4.0×10 ²	4.0×10 ³	4.0×10 ³	4.0×10 ³
<i>T.asahii</i> (2)	5.0×10 ³ -1.1×10 ⁶			
<i>T.montevideense</i> (1)	1.2×10 ⁶	1.2×10 ⁶	1.2×10 ⁶	1.2×10 ⁶
<i>T.inkin</i> (1)	2.0×10 ⁵	2.0×10 ⁵	2.0×10 ⁵	2.0×10 ⁵
<i>T.montevideense</i> (4)	9.0×10 ⁵ -1.7×10 ⁶			
<i>T.dohaense</i> (2)	5.1×10 ⁴ -1.9×10 ⁵			
<i>T.coremiiforme</i> (1)	7.0×10 ³	7.0×10 ³	7.0×10 ³	7.0×10 ³
<i>T.guehoae</i> (1)	2.0×10 ³	2.0×10 ³	2.0×10 ³	2.0×10 ³
<i>C. curvatum</i> (1)	8.0×10 ⁴	8.0×10 ⁴	8.0×10 ⁴	8.0×10 ⁴

Table 3 Inconsistent results detected by the four

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Name(number)	Dilution (0.5M×)	Dynamiker	Kangtai	Liming	IMMY
<i>C.gattii</i> (A3530)	10 ⁻⁴	+	+	—	—
<i>C.uzbekistanensis</i> (A5648)	10 ⁻¹	+	—	—	—
<i>C.gattii</i> (A5677)	10 ⁻⁴	+	+	—	—
<i>C.albidus</i> (A5680)	10 ⁻²	+	—	—	—
<i>C.neoformans</i> (A5676)	10 ⁻³	+	+	+	—
<i>C.neoformans</i> var.grubii (A5923)	10 ⁻³	+	+	+	—

Keyword 1

POCT

Keyword 2

Cryptococcal antigen

Keyword 3

performance

Conflicts of interest

Do you have any conflicts of interest to declare?

I have no potential conflict of interest to report