



# Can Multidrug-Resistant *Candida auris* Be Reliably Identified in Clinical Microbiology Laboratories?

Masako Mizusawa,<sup>a</sup> Heather Miller,<sup>a,b</sup> Rachel Green,<sup>b</sup> Richard Lee,<sup>b</sup> Mariann Durante,<sup>c</sup> Rosalie Perkins,<sup>d</sup> Caroline Hewitt,<sup>d</sup> Patricia J. Simner,<sup>a,b</sup> Karen C. Carroll,<sup>a,b</sup> Randall T. Hayden,<sup>d</sup> Sean X. Zhang<sup>a,b</sup>

Division of Medical Microbiology, Department of Pathology, Johns Hopkins School of Medicine,<sup>a</sup> and Microbiology Laboratory, Johns Hopkins Hospital, Johns Hopkins Medical Institutions,<sup>b</sup> Baltimore, Maryland, USA; Microbiology Laboratory, Suburban Hospital, Johns Hopkins Medical Institutions, Bethesda, Maryland, USA;<sup>c</sup> Department of Pathology, St. Jude Children's Research Hospital, Memphis, Tennessee, USA<sup>d</sup>

**KEYWORDS** API, BD Phoenix, Bruker MS, *Candida auris*, *Candida duobushaemulonii*, *Candida haemulonii*, MALDI-TOF MS, MicroScan, Vitek, Vitek MS

*Candida auris*, an emerging multidrug-resistant yeast associated with a high mortality rate, has been increasingly reported outside the United States to cause outbreaks in hospital settings (1). Although this organism is rare in the United States, its prevalence may be underestimated because of unreliable identification (2–4). The CDC has recently recommended that health care facilities place patients with *C. auris* colonization or infection in single rooms (2). Therefore, it is imperative for clinical microbiology laboratories to accurately identify this organism to aid in preventing health care-associated outbreaks.

Since a majority of U.S. clinical microbiology laboratories do not have experience in identifying *C. auris*, the CDC has recently prepared a panel of *C. auris* and related species to assist clinical microbiology laboratories with implementing and validating methods to identify this organism. The panel includes 10 isolates of *C. auris*, 3 of *C. duobushaemulonii*, 2 of *C. haemulonii*, 2 of *Saccharomyces*, and 1 each of *Kodamaea ohmeri*, *Candida krusei*, and *C. lusitanae*. We tested *C. auris* isolates, as well as phylogenetically closely related *C. haemulonii* and *C. duobushaemulonii* isolates, on four commercial biochemical identification platforms and two matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS) systems (Tables 1 and 2). The identities of the 15 isolates tested were all confirmed correctly to the species level by sequencing of the internal transcribed spacer and D1/D2 regions.

All *C. auris* isolates were misidentified as *Rhodotorula glutinis* by API 20C AUX (bioMérieux, Marcy l'Etoile, France), as *C. haemulonii* (except one as *C. catenulata*) by BD Phoenix (BD Diagnostics, Sparks, MD), as *C. haemulonii* by Vitek-2 (bioMérieux), and as *C. famata*, *C. lusitanae*, *C. guilliermondii*, or *C. parapsilosis* by MicroScan (Beckman Coulter, Pasadena, CA) (Table 1). Because of the lack of *C. auris* entries in the FDA-approved libraries, it was unidentified by both the Bruker Biotyper (Bruker, Billerica, MA) and Vitek-MS (bioMérieux) MALDI-TOF MS systems when queried on the FDA-approved libraries (Table 2). Incorporation of a research-use-only (RUO) library containing *C. auris* rendered correct identification of this organism by both MALDI-TOF MS systems. In the Vitek MS system, all were identified correctly by the direct extraction method. However, it requires the full-tube extraction method for the Bruker MS system because the direct on-plate extraction method resulted in low-score matches for 50% of the *C. auris* isolates and left another 50% unidentified. Although it was not tested in our study, a partial extraction method that is less laborious than full-tube extraction has been reported to achieve excellent identification by the Bruker MS system (5, 6).

Accepted manuscript posted online 23 November 2016

**Citation** Mizusawa M, Miller H, Green R, Lee R, Durante M, Perkins R, Hewitt C, Simner PJ, Carroll KC, Hayden RT, Zhang SX. 2017. Can multidrug-resistant *Candida auris* be reliably identified in clinical microbiology laboratories? *J Clin Microbiol* 55:638–640. <https://doi.org/10.1128/JCM.02202-16>.

**Editor** David W. Warnock, University of Manchester

**Copyright** © 2017 American Society for Microbiology. All Rights Reserved.

Address correspondence to Sean X. Zhang, [szhang28@jhmi.edu](mailto:szhang28@jhmi.edu).

**TABLE 1** Biochemical identification

Isolate no.	Species tested	Identification according to:			
		API 20C AUX <sup>a</sup>	BD Phoenix <sup>b</sup>	Vitek-2 <sup>c</sup>	MicroScan <sup>d</sup>
1	<i>C. auris</i>	<i>R. glutinis</i>	<i>C. catenulata</i>	<i>C. haemulonii</i>	<i>C. famata</i>
2	<i>C. auris</i>	<i>R. glutinis</i>	<i>C. haemulonii</i>	<i>C. haemulonii</i>	<i>C. famata</i>
3	<i>C. auris</i>	<i>R. glutinis</i>	<i>C. haemulonii</i>	<i>C. haemulonii</i>	<i>C. famata</i>
4	<i>C. auris</i>	<i>R. glutinis</i>	<i>C. haemulonii</i>	<i>C. haemulonii</i>	<i>C. lusitaniae</i>
5	<i>C. auris</i>	<i>R. glutinis</i>	<i>C. haemulonii</i>	<i>C. haemulonii</i>	<i>C. guilliermondii</i>
6	<i>C. auris</i>	<i>R. glutinis</i>	<i>C. haemulonii</i>	<i>C. haemulonii</i>	<i>C. famata</i>
7	<i>C. auris</i>	<i>R. glutinis</i>	<i>C. haemulonii</i>	<i>C. haemulonii</i>	<i>C. guilliermondii</i>
8	<i>C. auris</i>	<i>R. glutinis</i>	<i>C. haemulonii</i>	<i>C. haemulonii</i>	<i>C. parapsilosis</i>
9	<i>C. auris</i>	<i>R. glutinis</i>	<i>C. haemulonii</i>	<i>C. haemulonii</i>	<i>C. guilliermondii</i>
10	<i>C. auris</i>	<i>R. glutinis</i>	<i>C. haemulonii</i>	<i>C. haemulonii</i>	<i>C. guilliermondii</i>
11	<i>C. duobushaemulonii</i>	<i>R. glutinis</i>	<i>C. parapsilosis</i>	<i>C. haemulonii</i>	<i>C. guilliermondii</i>
12	<i>C. duobushaemulonii</i>	<i>R. glutinis</i>	<i>C. parapsilosis</i>	<i>C. haemulonii</i>	<i>C. guilliermondii</i>
13	<i>C. haemulonii</i>	<i>R. glutinis</i>	<i>C. haemulonii</i>	<i>C. haemulonii/K. ohmeri</i>	<i>C. catenulata</i>
14	<i>C. duobushaemulonii</i>	<i>R. glutinis</i>	<i>C. parapsilosis</i>	<i>C. haemulonii</i>	<i>C. parapsilosis</i>
15	<i>C. haemulonii</i>	<i>R. glutinis</i>	None	<i>C. haemulonii/K. ohmeri</i>	<i>C. parapsilosis</i>

<sup>a</sup>Identification at 48 and 72 h of incubation; API 20C AUX does not have *C. auris*, *C. haemulonii*, or *C. duobushaemulonii* in its library.

<sup>b</sup>*C. haemulonii* is in the BD Phoenix library, but *C. auris* and *C. duobushaemulonii* are not.

<sup>c</sup>The Vitek-2 library has *C. haemulonii* but not *C. auris* or *C. duobushaemulonii*.

<sup>d</sup>MicroScan does not have *C. auris*, *C. haemulonii*, or *C. duobushaemulonii* in its library.

In summary, *C. auris* cannot be reliably identified by standard biochemical identification platforms/kits primarily because of a lack of the organism in their databases. Identification of *Rhodotorula glutinis* by API 20C AUX should trigger further investigation if colonies on culture plates are not pink with a negative urease reaction. Likewise, identification of *C. haemulonii* by BD Phoenix and Vitek-2 requires further testing by DNA sequencing to rule out *C. auris*. MicroScan users may find this especially challenging, since *C. auris* was misidentified as several different *Candida* species. Particular attention needs to be paid to *C. famata*, since it has microscopic features very similar to those of *C. auris* (e.g., no pseudohypha production). While *C. auris* is not identified by both the Bruker and Vitek MALDI-TOF MS systems with FDA-approved libraries, it can be reliably identified by both MALDI-TOF MS systems with an RUO library with *C. auris* entries (Table 2). Importantly, however, Bruker MALDI-TOF MS users must be aware that *C. auris* could potentially be unidentified if the direct on-plate extraction

**TABLE 2** Identification by MALDI-TOF MS

Isolate no.	Species tested	Bruker Biotyper			Vitek-MS	
		FDA library <sup>a</sup> direct on-plate extraction (score)	RUO <sup>b</sup> library	Full-tube extraction (score)	Direct extraction (% identity)	
			Direct on-plate extraction (score)		IVD <sup>c</sup> library	RUO library <sup>d</sup>
1	<i>C. auris</i>	No ID <sup>e</sup>	<i>C. auris</i> (1.75)	<i>C. auris</i> (2.19)	No ID	<i>C. auris</i> (99)
2	<i>C. auris</i>	No ID	No ID	<i>C. auris</i> (2.02)	No ID	<i>C. auris</i> (98)
3	<i>C. auris</i>	No ID	<i>C. auris</i> (1.80)	<i>C. auris</i> (2.04)	No ID	<i>C. auris</i> (99)
4	<i>C. auris</i>	No ID	<i>C. auris</i> (1.73)	<i>C. auris</i> (2.10)	No ID	<i>C. auris</i> (99)
5	<i>C. auris</i>	No ID	No ID	<i>C. auris</i> (1.95)	No ID	<i>C. auris</i> (99)
6	<i>C. auris</i>	No ID	No ID	<i>C. auris</i> (1.97)	No ID	<i>C. auris</i> (87)
7	<i>C. auris</i>	No ID	No ID	<i>C. auris</i> (2.05)	No ID	<i>C. auris</i> (99)
8	<i>C. auris</i>	No ID	<i>C. auris</i> (1.73)	<i>C. auris</i> (1.99)	No ID	<i>C. auris</i> (99)
9	<i>C. auris</i>	No ID	No ID	<i>C. auris</i> (2.00)	No ID	<i>C. auris</i> (92)
10	<i>C. auris</i>	No ID	<i>C. auris</i> (1.75)	<i>C. auris</i> (1.92)	No ID	<i>C. auris</i> (99)
11	<i>C. duobushaemulonii</i>	<i>C. duobushaemulonii</i> (2.29)	<i>C. duobushaemulonii</i> (2.29)	Not tested	No ID	No ID
12	<i>C. duobushaemulonii</i>	<i>C. duobushaemulonii</i> (2.19)	<i>C. duobushaemulonii</i> (2.19)	Not tested	No ID	No ID
13	<i>C. haemulonii</i>	<i>C. haemulonii</i> (2.29)	<i>C. haemulonii</i> (2.29)	Not tested	<i>C. haemulonii</i> (99)	<i>C. haemulonii</i> (99)
14	<i>C. duobushaemulonii</i>	<i>C. duobushaemulonii</i> (2.27)	<i>C. duobushaemulonii</i> (2.27)	Not tested	No ID	<i>C. duobushaemulonii</i> (94)
15	<i>C. haemulonii</i>	<i>C. haemulonii</i> (2.21)	<i>C. haemulonii</i> (2.21)	Not tested	<i>C. haemulonii</i> (99)	<i>C. haemulonii</i> (99)

<sup>a</sup>The Bruker FDA library contains *C. haemulonii* (12 entries) and *C. duobushaemulonii* (7 entries).

<sup>b</sup>The Bruker RUO library has *C. auris* (three entries).

<sup>c</sup>IVD, *in vitro* diagnostic. The Vitek MS IVD library is an FDA-approved library, and it contains *C. haemulonii*.

<sup>d</sup>The Vitek MS RUO library has *C. auris* and *C. duobushaemulonii*.

<sup>e</sup>ID, identification.

method is used; thus, the full-tube extraction method or possibly a partial extraction method should be applied for reliable identification.

## REFERENCES

1. Pan American Health Organization/World Health Organization. 3 October 2016. Epidemiological alert: *Candida auris* outbreaks in health care services. Regional Office for the Americas of the World Health Organization, Washington, DC. [http://www.paho.org/hq/index.php?option=com\\_docman&task=doc\\_view&Itemid=270&gid=36354&lang=en](http://www.paho.org/hq/index.php?option=com_docman&task=doc_view&Itemid=270&gid=36354&lang=en).
2. Centers for Disease Control and Prevention. 2016. Clinical alert to U.S. healthcare facilities—June 2016: global emergence of invasive infections caused by the multidrug-resistant yeast *Candida auris*. Centers for Disease Control and Prevention, Atlanta, GA. <http://www.cdc.gov/fungal/diseases/candidiasis/candida-auris-alert.html>.
3. Chowdhary A, Sharma C, Duggal S, Agarwal K, Prakash A, Singh PK, Jain S, Kathuria S, Randhawa HS, Hagen F, Meis JF. 2013. New clonal strain of *Candida auris*, Delhi, India. *Emerg Infect Dis* 19:1670–1673. <https://doi.org/10.3201/eid1910.130393>.
4. Kathuria S, Singh PK, Sharma C, Prakash A, Masih A, Kumar A, Meis JF, Chowdhary A. 2015. Multidrug-resistant *Candida auris* misidentified as *Candida haemulonii*: characterization by matrix-assisted laser desorption ionization–time of flight mass spectrometry and DNA sequencing and its antifungal susceptibility profile variability by Vitek 2, CLSI broth microdilution, and Etest method. *J Clin Microbiol* 53:1823–1830. <https://doi.org/10.1128/JCM.00367-15>.
5. Fraser M, Brown Z, Houldsworth M, Borman AM, Johnson EM. 2016. Rapid identification of 6328 isolates of pathogenic yeasts using MALDI-ToF MS and a simplified, rapid extraction procedure that is compatible with the Bruker Biotyper platform and database. *Med Mycol* 54:80–88. <https://doi.org/10.1093/mmy/myv085>.
6. Borman AM, Szekely A, Johnson EM. 2016. Comparative pathogenicity of United Kingdom isolates of the emerging pathogen *Candida auris* and other key pathogenic *Candida* species. *mSphere* 1(4):e00189-16. <https://doi.org/10.1128/mSphere.00189-16>.