Development of Cobas® UC-TIB-CPO Assay for Detection of KPC, OXA-48, NDM, and VIM/IMP

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RES-113

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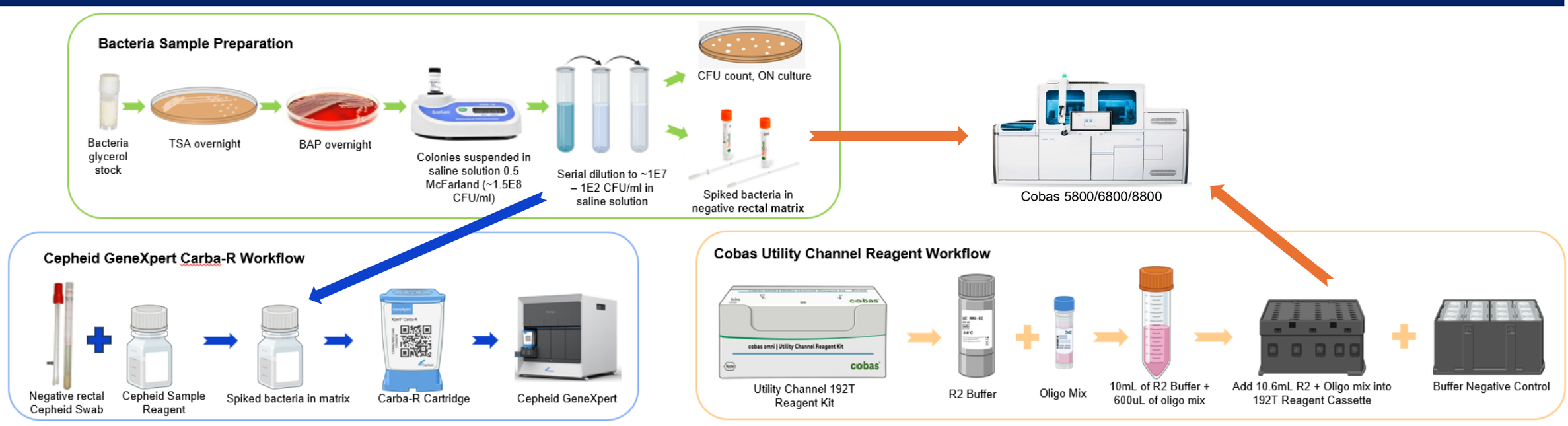
Background: Carbapenemase-producing organisms (CPO) are a significant cause of healthcare-associated infections and an urgent threat to public health. These critical pathogens have limited treatment options and are associated with high mortality, making resistance detection essential for infection prevention, antimicrobial stewardship, and epidemiological surveillance.
Methods: The Cobas® UC-TIB-CPO assay (UC-TIB-CPO assay) was designed for qualitative detection of the five major carbapenemases, KPC, OXA-48 like, NDM, and VIM/IMP (undifferentiated), on the Cobas Utility Channel of the automated, high-throughput Cobas 5800/6800/8800 Systems. Analytical performance was compared with the Cepheid Xpert Carba-R assay using contrived specimens spiked in rectal swab matrix with reference organisms carrying target genes or synthetic templates. Analytical exclusivity was conducted with 51 bacterial strains carrying closely related but off-target resistance markers, spiked at 1E7 colony-forming units (CFU)/mL. Additionally, in-silico inclusivity and specificity analyses were performed.
Results: With contrived swab samples, the assay demonstrated an analytical sensitivity of ~62.5 CFU/swab (KPC-2), 3.9 CFU/swab (OXA-232), 125 CFU/swab (VIM-2), 31.25 CFU/swab (NDM-1), and 3.9/7.81 CFU/swab (IMP-1/IMP-4), outperforming the Carba-R assay. Combined in silico and wet-lab studies demonstrated 100% inclusivity for all variants of the 5 major carbapenemases available in the National Center for Biotechnology Information GenBank database as of March 2025. No cross-reactivity was observed in wet-lab testing with 51 exclusivity strains.
Conclusion: Using contrived rectal swab samples, the UC-TIB-CPO assay demonstrated better analytical sensitivity than the Cepheid Carba-R assay with excellent inclusivity and exclusivity for the detection of the 5 most problematic carbapenemase-encoding genes carried by Gram-negative pathogens.

Background:

- Carbapenemase-producing organisms are urgent/critical threats to public health due to limited treatment options and high associated mortality
- Accurate and rapid detection of carbapenemases is essential to infection prevention, antimicrobial stewardship, and epidemiological surveillance
- We assessed the analytical performance of the UC-TIB-CPO assay, which was designed to detect the 5 major carbapenemases, KPC, OXA-48 like, NDM, and VIM/IMP (undifferentiated), on the Cobas Utility Channel of the automated, high-throughput Cobas 5800/6800/8800 Systems

Methods:



Results:

- When evaluated with contrived samples, UC-TIB-CPO assay had better analytical sensitivity when compared with Cepheid Carba-R assay (Table 1)
- In combined in silico and wet-lab studies, UC-TIB-CPO assay demonstrated 100% inclusivity for all variants of KPC, NDM, VIM, OXA-48, and IMP available in NCBI GenBank as of Mar 2025, including those not detected by Cepheid Carba-R (Table 2)
- No cross-reactivity was observed in wet-lab testing of 51 exclusivity strains (data not shown). However, in silico analysis found potential low-level cross-reactivity with AFM carbapenemases (NDM-like).

Table 1

Contrived Sample		KPC-2 K. pneumoniae CDC AR-0005		OXA-232 K. pneumoniae CDC AR-0068		VIM-2 P. aeruginosa CDC AR-0108		NDM-1 K. pneumoniae CDC AR-0068		IMP-1 P. aeruginosa CDC AR-0103		IMP-4 K. aerogenes CDC AR-0161	
CFU/Swab		UC-TIB	Carba-R	UC-TIB	Carba-R	UC-TIB	Carba-R	UC-TIB	Carba-R	UC-TIB	Carba-R	UC-TIB	Carba-R
L0	5000						1/1						0/1
L1	1000	5/5		5/5		5/5	0/1	5/5		5/5	1/1	5/5	0/2
L2	500	5/5		5/5		5/5	0/1	5/5		5/5	1/1	5/5	0/2
L3	250	5/5		5/5		5/5		5/5		5/5	1/1	5/5	0/1
L4	125	5/5	2/2	5/5		5/5		5/5	2/2	5/5	0/2	5/5	
L5	62.5	5/5	1/1	5/5		4/5		5/5	2/2	5/5	0/2	5/5	
L6	31.25	4/5	0/1	5/5		3/5		5/5	2/2	5/5	0/1	5/5	
L7	15.62	3/5		5/5	2/2	1/5		4/5	0/2	5/5		5/5	
L8	7.81	0/5		5/5	0/2	0/5		0/5	0/2	5/5		5/5	
L9	3.9	1/5		4/4	0/1	0/5		1/5	1/2	5/5		4/5	

Table 2

Target	UC-TIB-CPO Assay: Inclusivity (in silico)	UC-TIB-CPO Assay: Detected in Wet Lab Testing	UC-TIB-CPO Assay: Not Detected in Wet Lab Testing	Cepheid Carba-R: Inclusivity (package insert)	Cepheid Carba-R: Detected in Wet Lab Testing	Cepheid Carba-R: Not Detected in Wet Lab Testing
KPC	1-245	1, 2, 3, 6	-	2-16	-	-
NDM	1-78	1, 5, 7	-	1-9	-	-
VIM	1-92	1, 2, 4, 7, 13, 27, 69	-	1,2, 4, 5-20, 23-38	7, 13, 69	-
OXA-48-like	48, 54, 162, 163, 181, 199, 204, 232, 244, 245, 247, 252, 370, 405, 416, 436, 438, 439, 484, 505, 514, 515, 517, 519, 535, 538, 546, 547, 566, 567, 731, 788, 793, 833, 894, 918, 920, 922, 923, 924, 929, 933, 934, 1012, 1038, 1039, 1055, 1119, 1146, 1167, 1181, 1200, 1201, 1205, 1207, 1211, 1212, 1213, 1226, 1240, 1242, 1304, 1305, 1307, 1308, 1309	48, 54, 181, 204, 232, 535	-	48, 162, 163, 181, 204, 232, 244, 245, 247	204, 535	54
IMP	1-106	1, 4, 7, 8, 11, 13, 14, 15, 18, 22, 26, 27, 31, 44, 46, 48, 54, 63, 67, 74, 83	-	1 (9 strains), 2, 3, 4, 6, 8, 9, 10, 11, 13[a], 19-22, 24, 25, 27, 28, 30, 31, 33, 37, 40, 42	1, 4, 26	13, 14, 15, 18, 27, 67

[a] Inclusive in silico but not detected in wet lab testing by Cepheid

Conclusions:

- The UC-TIB-CPO assay demonstrated better analytical sensitivity than the Cepheid Carba-R assay, with excellent inclusivity and exclusivity in silico and in wet lab testing, for the detection of the 5 most problematic carbapenemase-encoding genes carried by Gram-negative pathogens.
- Limitations to this work include potential cross-reactivity with rare AFM carbapenemases (which can be mitigated by incorporating a signal cutoff), and the limited availability of CPO bacterial strains available for wet lab testing.

Disclaimers/disclosures:
- Cobas UC-TIB-CPO is for research purposes only and not approved for clinical use.
- The study was funded by Roche Molecular Systems. All authors are employees of Roche.