Supplementary Materials

Rapid and extensive karyotype diversification in haploid clinical *Candida auris* isolates

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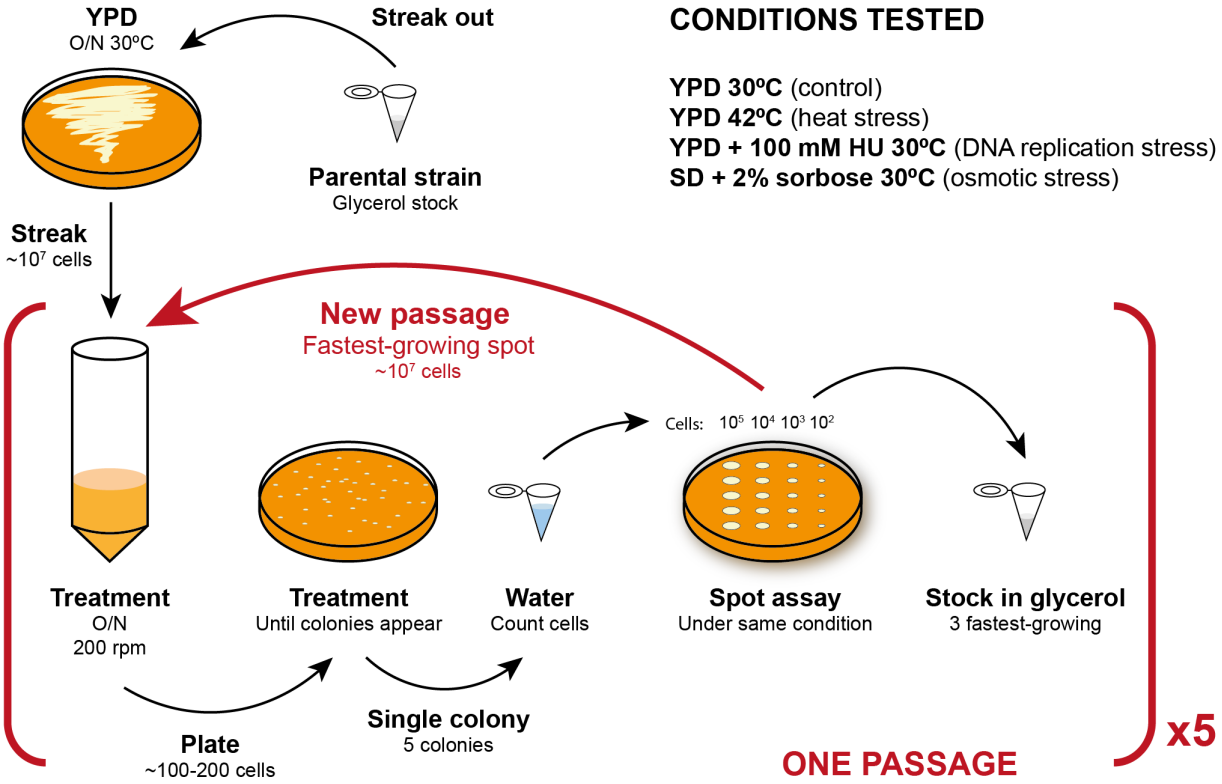

Figure S1. Microevolution assay. Schematic representation of the microevolution assay carried out in this study. Strains where separately passaged five times through YPD broth at 30°C (control), YPD broth at 42°C (heat stress), synthetic defined (SD) liquid medium containing 2 % sorbose at 30°C (osmotic stress), and YPD broth containing 100 mM hydroxyurea (HU) at 30°C (DNA replication stress). Parental strains, from glycerol stock, were grown on YPD plates over night at 30°C. ~10^7 cells from that plate were inoculated into liquid culture to initiate the different passages. A passage consisted of (1) growing cells in liquid culture overnight under treatment conditions, (2) plating 100-200 cells from that liquid culture on appropriate solid medium (under treatment conditions) until single colonies were visible, (3) selecting the five largest single colonies for spot assays under the treatment conditions, (4) picking the three fastest-growing isolates for long-term storage, and (5) the fastest one to inoculate ~10^7 cells in a fresh overnight liquid culture under the same treatment conditions to start the next passage.

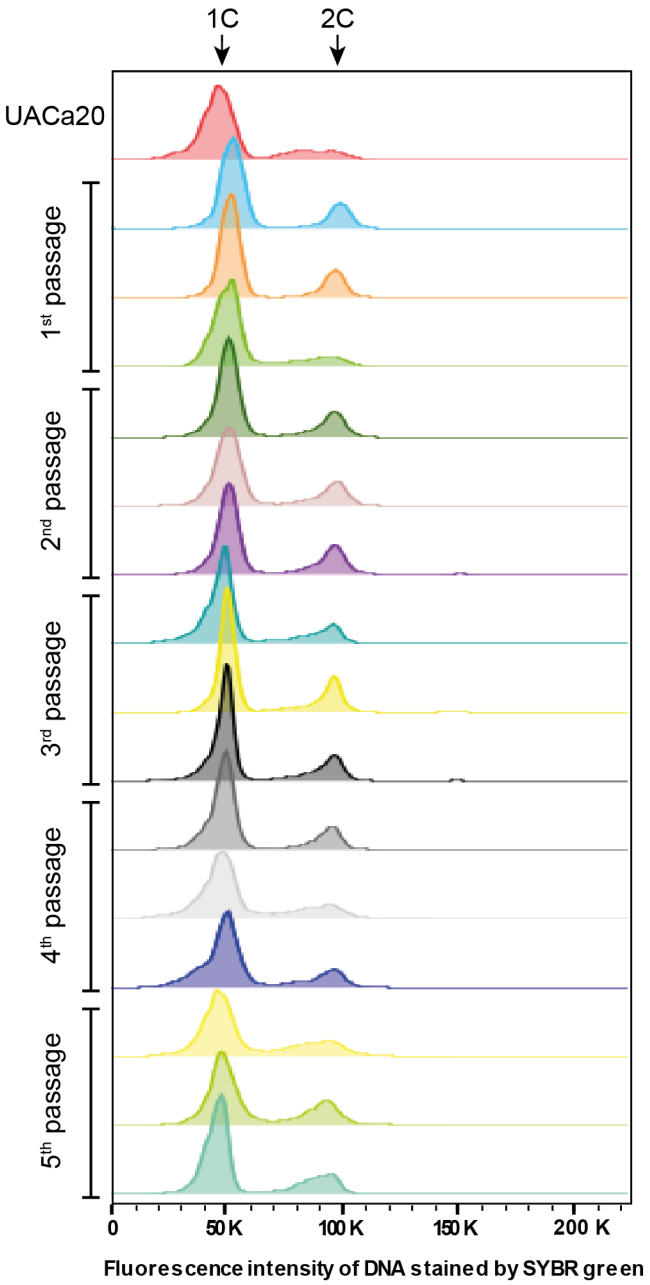

Figure S2. Cell cycle profile of *Candida auris* UACa20 and of isolates derived by heat stress from it. Histogram showing cell cycle profiles obtained by flow cytometry after staining DNA with SYBR green of *C. auris* strain UACa20 and its microevolved derivatives (Table S1). The isolates derived by heat stress from *C. auris* UACa20 through 5 consecutive passages have the same cell cycle profile as the parental *C. auris* strain. Approximate position of haploid G1 (1C) and haploid G2 (2C) peaks are indicated at the top.

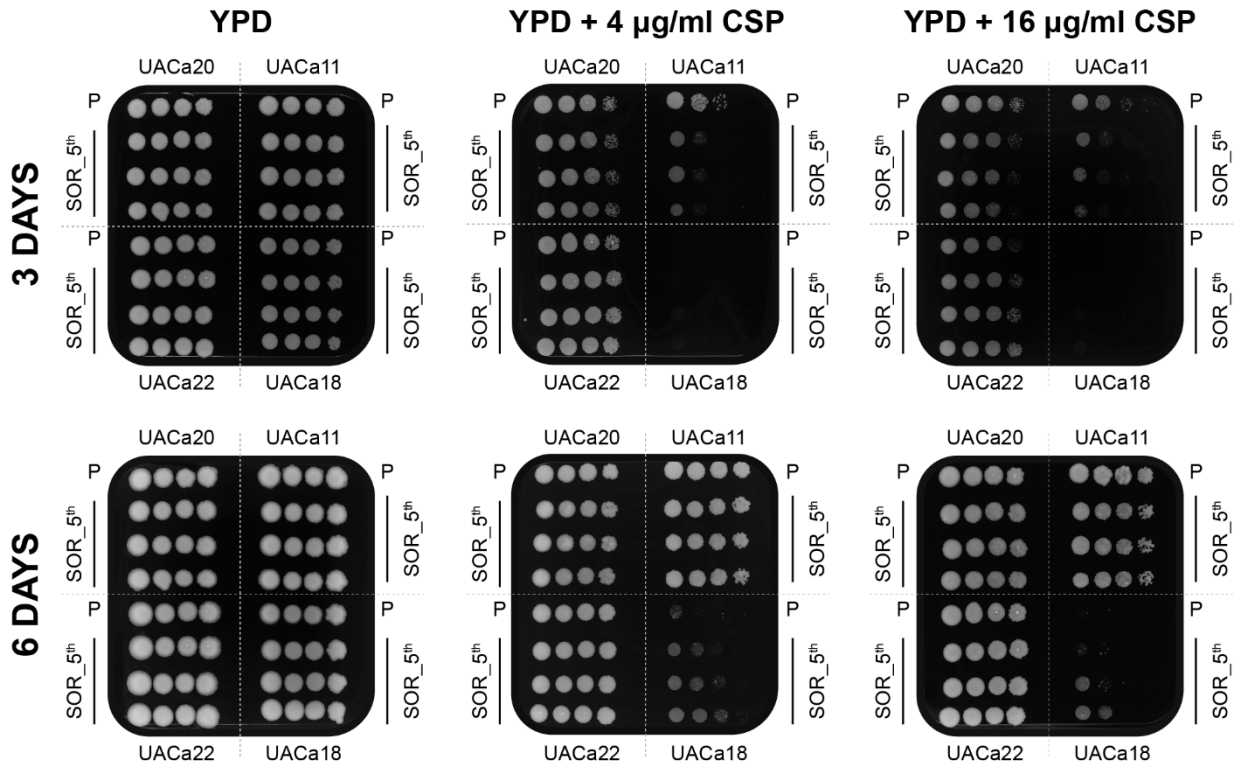

Figure S3. Growth of sorbose-microevolved isolates in presence of caspofungin (CSP). Spot assays on YPD (control), and YPD containing 4 or 16 µg/ml CSP after 3 and 6 days at 30°C of isolates obtained after the 5^{th} passage in the presence of 2% sorbose in synthetic defined medium at 30°C (SOR_5^{th}) from parental strains (P) UACa11, UACa18, UACa20, and UACa22. Serial dilutions contain 10^5, 10^4, 10^3, and 10^2 cells.

Table S1. Details of yeast strains used in this study

Strain	Collection No.	Species	Relevant genotype/Clade	Site of isolation	Known drug resistances[a]	Origin/Reference
470026	UACa1	*Candida auris*	WT, S. Asia (India)	BSI	FCZ, CSP	A. Chakrabarti[1]
470027	UACa2	*Candida auris*	WT, S. Asia (India)	BSI	FCZ, VCZ, CSP	A. Chakrabarti[1]
470028	UACa3	*Candida auris*	WT, S. Asia (India)	BSI	FCZ, CSP	A. Chakrabarti[1]
470029	UACa4	*Candida auris*	WT, S. Asia (India)	BSI	FCZ, VCZ, CSP	A. Chakrabarti[1]
470030	UACa5	*Candida auris*	WT, S. Asia (India)	BSI	FCZ, VCZ, CSP	A. Chakrabarti[1]
NCPF8980#9	UACa6	*Candida auris*	WT, S. Africa	BSI	FCZ, CSP	E. Johnson
NCPF8984#15	UACa7	*Candida auris*	WT, E. Asia (Japan)	unknown	FCZ	E. Johnson
NCPF8985#20	UACa8	*Candida auris*	WT, S. Asia (India)	wound	FCZ, ISA, PSZ, VCZ, 5-FC, AFG	E. Johnson
NCPF13001#16	UACa9	*Candida auris*	WT, S. Asia (India)	unknown	FCZ	E. Johnson
NCPF13005#95	UACa10	*Candida auris*	WT, S. Africa	urine	FCZ, VCZ, AFG, AMB, CSP	E. Johnson
VPCI479/P/13	UACa11	*Candida auris*	WT, S. Asia (India)	BSI	FCZ	A. Chowdhary[2]
RBH7723	UACa12	*Candida auris*	WT, Royal Brompton hospital	wound	CSP[a]	S. Schelenz[3]
RBH7728	UACa13	*Candida auris*	WT, Royal Brompton hospital	hospital environment	sensitive	S. Schelenz[3]
RBH7745	UACa14	*Candida auris*	WT, Royal Brompton hospital	skin swab	FCZ, VCZ, CSP	S. Schelenz[3]
RBH7748	UACa15	*Candida auris*	WT, Royal Brompton hospital	nose swab	FCZ, VCZ, CSP	S. Schelenz[3]
B11220	UACa18	*Candida auris*	WT, E. Asia (Japan)	auditory canal	FCZ, VCZ	S. Lockhart[4]
B11109	UACa19	*Candida auris*	WT, S. Asia (Pakistan)	burn wound	CSP	S. Lockhart[4]
B11221	UACa20	*Candida auris*	WT, S. Africa	BSI	FCZ, CSP	S. Lockhart[4]
B11222	UACa21	*Candida auris*	WT, S. Africa	BSI	FCZ, CSP	S. Lockhart[4]
B11244	UACa22	*Candida auris*	WT, S. America (Venezuela)	BSI	FCZ, VCZ, CSP	S. Lockhart[4]
B11245	UACa23	*Candida auris*	WT, S. America (Venezuela)	BSI	FCZ, VCZ, CSP	S. Lockhart[4]
B8441	UACa24	*Candida auris*	WT, S. Asia (Pakistan)	BSI	CSP	S. Lockhart[4]
B11098	UACa25	*Candida auris*	WT, S. Asia (Pakistan)	BSI	FCZ	S. Lockhart[4]
B11203	UACa26	*Candida auris*	WT, S. Asia (India)	BAL	FCZ, 5-FC	S. Lockhart[4]
B11205	UACa27	*Candida auris*	WT, S. Asia (India)	chest wound	FCZ, VCZ, 5-FC	S. Lockhart[4]
CBS10913T	UACa83	*Candida auris*	WT, E. Asia (Japan)	auditory canal	none	CBS-KNAW collection[5]

BY4741	UACa35	*Saccharomyces cerevisiae*	*MAT***a** *his3Δ1 leu2Δ0 met15Δ0 ura3Δ0*	n/a	n/a	lab strain[6]
BY4742	UACa36	*Saccharomyces cerevisiae*	*MATα his3Δ1 leu2Δ0 lys2Δ0 ura3Δ0*	n/a	n/a	lab strain[6]
BY4743	UACa37	*Saccharomyces cerevisiae*	*MAT***a**/α *his3Δ1/his3Δ1 leu2Δ0/leu2Δ0 LYS2/lys2Δ0 MET15/met15Δ0* ura3Δ0/*ura3Δ0*	n/a	n/a	lab strain; cross of BY4741×BY4742
SC5314	UACa38	*Candida albicans*	WT	n/a	n/a	lab strain[7]

[a]Using EUCAST clinical breakpoints for *Candida albicans*: (http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/AFST/Clinical_breakpoints/Antifungal_breakpoints_v_9.0_180212.pdf)

Abbreviations: BAL = broncho-alveolar lavage, BSI = bloodstream infection, FCZ = fluconazole, ISA = Isavuconazole, PSZ = Posaconazole, VCZ = Voriconazole, CSP = Caspofungin, AFG = Anidulafungin, 5-FC = flucytosine, AMB = Amphotericin B.

Supplementary References

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