Table S1: Specimen source of yeast isolates sent for AFST representing the first species per patient per infection episode, 2014-2018.

			Candida spp.		Other yeast		Total	
Sterile			3386	74.08%	120	83.33%	3506	74.36%
	Cardiovascular System		2607	57.03%	73	50.69%	2680	56.84%
		Blood	2596	56.79%	73	50.69%	2669	56.61%
		Bone marrow	2	0.04%	0	0.00%	2	0.04%
		Lymph node	1	0.02%	0	0.00%	1	0.02%
		Pericardial fluid	8	0.18%	0	0.00%	8	0.17%
	Respiratory System		170	3.72%	10	6.94%	180	3.82%
		Bronchial alveolar lavage	10	0.22%	3	2.08%	13	0.28%
		Bronchial washing	2	0.04%	2	1.39%	4	0.08%
		Bronchial, aspirate	2	0.04%	1	0.69%	3	0.06%
		Lung tissue/Biopsy	16	0.35%	2	1.39%	18	0.38%
		Pleural Fluid	140	3.06%	2	1.39%	142	3.01%
	Nervous System		16	0.35%	28	19.44%	44	0.93%
		Brain	2	0.04%	0	0.00%	2	0.04%
		Cerebral Spinal Fluid	12	0.26%	28	19.44%	40	0.85%
		Spinal	2	0.04%	0	0.00%	2	0.04%
	Organs and Fluids		337	7.37%	5	3.47%	342	7.25%
		Bile fluid	21	0.46%	0	0.00%	21	0.45%
		Dialysis fluid	46	1.01%	2	1.39%	48	1.02%
		Kidney	16	0.35%	0	0.00%	16	0.34%
		Liver/Liver aspirate	17	0.37%	0	0.00%	17	0.36%
		Pancreas/Pancreatic fluid	7	0.15%	0	0.00%	7	0.15%
		Peritoneal fluid	229	5.01%	3	2.08%	232	4.92%
		Spleen	1	0.02%	0	0.00%	1	0.02%
	Skeletal		45	0.98%	2	1.39%	47	1.00%
		Bone	36	0.79%	0	0.00%	36	0.76%
		Synovial fluid	9	0.20%	2	1.39%	11	0.23%
	Genitourinary Tract/Reproductive		1	0.02%	0	0.00%	1	0.02%

		Amniotic fluid	1	0.02%	0	0.00%	1	0.02%
	Other		210	4.59%	2	1.39%	212	4.50%
		Biopsy	184	4.03%	2	1.39%	186	3.94%
		Body fluid	21	0.46%	0	0.00%	21	0.45%
		Cyst	2	0.04%	0	0.00%	2	0.04%
		Vitreous Fluid	3	0.07%	0	0.00%	3	0.06%
Non-Sterile			555	12.14%	8	5.56%	563	11.94%
	Cardiovascular System		24	0.53%	0	0.00%	24	0.51%
		IV/Catheter tip	24	0.53%	0	0.00%	24	0.51%
	Respiratory System		35	0.77%	2	1.39%	37	0.78%
		Tracheal aspirate	6	0.13%	0	0.00%	6	0.13%
		Esophagus	12	0.26%	1	0.69%	13	0.28%
		Nose/Sinus	4	0.09%	0	0.00%	4	0.08%
		Sputum	5	0.11%	1	0.69%	6	0.13%
		Throat	8	0.18%	0	0.00%	8	0.17%
	Genitourinary Tract/Reproductive		245	5.36%	2	1.39%	247	5.24%
		Penile swab	2	0.04%	0	0.00%	2	0.04%
		Pelvic	11	0.24%	0	0.00%	11	0.23%
		Urine	189	4.13%	2	1.39%	191	4.05%
		Vaginal swab	43	0.94%	0	0.00%	43	0.91%
	Other		251	5.49%	4	2.78%	255	5.41%
		Arm/hand/finger	11	0.24%	0	0.00%	11	0.23%
		Aspirate	59	1.29%	1	0.69%	60	1.27%
		Corneal Scraping	24	0.53%	0	0.00%	24	0.51%
		Drainage	25	0.55%	0	0.00%	25	0.53%
		Ear	8	0.18%	0	0.00%	8	0.17%
		Eye	7	0.15%	0	0.00%	7	0.15%
		Leg/foot/toe	25	0.55%	0	0.00%	25	0.53%
		Oral	13	0.28%	1	0.69%	14	0.30%
		Nail	2	0.04%	0	0.00%	2	0.04%
		Neck	3	0.07%	1	0.69%	4	0.08%

	Oral	4	0.09%	0	0.00%	4	0.08%
	Skin	3	0.07%	1	0.69%	4	0.08%
	Ulcer	1	0.02%	0	0.00%	1	0.02%
	Wound	66	1.44%	0	0.00%	66	1.44%
Unknown		630	13.78%	16	11.11%	646	13.70%
	Hip	13	0.28%	0	0.00%	13	0.28%
	Abdomen	64	1.40%	0	0.00%	64	1.36%
	Abscess	113	2.47%	5	3.47%	118	2.50%
	Breast	1	0.02%	0	0.00%	1	0.02%
	Chest	3	0.07%	1	0.69%	4	0.08%
	Effluent	1	0.02%	0	0.00%	1	0.02%
	Fluid	171	3.74%	3	2.08%	174	3.69%
	Mass	2	0.04%	0	0.00%	2	0.04%
	Source unspecified	262	5.73%	7	4.86%	269	5.71%
Total		4571		144		4715	

Table S2: Specimen source of all non-susceptible isolates of *Candida* spp. including multiple isolates per patient.

	Azole Non-susceptible isolates				Echinocandin Non-susceptible isolates					
	C. alb.	*C. para.*	*C. trop.*	*C. kru.*	*C. alb.*	*C. gla.*	*C. para.*	*C. trop.*	*C. kru.*	*C. guil.*
Sterile										
Cardiovascular System										
Blood	8	114	89	1	9	59	1	2	12	
Respiratory System										
Bronchial Washing			1							
Pleural fluid	2	7	6	1		2			1	
Abdominal Cavity										
Dialysis fluid				1		1				
Liver/Liver aspirate			1							
Peritoneal fluid		1	7	1	1	4				
Skeletal										
Bone			2							
Other										
Biopsy	4	2	3			1				
Non-Sterile										
Cardiovascular System										
IV/Catheter Tip		4	1							
Respiratory System										
Esophagus	2				1					
Nose/Sinus	1									
Sputum	1		1							
Throat	4			1					1	
Genitourinary Tract/Reproductive										
Urine	4		7	1		6				
Pelvic			1	1						
Vaginal Swab	5									
Other										

	Arm/Hand/Finger			1							
	Aspirate					1	2			1	
	Drainage									1	
	Leg/Foot/Toe							1			
	Neck		1								
	Oral	4									
	Wound	1	3	5			2				
Unknown											
	Hip			1							
	Abdomen			3			4				
	Abscess	2	1	1		1	2			1	
	Chest			1			1			1	
	Fluid	1	6	2	1	1	2				
	Source unspecified	4	9	6			4	1			
Total		43	148	139	8	14	90	3	2	18	0

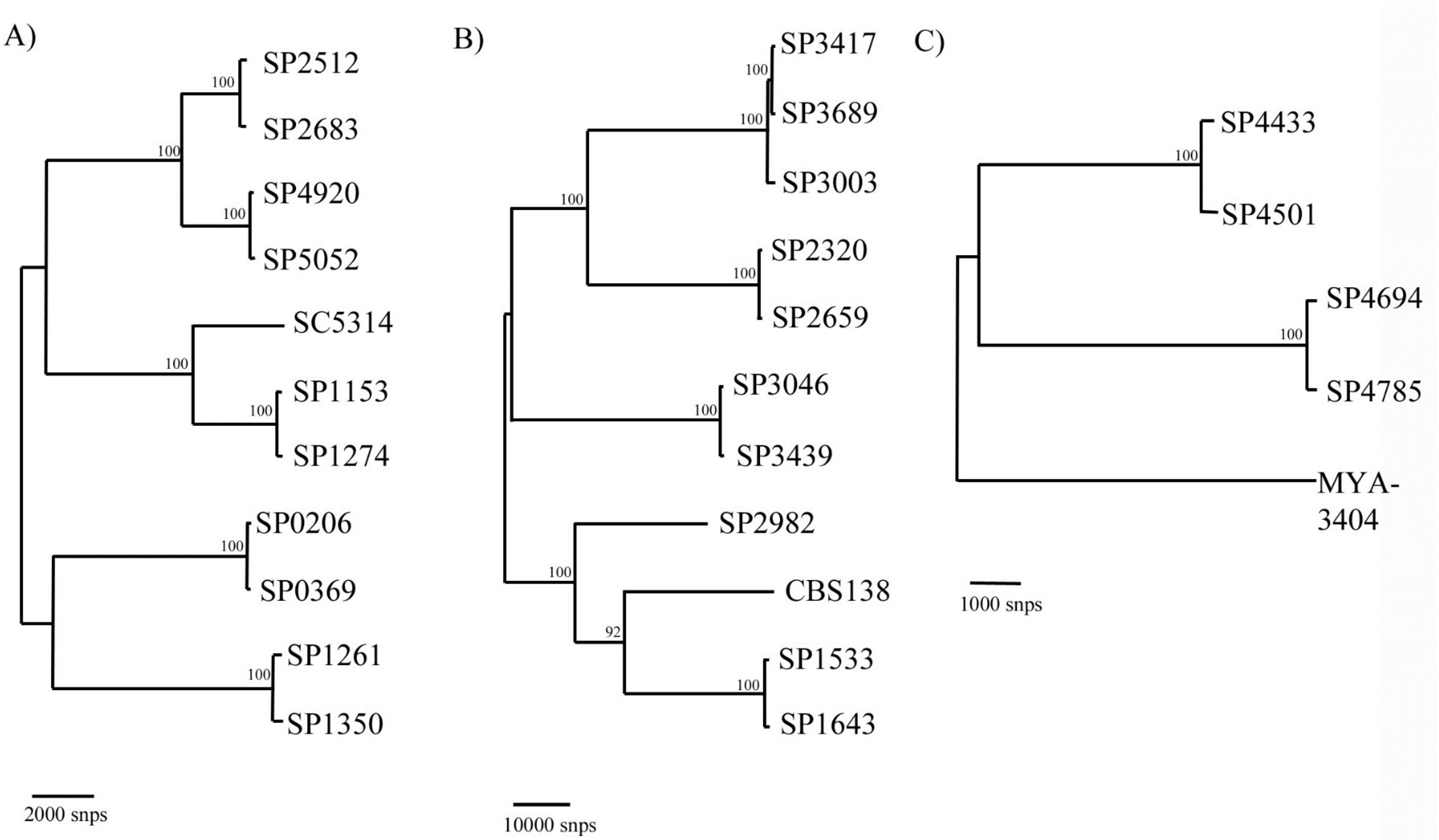


Fig. S1: Maximum Parsimony analysis of whole-genome snps of pairs of isolates from individual patients isolated within 6 months of each other representing a single infection episode where the initial isolate was susceptible and the subsequent isolate resistant to an antifungal agent. FASTA sequences of whole-genome snps were aligned using CLUSTAL W (Larkin 2007). Maximum parsimony analysis was conducted in MEGA X

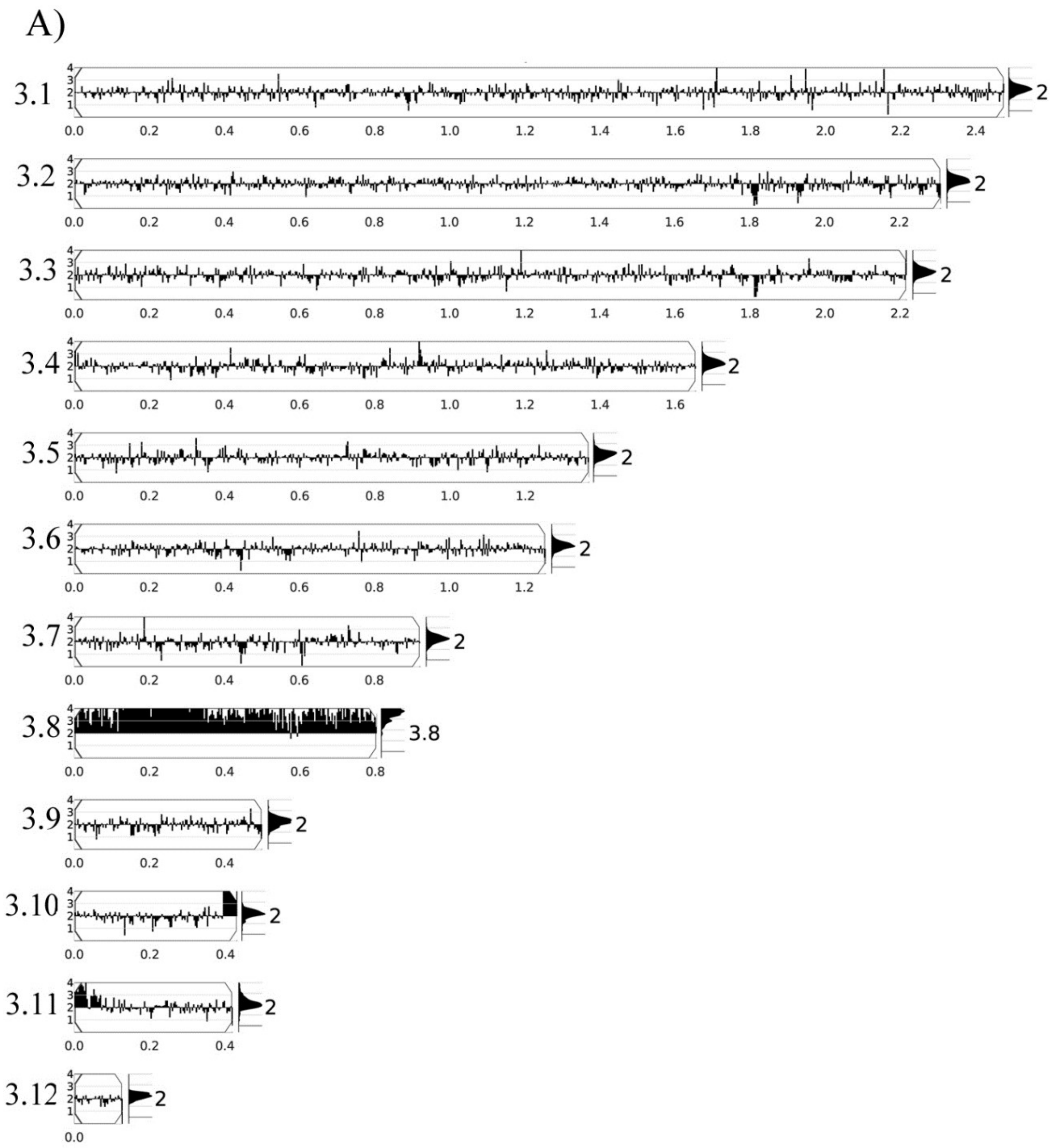
(Kumar et al 2018). All positions containing gaps and missing data were eliminated (complete deletion option). Branches with bootstrap (n=500) percentages >90% are indicated. (A) Five pairs of *C. albicans* and reference strain SC5314. (B) Five pairs of *C. glabrata* and reference strain CBS 138 (C) Two pairs of *C. tropicalis* and reference strain MYA-3404.

Table S3: List of non-synonymous genetic alterations in genes associated with azole resistance in the azole-resistant isolates of *C. albicans* and *C. tropicalis* compared with the azole susceptible progenitor derived from the same patient.

Species			*C. albicans*	*C. albicans*		*C. tropicalis*
Initial susceptible isolate MICs of initial isolate			SP0206 FLU 0.5 (S), VORI <0.008 (S)	SP2512 FLU 2 (S), VORI 0.015 (S)		SP4694 FLU 1 (S), VORI 0.12 (S)
Final resistant isolate MICs of final isolate			SP0369 FLU >256 (R), VORI 8 (R)	SP2683 FLU 256 (R), VORI 8 (R)		SP4785 FLU 32 (R), VORI 2 (R)
No. days between initial and final isolates			83	55		28
Gene	**Description**	***C. albicans* SC5314 locus tag or genome location**			***C. tropicalis* MYA-3404 locus tag or genome location**	
ERG3	C-5 sterol desaturase	CAALFM_C104770CA	--	G/G763A/A| A255T	CTRG_04480	--
ERG11	sterol 14-demethylase	CAALFM_C500660CA	--	--	CTRG_05283	--
ERG11	sterol 14-demethylase	isochromosome of left arm chr5	no evidence	no evidence	Aneuploidy of supercontig 3.8	Ploidy estimate of 6.0
MDR1 promoter allele	MDR/MFS multidrug efflux pump promoter	chr6:668214,668229,668231,668383,668420, complement	both strains are heterozygous A/G	both strains have same hybrid G-A allele	n/a	n/a
MDR1	MDR/MFS multidrug efflux pump	CAALFM_C603170CA	--	--	CTRG_02412 CTRG_03501	-- --
MMR1	putative Zn(II)2Cys6 transcription factor; regulator of MDR1 transcription	CAALFM_C305920WA	--	--	CTRG_02269	--

MMR1	putative Zn(II)2Cys6 transcription factor; regulator of MDR1 transcription	MMR1 loss of heterozygosity on chr3	no evidence	Gain of heterozygosity with all synonymous substitutions noted in MMR1 on chr 3.	MRR1 Loss of heterozygosity on Supercontig 3.3	No evidence
CDR1	ATP-binding cassette multidrug transporter	CAALFM_C305229WA	--	A/A1280A/T| Y427F	CTRG_02526 CTRG_02606	-- --
CDR2	ATP-binding cassette multidrug transporter	CAALFM_C304890WA	--	--	n/a	n/a
CDR11	Putative transporter of PDR subfamily of ABC family	CAALFM_C304070CA	--	--	CTRG_02576	A/A1237A/C|K413Q
FLU1	MDR/MFS multidrug efflux pump	CAALFM_C701520WA	--	TACCAAC/TACCAAC > T/TACCAAC disruptive inframe deletion; G/G25C/G| D9H; G/G496G/T| V166L; T/T1540T/G| S514A	CTRG_04985	--
SNQ2	ATP-binding cassette transporter	CAALFM_C603840CA	--	C/C2504T/C| A835V	CTRG_05971	--
TPO3	putative polyamine transporter; MFS-MDR family	CAALFM_C108790WA	--	A/G880G/G| N294D	CTRG_03231	--
YOR1	ATP-binding cassette transporter	CAALFM_C209990CA	--	--	CTRG_02100	--
STB5	Putative transcription factor with zinc cluster DNA-binding motif	CAALFM_C101200WA	--	--	CTRG_04421	--

TAC1	Zn(2)-Cys(6) transcriptional activator of drug-responsive genes (CDR1 and CDR2)	CAALFM_C501840CA	--	--	CTRG_05307	--
TAC1	Zn(2)-Cys(6) transcriptional activator of drug-responsive genes (CDR1 and CDR2)	isochromosome of left arm chr5	no evidence	no evidence	Aneuploidy of supercontig 3.8	Ploidy estimate of 6.2
Ndt80	activator of CDR1 induction by antifungal drugs	CAALFM_C200140WA	--	GCAGCAGCAACAA/GCAGCAGCAACAA>GCAACAGCAGCAACAA/GCAACAGCAGCAACAA 239_240insACA|p.Q80dup; A/A424G/A|T142A; C/C480A/C|H160Q	CTRG_01097	--
UPC2	Zn2-Cys6 transcript factor; regulator of ergosterol biosynthetic genes and sterol uptake	CAALFM_C108460CA	--	--	CTRG_03159	--


A)
3.1
3.2
3.3
3.4
3.5
3.6
3.7
3.8
3.9
3.10
3.11
3.12
1
2
3
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0.0
0.2
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2
3.8

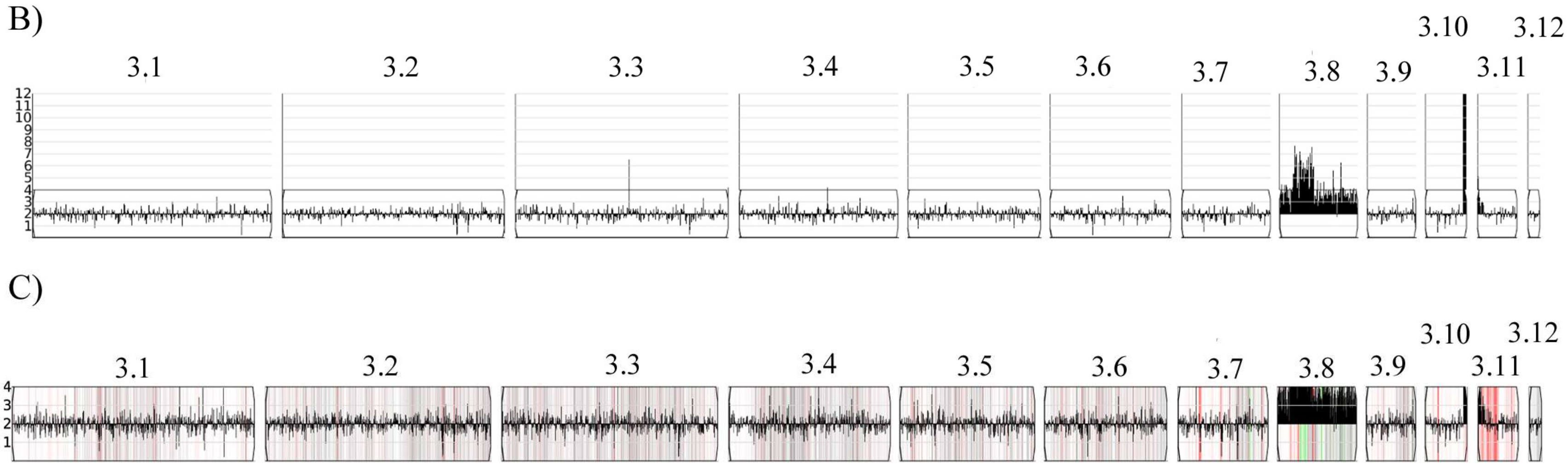

Fig. S2: Comparison and visualization of whole genome sequence data of *C. tropicalis* SP4785 relative to parental strain SP4694 using YMAP (Abbey et al 2014). (A) Copy number variation (CNV) between 0 and 4 is illustrated by black bars. Ploidy estimates are given for each of supercontigs 3.1-3.12. (B) Supercontigs 3.1-3.12 with CNV between 0 and 12 illustrated by black bars. (C) Supercontigs 3.1-3.12 with copy number variation changes in black and loss of heterozygosity events in red with green indicating unusual allelic ratios between 0.5 and 1 but not including 1.