



Draft Genome Sequences of 19 Clinical Isolates of *Candida auris* from Hong Kong

Herman Tse,^a 💿 Alan K. L. Tsang,^a Yiu-Wai Chu,^a Dominic N. C. Tsang^a

^aMicrobiology Division, Public Health Laboratory Services Branch, Centre for Health Protection, Department of Health, Hong Kong SAR, China

ABSTRACT Candida auris is an emerging human pathogen associated with multidrug resistance and nosocomial outbreaks. We report the draft genome sequences of 19 *C. auris* isolates that were associated with a cluster of cases in a hospital in Hong Kong.

C andida auris was first described in Japan in 2009 (1). Since then, *C. auris* infections and nosocomial outbreaks have been reported globally (2, 3). Of particular concern is the high rate of multidrug resistance, which has contributed to significant mortality among hospitalized patients suffering from invasive *C. auris* infections (4). In 2019, a cluster of *C. auris* colonizations occurred in a public hospital in Hong Kong and affected 15 patients.

Whole-genome sequencing for the isolates was performed for outbreak investigation. *C. auris* isolates were cultured from clinical specimens, including endotracheal aspirate, nasal swab, axilla swab, groin swab, and rectal swab specimens (Table 1). The isolates were grown overnight on blood agar at 37°C. Genomic DNA was extracted using the cetyltrimethylammonium bromide-based method (5), followed by library preparation using the Nextera XT kit (Illumina, CA) and sequencing on a MiSeq sequencer (Illumina). Paired-end reads were processed using Trimmomatic v0.38 (6) to remove low-quality bases and adapter sequences with the following parameters: ILLUMINACLIP, 1:30:10; LEADING, 10; TRAILING, 10; SLIDINGWINDOW, 4:15; and MINLEN, 30. Quality-trimmed reads were *de novo* assembled using SPAdes v3.13.1 with the parameters only-assembler, careful, and cov-cutoff auto (7). Ragout v2.1.1 was utilized for reference-assisted scaffolding against reference genomes of strains B11220 (GenBank accession no. GCA_003013715.2) and B11245 (GenBank accession no. GCA_008275145.1) (8). Contigs and scaffolds smaller than 500 bp were filtered and excluded from the draft assemblies.

The draft assemblies of these 19 isolates varied in length from 12.6 to 14.2 Mb, with a mean \pm standard deviation scaffold count of 265 \pm 180, GC content of 45.1% \pm 0.06%, scaffold N_{50} value of 217 \pm 44 kb, and coverage depth of 86-fold \pm 26-fold for quality-trimmed reads. Summary statistics for individual assemblies are presented in Table 1.

Single nucleotide polymorphism (SNP) analysis was performed using Snippy v4.41 (https://github.com/tseemann/snippy). *C. auris* strain B8411 (GenBank accession no. GCA_002759435.2) was selected as the reference genome, and the raw reads of sequenced *C. auris* isolates from each of the four established clades, including strains B11215 (GenBank accession no. SRR3883446 [clade I/South Asia]), B11220 (GenBank accession no. SRR3883452 [clade II/East Asia]), B11223 (GenBank accession no. SRR3883455 [clade III/South Africa]), and B11244 (GenBank accession no. SRR3883465 [clade IV/South America]), were added to the analysis (9). A maximum likelihood phylogeny was constructed from the SNP data using IQ-TREE v1.6.9 with a GTR+gamma model and the fast option. All isolates are closely related to B11215, with 40 to 45 SNPs, which

Citation Tse H, Tsang AKL, Chu Y-W, Tsang DNC. 2021. Draft genome sequences of 19 clinical isolates of *Candida auris* from Hong Kong. Microbiol Resour Announc 10:e00308-20. https://doi.org/10.1128/MRA.00308-20.

Editor Antonis Rokas, Vanderbilt University

Copyright © 2021 Tse et al. This is an openaccess article distributed under the terms of the Creative Commons Attribution 4.0 International license.

Address correspondence to Alan K. L. Tsang, alan_kl_tsang@dh.gov.hk.

Received 4 May 2020 Accepted 5 December 2020 Published 7 January 2021

TABLE 1 C	haracteris	cics and accession numbers of g	enomes of C.	<i>auris</i> in the p	present stu	dy					
			Genome	No. of	No. of	No. of	Scaffold	Scaffold GC	Contig	Scaffold	Read
Isolate	Patient	Isolation source	size (Mb)	reads	contigs	scaffolds	N ₅₀ (bp)	content (%)	accession no.	accession no.	accession no.
Cau1901	-	Endotracheal aspirate	13.05	3,292,066	1,986	362	243,019	45.06	CACTHW010000000	CACTHW030000000	ERR3503255
Cau1902	-	Pooled swab (nasal, axilla,	13.19	3,210,208	2,159	433	258,084	45.04	CACTGN010000000	CACTGN030000000	ERR3503256
		and groin)									
Cau1903	-	Rectal swab	12.92	6,090,642	756	109	161,728	45.14	CACTGL010000000	CACTGL030000000	ERR3503257
Cau1904	2	Pooled swab (nasal, axilla,	12.85	5,160,246	1,581	238	233,558	45.06	CACTGM010000000	CACTGM030000000	ERR3503258
		and groin)									
Cau 1905	2	Pooled swab (axilla and	12.95	3,797,138	1,685	278	241,804	45.05	CACTHC010000000	CACTHC03000000	ERR3503259
		groin)									
Cau1906	2	Nasal swab	12.88	5,245,386	1,424	348	235,153	45.05	CACTGS010000000	CACTGS030000000	ERR3503260
Cau1907	ŝ	Skin swab (axilla and groin)	12.60	3,666,438	733	133	260,717	45.16	CACTHB010000000	CACTHB030000000	ERR3503261
Cau1908	4	Skin swab (axilla and groin)	13.61	1,979,612	2,376	707	308,895	45.07	CACTGV010000000	CACTGV030000000	ERR3503262
Cau1909	5	Skin swab (axilla and groin)	13.32	2,125,554	2,416	575	235,706	45.03	CACTHA010000000	CACTHA030000000	ERR3503263
Cau1910	9	Skin swab (axilla and groin)	13.05	5,992,296	1,842	330	204,007	45.06	CACTGU010000000	CACTGU030000000	ERR3503264
Cau1911	7	Skin swab (axilla and groin)	13.29	2,556,728	2,447	527	263,577	45.01	CACTGZ010000000	CACTGZ030000000	ERR3503265
Cau1912	8	Pooled swab (axilla and	13.46	4,233,504	837	154	167,847	45.18	CACTGW010000000	CACTGW03000000	ERR3503266
		groin)									
Cau1913	6	Nasal swab	12.71	5,291,608	749	101	232,540	45.15	CACTGY010000000	CACTGY030000000	ERR3503267
Cau1914	10	Nasal swab	12.83	3,683,864	813	126	172,921	45.18	CACTGX010000000	CACTGX030000000	ERR3503268
Cau1915	11	Nasal swab	13.08	3,481,116	784	112	194,566	45.13	CACTGQ010000000	CACTGQ03000000	ERR3503269
Cau1916	12	Pooled swab (nasal, axilla,	13.19	5,254,784	606	126	199,353	45.17	CACTGR010000000	CACTGR030000000	ERR3503270
		and groin)									
Cau1917	13	Pooled swab (nasal, axilla,	14.25	4,755,080	966	213	113,160	45.18	CACTGT010000000	CACTGT030000000	ERR3503271
		and groin)									
Cau1918	14	Pooled swab (nasal, axilla,	13.28	5,222,686	758	100	192,279	45.17	CACTGP010000000	CACTGP030000000	ERR3503272
		and groin)									
Cau1919	15	Pooled swab (nasal, axilla,	12.58	4,471,008	656	69	208,443	45.13	CACTGO010000000	CACTGO03000000	ERR3503273
		and groin)									



FIG 1 (A) Phylogenetic tree showing the genetic relationships among isolates representing four distinct clades. The isolates from the 15 patients are highlighted in blue. The scale bar indicates the number of SNP differences. (B) Phylogenetic tree showing the genetic relationships among isolates within the South Asia clade. The isolates from the 15 patients are highlighted in blue. The scale bar indicates the number of SNP differences.

identifies them as strains of clade I/South Asia (Fig. 1A) (2). The maximum number of pairwise SNP differences between isolates is 13, suggesting a high degree of genetic relatedness (Fig. 1B). Our results are comparable to those of a previous study, which suggested a genetic distance of \leq 12 SNPs between patients as being indicative of recent transmission (10).

Gene mutations associated with antifungal resistance, including a reported *ERG11* mutation, were observed (9, 11). The present work adds to the growing body of knowledge on this increasingly important human pathogen.

Data availability. The whole-genome sequencing project has been deposited in DDBJ/ENA/GenBank under the accession no. PRJEB34199. The accession numbers for the assembly and raw reads for individual isolates are provided in Table 1.

REFERENCES

- Satoh K, Makimura K, Hasumi Y, Nishiyama Y, Uchida K, Yamaguchi H. 2009. Candida auris sp. nov., a novel ascomycetous yeast isolated from the external ear canal of an inpatient in a Japanese hospital. Microbiol Immunol 53:41–44. https://doi.org/10.1111/j.1348-0421.2008.00083.x.
- Rhodes J, Fisher MC. 2019. Global epidemiology of emerging *Candida* auris. Curr Opin Microbiol 52:84–89. https://doi.org/10.1016/j.mib.2019 .05.008.
- Cuomo CA, Alanio A. 2020. Tracking a global threat: a new genotyping method for *Candida auris*. mBio 11:e00259-20. https://doi.org/10.1128/ mBio.00259-20.
- 4. Cortegiani A, Misseri G, Fasciana T, Giammanco A, Giarratano A, Chowdhary

A. 2018. Epidemiology, clinical characteristics, resistance, and treatment of infections by *Candida auris*. J Intensive Care 6:69. https://doi.org/10.1186/ s40560-018-0342-4.

- Hildén K, Martínez AT, Hatakka A, Lundell T. 2005. The two manganese peroxidases Pr-MnP2 and Pr-MnP3 of *Phlebia radiata*, a lignin-degrading basidiomycete, are phylogenetically and structurally divergent. Fungal Genet Biol 42:403–419. https://doi.org/10.1016/j.fgb.2005.01.008.
- Bolger AM, Lohse M, Usadel B. 2014. Trimmomatic: a flexible trimmer for Illumina sequence data. Bioinformatics 30:2114–2120. https://doi.org/10 .1093/bioinformatics/btu170.
- 7. Nurk S, Bankevich A, Antipov D, Gurevich AA, Korobeynikov A, Lapidus A,

Prjibelski AD, Pyshkin A, Sirotkin A, Sirotkin Y, Stepanauskas R, Clingenpeel SR, Woyke T, McLean JS, Lasken R, Tesler G, Alekseyev MA, Pevzner PA. 2013. Assembling single-cell genomes and mini-metagenomes from chimeric MDA products. J Comput Biol 20:714–737. https://doi.org/10.1089/cmb.2013.0084.

- Kolmogorov M, Armstrong J, Raney BJ, Streeter I, Dunn M, Yang F, Odom D, Flicek P, Keane TM, Thybert D, Paten B, Pham S. 2018. Chromosome assembly of large and complex genomes using multiple references. Genome Res 28:1720–1732. https://doi.org/10.1101/gr.236273.118.
- Lockhart SR, Etienne KA, Vallabhaneni S, Farooqi J, Chowdhary A, Govender NP, Colombo AL, Calvo B, Cuomo CA, Desjardins CA, Berkow EL, Castanheira M, Magobo RE, Jabeen K, Asghar RJ, Meis JF, Jackson B, Chiller T, Litvintseva AP. 2017. Simultaneous emergence of multidrug-resistant *Candida auris* on

3 continents confirmed by whole-genome sequencing and epidemiological analyses. Clin Infect Dis 64:134–140. https://doi.org/10.1093/cid/ciw691.

- Chow NA, Gade L, Tsay SV, Forsberg K, Greenko JA, Southwick KL, Barrett PM, Kerins JL, Lockhart SR, Chiller TM, Litvintseva AP, US Candida auris Investigation Team. 2018. Multiple introductions and subsequent transmission of multidrug-resistant Candida auris in the USA: a molecular epidemiological survey. Lancet Infect Dis 18:1377–1384. https://doi.org/10 .1016/S1473-3099(18)30597-8.
- 11. Chowdhary A, Prakash A, Sharma C, Kordalewska M, Kumar A, Sarma S, Tarai B, Singh A, Upadhyaya G, Upadhyay S, Yadav P, Singh PK, Khillan V, Sachdeva N, Perlin DS, Meis JF. 2018. A multicentre study of antifungal susceptibility patterns among 350 *Candida auris* isolates (2009–17) in India: role of the *ERG11* and *FKS1* genes in azole and echinocandin resistance. J Antimicrob Chemother 73:891–899. https://doi.org/10.1093/jac/dkx480.