Supplementary Information



Supplementary Fig. 1 | Representative images of PAS-stained main organs.

Kidney, brain, liver and spleen sections of mice (n = 3) at 1, 24, 48, and 72 h after intravenous injection with NS and infection with WT, *atp16* Δ/Δ , and *atp16* $\Delta/ATP16$ (5 × 10⁵ CFU per mice). **a**, Kidneys. *atp16* Δ/Δ displayed similar results to NS control. WT and *atp16* $\Delta/ATP16$ showed *C. albicans* filamentation at 1 h after infection, and the number of hyphae continued to increase throughout the entire course of the experiment. *C. albicans* colocalized with phagocytes to form abscesses at 24, 48, and 72 h after infection. **b**, Brains. *atp16* Δ/Δ displayed similar results to NS control. WT and *atp16* $\Delta/ATP16$ showed *C. albicans* filamentation. *C. albicans* colocalized with phagocytes to form abscesses at 24, 48, and 72 h after infection. *C. albicans* colocalized with phagocytes to form small scattered multifocal abscesses. **c** and **d**, Livers and spleens. *C. albicans* filamentation was not observed at any time point after infection; rather, phagocytes accumulated in large numbers but did not organize into abscesses in NS, WT, *atp16* Δ/Δ and *atp16* $\Delta/ATP16$. In **a**, **b**, **c** and **d**, one representative experiment out of three independent experiments is shown. Arrowheads indicate fungal hyphae. Magnification × 400. Scale bar is 50 μ M.



Supplementary Fig. 2 | Overexpression of the δ subunit does not enhance lethal *C. albicans* infection.

a, Survival curves of mice (n = 10) after intravenous infection with *C. albicans* Atp16 O/E (5 × 10⁵ CFU per mice). **b**, *C. albicans* fungal burdens (CFU per g tissue) in organs (n = 3) 48 h after systemic infection with Atp16 O/E (5 × 10⁵ CFU per mice). **c** and **d**, Representative images of PAS-stained kidney sections of mice (n = 3) (**c**) and combined inflammatory score based on renal immune cell infiltration (inflammation) and tissue destruction (n = 3) (**d**) 48 h after intravenous infection with Atp16 O/E (5 × 10⁵ CFU per mice). **f** CFU per mice). Magnification × 400. Scale bar is 50 µM. In **a**, **b**, **c** and **d**, there were no significant differences in the phenotypes of Atp16 O/E compared with that of WT. In **c**, one representative experiment out of three independent experiments is shown. In **a**, **b** and **d**, data are expressed as the mean ± SD. ns, not significant; by log-rank test (**a**), or two-tailed unpaired Student's *t*-test (**b**, **d**).



Supplementary Fig. 3 | Deletion of the δ subunit does not lead to remarkable *C. albicans* growth defects.

a-**d**, The growth of WT, *atp16* Δ/Δ and *atp16* $\Delta/ATP16$ in YPD (**a**, **b**) and YPS (**c**, **d**) media over time determined by cell density (OD₆₀₀) (**a**, **c**) and viable cell counts (CFU/ml) (**b**, **d**). **e**-**g**, The growth of WT, *atp16* Δ/Δ and *atp16* $\Delta/ATP16$ in liver, kidney, brain, spleen, and heart fresh tissue homogenates (500 mg/ml, without inactivation) and serum (100%, without inactivation) (**e**) and in kidney (**f**) and brain (**g**) homogenates (500 mg/ml, without inactivation) supplemented with 0.1%, 0.2%, and 0.4% glucose for 24 h determined by viable cell counts (CFU/ml). The initial density of *C*. *albicans* was 5×10³ CFU/ml. **h** and **i**, *C*. *albicans* fungal burdens (CFU per g tissue) in kidneys (**h**) and brains (**i**) of BALB/c mice that were injected with PBS liposomes (*n* = 3) or clodronate liposomes (*n* = 3) 24 h before and 24 h after intravenous infection with WT and *atp16* Δ/Δ (2 × 10⁵ CFU per mice). In **a**, **b**, **c**, **d**, **e**, **f**, **g**, **h** and **i**, data are expressed as the mean ± SD of three independent experiments. **P* < 0.05, ***P* < 0.01, ****P* < 0.001; ns, not significant; by two-way ANOVA (**a**, **b**, **c**, **d**, **f**, **g**, **h** and **i**), or two-tailed unpaired Student's *t*-test (**e**).



Supplementary Fig. 4 | The role of the δ subunit in the mitochondrial morphology and mRNA expression levels of mitochondrial genes.

a, The mitochondrial morphology of WT, *atp16* Δ/Δ and *atp16* $\Delta/ATP16$ cultured in YNB + 2% glucose medium for 12 h were observed by TEM. Arrowheads indicate the mitochondrial cristae. Magnification × 23000. Scale bar is 0.2 µM. **b**, The mRNA expression levels of the mitochondrial genes *COB* (encoded complex IV subunit 3), *COX1*, *COX2*, *COX3* (encoded complex IV subunits 1, 2, 3), *ATP6*, *ATP8*, and *ATP9* (encoded F₁F₀-ATP synthase subunits a, 8, c) in WT, *atp16* Δ/Δ and *atp16* $\Delta/ATP16$ were assessed by RT–qPCR. In **b**, Data are expressed as the mean ± SD of three independent experiments. ***P* < 0.01, ****P* < 0.001; by two-tailed unpaired Student's *t*-test.



Supplementary Fig. 5 | The role of the δ subunit in the mRNA and protein expression levels of key enzymes in glycolysis.

a, Relative mRNA expression levels of glycolytic enzymes in WT, $atp16\Delta/\Delta$ and $atp16\Delta/ATP16$ were assessed by RT-qPCR. **b**, The expression levels of proteins involved in glycolysis were assessed by proteomics analysis. The three columns for each strain represent three experiments performed with 3 biological replicates. In **a**, data are expressed as the mean ± SD of three independent experiments. ns, not significant; two-tailed unpaired Student's *t*-test.



Supplementary Fig. 6 | The role of the δ subunit in the mRNA expression levels of the MAPK pathway transcription factors and activation of Ras1.

a, Relative mRNA expression levels of the MAPK pathway transcription factors Cph1 and Tec1 in WT, $atp16\Delta/\Delta$ and $atp16\Delta/ATP16$ were assessed by RT–qPCR. **b**, Total Ras1 protein and GTP-Ras1 fraction in WT, $atp16\Delta/\Delta$ and $atp16\Delta/ATP16$ were assessed by immunoprecipitation. GAPDH blots were shown as loading control. In **a**, data are expressed as the mean ± SD of three independent experiments. ns, not significant; by two-tailed unpaired Student's *t*-test. In **b**, one representative experiment out of three independent experiments is shown.



Supplementary Fig. 7 | The effects of pyruvate on *C. albicans* hyphal formation.

a, Intracellular pyruvate concentration per mg protein in WT, *atp16* Δ/Δ and *atp16* $\Delta/ATP16$. **b**, Hyphae formation of WT, *atp16* Δ/Δ and *atp16* $\Delta/ATP16$ in the presence of exogenous pyruvate (0, 1, 5 mM) in Spider medium after incubation at 37 °C for 3.5 h. Magnification × 400. Scale bar is 50 µM. In **a**, data are expressed as the mean ± SD of three independent experiments. ***P* = 0.0037; ns, not significant; by two-tailed unpaired Student's *t*-test. In **b**, one representative experiment out of three independent experiments is shown.



Supplementary Fig. 8 | The effects of antimycin/oligomycin on *C. albicans* hyphal formation and Pfk1 activity.

a, Hyphae formation of WT in the presence of the oxidation respiratory chain inhibitor antimycin (0, 2, 4, 8,16 μ M) and F₁F₀-ATP synthase inhibitor oligomycin (0, 5,10, 20, 40 μ M) after cultured in 10% FBS and Spider media at 37 °C for 3.5 h. Magnification × 400. Scale bar is 50 μ M. **b**, The activity of Pfk1 in WT in the presence of the oxidation respiratory chain inhibitor antimycin (8 μ M) and F₁F₀-ATP synthase inhibitor oligomycin (20 μ M) after cultured in YPD medium at 30 °C for 12 h. In **b**, Data are expressed as the mean ± SD of three independent experiments. **P* < 0.05; by two-tailed unpaired Student's *t*-test.



Supplementary Fig. 9 | Diagram illustrating that δ subunit deletion failed to cause lethal systemic candidiasis by regulating FBP-mediated cAMP-PKA signalling dependent virulence traits.

Compared with WT (left), δ subunit deletion interrupted Pfk1 phosphorylation, reduced enzymatic activity, decreased the downstream FBP level, blocked Ras1-dependent and -independent cAMP-PKA pathways, curtailed virulence factors, and finally protected mice from fatal infection (**right**). Red font and arrowhead represent increases, and blue font and arrowhead represent decreases.



Supplementary Fig. 10 | Schematic diagram of the *ATP16* gene disruption by the *SAT1*-Flipper method.



Supplementary Fig. 11 | Schematic diagram of the intact ATP16 allele complemented into the ATP16 homozygous

mutant.



Supplementary Fig. 12 | Schematic diagram of the *ATP16* overexpression strain obtained by introducing an *ATP16* gene ORF to SC5314.



Supplementary Fig. 13 | Confirmation of *ATP16* gene deletion and complementation by PCR and RT–qPCR analysis. **a**, The *ATP16* gene was PCR-amplified from the genomic DNA of the WT, $atp16\Delta/\Delta$ and $atp16\Delta/ATP16$ with primers ATP16-F+ATP16-R. 1, WT was amplified stripe at 314 bp; 2, $atp16\Delta/\Delta$ was without an amplified stripe; 3, $atp16\Delta/ATP16$ amplified stripe at 314 bp. **b**, RT–qPCR analysis of the mRNA level in *ATP16* from the three strains was performed. The relative mRNA level of *ATP16* in $atp16\Delta/\Delta$ showed a 0.00015-fold change compared with WT; the relative mRNA level of *ATP16* in $atp16\Delta/ATP16$ showed a 0.47-fold change compared with WT. In **b**, data are expressed as the mean ± SD of three independent experiments. ****P* < 0.001; ns, not significant; by two-tailed unpaired Student's *t*-test.



Supplementary Fig. 14 | Confirmation of ATP16 gene overexpression by RT-qPCR analysis.

The relative mRNA level of *ATP16* in Atp16 O/E was approximately 12-fold different from that in WT. Data are expressed as the mean \pm SD of three independent experiments. ****P* < 0.001; by two-tailed unpaired Student's *t*-test.



Supplementary Fig. 15 | Summary of the gating strategy from the ROS assay and $\Delta \Psi m$ assay.

Pseudocoloured density plots displaying the side-scatter and forward-scatter data for WT, $atp16\Delta/\Delta$ and $atp16\Delta/ATP16$ cells when run on the FACScan flow cytometer and analysed with the FACSDiva Software. Gates displayed in black are the gates that were applied to all samples for data shown in Fig. 3e (**a**) and Fig. 3f (**b**).

Supplementary Table 1. Summary of pathogenicity-related proteins of *C. albicans* as determined in a murine model of candidiasis.

Homology with common pathogenic fungi	Non-homology with <i>Homo</i> sapiens and gut flora	Essentiality in lethal infection	Gene name	Protein accession	Protein name	Function	Biological process	Virulence in a disseminated candidiasis model	Reference
Yes	Yes	Yes	ATP16	A0A1D8PUD2	F1Fo-ATP synthase subunit delta	produces ATP from ADP	ATP synthesis coupled proton transport	avirulent	this study
Yes	Yes	Yes	FAS2	A0A1D8PK65	Fatty acid synthase subunit alpha	fatty-acid synthesis	Alpha subunit of fatty-acid synthase	avirulent	Zhao XJ, et al., Infect Immun, 1997; 65:829.
Yes	Yes	Yes	RFG1	Q5A220	Repressor of filamentous growth 1	filamentous, hyphal growth	transcriptional regulator	avirulent	Kadosh D, Johnson AD. Mol Cell Biol, 2001; 21: 2496.
					V-type proton	acidifying a variety of intracellular	vacuolar proton-transporting V-type ATPase complex		Jia C, et al., Fungal Genet
Yes	Yes	Yes	VMA6 VMA7	A0A1D8PKX3 A0A1D8PH17	ATPase subunit V-type proton ATPase subunit F	compartments vacuole acidification	assembly putative vacuolar H+-ATPase (V-ATPase) subunit	avirulent avirulent	Biol, 2018; 114:1. Poltermann S, et al., Microbiology, 2005; 151: 1645.
Yes	Yes	Yes	TPS1	Q92410	Alpha,alpha-trehalos e-phosphate synthase	stress response, hyphal growth	trehalose-6-phosphate synthase	avirulent	Zaragoza O, et al., J Bacteriol, 1998; 180: 3809.
No	Yes	Yes	ACE2	Q59RR0	Cell wall transcription factor ACE2	morphogenesis	transcription activator	avirulent	Kelly MT, et al., Mol Microbiol, 2004; 53: 969.
No	Yes	Yes	ARG2	Q59MB6	Amino-acid acetyltransferase, mitochondrial, EC	N-acetylglutamate synthase involved in arginine biosynthesis	arginine biosynthetic process	avirulent	Epp E, et al., Mol Microbiol, 2010; 75: 1182.
No	Yes	Yes	ARV1	Q5ANH2	Protein ARV1	Mediator of sterol homeostasis	intracellular sterol transport	avirulent	Gallo-Ebert C, et al., Fungal Genet Biol, 2012; 49: 101.
No	Yes	Yes	CAP1 (SRV2)	Q5AJU7	AP-1-like transcription factor CAP1	cAMP-mediated signaling	Adenylate cyclase-associated protein	avirulent	Bahn YS, Sundstrom P. J Bacteriol, 2001; 183: 3211.
No	Yes	Yes	CDC35	A0A1D8PR83	Adenylate cyclase	cAMP-mediated signaling	adenylyl cyclase	avirulent	Rocha CR, et al., Mol Biol Cell, 2001; 12: 3631.

			CDV1		Serine/threonine-prot	hyphal growth,	Protein kinase of the	· • •	Chen J, et al., Mol Cell
No	Yes	Yes	CRKI	Q9Y7W4	ein kinase BUR1	pathogenesis	Cdc2 subfamily	avirulent	Biol, 2000; 20: 8696.
					Cell surface				Martinez-Lopez R, et al.,
					GPI-anchored protein		cell surface GPI protein	avirulent	Microbiology, 2004; 150:
No	Yes	Yes	ECM33	Q5AGC4	ECM33	cell wall			3341.
					Enhancer of		cytoplasmic mRNA		
					mRNA-decapping		processing body		Jeong J, et al., Fungal
No	Yes	Yes	EDC3	A0A1D8PM93	protein 3	filamentous growth	assembly	avirulent	Genet Biol, 2016; 97: 18.
					Transcriptional				
					regulator of				Cao F, et al., Mol Biol
					filamentous growth	hyphal formation	transcription factor	avirulent	Cell, 2006; 17: 295.
No	Yes	Yes	FLO8	Q59QW5	FLO8				
					High-affinity iron		High-affinity iron		Ramanan N, Wang Y.
No	Yes	Yes	FTR1	A0A1D8PFV0	permease	iron transport	permease	avirulent	Science, 2000; 288: 1062.
					Histone		_		Chang P. et al., Fungal
No	Yes	Yes	GCN5	O59PZ5	acetvltransferase	Catalytic activity	pathogenesis	avirulent	Genet Biol. 2015: 81:132.
				<u>`</u>	GOA1 orf19 3818.				Bambach A. et al.
					CAALEM C404640	oxidative stress	Protein required for	avirulent	Eukarvot Cell. 2009: 8:
No	Yes	Yes	GOA1	O5A672	CA		respiratory growth		1706.
									Gácser A Stehr F Infect
No	Ves	Yes	LIP8	O9P8V9	Linase 8	Catalytic activity	pathogenesis	avirulent	Immun 2007: 75: 4710
				2,1017			patriogeneous		Guan G. et al. Fungal
No	Vec	Vec	MCU1	054874	Moulp	carbon utilization	pathogenesis	ovirulant	Genet Piol 2015: 81: 150
			MCOT	QJAKZ4	Danaira		patilogenesis	avirulent	Line O stal E seal
Na	Ver	Var	MOMI	054507	CTD	CTD		. in land	Liang C, et al., Fungal
INO	res	res	MGM1	Q5AFB/	GIPase	GTPase activity	memorane fusion	avirulent	Genet Biol, 2018; 120: 42.
					N-acetylglucosamine	N-acetylglucosamine	N-acetylglucosamine		Yamada-Okabe T, et al.,
	* 7			0.500.015	kinase I, GlcNAc	catabolic process	(GlcNAc) kinase	avirulent	Eur J Biochem, 2001; 268:
No	Yes	Yes	NAG5	Q59RW5	kinase I				2498.
						filamentous, hyphal	transcription factor	avirulent	Sellam A, et al., Eukaryot
No	Yes	Yes	NDT80	Q5ACU9	Transcription factor	growth		avirulent	Cell, 2010; 9: 634.
					*	histone			
					Histone	acetyltransferase			Li D, et al., Future
No	Yes	Yes	NGG1	O5AI28	acetyltransferase	activity	histone H3 acetylation	avirulent	Microbiol, 2017; 12: 1497.
				-	CCR4-NOT core				Krueger KE, et al.,
					ubiquitin-protein	filamentous growth,	Putative E3		Microbiology, 2004; 150:
No	Yes	Yes	NOT4	A0A1D8PSH4	ligase subunit	pathogenesis	ubiquitin-protein ligase	avirulent	229.
					Histone	-			Lopes da Rosa J, et al.,
					acetyltransferase	histone acetylation,	histone	avirulent	Proc Natl Acad Sci USA.
No	Yes	Yes	RTT109	Q5AAJ8	RTT109	pathogenesis	acetyltransferase		2010; 107: 1594.
							Transporter of		
					Basic amino acid	ferrichrome transport	ferrichrome	avirulent	Heymann P, et al., Infect
No	Yes	Yes	SIT1	A0A1D8PEJ7	transporter		siderophores		Immun, 2002; 70: 5246.
				1	1	1	1		1

Νο	Yes	Yes	SSK1	O5AKU6	Oxidative stress response two-component system protein SSK1	cell wall organization, filamentous growth	Response regulator of two-component system	avirulent	Calera JA, et al., Infect Immun, 2000; 68: 518.
No	Yes	Yes	SWI1	Q59UR3	Swi1p	adhesion,hyphal growth	Protein involved in transcription regulation	avirulent	Mao X, et al., FEBS Letts, 2006; 580: 2615.
				<u> </u>	Transcriptional	Represses			Murad AM, et al., EMBO
No	Yes	Yes	TUP1	P0CY34	repressor TUP1	transcription	pathogenesis	avirulent	J, 2001; 20: 4742.
					V-type proton	*			Zhang K. et al., Future
No	Yes	Yes	VMA5	O5A2U9	ATPase subunit C	catalytic activity	Hvdrogen ion transport	avirulent	Microbiol. 2017: 12: 1147.
					V-type proton	catalyzes the translocation of protons across the			Patenaude C, et al., J Biol
No	Yes	Yes	VPH1	Q59R99	ATPase subunit a	membranes	vacuolar acidification	avirulent	Chem, 2013; 288: 26256.
No	Yes	Yes	VPS34	A0A1D8PDV7	Phosphatidylinositol 3-kinase VPS34	autophagy, endocytosis	phosphatidylinositol 3-kinase	avirulent	Bruckmann A, et al., Microbiology, 2000; 146: 2755.
No	Yes	Yes	PHR1	P43076	pH-responsive protein 1	fungal type cell wall organization, hyphal growth	Glycosidase of cell surface;high pH or filamentation induced	avirulent	De Bernardis F, et al., Infect Immun, 1998; 66: 3317.
No	Yes	Yes	SSN6	Q5ADP3	Transcription regulator	hyphal, filamentous growth	putative global transcriptional co-repressor	avirulent	Hwang C, et al., Mol Microbiol, 2003; 47: 1029.
No	Yes	Yes	SUN41	Q59NP5	Secreted beta-glucosidase SUN41	adhesion, biofilm formation	Putative cell wall glycosidase	avirulent	Norice CT, et al., Eukaryot Cell, 2007; 6: 2046.
No	Yes	Yes	CHS1	Q5A594	Chitin synthase	cell wall biosynthetic process	chitin sythase	avirulent	Munro CA, et al., Mol Microbiol, 2001; 39: 1414.
					Histidine protein			avirulent in	Calera JA, et al., Infect
No	Yes	Yes	CHK1	Q5AHA0	kinase 1	hyphal growth defect	cell wall synthesis	mouse	Immun, 1999; 67: 4280.
No	No	Yes	CHO1	A0A1D8PF32	CDP-diacylglycerol serine O-phosphatidyltransf erase	Catalytic activity	phosphatidylethanolami ne biosynthesis	avirulent in mouse	Chen YL, et al., Mol Microbiol, 2010; 75:1112.
					F1F0 ATP synthase	Produces ATP from	ATP synthesis counled		LiS et al Front
No	No	Yes	ATP1	A0A1D8PDC4	subunit alpha	ADP	proton transport	avirulent	Microbiol, 2017; 8: 285.
No	No	Yes	ATP2	A0A1D8PKZ9	F1F0 ATP synthase subunit beta	Produces ATP from ADP	ATP synthesis coupled proton transport	avirulent	Li S, et al., Front Microbiol, 2018; 9: 1025.
No	No	Yes	ADE5,7	A0A1D8PE67	Bifunctional aminoimidazole ribotide synthase/glycinamide ribotide synthase	de novo purine nucleotide biosynthetic pathway	putative aminoimidazole ribotide synthetase (AIRS) and glycinamide ribotide synthetase (GARS)	avirulent	Jezewski S, et al., Microbiology, 2007; 153: 2351.

No	No	Vas	A D D 2	AOW21565	Putative component of the Arp2/3	fungal type cell wall organization	Putative component of the Arp2/3 complex	avirulent	Epp E, et al., Mol Microbiol, 2010; 75: 1182.
No	No	Yes	CLA4	O5APR8	Serine/threonine-prot	filamentous growth,chlamydospo re formation and virulence	activation of protein	avirulent	Leberer E, et al., Curr Biol, 1997; 7: 539.
No	No	Yes	GAT1	Q5A432	Transcriptional regulatory protein GAT1	Transcriptional regulator of nitrogen utilization	negative regulation of transcription by RNA polymerase II	avirulent	Limjindaporn T, et al., Mol Microbiol, 2003; 50: 993.
No	No	Yes	HOG1	Q92207	Mitogen-activated protein kinase HOG1	filamentous growth, fungal cell wall organization	mitogen-activated protein (MAP) kinase	avirulent	Cheetham J, et al., J Biol Chem, 2011; 286: 42002.
No	No	Yes	KRE5	A0A1D8PJN6	Kre5p	1,6 beta-glucan biosynthetic process	UDP-glucose:glycoprot ein glucosyltransferase (UGGT)	avirulent	Herrero AB, et al., Eukaryot Cell, 2004; 3: 1423.
No	No	Yes	PMR1	A0A1D8PQK6	Calcium-transporting ATPase	cell wall maintenance, protein glycosylation	P-type Ca2+/Mn2+-ATPase	avirulent	Jiang L, et al., Fungal Genet Biol, 2018; 115: 1.
No	No	Yes	SAC1	A0A1D8PEV5	Phosphatidylinositol- 3-phosphatase	phosphatidylinositol- 4-phosphate phosphatase activity	pathogenesis	avirulent	Zhang B, et al., Fungal Genet Biol, 2015; 81: 261.
No	No	Yes	SSQ1	A0A1D8PRH1	Hsp70 family ATPase	ATPase activity	cellular response to unfolded protein	avirulent	Dong Y, et al., Int J Biochem Cell Biol, 2017; 85: 44.
No	No	Yes	TFP 1	Q5AJB1	V-type proton ATPase catalytic subunit A	Catalytic activity	pathogenesis	avirulent	Jia C, et al., Fungal Genet Biol, 2014; 71: 58.
No	No	Yes	VAC1 (PEP7)	Q59UQ8	Рер7р	adhesion, filamentous growth	vesicle transport pt	avirulent	Franke K, et al., Microbiology, 2006; 152: 3111.
No	No	Yes	YPT72	A0A1D8PHR9	Rab family GTPase	GTPase activity	pathogenesis	avirulent	Johnston DA, et al., Infect Immun, 2009; 77: 2343.
No	No	Yes	CMP1	A0A1D8PCA8	Serine/threonine-prot ein phosphatase	hyphal growth, pH stress	Catalytic subunit of calcineurin	avirulent	Bader T, et al., Infect Immun, 2003; 71: 5344.
No	No	Yes	NAG1	Q04802	Glucosamine-6-phos phate isomerase	N-acetylglucosamine catabolic process	Glucosamine-6-phospha te deaminase	avirulent	Singh P, et al., Infect Immun, 2001; 69: 7898.
No	No	Yes	PMT1	O74189	Dolichyl-phosphate- mannoseprotein mannosyltransferase 1	cell wall organization, hyphal growth	isoforms of protein mannosyltransferases	avirulent	Timpel C, et al., J Biol Chem, 1998 ; 273: 20837.

No	No	Yes	VPS4	Q5AG40	Vacuolar protein sorting-associated protein 4	vacuole organization, filamentous growth	Protein involved in transport from multivesicular body (MVB) to the vacuole	avirulent	Lee SA, et al., Mycopathologia, 2009 ; 167: 55.
No	No	Yes	RAD52	Q59NG2	Recombinase	DNA double strand break repair	required for DNA homologous recombination	avirulent	Chauhan N, et al., Infect Immun, 2005 ; 73: 8069.
No	No	Yes	CDC24	AAO25556	GDP-GTP exchange factor for Cdc42p	hyphal growth, pathogenesis	GDP-GTP exchange factor for Cdc42p	avirulent (induc prom)	Bassilana M, et al., Eukaryot Cell, 2003; 2: 9.
No	No	Yes	CEF3 (YEF3/EFT 3)	CAA78282	Translation elongation factor 3	translational elongation	Translation elongation factor 3	avirulent (induc prom)	Nakayama, et al., Infect Immun, 2000; 68: 6712.
No	No	Yes	RHO1	O42825	GTP-binding protein RHO1	1,3 beta-glucan biosynthetic process	GTPase of Rho family>>regulates beta 1,3-glucan synthesis	avirulent (induc.prom)	Smith SE, et al., FEMS Yeast Res, 2002; 2: 103.
No	No	No	ADE2	Q92210	Phosphoribosylamin oimidazole carboxylase	adenine biosynthesis	phosphoribosylaminoim idazole carboxylase	reduced virulence	Kirsch DR, Whitney RR. Infect Immun, 1991; 59: 3297.
No	No	No	AGE3	A0A1D8PCP6	Age3p	pathogenesis	Putative transcription factor with zinc finger DNA-binding motif	reduced virulence	Epp E, et al., PLoS Pathog, 2010; 6: e1000753
No	No	No	ALS1	Q5A8T4	Agglutinin-like protein 1 (Adhesin 1)	cell adhesion, hyphal growth	adhesin	reduced virulence	Fu Y, et al., Mol Microbiol, 2002; 44: 61.
No	No	No	ARF1	P22274	ADP-ribosylation factor	GTP-binding	intracellular protein transport	reduced virulence	Zhang B, et al., Fungal Genet Biol, 2015; 81: 261.
No	No	No	ATC1	Q5AAU5	Cell wall acid trehalase ATC1	trehalose catabolic process	cell wall acid trehalase	reduced virulence	Pedreno Y, et al., FEBS J, 2018; 285: 2004.
No	No	No	ATG8	90C075	Autophagy-related			reduced virulence	Li J, et al., Int J Med Microbiol, 2018; 308: 378.
No	No	No	BIG1	Q59WG7	Protein BIG1	adhesion, filamentation	involved in beta-1,6 glucan synthesis	reduced virulence	Umeyama T, et al., Infect Immun, 2006; 74: 2373.
No	No	No	BMH1	O42766	14-3-3 protein homolog	hyphal growth	multifunctional signal-modulating 14-3-3 protein	reduced virulence	Kelly MN, et al., Microbiology, 2009; 155: 1536.

No	No	No	CAS5	Q5AMH6	Cell wall integrity transcriptional regulator CAS5	cell wall damage response	Putative zinc finger transcription factor	reduced virulence	Chamilos G, et al., J Infect Dis, 2009; 200: 152.
No	No	No	CAT1	O13289	Peroxisomal catalase	hydrogen pyroxide catabolic process, hyphal growth	catalase	reduced virulence	Wysong DR, et al., Infect Immun, 1998; 66: 1953.
No	No	No	CCZ1	A0A1D8PQ69	Uncharacterized protein		autophagy	reduced virulence	Dong Y, et al., Int J Biochem Cell Biol, 2015; 69: 41.
No	No	No	CDC10	P39827	Cell division control protein 10	cell cycle	pathogenesis	reduced virulence	Gonzalez-Novo A, et al., Microbiol Immunol, 2006; 50: 499.
No	No	No	CDC11	G1UB61	Cell division control protein 11	cell cycle	pathogenesis	reduced virulence	Warenda AJ, et al., Infect Immun, 2003; 71: 4045.
Νο	No	No	CEK1	0541D3	Extracellular signal-regulated kinase 1	fungal cell wall biogenesis, hyphal growth	ERK-family protein kinase	reduced virulence	Csank C, et al., Infect Immun, 1998; 66: 2713.
No	No	No	CHS3	A0A1D8PFK5	Chitin synthase	cell wall biosynthetic process	chitin synthase	reduced virulence	Mio T, et al., J Bacteriol, 1996; 178: 2416.
No	No	No	CHS7	Q5AA40	Chitin synthase export chaperone	cell wall biosynthetic process	Protein required for wild-type chitin synthase III activity	reduced virulence	Sanz M,et al., Microbiol, 2005;151: 2623.
No	No	No	CNB1	A0A1D8PP58	Calcineurin regulatory subunit B	hyphal growth, pH stress	Regulatory subunit of calcineurin	reduced virulence	Blankenship JR, et al., Eukaryot Cell, 2003; 2: 422.
No	No	No	CNH1	A0A1D8PKY1	Cnh1p	morphogenesis, metal ion transport	Na+/H+ antiporter	reduced virulence	Soong TW, et al., Microbiology, 2000; 146: 1035.
No	No	No	COS1(NIK1)	Q5A599	Histidine protein kinase NIK1	cell wall biosynthetic process	Histidine kinase	reduced virulence	Selitrennikoff CP, et al., Med Mycol, 2001; 39: 69.
No	No	No	CPH1	P43079	Transcription factor CPH1	mating and hyphal growth	Transcription factor	reduced virulence	Lo JH, et al., Cell, 1997; 90: 939.
No	No	No	CPP1	Q5APU2	Dual specificity protein tyrosine phosphatase CCP1	pheromone response MAP kinase cascade	MAPK phosphatase of the VH1 family	reduced virulence	Csank C, et al., Mol Biol, 1997, Cell; 8: 2539.

					Extracellular	cell wall org	glycosylphosphatidylin ositol-dep cell wall pts	reduced virulence	Pardini G, et al., J Biol Chem 2006: 281: 40399.
No	No	No	CRH11	Q5AFA2	glycosidase CRH11				Pardini G. et al., J Biol
No	No	No	CRH12	Q5AK54	Extracellular glycosidase CRH12	cell wall org	glycosylphosphatidylin ositol-dep cell wall pts	reduced virulence	Chem, 2006; 281: 40399.
No	No	No	CSD27	0540D4	Con 27n	pathogenesis, cell	Plasma membrane,	reduced virulence	Sentandreu M, et al., J Bacteriol 1997: 179: 4654.
		110	0.51.57	QJAJD4	Csp37p	protein	nyphar cen wan protein		Leberer E. et al., Proc Natl
					Serine/threonine-prot	serine/threonine			Acad Sci USA, 1996; 93:
No	No	No	CST20	P0CY24	ein kinase CST20	kinase activity	pathogenesis	reduced virulence	13217.
No	No	No	CTF1	A0A1D8PGH7	Ctflp	fatty acid catabolic process	Putative zinc-finger transcription factor	reduced virulence	Ramirez MA, Lorenz MC. Eukaryot Cell, 2009; 8: 1604.
No	No	No	DPP3	Q5AH74	Bifunctional diacylglycerol diphosphate phosphatase	farnesol biosynthesis	phosphatase, converts farnesyl PP to farnesol	reduced virulence	Navarathna DH, et al., Infect Immun, 2007; 75: 1609.
No	No	No	DRG1	Q5A779	GTP-binding protein	filamentous growth	cytoplasmic G protein>>filamentous growth	reduced virulence	Chen X, Kumamoto CA. Microbiology, 2006; 152: 3691.
No	No	No	ECM25	A0A1D8PFN0	Ecm25p	morphogenesis, cell wall organization	protein involved in cell morphogenesis	reduced virulence	Zhang T, et al., Sci China C Life Sci, 2008; 51: 362.
No	No	No	EFG1	Q59X67	Enhanced filamentous growth protein 1	hyphal growth, metabolism	Transcriptional repressor	reduced virulence	Lo JH, et al., Cell, 1997; 90: 939.
No	No	No	ERG24	AOW27923	sterol C-14 reductase	ergosterol biosynthetic process	sterol C-14 reductase	reduced virulence	Jia N, et al., Antimicrob Agents Chemother, 2002; 46: 947.
No	No	No	ERG3	Q59VG6	C-5 sterol desaturase	ergosterol synthesis, hyphal growth	sterol C5,6-desaturase	reduced virulence	Chau AS, et al., Antimicrob Agents Chemother, 2005; 49: 3646.
No	No	No	FOX2	A0A1D8PJ13	Bifunctional hydroxyacyl-CoA dehydrogenase/enoyl -CoA hydratase	fatty acid B oxidation	peroxisomal enzyme;Predicted 3-hydroxyacyl-CoA epimerase	reduced virulence	Piekarska K, et al., Eukaryot Cell, 2006; 5: 1847.
No	No	No	GLN3	A0A1D8PNX9	Nitrogen-responsive transcriptional regulator	transcriptional regulator	pathogenesis	reduced virulence	Liao WL, et al., Fungal Genet Biol, 2008; 45: 514.
No	No	No	GNA1	Q5AHF9	Glucosamine 6-phosphate N-acetyltransferase	UDP-N-acetylglucos amine biosynthetic process	glucosamine-6-phospha te acetyltransferase	reduced virulence	Mio T, et al., Microbiology, 2000; 146:1753.

							Protein involved in		
					GPI ethanolamine	GPI anchor	attachment of		Richard M, et al., Mol
					phosphate transferase	biosynthesis	GPI-linked proteins to	reduced virulence	Microbiol, 2002; 44: 841.
No	No	No	GPI7	Q8TGB2	2		cell wall		
				<u> </u>					
			GRX2(TTR			pathogenesis,	putative glutathione	reduced virulence	Chaves GM, et al., Genet
No	No	No	1)	Q5ABB1	Dithiol glutaredoxin	oxidative stress	reductase		Mol Res, 2007; 6: 1051.
							Hydroxymethylbilane		
						heme biosynthetic	synthase		Kirsch DR, Whitney RR.
					Porphobilinogen	process	(uroporphyrinogen I	reduced virulence	Infect Immun, 1991; 59:
No	No	No	HEM3	O94048	deaminase, PBG		synthase		3297.
					Hypha-specific G1				
					cyclin-related protein	hyphal	G1 cyclin-related	reduced virulence	Zeng X, et al., EMBO,
No	No	No	HGC1	O5ABE2		morphogenesis	protein	reduced virtuience	2004; 23: 1845.
	110	110		QJABEZ	1				
						CHO transport	glucose and galactose	reduced virulence	Brown V, et al., Eukaryot
No	No	No	HGT4	Q5ANE1	Glucose sensor	erro unisport	sensor		Cell, 2006; 5: 1726.
						3-hydroxyisobutyrat			
						e dehvdrogenase	propionyl-CoA		Otzen C. et al., J Biol
No	No	No	HPD1	A0A1D8PO07	Hpd1p	activity	catabolic process	reduced virulence	Chem. 2014: 289: 8151
					Sarina/thraonina prot				Umayama T et al. Mol
No	No	No	USI 1	054671	ain kinasa USI 1	filomentous growth	Sar/Thr protein kinasa	reduced virulence	Microbiol 2005: 55: 281
INO	110	110	115L1	QJAU/I		mamentous growm	Sel/Thi protein kinase	reduced viruience	Wilciobiol, 2005, 55. 581.
					Hyphal wall protein	adhesion,cell wall			Tsuchimori N, et al., Infect
	. .				I (Cell elongation	organization	hyphal cell wall protein	reduced virulence	Immun, 2000; 68: 1997.
No	No	No	HWPI	P46593	protein 2)				
					Hyphal wall protein	filamentous growth,			Hayek P, et al., Microbiol
					2(GPI-anchored	pathogenesis	GPI-anchored protein	reduced virulence	Res, 2010; 165: 250.
No	No	No	HWP2	Q59PF9	protein 8)	* -			
					Cell wall protein	cell wall structure.			Bates S. et al., Infect
					IFF11 (Adhesin-like	virulence	Secreted protein	reduced virulence	Immun 2007: 75: 2922
No	No	No	IFF11	Q5A7R7	protein IFF11)				
					Cell wall protein	adhasian			Kempf M, et al.,
					IFF4(Adhesin-like	auticsion,	GPI anchor protein	reduced virulence	Mycopathologia, 2009;
No	No	No	IFF4	Q5AAL9	protein IFF4)	pathogenesis			168: 73.
							phosphatidylinositol-(4,		
						cell integrity	5)-bisphosphate		Badrane H, et al.,
					Phosphoinositide	pathway, hyphal	[PI(4,5)P2]	reduced virulence	Microbiology, 2008; 154:
No	No	No	INP51	A0A1D8PIH6	5-phosphatase	growth	5-phosphatase		3296.
						, ·			
					Bud site selection	morphogenesis,	Integrin-like protein	reduced virulence	Gale, CA, et al., Science,
No	No	No	INT1	P53705	protein BUD4	adhesion			1998; 279: p1355.
						adhasion call wall	Protein with roles in		Badrane H, et al.,
					Increased rDNA	organization	coll well integrity	reduced virulence	Microbiology, 2005; 151:
No	No	No	IRS4	Q59SR6	silencing protein 4	organization	cen wan integrity		2923.

						hyphal growth	Subtilisin-like protease		Newport G, et al.,
						pathogenesis	(proprotein convertase)	reduced virulence	J.Biol.Chem. 2003;
No	No	No	KEX2	A0A1D8PEG3	Kexin	F	(+-++)		278:1713.
						DNA double strand	DNA ligase	reduced virulence	Andaluz E, et al., Infect
No	No	No	LIG4	P52496	DNA ligase 4	break repair	Divit inguot		Immun, 2001; 69: 137.
					Spindle assembly	mitotic cell cycle	spindle assembly		Bai C. et al., Mol
					checkpoint	spindle assembly	checkpoint (SAC)	reduced virulence	Microbiol. 2002: 45: 31.
No	No	No	MAD2	Q59VQ3	component MAD2	-p	component		,,
									Jeong J, et al., Fungal
No	No	No	MCA1	Q5ANA8	Metacaspase-1	apoptosis	apoptotic process	reduced virulence	Genet Biol, 2016; 97: 18.
					Multidrug resistance				
					protein 1 (Benomyl	biofilm formation,	Multidrug efflux pump		Becker JM, et al., Infect
No	No	No	MDR1	Q5ABU7	resistance protein 1)	drug export	of plasma membrane	reduced virulence	Immun, 1995; 63: 4515.
						pH induced hyphal	required for growth and		Davis DA, et al., Genetics
					Negative regulator of	formation	hyphal formation at	reduced virulence	2002: 162: 1573
No	No	No	MDS3	Q59WF4	sporulation MDS3		alkaline pH		
					Mannosylinositol		GDP-mannose inositol-		
					phosphorylceramide	glycosphingolipid	phospho-ceramide	reduced virulence	Mille C, et al., J Biol
					synthase catalytic	synthesis	mannose transferase		Chem, 2004; 279: 47952.
No	No	No	MIT1	A0A1D8PIF7	subunit				
					Mitogen-activated	filamentous, hyphal	mitogen-activated	reduced virulence	Diez-Orejas R, et al., Infect
No	No	No	MKC1	Q5AAG6	protein kinase MKC1	growth	protein kinase		Immun, 1997; 65: 833.
					Multiple drug				
					resistance-associated	Vacuolar multi-drug	a i		Khandelwal NK, et al.,
					protein-like	resistance ABC	pathogenesis	reduced viruience	Biochem J, 2016; 473:
No	No	No	MLT1	Q5A762	transporter 1	transporter			1537.
			MNN5		Alpha-1,2-mannosylt	filamentous, hyphal	alpha-1,2-mannosyltran		Bai C, et al., Eukaryot
No	No	No	(MNN2)	Q59WF4	ransferase MNN2	growth	sferase	reduced virulence	Cell, 2006; 5: 238.
					Glycolipid				Buurman ET, et al., Proc
					2-alpha-mannosyltra	adhesion,	Alpha-1,2-mannosyl	reduced virulence	Natl Acad Sci U S A,
No	No	No	MNT1	Q00310	nsferase 1	filamentous growth	transferase		1998; 95: 7670.
						iron ion			Xu N, et al., Biochim
						transmembrane			Biophys Acta, 2014; 1843:
No	No	No	MRS4	Q5A2T7	Fe(2+) transporter	transporter activity	iron ion homeostasis	reduced virulence	629.
					N-acetylglucosamine		N-acetylglucosamine-6-		Yamada-Okabe T, et al.,
			NAG2		-6-phosphate	N-acetylglucosamine	phosphate (GlcNAcP)		Eur J Biochem, 2001; 268:
No	No	No	(DAC1)	A0A1D8PQG3	deacetylase	catabolic process	deacetylase	reduced virulence	2498.
					Major facilitator		Putative transporter of		Yamada-Okabe T,
					superfamily	drug transport	the major facilitator	reduced virulence	Yamada-Okabe H. FEMS
					multidrug transporter		superfamily (MFS)		Microbiol Lett, 2002; 212:
No	No	No	NAG3	A0A1D8PQG0	NAG3		······································		15.

					Major facilitator				Yamada-Okabe T,
					superfamily	1			Yamada-Okabe H. FEMS
					multidrug transporter	drug transport	Putative transporter	reduced virulence	Microbiol Lett, 2002; 212:
No	No	No	NAG4	Q59RG0	NAG4				15.
							Protein required for		
							wild-type mouse		Yamada-Okabe T,
						hexose transport	virulence and wild-type	reduced virulence	Yamada-Okabe H. FEMS
							cycloheximide		Microbiol Lett, 2002; 212:
No	No	No	NAG6	Q9C0L9	Protein SEY1		resistance		15.
							member of CCR-NOT		
						adhesion, hyphal	complex>>global		Cheng S, et al., Infect
					CCR4-NOT core	growth	regulator of	reduced virulence	Immun, 2005; 73: 7190.
No	No	No	NOT5	A0A1D8PE87	subunit	-	transcription		
					Transcriptional		Transcriptional		Murad AM. et al., EMBO
No	No	No	NRG1	O5A0E5	regulator NRG1	hyphal growth	repressor	reduced virulence	J. 2001: 20: 4742.
						cAMP-mediated			- , - ,
						signal transduction			
						pathway for	nhosnhodiesterase>>hig		Bahn YS et al Mol
						morphologic	h affinity for cAMP	reduced virulence	Microbiol 2003: 50: 391
						switching (hyphal			
No	No	No	PDE2	A0A1D8PCV9	Phosphodiesterase	formation)			
						vacuolar transport			Palanisamy SK et al
						endocytosis and	t-SNARE (pre-vacuolar	reduced virulence	Fukarvot Cell 2010: 9
No	No	No	PEP12	4041D8PNI0	SNAP receptor	secretion	trafficking gene)		266
			11112		CPI anahored protein	secretion			Calic S. at al. Europal
No	No	No	PGA13	054343		cell wall synthesis	pathogenesis	reduced virulence	Genet Biol 2012: 40: 322
	110	110	IGAIS	QJAJAJ	Dhamhata ann ing	cen wan synthesis			Halt Marstal Mal Dial
NI.	NT-	N.	NIOA		Phosphate-sensing	protein dimerization	centular phosphate ion		
INO	INO	INO	РНО4	AUATD8PMD1	transcription factor	activity	nomeostasis	reduced viruience	Cell, 2016; 27: 2784.
						migration in host,	nhosnholinase B	reduced virulence	Leidich SD, et al., J Biol
No	No	No	PLB1	Q9UWF6	Lysophospholipase 1	pathogenesis	phospholipuse D	reduced virturence	Chem, 1998; 273: 26078.
						multigene			
						phospholipase	phospholipase B	reduced virulence	Theiss S, et al., Int J Med
No	No	No	PLB5	A0A1D8PEB1	Lysophospholipase	family			Microbiol, 2006; 296: 405.
						hyphal growth,			Dolan JW, et al., Med
No	No	No	PLD1	A0A1D8PF62	Phospholipase	pathogenesis	Phospholipase D1	reduced virulence	Mycol, 2004; 42: 439.
					Dolichyl-phosphate-	cell wall			
					mannoseprotein	organization, hyphal	isotorms of protein	reduced virulence	Kouabhia M, et al., Infect
					mannosyltransferase	growth	mannosyltransferases		Immun, 2005; 73: 4571.
No	No	No	PMT4	Q59X23	4				

No	No	No	PMT5	Q5ACU3	Dolichyl-phosphate- mannoseprotein mannosyltransferase 5	cell wall organization, hyphal growth	isoforms of protein mannosyltransferases	reduced virulence	Rouabhia M, et al., Infect Immun, 2005; 73: 4571.
No	No	No	РМТ6	Q5A688	Dolichyl-phosphate- mannoseprotein mannosyltransferase 6	cell wall organization, hyphal growth	Protein mannosyltransferases	reduced virulence	Timpel C, et al., J Bacteriol, 2000 ; 182: 3063.
					Ras-like protein 1				
No	No	No	RAS1	O59XU5	(Ras homolog type B)	cAMP-mediated	RAS signal transduction GTPase	reduced virulence	Leberer E, et al., Mol Microbiol, 2001: 42: 673.
				(,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	Regulator of	88			
					cytoskeleton and	cytoskeletal protein			Douglas LM, et al., Infect
No	No	No	Rvs161	Q5AFE4	endocytosis RVS161	binding	pathogenesis	reduced virulence	Immun, 2009; 77: 4150.
					Regulator of				
					cytoskeleton and	cytoskeletal protein			Douglas LM, et al., Infect
No	No	No	Rvs167	Q59LF3	endocytosis RVS167	binding	pathogenesis	reduced virulence	Immun, 2009; 77: 4150.
						negatively regulates			
						the cytosolic			Jiang L, et al., Fungal
No	No	No	RCH1	Q59UQ7	Solute carrier RCH1	homeostasis	calcium ion import	reduced virulence	Genet Biol, 2018; 115: 1.
No	No	No	RFX2	O5AMO6	RFX-like DNA-binding protein RFX2	filamentation, adhesion	Transcriptional repressor	reduced virulence	Hao B, et al., Eukaryot Cell, 2009; 8: 627.
No	No	No	RIM101	Q9UW14	pH-response transcription factor pacC	filamentous, hyphal growth	Transcription factor involved in alkaline pH response	reduced virulence	Davis D, et al., Infect Immun, 2000; 68: 5953.
No	No	No	RIM8	Q9UW13	pH-response regulator protein palF	filamentous, hyphal growth	Transcription factor involved in alkaline pH response	reduced virulence	Davis D, et al., Infect Immun, 2000; 68: 5953.
No	No	No	RVS161	Q5AFE4	Regulator of cytoskeleton and endocytosis RVS161	endocytosis, cell wall organization	Amphiphysin membrane protein containing a BAR domain	reduced virulence	Douglas LM, et al., Infect Immun, 2009; 77: 4150.
No	No	No	RVS167	Q59LF3	Regulator of cytoskeleton and endocytosis RVS167	endocytosis, cell wall organization	Protein containing a BAR domain	reduced virulence	Douglas LM, et al., Infect Immun, 2009; 77: 4150.
No	No	No	SAP7	Q59VH7	Candidapepsin-7	protein metabolic process, pathogenesis	Member of the secreted aspartyl proteinase family	reduced virulence	Taylor BN, et al., Infect Immun, 2005; 73: 7061.
					Succinate				
					dehydrogenase	transferring electrons			
					[ubiquinone]	from succinate to	respiratory electron		Bi S, et al., Future
No	No	No	SDH2	Q59QN7	iron-sulfur subunit	ubiquinone	transport chain	reduced virulence	Microbiol, 2018; 13: 1141.

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No. No. State Sta	No. No. Series Filter of point in the series of point in the se	No	No	No	SEF1	Q59UY7	SEF1	Transcription factor	pathogenesis	reduced virulence	Microbe, 2011; 10: 118.	
No. No. No. Str. St	No. No. STI SCAL SC						Histone-lysine	cellular				
NM No <	No. No. STI SAGG1 protein point process, protein point methytransferase protein point Macro point <td></td> <td></td> <td></td> <td></td> <td></td> <td>N-methyltransferased</td> <td>developmental</td> <td>putative lysine histone</td> <td></td> <td>Raman SB, et al., Mol</td>						N-methyltransferased	developmental	putative lysine histone		Raman SB, et al., Mol	
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No No SFL1 Q5A287 SFL1 Interscription factor SFL1 Interscription factor becalation Interscription repressor reduced virulence Li V, et al., Eukaryot Cel 2007, 6: 2112. No No No SH01 Q5A036 SFL1 Predicted daptor rotein involved in activation of MAP Predicted daptor rotein involved in activation of MAP Roman E, et al., Eukaryot Cell, 2009, 8: 1235. No No SH01 Q5A036 SH01 Predicted daptor rotein involved in activation of MAP Predicted daptor rotein involved in activation of MAP Roman E, et al., Eukaryot Cell, 2009, 8: 1235. No No SH01 Q5A036 Stf101 Predicted virulence in phosphatase STr4 Predicted virulence preports regulator roteined virulence for phoreary status Roman E, et al., Eukaryot Cell, 2009, 8: 1235. No No Stf14 Q5AVS Stf101 Prepint growth, inspected virulence preports regulator roteined virulence for phoreary status Roman E, et al., Eukaryot Cell, 2009, 81: 2007. No No No Stf19 Stf19 Prepint growth, inspected virulence preporte dismutes Roman E, et al., Eukaryot cell wall Roman E, et al., Eukaryot cell wall No No Stf19	No No SFL 1 Q5A287 Transcription factor SFL 1 filamentous growth, ficoculation transcriptional repressor protein involved in activation of MAP reduced vinulence involved in activation of MAP L1 Y, et al., Eakaryy 2007, 6 : 2112. No No No SH01 Q5AQ36 SH01 predicted adaptor protein involved in activation of MAP reduced vinulence (Cell, 2009, 8: 1235. Roman E, et al., Edd Cell, 2009, 8: 1235. No No No SH01 Q5AQ36 SH01 predicted adaptor protein insolved in signaling pathways reduced vinulence (Cell, 2009, 8: 1235. Roman E, et al., Edd Cell, 2009, 8: 1235. No No No SH01 Q5AQ36 SH01 prephytel growth, in phosphatase callytic subunit of a type2A-related protein phosphatase reduced vinulence finantu, 2004, 7: 1 No No SKN7 Q5AUX5 SKN7 response to oxidative growth response regulator phospherelay grant reduced vinulence finantu, 2004, 7: 2 No No SLR19 Q5ADT0 SIL19 cell wall organization alkaleni-induced regiones to oxidative growth reduced vinulence finantu, 2013, 81 : cell wall repressor reduced vinulence finanduced reduced vinulence	No	No	No	SET1	Q5ABG1	protein 1)	filamentation				
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Image: series in the	No. No. No. NO. NO. NO. SHO. Q5Q. SHO. S	No	No	No	SFL1	Q5A287	SFL1	flocculation	transcriptional repressor	reduced virulence	2007; 6: 2112.	
No. No. No. SHO. SHO. <t< td=""><td>No. No. No. No. SHO1 SAO3 SHO1 State State<!--</td--><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td>Predicted adaptor</td><td></td><td></td></td></t<>	No. No. No. No. SHO1 SAO3 SHO1 State State </td <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td>Predicted adaptor</td> <td></td> <td></td>								Predicted adaptor			
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No No IEC1 QSANJ4 activator IEC1 filamentous growth transcription factor Microbiol, 2000; 38: 435 Microbiol, 2000; 38: 435 cAMP-dependent morphogenesis, catalytic subunit of a Sonneborn A, et al., Mol protein kinase protein kinase husbal growth reduced virulence Microbiol, 2000; 35: 266	No No SWE1 Q5AP97 protein kinase SWE1 pathogenesis checkpoint kinase reduced virulence 2009; 155: 3847. No No No TEC1 Q5ANJ4 Transcription cell adhesion, TEA/ATTS reduced virulence Schweizer A, et al., No No TEC1 Q5ANJ4 activator TEC1 filamentous growth transcription factor reduced virulence Schweizer A, et al., Microbiol, 2000; 38 CAMP-dependent morphogenesis, protein kinase A (PKA) reduced virulence Sonneborn A, et al.,							hyphal growth			Microbiol 2000. 25. 204	
	i reduced virulence	No	No	No	SWE1	Q5AP97	protein kinase SWE1	pathogenesis	checkpoint kinase		2009; 155: 3847.	
Transcription cell adhesion, TEA/ATTS Schweizer A, et al., Mol	No No SWE1 Q5AP97 protein kinase SWE1 pathogenesis checkpoint kinase 2009; 155: 3847.						Transcription	cell adhesion,	TEA/ATTS		Schweizer A, et al., Mol	
reduced virulence	No No SWE1 Q5AP97 protein kinase SWE1 pathogenesis checkpoint kinase reduced virulence 2009; 155: 3847. Image: Comparison of the system of the	No	No	No	TEC1	Q5ANJ4	activator TEC1	filamentous growth	transcription factor	reduced virulence	Microbiol, 2000; 38: 435.	
No No IECI QSANJ4 activator IECI filamentous growth transcription factor Microbiol, 2000; 38: 435	NoNoSWE1Q5AP97protein kinase SWE1pathogenesischeckpoint kinasereduced virulence2009; 155: 3847.NoNoTEC1Q5ANJ4Transcription activator TEC1cell adhesion, filamentous growthTEA/ATTS transcription factorreduced virulence kinaseSchweizer A, et al., Microbiol, 2000; 38						cAMP-dependent		catalytic subunit of a		Communities and the local state	
No No IEC1 QSANJ4 activator IEC1 filamentous growth transcription factor Microbiol, 2000; 38: 435 Image: Comparison of the second se	No No SWE1 Q5AP97 protein kinase SWE1 pathogenesis checkpoint kinase reduced virulence 2009; 155: 3847. No No No TEC1 Q5ANJ4 Transcription cell adhesion, TEA/ATTS reduced virulence Schweizer A, et al., No No TEC1 Q5ANJ4 cell adhesion, TEA/ATTS reduced virulence Schweizer A, et al., Microbiol, 2000; 38 CAMP-dependent morphogenesis, catalytic subunit of a Sonneborn A, et al.,						protein kinase		protein kinase A (PKA)	reduced virulence		
No No Tech QSANJ4 activator TEC1 filamentous growth transcription factor Microbiol, 2000; 38: 435 No No Tech QSANJ4 activator TEC1 filamentous growth transcription factor Microbiol, 2000; 38: 435 Image: Comparison factor Image: Comparison factor catalytic subunit of a protein kinase catalytic subunit of a protein kinase A (PKA) Sonneborn A, et al., Mol Microbiol, 2000; 35: 386	NoNoSWE1Q5AP97protein kinase SWE1pathogenesischeckpoint kinasereduced virulence2009; 155: 3847.NoNoTEC1Q5ANJ4Transcriptioncell adhesion, filamentous growthTEA/ATTS transcription factorSchweizer A, et al., Microbiol, 2000; 38NoNoTEC1Q5ANJ4cAMP-dependent protein kinasemorphogenesis, protein kinase A (PKA)reduced virulence reduced virulenceSchweizer A, et al., Microbiol, 2000; 38							hyphal growth			Microbiol, 2000; 35: 386.	

						stress response	trehalose-6-phospate		Zaragoza O, et al.,
					Trehalose-phosphata	hyphal growth	phosphatase	reduced virulence	Microbiology, 2002; 148:
No	No	No	TPS2	Q5AI14	se	nyphur growth	phosphilase		1281.
					Transcriptional	hyphal growth			Baneriee Metal Mol
					regulatory protein	nathogenesis	Transcription factor	reduced virulence	Biol Cell 2008: 19: 1354
No	No	No	UME6	Q59MD2	UME6	patilogenesis			Bioi Cell, 2008, 17. 1354.
					Orotidine	adhesion	orotidine		Kirsch DR, Whitney RR.
					5'-phosphate	filementous growth	5'-monophosphate	reduced virulence	Infect Immun, 1991; 59:
No	No	No	URA3	P13649	decarboxylase	mamentous growth	decarboxylase		3297.
						cell wall			
					Extracellular	organization, hyphal	GPI anchored cell wall	reduced virulence	Pardini G, et al., J Biol
No	No	No	UTR2	Q5AJC0	glycosidase UTR2	growth	putative glycosidase		Chem, 2006; 281: 40399.
						vacuolar			
						proton-transporting			
						V-type ATPase			Jia C, et al., Fungal Genet
No	No	No	VPH2	A0A1D8PFF4	Vph2p	complex assembly		reduced virulence	Biol, 2018; 114: 1.
						protein transport to			Johnston DA et al Infect
						vacuole	Rab GTPase	reduced virulence	Immun 2009: 77: 2343
No	No	No	VPS21	Q59X89	Rab family GTPase				ininian, 2009, 77: 23 15:
					Vacuolar protein	cell wall	Protein involved in		Cornet M, et al., Infect
					sorting-associated	organization, pH	proteolytic activation of	reduced virulence	Immun, 2005; 73: 7977.
No	No	No	VPS28	Q59SD1	protein 28	response	Rim101p		
						filamentous growth,	Protein involved in		Connet Mart al Infrast
					Vacuolar-sorting	cell wall	proteolytic activation of	reduced virulence	Cornet M, et al., infect
No	No	No	VPS32	Q5ABD0	protein SNF7	organization	Rim101p		ininian, 2005, 75. 7977.
						nitric oxide			Hromatka BS et al. Mol
No	No	No	VHB1	O59MV9	Flavohemoprotein	dioxygenase activity	nathogenesis	reduced virulence	Biol Cell 2005: 16: 4814
						aloxygenuse ueuvity	puttogenesis		
								reduced virulence	Johnston DA, et al., Infect
No	No	No	YPT72	A0A1D8PHR9	Rab family GTPase	GTPase activity	pathogenesis		Immun, 2009; 77: 2343.
					Stress-associated				
					endoplasmic				Li J, et al., Int J Med
No	No	No	YSY6	A0A1D8PJJ9	reticulum protein		protein transport	reduced virulence	Microbiol, 2018; 308: 378.
					Calcium channel	hyphal growth,			Yu O, et al., Int J Med
No	No	No	YVC1	Q5A2J7	YVC1	pathogenesis	protein phosphatase	reduced virulence	Microbiol, 2014; 304: 339.
				-		protein			
						tyrosine/serine/three			Hanaoka N. et al.
					Tyrosine protein	nine phosphatase			Microbiology 2005 151
No	No	No	YVH1	A0A1D8PSH7	phosphatase	activity	pathogenesis	reduced virulence	2223.
	1	1	1		r · · · ·	1 1	r ~ -		1

No	No	No	PMT2	Q5ADM9	Dolichyl-phosphate- mannoseprotein mannosyltransferase 2	cell wall organization, hyphal growth	isoforms of protein mannosyltransferases	reduced virulence (heterozygote)	Rouabhia M, et al., Infect Immun, 2005; 73: 4571.
No	No	No	FBA1	Q9URB4	Fructose-bisphosphat e aldolase	glycolysis	fructose-1,6-bisphophat e aldolase	reduced virulence (induc prom)	Rodaki A, et al., Eukaryot Cell, 2006; 5: 1371.
No	No	No	NMT1	P30418	Glycylpeptide N-tetradecanoyltrans ferase	drug binding, pathogenesis	MyristoylCoA:protein N-myristoyltransferase	reduced virulence (knock-down strain)	Weinberg RA, et al., Mol Microbiol, 1995; 16: 241.
No	No	No	SAP4	Q5A8N2	Candidapepsin-4	adhesion, pathogenesis	secreted aspartyl proteinases	reduced virulence of triple deletion mutant	Sanglard D, et al., Infect Immun, 1997; 65: 3539.
No	No	No	SAP5	P43094	Candidapepsin-5	adhesion, pathogenesis	secreted aspartyl proteinases	reduced virulence of triple deletion mutant	Sanglard D, et al., Infect Immun, 1997; 65: 3539.
No	No	No	SAP6	Q5AC08	Candidapepsin-6	adhesion, pathogenesis	secreted aspartyl proteinases	reduced virulence of triple deletion mutant	Sanglard D, et al., Infect Immun, 1997; 65: 3539.
No	No	No	ATP18	A0A1D8PG50	F1F0 ATP synthase subunit i/j	proton transmembrane transporter activity	ATP synthesis coupled proton transport	reduced virulence	Zhao Y, et al., Med Mycol, 2021; 59: 639.

<i>C. albicans</i> gene name	Protein accession	Protein name	Function	Biological process	Status
1701		F ₁ F ₀ -ATP synthase		ATP synthesis coupled	Protein inferred from
AIPI	A0A1D8PDC4	subunit α	produces ATP from ADP	proton transport	homology
		F ₁ F ₀ -ATP synthase		ATP synthesis coupled	Protein inferred from
ATP2	A0A1D8PKZ9	subunit β	produces ATP from ADP	proton transport	homology
		F ₁ F ₀ -ATP synthase		ATP synthesis coupled	Protein inferred from
ATP3	A0A1D8PRY3	subunit γ	produces ATP from ADP	proton transport	homology
		F_1F_0 -ATP synthase		ATP synthesis coupled	
ATP4	Q59ZE0	subunit 4	produces ATP from ADP	proton transport	Protein predicted
		F_1F_0 -ATP synthase		ATP synthesis coupled	Protein inferred from
ATP5	Q5A7P7	subunit 5	produces ATP from ADP	proton transport	homology
		F_1F_0 -ATP synthase		ATP synthesis coupled	Protein inferred from
ATP6	Q9B8D4 (I2BJX7)	subunit a	produces ATP from ADP	proton transport	homology
		F_1F_0 -ATP synthase		ATP synthesis coupled	Protein inferred from
ATP7	Q59PV8	subunit d	produces ATP from ADP	proton transport	homology
		F_1F_0 -ATP synthase		ATP synthesis coupled	Protein inferred from
ATP8	Q9B8D3	subunit 8 (A6L)	produces ATP from ADP	proton transport	homology
		F_1F_{\circ} -ATP synthase		ATP synthesis coupled	Protein inferred from
ATP9	Q9B8D5	subunit 9	produces ATP from ADP	proton transport	homology
		F_1F_0 -ATP synthase		ATP synthesis coupled	
ATP14	A0A1D8PHL7	subunit h	produces ATP from ADP	proton transport	Protein predicted
		predicted F ₁ F ₀ -ATP		ATP synthesis coupled	Protein inferred from
orf19.5597.1	A0A1D8PQ38	synthase subunit ε	produces ATP from ADP	proton transport	homology
		F_1F_0 -ATP synthase		ATP synthesis coupled	Protein inferred from
ATP16	A0A1D8PUD2	subunit δ	produces ATP from ADP	proton transport	homology
		F_1F_0 -ATP synthase		ATP synthesis coupled	
ATP17	A0A1D8PRM5	subunit f	produces ATP from ADP	proton transport	Protein predicted
		F_1F_0 -ATP synthase		ATP synthesis coupled	Ĩ
ATP18	A0A1D8PG50	subunit i/j	produces ATP from ADP	proton transport	Protein predicted
		F_1F_2 -ATP synthase		ATP synthesis coupled	Ĩ
ATP19	A0A1D8PFD4	subunit k	produces ATP from ADP	proton transport	Protein predicted
		F_1F_0 -ATP synthase		ATP synthesis coupled	Protein inferred from
ATP20	Q59M30	subunit g	produces ATP from ADP	proton transport	homology
		F_1F_0 -ATP synthase	-	ATP synthesis coupled	Protein inferred from
TIMI I	A0A1D8PL02	subunit e	Produces ATP from ADP	proton transport	homology

Supplementary Table 2. Summary of F₁F₀-ATP synthase subunits of *C. albicans*.

Strain	Parent	Genotype	Reference
SC5314		Wild-type strain	1
$ATP16/atp16\Delta$	SC5314	orf19.7678-14::FRT/orf19.7678-2	
$atp16\Delta/\Delta$	$ATP16/atp16\Delta$	orf19.7678-14::FRT/orf19.7678-24::FRT	This study
$atp16\Delta/ATP16$	$atp16\Delta/\Delta$	orf19.7678-14::FRT/orf19.7678-2::FRT	This study
Atp16 O/E	SC5314	ADH1/adh1::PADH1-orf19.7678-1-caSAT1	This study
SN250		wild-type (leu2A::C.d.HIS1/leu2A::C.m.LEU2,	2
		ura 3Δ /URA3, his 1Δ /his 1Δ , arg 4Δ /arg 4Δ ,	
		iro1Δ/IRO1, MTLa/ MTLα)	
$ras1\Delta/\Delta$		ura3::limm434/ura3::limm434	3
		ras1::hisG/ras1::hisG:URA3	

Supplementary Table 3. Strains used in this study.

Supplementary Table 4. Primers used in this study.

Primers	Sequence (5' to 3') ^a
$atp16\Delta/\Delta$ and $atp16\Delta/ATP16$ construction	
ATP16-1	CCCgggcccATCAACGACATGCAGAAC
ATP16-2	CCCctcgagGCCTCGGTGGCATAAGTT
ATP16-3	ATAAGAATgcggccgcAGAGCTGAATCTAGTGATG
ATP16-4	TCCccgcggTAAGCACTAAAGAAGGGT
CassetF	GCTTTCGGTCGCTGTTCTCA
CassetR	TGTTAGGCGTCATCCTGTGC
ATP16-5	AAGTCATAGAAGMAGCGGCAAG
ATP16-6	TCCAGACAGTCGAGTTAG
ATP16-7	TCTCGGGAGCACAGGATG
ATP16-8	GTTGACTGGTGGCGTAGC
ATP16-F	GAAATTATCCTTGGCATTG
ATP16-R	TGGTCAGAGTCTCCGTTT
Atp16 O/E construction	
ATP16orf-F	CCCctcgagATGTTCAGACAAGTTTTCCGTCAAG
ATP16orf-R	CCCagatetTTACTTAGTAAAATGTTGTAAAGC
pADH1E2-ATP16-up-F	TCTTGTTCGAAACGGCAGTGCCTC
pADH1E2-ATP16-up-R	AACCAGATTTCCAGATTTCCAG
pADH1E2-ATP16-down-F	TAAGCAGACAGCTCCTTGGCATAC
pADH1E2-ATP16-down-R	GAGTTGTTGGAGAGGTAAACCCAG
RT_aPCR	
SSA1-F	
SSA1-R	GGTGGCTTGTCTTTGAGAATC
HWP1-F	TGTCTACACTACATTCTGTC
HWP1-R	AGGAATAGATGGTTGTGAAC
ALS3-F	CTCATTACACCAACCATACA
ALS3-R	GGATTCTGTGGTTGTAGTAT
HGC1-F	GTATCGCTGGTTCTCGTGCT
HGC1-R	AGGTGTACCACTACCACCATT
RAS1-F	ATCAAGATGGATTAGCATTGG
RAS1-R	TGTTGTTGCTGTTGTTGTTG
CYR1-F	AGAAAGAAGACGATGAAACAG
CYR1-R	AGGAGAACTAGAGGATGTAGAC
TPK1-F	AGAACTTGCCAACAAACAAC
TPK1-R	TTTCTTGGTCAAGGAAAGAC
TPK2-F	TTGTTGCCTGAACGTTCTAC
TPK2-R	CTACCATTGTGAACTGATCTC

EFG1-F	ACAACCTCAGCATTACAATG
EFG1-R	ATAGGTACTGCTTGTTGACC
FLO8-F	AGCAAATGACTAAGATGGCTG
FLO8-R	AGTCGGAATTACCAGTGTTTC
CPH1-F	ATGCAACACTATTTATACCTC
CPH1-R	CGGATATTGTTGATGATGATA
TEC1-F	AGGTTCCCTGGTTTAAGTG
TEC1-R	ACTGGTATGTGTGGGGTGAT
COX1-F	GCACTTCTTAGGATTGAATG
COX1-R	TTCTTCACGCTCATTCTCAC
COX2-F	AGATGCTACTCCAGGTCG
COX2-R	ACTGCTCTACCATTGAGC
COX3-F	CCCTACTATATCACCAGCTG
COX3-R	TCACTAAGTGTAAATCCAGC
COB-F	GATAGATTGCCAATGCATCC
COB-R	CGAAGTATAGCATAGAATGG
ATP6-F	GCTGGAGGTCATTTCTTCCCT
ATP6-R	TAGCACCAAGACGTAGACCT
ATP8-F	CAGGTATTGCAGCTGTATCAA
ATP8-R	AGCTCTAGCTACTAATAAACGTA
ATP9-F	ACAGGTATTGCAGCTGTATCAAT
ATP9-R	AGCTCTAGCTACTAATAAACGTAAT

^a Lowercase sequences represent the following restriction sites: ApaI for ATP16-1, XhoI for ATP16-2, NotI for

ATP16-3, SacII for ATP16-4.

Strains	Р	y (PE)	
	1 st experiment 2 nd experiment		3 rd experiment
WT	2181	1205	1361
$atp16\Delta/\Delta$	1795	1197	1243
$atp16\Delta/ATP16$	2635	1116	1352

Supplementary Table 5. The mean fluorescence intensity value of ROS.

Supplementary Table 6. The red/green mean fluorescent intensity value of $\Delta \Psi m$.

Strains	P1 Mean Fluorescence Intensity (PE)							
	1 st exp	eriment	2 nd exp	eriment	3 rd experiment			
	JC-1 Red	JC-1 green	JC-1 Red	JC-1 green	JC-1 Red	JC-1 green		
WT	6544	8971	23322	31970	11599	17164		
$atp16\Delta/\Delta$	2954	7766	6310	16929	15127	46298		
$atp16\Delta/ATP16$	4351	6800	13057	15592	17026	22645		

Supplementary References

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- Noble, S. M., French, S., Kohn, L. A., Chen, V. & Johnson, A. D. Systematic screens of a *Candida albicans* homozygous deletion library decouple morphogenetic switching and pathogenicity. *Nat. Genet.* 42, 590-598 (2010).
- 3. Grahl, N., *et al.* Mitochondrial Activity and Cyr1 Are Key Regulators of Ras1 Activation of *C. albicans* Virulence Pathways. *PLoS pathog.* **11**, e1005133 (2015).