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Corynebacterium Prosthetic Joint Infection

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Identification of *Corynebacterium* species may be challenging. *Corynebacterium* species are occasional causes of prosthetic joint infection (PJI), but few data are available on the subject. Based on the literature, *C. amycolatum*, *C. aurimucosum*, *C. jeikeium*, and *C. striatum* are the most common *Corynebacterium* species that cause PJI. We designed a rapid PCR assay to detect the most common human *Corynebacterium* species, with a specific focus on PJI. A polyphosphate kinase gene identified using whole-genome sequence was targeted. The assay differentiates the antibiotic-resistant species *C. jeikeium* and *C. urealyticum* from other species in a single assay. The assay was applied to a collection of human *Corynebacterium* isolates from multiple clinical sources, and clinically relevant species were detected. The assay was then tested on *Corynebacterium* isolates specifically associated with PJI; all were detected. We also describe the first case of *C. simulans* PJI.

While Gram-positive aerobic cocci cause most cases of prosthetic joint infection (PJI), *Corynebacterium* species are occasional causes. Since the publication of the few reports on *Corynebacterium* PJI, several new *Corynebacterium* species have been described. The genus now includes over 85 species (http://old.dsmz.de/microorganisms/bacterial_nomenclature_info.php?genus=Corynebacterium), not all isolated from humans. As normal human flora, *Corynebacterium* species are common contaminants in clinical specimens. Because of this, as well as challenges in their identification, they have not received a great deal of attention in clinical practice. They are, however, increasingly recognized as causes of significant human infection, including PJI (1, 16, 20, 22).

Corynebacterium species commonly isolated in the clinical laboratory include *C. amycolatum*, *C. aurimucosum*, *C. glucuronolyticum*, *C. jeikeium*, C. *pseudodiphtheriticum*, *C. striatum*, *C. tuberculostearicum*, and *C. urealyticum* (8). *C. glucuronolyticum* and *C. urealyticum* are involved predominantly in urinary tract infection and *C. pseudodiphtheriticum* in respiratory tract infection (8); the other five commensal flora species (10) are potential causes of device-associated infections, including PJI (13, 19). Corynebacteria that cause orthopedic device-associated infections are not usually identified to the species level, and specific *Corynebacterium* species involved in PJI are not definitively known.

As mentioned, many laboratories do not routinely identify *Corynebacterium* species, because they are frequently isolated as contaminants and their identification is challenging. In our laboratory, the term "small non-spore-forming Gram-positive bacillus resembling *Corynebacterium* species" is often used for coryneform organisms, since it can be challenging to differentiate *Corynebacterium* species from *Turicella otidis*, *Arthrobacter* species, *Brevibacterium* species, *Dermabacter hominis*, *Rothia dentocariosa*, *Exiguobacterium acetylicum*, *Helcobacillus* species, *Oerskovia turbata*, *Cellulomonas* species, *Cellulosimicrobium* species, *Microbacterium* species, *Curtobacterium* species, and *Leifsonia aquatica* using a simplistic strategy (8). For species-level identification, phenotypic testing such as with API Coryne (bioMérieux, Durham, NC) has been used. Sequencing-based methods targeting the 16S rRNA gene or *rpoB* give more precise species identification (11). Of these, *rpoB* sequencing is ideal but not commonly available; none of these methods is rapid.

As an alternative approach for rapid identification of *Corynebacterium* species, a PCR assay targeting the *Corynebacterium* species that most frequently cause human infection, with a specific focus on those causing PJI, was designed. In addition to detection of *Corynebacterium* species, the assay differentiates the antibiotic-resistant species *C. jeikeium* and *C. urealyticum* from other species. The assay was first tested on a collection of *Corynebacterium* isolates representing multiple species. It was then tested on isolates specifically associated with PJI, which were also identified using *rpoB* or 16S rRNA gene sequencing. Finally, we compared our results on the microbial ecology of PJI to the literature on the topic.

MATERIALS AND METHODS

Control isolates. Nineteen clinical *Corynebacterium* species characterized by partial *rpoB* gene sequencing (2) and *C. glutamicum* ATTC 13032 were studied (Table 1). The five specifically targeted clinical species are in bold in Table 1. In addition, 338 non-*Corynebacterium* isolates, identified using phenotypic methods or 16S rRNA gene sequencing, from patients with biofilm-associated infections were used to assess cross-reactivity (Table 2).

Clinical isolates from the site of PJI. Nine *Corynebacterium* species isolated from the site of hip or knee PJI between 1999 and 2008 were studied. They were characterized by partial *rpoB* (2) or (if *rpoB* failed) partial 16S rRNA gene (12) sequencing, and their antimicrobial susceptibilities were determined following current guidelines (4).

DNA extraction. DNA was extracted using the QIAamp DNA Minikit (Qiagen, Valencia, CA).

Real-time PCR assay design. A potential target corresponding to a polyphosphate kinase gene, *pvdS2*, of *C. jeikeium* strain K411 (accession number NC_007164) was identified in the genomes of *C. aurimucosum* ATCC 700975, *C. jeikeium* K411, and *C. urealyticum* DSM7109 (14, 15, 18). A consensus sequence was created using Sequencher

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TABLE 1 Characteristics of *Corynebacterium* species and their detection by the described real-time PCR assay

Species[a]	Clinical source(s)[b]	Antimicrobial susceptibility[b]	Frequency in clinical specimens[b,c]	Frequency in PJI[c,d]	No. of isolates tested	Melting temp (°C)	
						Channel 1[e]	Channel 2[f]
C. accolens	Eyes, ENT[g]	Susceptible	−	−	1	−	−
C. afermentans	Skin, blood	β-Lactam susceptible	−	−	4	+61, 67[h]	−
C. amycolatum	Skin, foreign body, blood	Possible resistance	+++	+++	3	+64	−
C. aurimucosum	Skin, female genitourinary tract		+++	+++	4	+∼56	+50[i]
C. confusum	Foot, breast		−	−	1	+60	−
C. diphtheriae	Oropharynx	Susceptible	+	−	1	+57	
C. durum	Respiratory tract, blood		+	−	1	−	−
Corynebacterium group F1	Urinary tract	Penicillin susceptible, often macrolide resistant	−	−	2	−	−
C. glucuronolyticum	Male genitourinary tract, blood	Often tetracycline resistant	++	−	1	+63	−
C. glutamicum	Animal species		−	−	1	+64	
C. imitans	Skin, blood		+	−	1	+56	−
C. jeikeium	Skin, foreign body, endocarditis	Often resistant to multiple agents	+++	++	2	−	+61
C. mucifaciens	Blood, peritoneal fluid	Susceptible	+	−	1	+62	−
C. propinquum	Oropharynx		−	−	1	+55	−
C. pseudodiphtheriticum[j]	Oropharynx, Respiratory tract, endocarditis	β-Lactam susceptible	++	−	1	+55	−
C. riegelii	Female urinary tract, blood		+	−	1	−	−
C. singulare	Skin		−	−	1	+52	−
C. striatum	Skin, respiratory tract, foreign body	Possible macrolide, fluoroquinolone, tetracycline resistance	+++	+++	2	+50	−
C. tuberculostearicum	Skin, foreign body, endocarditis		+++	−	2	+56, 64[h]	−
C. urealyticum	Urinary tract, blood, groin	Often resistant to multiple agents	++	−	1	−	+61

[a] Boldface indicates species most frequently isolated in the clinical laboratory.
[b] Based on data from references 3, 8, and 9.
[c] −, exceptionally or never observed; +, rarely observed; ++, frequently observed; +++, very frequently observed.
[d] Based on data from references 13 and 19.
[e] Measured using F2/F1 color compensation.
[f] Measured using F3/F2 color compensation.
[g] ENT, ear, nose, and throat.
[h] Double peak on melting curve.
[i] No crossing point on quantification curve.
[j] *C. pseudodiphtheriticum* is closely related to *C. propinquum* based on *rpoB* sequence; they also share the same PCR profile (positive only with probes 1 and 2, with a T_m of 55°C).

(GeneCodes, Ann Arbor, MI) and primers (forward and reverse 1 [Table 3]) designed with Roche LightCycler Primer Design software. Primers (Integrated DNA Technologies, Coralville, IA) were initially evaluated on DNA from control organisms with SYBR green (Roche Applied Science, Indianapolis, IN) detection using the LightCycler 1.0 (Roche Applied Science, Indianapolis, IN). *C. jeikeium*, *C. urealyticum*, *C. aurimucosum*, and *C. striatum*, but not *C. amycolatum* or *C. tuberculostearicum*, were detected. The putative kinase genes of the two nondetected species were amplified with primers Seq Coryne kin F and R (Table 3) and sequenced, as previously described (12). Based on known and new sequence data, a third primer (reverse 2) was designed to enable the detection of the five clinically relevant PJI species with all three primers combined. Three fluorescence resonance energy transfer (FRET) probes, i.e., a donor probe labeled with fluorophore (fluorescein isothiocyanate [FITC]) at the 3′ end (probe 1) and two acceptor probes, one labeled with the fluorophore LC705 at the 5′ end (probe 3, specific for *C. jeikeium*) and the other with the fluorophore LC640 at the 5′ end (probe 2, detects other *Corynebacterium* species), were incorporated (Table 3). Primers and probes (TIB Molbiol, Berlin, Germany) were evaluated with DNA from *Corynebacterium* species (Table 1) and non-*Corynebacterium* species (Table 2).

PCR optimization. Two microliters of template DNA was added to 18 μl PCR mix (LightCycler FastStart DNA Master HybProbe mixture; Roche Applied Science) for a 20-μl final reaction volume. The cycling parameters initially evaluated were preincubation for 10 min at 95°C followed by 35 cycles of 95°C for 10 s, 55°C for 10 s, and 72°C for 22 s. Melting curve analysis (starting at 45°C) was performed with a temperature transition rate of 0.8°C/s to determine the melting temperature (T_m). The assay was optimized for primer concentration, forward/reverse primer ratio, Mg^{2+} concentration, annealing temperature, and number of cycles. Parameters giving the lowest crossing point for standardized positive controls were selected.

Optimization of the LightCycler PCR assay. The optimal Mg^{2+}, probe, and forward primer and reverse primer concentrations were 4 mM, 0.2 μM, 0.4 μM, and 2.0 μM, respectively. The optimal annealing temperature and cycle number were 57°C and 35, respectively.

TABLE 2 Non-*Corynebacterium* isolates ($n = 338$) from patients with biofilm-associated diseases tested for cross-reactivity

Group, genus, or species	No. of isolates
Staphylococci	201
S. aureus	85
Coagulase-negative staphylococci	116
S. epidermidis	80
S. lugdunensis	16
S. warneri	8
S. capitis	3
S. caprae	3
S. simulans	3
Other[a]	3
Propionibacterium spp.	41
P. acnes	29
P. avidum	10
P. granulosum	2
Enterobacteriaceae	28
Escherichia coli	5
Enterobacter cloacae	4
Proteus mirabilis	3
Klebsiella pneumoniae	3
K. oxytoca	2
Other[b]	11
Streptococcus spp.	15
S. agalactiae	3
S. dysgalactiae	3
S. pyogenes	2
S. pneumoniae	2
S. salivarius	2
Other[c]	3
Bacteroides fragilis group	13
B. fragilis	8
B. thetaiotaomicron	2
Other[d]	3
Gram-positive anaerobic cocci	12
Finegoldia magna	8
Other[e]	4
Pseudomonas aeruginosa	10
Enterococcus faecalis	9
Granulicatella adiacens	3
Other[f]	6

[a] 1 *S. haemolyticus*, 1 *S. hominis*, 1 *S. saprophyticus*.
[b] 1 *Citrobacter freundii*, 1 *C. koseri*, 1 *E. aerogenes*, 1 *Morganella morganii*, 1 *Pantoea agglomerans*, 1 *P. vulgaris*, 1 *Providencia rettgeri*, 1 *Salmonella* sp., 1 *Serratia liquifaciens*, 1 *S. marcescens*, 1 *Shigella flexneri*.
[c] 1 *S. anginosus*, 1 *S. mitis*, 1 *S. mutans*.
[d] 1 *B. caccae*, 1 *B. distasonis*, 1 *B. ovatus*.
[e] 1 *Peptoniphilus asaccharolyticus*, 1 *P. harei*, 1 *Parvimonas micra*, 1 *Anaerococcus prevotii*.
[f] 1 *Candida parapsilosis*, 1 *Dermabacter hominis*, 1 *Gordonae terrae*, 1 *Pseudomonas fluorescens*, 1 *Rhodococcus equi*, 1 *Staphylococcus saccharolyticus*.

LOD. The limit of detection (LOD) was determined by testing serial 10-fold dilutions of known concentrations of *C. tuberculostearicum* and *C. jeikeium*.

RESULTS

Inclusivity and cross-reactivity. All isolates of the five common human PJI species (*C. amycolatum*, *C. aurimucosum*, *C. jeikeium*, *C. striatum*, and *C. tuberculostearicum*) were detected (Table 1). Nine other species, including *C. glucuronolyticum*, *C. pseudodiphtheriticum*, and *C. urealyticum*, were also detected. Four unusual species (*C. accolens*, *C. durum*, *Corynebacterium* group F1, and *C. riegelii*) and non-*Corynebacterium* isolates (Table 2) were not detected.

TABLE 3 Oligonucleotide primers and probes

Primer or probe	Sequence (5′ → 3′)
Forward	CGRTTGTACCARGARCGGT
Reverse 1[a]	GCACCTSAAYCCSCGT
Reverse 2[b]	CAACGAGCACCTSAACCC
Seq Coryne kin F	GTRCAGAAKCCCATSACGCGC
Seq Coryne kin R	GCSGGYAAGGGYGGCWCC
Probe 1	TAGCGCTGGAAGTACCASGAGGT-FL
Probe 2	LC640-GACTCRCGCGGCGACGG
Probe 3	LC705-GACTCGCGCTCGGAAGG

[a] Fragment size with primers forward and reverse 1, 143 bp.
[b] Fragment size with primers forward and reverse 2, 149 bp.

Limit of detection. The LODs were 200 and 440 CFU/ml for *C. tuberculostearicum* and *C. jeikeium*, respectively.

Melting curve analysis. The LC640 probe is detected in channel 1 of the LightCycler (measured using F2/F1 color compensation) and the LC705 probe in channel 2 (measured using F3/F2 color compensation). In the melting curve analysis (Table 1), most species tested yielded a T_m only in channel 1. Characteristic T_m values were found for some species (e.g., 64°C for *C. amycolatum*). *C. jeikeium* and the closely related *C. urealyticum* yielded a T_m in channel 2 only. Only *C. aurimucosum* yielded T_m values in both channels, but with a T_m different from that of *C. jeikeium* in channel 2, allowing differentiation. *C. aurimucosum* did not yield a crossing point in channel 2 using quantification curve analysis.

Interpretative criteria. Interpretative criteria were established by assessment of the bacteria shown in Tables 1 and 2. A T_m of >60°C in only channel 2, in conjunction with a quantification curve, was considered positive for *C. jeikeium* or the closely related *C. urealyticum*; the absence of a quantification curve or the presence of a quantification curve and the absence of a corresponding T_m of >60°C was considered negative for *C. jeikeium* and *C. urealyticum*. A T_m in channel 1, in conjunction with a quantification curve, was considered positive for non-*jeikeium*/*urealyticum Corynebacterium* species. Certain species are differentiated by their T_ms. The absence of a T_m in both channels was considered negative for *Corynebacterium* species (with the caveat that *C. accolens*, *C. durum*, *Corynebacterium* group F1, and *C. riegelii* are not detected).

Clinical isolates from the site of PJI. All isolates from the site of clinically defined PJI (5) were detected (Tables 4 and 5). IDRL-6128 yielded a T_m of >60°C in channel 2 only and was identified as *C. jeikeium* by *rpoB* sequencing. IDRL-8271 yielded a T_m in both channels (T_m of <60°C in channel 2) and was identified by partial 16S rRNA gene sequencing as *C. aurimucosum* (*rpoB* sequencing failed). The remaining isolates had a T_m in channel 1 only. Three (IDRL-6031, -6110, and -6281) had a T_m of 64°C and were identified as *C. amycolatum*, and one (IDRL-7596) had a T_m of 55°C and was identified as *Corynebacterium propinquum*. IDRL-7734 yielded an unexpected T_m of 52°C and was identified as *Corynebacterium simulans* by *rpoB* sequencing. Finally, IDRL-6330 yielded a T_m of 66°C; *rpoB* sequencing failed, and partial 16S rRNA

TABLE 4 Clinical characteristics and culture results for nine *Corynebacterium* species isolated from the site of hip and knee PJI

Isolate no.[a]	Source	Criteria for PJI (acute inflammation/ visible purulence/ sinus tract)	Antibiotics (MIC, μg/ml)	Tissue culture (no. of culture-positive tissues/ no. of tissues cultured, organism detected)	Sonicate fluid culture[b]	Synovial fluid culture	Colony morphology
6031	Hip	ND[c]/+/−	Penicillin (>8), ciprofloxacin (>2), minocycline (1), TMP-SMX[d] (>2-38)	3/4, *Corynebacterium* sp.	ND	ND	White, tiny
6110	Knee	+/+/−	Penicillin (1), cefazolin (8), levofloxacin (>4), minocycline (1), TMP-SMX (>2-38), vancomycin (2)	1/2, *Corynebacterium* sp.	ND	ND	White, tiny
6128	Hip	−/+/−	Penicillin (8), cefazolin (8), levofloxacin (2), minocycline (1)	2/5, *C. jeikeium*	ND	ND	Translucent, tiny
6281	Knee	+/−/−	Penicillin (2), cefazolin (8), erythromycin (>4), levofloxacin (>4), vancomycin (2)	2/4, *Corynebacterium* sp.; 1/4, *Enterococcus* sp.	*Corynebacterium* sp. (probable contaminant)	ND	White, tiny, dry
6330	Knee	+/+/−	ND	0/3, *Corynebacterium* sp.; 1/3, SCN[e]	*Corynebacterium* sp., *S. lugdunensis*	SCN	White, tiny, slow growing
7065	Knee	+/−/−	ND	0/4	*Corynebacterium* sp.	ND	Translucent, tiny, creamy
7596	Knee	ND/+/+	ND	1/5, *Corynebacterium* sp.; 2/5, yeast	*Corynebacterium* sp.	−	White, tiny
7734	Knee	+/+/−	Penicillin (1), vancomycin (≤2)	4/6, *Corynebacterium* sp.	*Corynebacterium* sp.	*Coryne.* sp.	White, small, dry
8271	Knee	ND/−/+	Penicillin (1), ceftriaxone (2), vancomycin (≤1)	1/5, *Corynebacterium* sp., 5/5, *Escherichia coli*, SCN	*Corynebacterium* sp., *E. coli*, SCN	ND	White, large (2 mm)

[a] Isolates from monomicrobial *Corynebacterium* PJI cases are in bold.
[b] Implant sonication as described by Trampuz et al. (17).
[c] ND, not done.
[d] TMP-SMX, trimethoprim-sulfamethoxazole.
[e] SCN, coagulase-negative *Staphylococcus* species.

gene sequencing showed 100% and 99.7% homology with two unnamed *Corynebacterium* sp. strains, *Corynebacterium* sp. strain 96447 (6) and *Corynebacterium* sp. strain 3301750 (11), respectively (Table 5). All results were therefore as expected (Table 1).

Four of the 9 isolates (IDRL-6031, -6128, -6281, and -7734) were isolated from at least two tissue cultures, and these were all monomicrobial infections. For the remaining isolates, whether they were the cause of the PJI with which they were associated is unknown; some may be contaminants (Table 4). Most isolates were susceptible to the antimicrobial agents tested, with some exceptions. *C. amycolatum* IDRL-6281 was intermediate to penicillin and resistant to cefazolin, erythromycin, clindamycin, and levofloxacin; *C. jeikeium* IDRL-6128 was resistant to penicillin and cefazolin and intermediate to levofloxacin (Table 4).

DISCUSSION

Corynebacterium genus-specific real-time PCR allows more rapid identification than API Coryne or sequencing-based approaches.

TABLE 5 Molecular identification of *Corynebacterium* species isolated from the site of hip and knee PJI

Isolate no.	Real-time PCR melting temp (°C)		Sequence (% identity)	
	Channel 1[a]	Channel 2[b]	*rpoB*	16S rRNA gene
6031	+64	−	*C. amycolatum* (99)	
6110	+64	−	*C. amycolatum* (99)	
6128	−	+61	*C. jeikeium* (95)	
6281	+64	−	*C. amycolatum* (99)	
6330	+66	−	−	*Corynebacterium* sp. strain 96447 (100) (6), *Corynebacterium* sp. strain 3301750 (99.7) (11)
7065	+62, 68	−	*C. afermentans* (97)	
7596	+55	−	*C. propinquum* (98)	
7734	+52	−	*C. simulans* (98)	
8271	+56	+54	−	*C. aurimucosum* (99)

[a] Measured using F2/F1 color compensation.
[b] Measured using F3/F2 color compensation.

We are not aware of another *Corynebacterium*-specific real-time PCR assay. We developed an assay that detects the most common human *Corynebacterium* species, with a specific focus on PJI. Based on our review of the literature and clinical laboratory experience, we focused on five species. A novel polyphosphate kinase was targeted, and three probes with two detection fluorophores were incorporated to differentiate *C. jeikeium* (and *C. urealyticum*) from other *Corynebacterium* species.

There are only a few published studies about *Corynebacterium* and PJI, most of which were performed before the identification of recently described *Corynebacterium* species. In 2004, Roux et al. published a study of *Corynebacterium* species isolated from bone and joint infections (13). Of the 31 patients reported, 8 presented with prosthetic joint infection (2 each with *C. amycolatum* and *C. striatum*, 3 with *C. aurimucosum*, and 1 with *C. jeikeium*). In 1998, von Graevenitz and al. published a study analyzing 60 patients presenting with PJI or open fracture infection (19). Seventy-three coryneform bacteria were identified to the species level; the most frequent species were *C. amycolatum*, *C. striatum*, and *C. jeikeium*. Nine isolates were considered clinically significant as sole agents of PJI (4 *C. striatum*, 3 *C. amycolatum*, and 1 each *C. jeikeium* and *Corynebacterium* species). At the time, *C. aurimucosum* and *C. tuberculostearicum* had not been described (they were described in 2002 [21] and 2004 [7], respectively). In both studies, *C. amycolatum* was highlighted as a cause of PJI.

A retrospective analysis of *Corynebacterium* species isolated at our institution from the site of hip or knee PJI was performed. Nine available isolates were analyzed with the described assay, all were detected, and the sole *C. jeikeium* isolate was correctly identified. This study confirms *Corynebacterium* species as causes of PJI. *Corynebacterium* PJI is rare. Four monomicrobial infection cases were found, which is unusual, with five case reports (1, 16, 20, 22) and the cases in the von Graevenitz study (19), previously describing this entity. We describe a case of *C. jeikeium* PJI, which has been previously reported (16); as expected, this isolate was resistant to penicillin and cefazolin. Two cases of *C. amycolatum* PJI are also described; this commensal flora organism has been previously described as a cause of PJI (13, 19). Finally, we describe one case of *C. simulans* PJI which, to best of our knowledge, has not been previously described. The isolate was susceptible to penicillin and vancomycin, and the patient's outcome was favorable following two-stage implant exchange and a course of intravenous ertapenem. Overall, *C. amycolatum* was identified in three cases. We also identified *C. propinquum* in one case, with the same T_m (55°C) as the closely related species *C. pseudodiphtheriticum* (11) (Table 1). *C. propinquum* and *C. pseudodiphtheriticum* are commensal flora and/or pathogens of the respiratory tract, especially the oropharynx. Finally, for IDRL-6330, *rpoB* sequencing failed and 16S rRNA gene sequencing showed 100 and 99.7% homology with two unnamed *Corynebacterium* sp. strains, *Corynebacterium* sp. strain 96447 (6) and *Corynebacterium* sp. strain 3301750 (11), respectively. This isolate may represent a yet-to-be described species.

This study highlights the need for antimicrobial susceptibility testing on clinically significant *Corynebacterium* species. *C. jeikeium* is not the only penicillin-resistant species; furthermore, some *C. jeikeium* strains lack penicillin resistance (9).

Human microbiome studies are now frequent in the literature. Gao et al. analyzed superficial skin bacterial biota of the human forearm and found that the *Corynebacterium* genus was one of the most frequent genera present, with *C. tuberculostearicum* being the most frequent *Corynebacterium* species detected (10).

In conclusion, we designed a *Corynebacterium* real-time PCR assay which detects *Corynebacterium* species frequently described in human pathology and specifically in PJI. This assay is rapid and specific and can differentiate *C. jeikeium* and *C. urealyticum*, which are usually resistant to multiple antibiotics, from other species. Our analysis of clinical isolates from the site of PJI (all detected by our assay) and review of the literature highlight two points: the need for identification and antimicrobial susceptibility testing of clinically significant *Corynebacterium* isolates.

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