GLYOXYLATE CYCLE AND ALTERNATIVE CARBON METABOLISM IN METABOLIC FLEXIBILITY AND PATHOGENICITY OF Candida glabrata

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By

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Thesis submitted to the School of Graduate Studies, Universiti Putra Malaysia, in fulfilment of the requirements for the Degree of Doctor of Philosophy

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GLYOXYLATE CYCLE AND ALTERNATIVE CARBON METABOLISM IN METABOLIC FLEXIBILITY AND PATHOGENICITY OF *Candida glabrata*

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November 2019

Chairman : Leslie Than Thian Lung, PhD
Faculty : Medicine and Health Sciences

Distinct microenvironments in the host can differ significantly (e.g. nutrients availability) and that *Candida glabrata*, in order to be an effective human pathogen, must transit between these niches and adapt to the differences. In addition, most of the immune cells also actively deprive nutritional resources from invading pathogens, which makes the survival of intracellular pathogens even more challenging. *Candida glabrata* appears to utilise unique stealth, evasion and persistence strategies in subverting the onslaught of host immune response during systemic infection. In fact, it is surprising that *C. glabrata* triggers its own engulfment by macrophages. Considering the glucose-deficient condition within the macrophages, *C. glabrata* must be able to assimilate endogenous resources such as alternative carbon sources for their survival. The present study concentrated on the impact of alternative carbon metabolism in the metabolic flexibility and pathogenicity of *C. glabrata*. Growth on alternative carbon sources such as acetate, lactate, ethanol and oleic acid induced alteration in several fitness and pathogenic attributes of *C. glabrata*. These include the reduction in planktonic growth, biofilm formation, and oxidative stress resistance. Alternative carbon sources also modulated the cell wall architecture of *C. glabrata*, as demonstrated by the reduction of β-glucan and chitin layer, and the increase of mannan layer. Furthermore, the antifungal resistance of C. *glabrata* grown in alternative carbon sources was significantly enhanced. The metabolic regulation of alternative carbon metabolism in *C. glabrata* was subsequently explored using high-throughput transcriptomic and proteomic analyses in response to acetate, an alternative carbon source that has been proven to be

relevant *in vivo*. Collectively, both transcriptome and proteome data revealed that the regulation of alternative carbon metabolism in *C. glabrata* substantially resembled human fungal pathogens such as *Candida albicans* and *Cryptococcus neoformans*, with up-regulation of many proteins and transcripts from the glyoxylate cycle and gluconeogenesis, namely isocitrate lyase (*ICL1*), malate synthase (*MLS1*), phosphoenolpyruvate carboxykinase (*PCK1*) and fructose 1,6-biphosphatase (*FBP1*). In the absence of glucose, *C. glabrata* shifted its metabolism to hexose anabolism from the available carbon source. The results essentially suggest that the gluconeogenic metabolism are possibly critical for the survival of phagocytosed *C. glabrata* within the glucose-deficient macrophages. The importance of the glyoxylate cycle enzyme gene *ICL1* in the metabolic flexibility and pathogenicity of *C. glabrata* was further substantiated by the comprehensive analyses of *icl1*Δ mutant strains. Indeed, disruption of *ICL* rendered *C. glabrata* unable to assimilate several alternative carbon sources, as well as reduced its biofilm formation capability. In addition, *ICL1* is also pivotal for the survival of phagocytosed *C. glabrata*, as the *icl1*Δ mutant strains were significantly more susceptible to macrophage killing relative to wild-type strain. Finally, evaluation of *icl1*Δ mutant strains in a mouse model of invasive candidiasis showed that *ICL1* is essentially required for the full virulence of *C. glabrata in vivo*. In conclusion, the present study demonstrated that alternative carbon metabolism and the glyoxylate cycle is crucial for the metabolic flexibility and pathogenicity of *C. glabrata in vitro* and *in vivo*. The findings implicate *ICL1* as a promising target in the development of novel and innovative treatments for a better management of invasive candidiasis.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia
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KITAR GLIOKSILAT DAN METABOLISME KARBON ALTERNATIF DALAM FLEKSIBILITI METABOLIK DAN KEPATOGENAN *Candida glabrata*

Oleh

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Persekitaran mikro dalam perumah boleh berbeza dengan ketara (ketersediaan nutrien) dan *Candida glabrata*, untuk menjadi patogen manusia yang berkesan, mesti transit antara nic perumah dan menyesuaikan diri dengan perbezaan ini. Tambahan pula, kebanyakan sel-sel imun juga melucutkan sumber pemakanan secara aktifnya daripada pathogen penyerang, dan ini menjadikan survival pathogen intraselular lebih mencabar. *Candida glabrata* menggunakan strategi penyelinapan, pengelakan dan pengekalan yang unik untuk melawan gerak balas imun perumah semasa jangkitan sistemik. Malah, *C. glabrata* juga mencetuskan fagositosisnya oleh sel makrofaj. Memandangi keadaan kekurangan glukosa dalam sel makrofaj, *C. glabrata* mesti mengasimilasi sumber endogen seperti sumber karbon alternatif untuk menjamin survival mereka. Penyelidikan ini bertujuan untuk mengkaji kesan metabolisme karbon alternatif terhadap fleksibiliti metabolik dan kepatogenan *C. glabrata*. Pertumbuhan dalam sumber karbon alternatif seperti asetat, laktat, etanol dan asid oleik membawa perubahan kepada beberapa sifat kecergasan dan patogen *C. glabrata*. Ini termasuk pengurangan pertumbuhan planktonik, pembentukan biofilm, dan rintangan oksidatif. Sumber karbon alternatif juga memodulasi seni bina dinding sel *C. glabrata*, seperti yang ditunjukkan dalam pengurangan lapisan β-glukan dan kitin, dan peningkatan lapisan manan. Tambahan pula, rintangan antikulat *C. glabrata* dalam sumber karbon alternatif juga telah dipertingkatkan dengan ketara. Pengawalaturan metabolisme karbon alternatif *C. glabrata* dalam asetat dikaji dengan menggunakan analisis transkrip dan protein keupayaan celusan tinggi. Secara keseluruhannya, data transkrip dan protein menunjukan bahawa pengawalaturan metabolisme karbon alternatif *C. glabrata* menyerupai

patogen kulat manusia seperti *Candida albicans* dan *Cryptococcus neoformans*, dengan peningkatan pengawalaturan protein dan transkrip dari kitaran glioksilat dan glukoneogenesis, termasuk isositrat liase (*ICL1*), malat sintase (*MLS1*), fosfoenolpiruvat karboksikinase (*PCK1*) dan fruktosa 1,6-bifosfat (*FBP1*). Semasa ketidakhadiran glukosa, *C. glabrata* mengalih metabolismenya ke anabolisme glukosa dengan menggunakan sumber karbon yang sedia ada. Hasil kajian mencadangkan bahawa kitaran glioksilat dan glukoneogenesis berkemungkinan kritikal kepada survival *C. glabrata* dalam sel makrofaj yang kekurangan glukosa. Kepentingan kitaran glioksilat dalam fleksibiliti metabolik dan kepatogenan *C. glabrata* juga dibuktikan oleh analisis komprehensif strain mutan *icl1*Δ. Penghapusan gen *ICL1* menghalang *C. glabrata* daripada mengasimilasi beberapa sumber karbon alternatif, dan juga mengurangi keupayaannaya dalam pembentukan biofilm. Di samping itu, *ICL1* adalah penting untuk survival fagositosis *C. glabrata*, kerana strain mutan *icl1*Δ lebih mudah terdedah kepada pembunuhan makrofaj berbanding dengan strain jenis liar. Akhir sekali, penilaian strain mutan *icl1*Δ dalam model tikus kandidiasis invasive menunjukkan bahawa *ICL1* diperlukan untuk virulens *C. glabrata in vivo*. Kesimpulannya, kajian ini menunjukkan bahawa metabolisme karbon alternatif dan kitaran glioksilat adalah penting untuk fleksibiliti metabolik dan kepatogenan *C. glabrata in vitro* dan *in vivo*. Penemuan ini mencadangkan *ICL1* sebagai sasaran berpotensi dalam perkembangan rawatan baru dan inovatif untuk pengurusan kandidiasis yang lebih baik.

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ABC	ATP-binding cassette
ABPA	Allergic bronchopulmonary aspergillosis
AFB1	Aflatoxin B1
AGC	Automatic gain control
AIDS	Acquired immunodeficiency syndrome
ATCC	American Type Culture Collection
BLAST	Basic local alignment search tool
BSI	Bloodstream infection
CDS	Coding sequences
CFU	Colony-forming-unit
CHAPS	3-[(3-Cholamidopropyl)dimethylammonio]-1-propanesulfonate
CLSI	Clinical and Laboratory Standards Institute
CNA	Chronic necrotising aspergillosis
CNS	Central nervous systems
CO_2	Carbon dioxide
CoA	Coenzyme A
COMeT	Comparative Medicine and Technology Unit
CSRE	Carbon source-responsive element
CT	Cycle threshold
CWPs	Cell wall proteins
DAVID	Database for Annotation, Visualization, and Integrated Discovery
DEGs	Differential expressed genes
DEPs	Differential expressed proteins
DHA	Drug:H+ antiporter
DHAP	Dihydroacetone phosphate
DMEM	Dulbecco's Modified Eagle's Medium
DTT	Dithiothreitol
EASE	Expression analysis systematic explorer
ECM	Extracellular matrix
EDTA	Ethylenediaminetetraacetic acid
ELISA	Enzyme-linked immunosorbent assay
FBS	Foetal bovine serum
FDR	False discovery rate
FPKM	Fragments per kilobase of transcript per million mapped fragments
GFP	Green fluorescent protein
GI	Gastrointestinal
GM-CFS	Granulocyte-macrophage colony-stimulating factor
GO	Gene ontology
GPI	Glycosylphosphatidylinositol
H_2O_2	Hydrogen peroxide
HAART	Highly active anti-retroviral therapy

HCC	Hepatocellular carcinoma
HCD	High-energy collisional dissociation
HIV	Human immunodeficiency virus
HSCT	Haematopoietic stem-cell transplantation
IACUC	Institutional Animal Care and Use Committee
ICR	Institute of Cancer Research
ICU	Intensive care unit
IPA	Invasive pulmonary aspergillosis
iTRAQ	Isobaric tags for relative and absolute quantitation
ITS	Internal transcribed spacer
KEGG	Kyoto Encyclopedia of Genes and Genomes
LOS	Length of stay
m/z	Mass-to-charge ratio
MAPK	Mitogen-activated protein kinase
MDR	Multidrug-resistance
MFS	Major facilitator superfamily
MIC	Minimum inhibitory concentration
MOI	Multiplicity of infection
MPO	Myeloperoxidase
MPOB	Malaysian Palm Oil Board
MTL	Mating type-like locus
NADPH	Nicotinamide adenine dinucleotide phosphate
NCAC	Non-albicans *Candida* species
NCBI	National Centre for Biotechnology Information
NGS	Next generation sequencing
OD	Optical density
OPC	Oropharyngeal candidiasis
OTC	Over-the-counter
PAS	Periodic acid-Schiff
PATH	Prospective antifungal therapy
PBS	Phosphate buffered saline
PCP	*Pneumocystis* pneumonia
PCR	Polymerase chain reaction
PDB	Protein Data Bank
PMN	Polymorphonuclear neutrophils
PRR	Pattern recognition receptor
qPCR	Quantitative real-time PCR
RIN	RNA integrity number
ROS	Reactive oxygen species
RPMI	Roswell Park Memorial Institute
SC	Synthetic complete
SCFAs	Short chain fatty acids
SD	Standard deviations
SDA	Sabouraud dextrose agar
SDS	Sodium dodecyl sulphate
SEM	Scanning electron microscopy
SOT	Solid organ transplantation

SPE	Solid phase extraction
SV	Spin/vacuum
TBE	Tris-Borate-EDTA
TCA	Tricarboxylic acid
TCEP	Tris(2-carboxyethyl)phosphine
TEM	Transmission electron microscopy
UHPLC	Ultra-high-performance liquid chromatography
UV	Ultraviolet
VVC	Vulvovaginal candidiasis
WT	Wild type
XTT	2, 3-bis-(2-methoxy-4-nitro-5-sulfophenyl)-2H tetrazolium-5-carboxanilide
YNB	Yeast nitrogen base
YPD	Yeast-peptone-dextrose

CHAPTER 1

INTRODUCTION

1.1 Introduction

Nearly 150 million of human populations are affected by potentially life-threatening fungal infections worldwide (Bongomin et al., 2017). However, these fungal diseases are as yet a disregarded issue by public health authorities even though most deaths caused by fungal infections are preventable (Bongomin et al., 2017). Invasive candidiasis, a systemic fungal infection caused by *Candida* species arises regularly among hospitalised individuals in the developed countries and is widely acknowledged as the cause of high morbidity and mortality (>50,000 deaths annually), primarily due to delay in diagnosis and commencement of fitting antifungals (Kullberg and Arendrup, 2015; Ben-Ami, 2018). Invasive candidiasis is one of the most common invasive mycoses and comprises of bloodstream infection (candidaemia) and deep-seated infection (Kullberg and Arendrup, 2015; Calandra et al., 2016). Also, candidaemia is associated with longer length of stay (LOS) and high financial burden up to USD 40,000 per person (Zaoutis et al., 2005; Strollo et al., 2017).

Approximately 10 - 20% of the *Candida* species discovered, including common species such as *Candida albicans*, *Candida glabrata*, *Candida krusei, Candida tropicalis*, and *Candida parapsilosis* have been implicated to cause invasive candidiasis in human (Pfaller et al; 2014; Yapar, 2014). Distribution of *Candida* species that cause infection has been changing throughout the last decade, with a diminishing prevalence of *C. albicans* and emergence of non-*albicans Candida* species (NCAC) (Lamoth et al., 2018). Notably, *C. glabrata* has been recognised as either second or third commonest cause of invasive candidiasis after *C. albicans*, and similar epidemiology have also been highlighted in multiple global surveillance programmes such as SENTRY, ARTEMIS and TRANSNET (Messer et al., 2006; Messer et al., 2009; Pfaller et al., 2010; Andes et al., 2016). Invasive candidiasis caused by *C. glabrata* is most commonly associated with patients with solid tumours and solid organ transplantation (Pfaller et al., 2014). Furthermore, *C. glabrata* candidaemia often has a longer LOS and imposes higher costs when compared to candidaemia caused by *C. albicans* (Moran et al., 2010).

Host immunity and pathogenicity of *Candida* are believed to be crucial for establishment of candidiasis (Silva et al., 2012). For instance, fitness and pathogenic attributes such as biofilm formation, phenotypic switching, secretion of hydrolytic enzymes, drug resistance and enhanced metabolic flexibility are all associated with the virulence of *Candida* species (Sardi et al., 2013). Relative to *C. albicans*, the fitness and pathogenic attributes of *C. glabrata* are not well-studied,

particularly in their natural niche. It has been shown that higher proportion of *C. glabrata* candidaemia shows increased resistance to antifungals such as azoles and echinocandins (Lee et al., 2009; Perlin, 2015) compared to *C. albicans*. However, *C. glabrata* is incapable to form hyphae and produce tissue-damaging hydrolytic enzymes (Silva et al., 2012), which explains the relatively less aggressive nature of this particular fungal pathogen.

Compared to the aggressive *C. albicans*, *C. glabrata* elicits a weaker polymorphonuclear neutrophils (PMN) activation that could trigger the recruitment of monocytic cells to the site of infection and subsequent monocytic engulfment (Duggan et al., 2015). Since *C. glabrata* is able to survive within macrophages, but not within neutrophils, this fungal pathogen could use monocytes or macrophages as potential "Trojan horses" to gain protection against the host defence system, especially neutrophils attack (Seider et al., 2011; Seider et al., 2014; Duggan et al., 2015). *Candida glabrata* clearly pursues a different immune evasion and persistence strategies to *C. albicans*, as escape from the macrophages upon engulfment is not the priority of this fungal pathogen. In fact, *C. glabrata* persists and propagates within the microenvironment of macrophages without causing any significant damage to the host, but eventually leads to cell burst and release the fungal progenies.

While trapped within macrophages, *C. glabrata* relies on endogenous resources for survival as the microenvironment is often depicted as glucose-deficient (Lorenz et al., 2004; Kaur et al., 2007). It has been shown that the ability of *C. glabrata* in mobilisation of the intracellular resources through autophagy serves as a major contributor to sustain viability of this pathogen during glucose deprivation (Roetzer et al., 2010; Shimamura et al., 2019). Besides recycling the intracellular resources via autophagy, the ability to utilise alternative carbon sources other than glucose could also potentially assist in the survival of engulfed *C. glabrata*. In fact, fundamental metabolic pathways involved in alternative carbon metabolism, including β-oxidation of fatty acids, the glyoxylate cycle and gluconeogenesis have been shown to be highly induced in phagocytosed-*C. albicans* (Lorenz et al., 2004), signifying that glucose deprivation and the availability of alternative carbon sources are indeed relevant *in vivo*. The principle function of these interconnected pathways is the generation of key metabolic intermediates from alternative carbon sources for growth and survival of the pathogen *in vivo*.

Besides, the key metabolic enzyme genes from β-oxidation of fatty acids (*FOX2*, encoded for β-oxidation multifunctional protein), the glyoxylate cycle (*ICL1*, encoded for isocitrate lyase) and gluconeogenesis (*FBP1,* encoded for fructose-1,6-biphosphatase) have been proven to be essential for the full virulence of *C. albicans* (Ramírez and Lorenz, 2007), as disruption of these genes confers a severe attenuation in the virulence in a mouse model of invasive candidiasis. All these

findings suggest that enhanced metabolic flexibility through alternative carbon metabolism could be a virulence determinant in *Candida* species.

To date, little is known about the alternative carbon metabolism of *C. glabrata* in their natural niche. The contribution of alternative carbon metabolism in the physiological and pathogenic attributes of *C. glabrata*, as well as the regulation of transcriptional and proteomic network still remain unresolved. In addition, the essential role of one of the metabolic pathways, the glyoxylate cycle (*ICL1*) in the metabolic flexibility and virulence of *C. glabrata* also warrants further investigation. It is envisaged that the knowledge generated from investigating the glyoxylate cycle and alternative carbon metabolism of *C. glabrata* will provide insights into devising novel and innovative strategies for reducing the severity of invasive candidiasis worldwide.

1.2 Objectives

General objective:

To investigate the role of alternative carbon metabolism and the glyoxylate cycle in the metabolic flexibility and pathogenicity of *C. glabrata*.

Specific objectives:

1. To investigate the impact of alternative carbon metabolism on the fitness attributes of *C. glabrata*.
2. To decipher the impact of alternative carbon metabolism on the transcriptional and proteomic landscapes of *C. glabrata*.
3. To investigate the essential role of glyoxylate cycle gene *ICL1* in the metabolic flexibility and virulence of *C. glabrata*.

REFERENCES

Abu Kwaik, Y. and Bumann, D. (2013). Microbial quest for food *in vivo*: 'nutritional virulence' as an emerging paradigm. *Cellular Microbiology* 15: 882–890.

Aguirre, J., Hansberg, W. and Navarro, R. (2006). Fungal responses to reactive oxygen species. *Medical Mycology* 44: S101–S107.

Ahn, C.H., Won, T.H., Kim, H., Shin, J., Oh, K.B. (2013). Inhibition of *Candida albicans* isocitrate lyase activity by cadiolides and synoilides from the ascidian *Synoicum* sp. *Bioorganic and Medicinal Chemistry Letters* 23(14) :4099–4101.

Alexander, B.D., Johnson, M.D., Pfeiffer, C.D., Jiménez-Ortigosa, C., Catania, J., Booker, R., Castanheira, M., Messer, S.A., Perlin, D.S., Pfaller, M.A. (2013). Increasing echinocandin resistance in *Candida glabrata*: clinical failure correlates with presence of FKS mutations and elevated minimum inhibitory concentrations. *Clinical Infectious Diseases* 56: 1724–1732.

Almeida, R.S., Wilson, D. and Hube, B. (2009). *Candida albicans* iron acquisition within the host. *FEMS Yeast Research* 9: 1000–1012.

Andes, D.R., Safdar, N., Baddley, J.W., Alexander, B., Brumble, L., Freifeld, A., Hadley, S., Herwaldt, L., Kauffman, C., Lyon, G.M., Morrison, V., Patterson, T., Perl, T., Walker, R., Hess, T., Chiller, T., Pappas, P.G.; TRANSNET Investigators. (2016). The epidemiology and outcomes of invasive *Candida* infections among organ transplant recipients in the United States: results of the Transplant-Associated Infection Surveillance Network (TRANSNET). *Transplant Infectious Disease* 18: 921–931.

Andes, D.R., Safdar, N., Baddley, J.W., Pappas, P.G., Reboli, A.C., Rex, J.H., Sobel, J.D., Playford, G., Kullberg, B.J. (2012). Impact of treatment strategy on outcomes in patients with candidemia and other forms of invasive candidiasis: a patient-level quantitative review of randomized trials. *Clinical Infectious Diseases* 54: 1110–1122.

Andrade, R.P., Kötter, P., Entian, K.D., Casal, M. (2005). Multiple transcripts regulate glucose-triggered mRNA decay of the lactate transporter *JEN1* from *Saccharomyces cerevisiae*. *Biochemical and Biophysical Research Communications* 332: 254–262.

Arendrup, M., Horn, T. and Frimodt-Møller, N. (2002). *In vivo* pathogenicity of eight medically relevant *Candida* species in an animal model. *Infection* 30: 286–291.

Arendrup, M.C. (2010). Epidemiology of invasive candidiasis. *Current Opinion in Critical Care* 16: 445–452.

Arendrup, M.C. (2014). Update on antifungal resistance in *Aspergillus* and *Candida*. *Clinical Microbiology and Infection* 20: 42–48.

Armstrong, A.W., Bukhalo, M. and Blauvelt, A. (2016). A clinician's guide to the diagnosis and treatment of candidiasis in patients with psoriasis. *American Journal of Clinical Dermatology* 17: 329–336.

Askew, C., Sellam, A., Epp, E., Hogues, H., Mullick, A., Nantel, A., Whiteway, M. (2009). Transcriptional regulation of carbohydrate metabolism in the human pathogen *Candida albicans*. *PLOS Pathogens* 5: e1000612.

Ballou, E.R., Avelar, G.M., Childers, D.S., Mackie, J., Bain, J.M., Wagener, J., Kastora, S.L., Panea, M.D., Hardison, S.E., Walker, L.A., Erwig, L.P., Munro, C.A., Gow, N.A., Brown, G.D., MacCallum, D.M., Brown, A.J. (2016). Lactate signalling regulates fungal β-glucan masking and immune evasion. *Nature Microbiology* 12: 16238.

Barelle, C.J., Priest, C.L., MacCallum, D.M., Gow, N.A., Odds, F.C., Brown, A.J.P. (2006). Niche-specific regulation of central metabolic pathways in a fungal pathogen. *Cellular Microbiology* 8: 961–971.

Beardmore, R.E., Cook, E., Nilsson, S., Smith, A.R., Tillmann, A., Esquivel, B.D., Haynes, K., Gow, N.A.R., Brown, A.J.P., White, T.C., Gudelj, I. (2018). Drug-mediated metabolic tipping between antibiotic resistant states in a mixed-species community. *Nature Ecology and Evolution* 2: 1312–1320.

Beese-Sims, S.E., Pan, S.J., Lee, J., Hwang-Wong, E., Cormack, B.P., Levin, D.E. (2012). Mutants in the *Candida glabrata* glycerol channels are sensitized to cell wall stress. *Eukaryotic Cell* 11: 1512–1519.

Ben-Ami, R. (2018). Treatment of invasive candidiasis: a narrative review. *Journal of Fungi* 4: 97.

Bennett, R.J. and Johnson, A.D. (2003). Completion of a parasexual cycle in *Candida albicans* by induced chromosome loss in tetraploid strains. *The EMBO Journal* 22: 2505–2515.

Bennett, R.J. and Johnson, A.D. (2005). Mating in *Candida albicans* and the search for a sexual cycle. *Annual Review of Microbiology* 59: 233–255.

Bertram, G.1., Swoboda, R.K., Gooday, G.W., Gow, N.A., Brown, A.J. (1996). Structure and regulation of the *Candida albicans* ADH1 gene encoding an immunogenic alcohol dehydrogenase. *Yeast* 12: 115–127.

Black, P.N. and DiRusso, C.C. (2007). Yeast acyl-CoA synthetases at the crossroads of fatty acid metabolism and regulation. *Biochimica et Biophysica Acta* 1771: 286–298.

Bongomin, F., Gago, S., Oladele, R.O., Denning, D.W. (2017). Global and multi-national prevalence of fungal diseases-estimate precision. *Journal of Fungi* 3: 57.

Bonifaz, A., Rojas, R., Tirado-Sánchez, A., Chávez-López, D., Mena, C., Calderón, L., María, P.O. (2016). Superficial mycoses associated with diaper dermatitis. *Mycopathologia* 181: 671–679.

Brand, A., MacCallum, D.M., Brown, A.J., Gow, N.A., Odds, F.C. (2004). Ectopic expression of URA3 can influence the virulence phenotypes and proteome of *Candida albicans* but can be overcome by targeted reintegration of URA3 at the RPS10 locus. *Eukaryotic Cell* 3: 900–909.

Britton, K., Langridge, S., Baker, P.J., Weeradechapon, K., Sedelnikova, S.E., De Lucas, J.R., Rice, D.W., Turner, G. (2000). The crystal structure and active site location of isocitrate lyase from the fungus *Aspergillus nidulans*. *Structure* 8: 349–362.

Britton, K.L., Abeysinghe, I.S., Baker, P.J., Barynin, V., Diehl, P., Langridge, S.J., McFadden, B.A., Sedelnikova, S.E., Stillman, T.J., Weeradechapon, K., Rice, D.W. (2001). The structure and domain organization of *Escherichia coli* isocitrate lyase. *Acta Crystallographica Section D* 57: 1209–1218.

Brown, A., Gow, N., Warris, A., Brown, G.D. (2019). Memory in fungal pathogens promotes immune evasion, colonisation, and infection. *Trends in Microbiology* 27: 219–230.

Brown, A.J., Brown, G.D., Netea, M.G., Gow, N.A. (2014a). Metabolism impacts upon *Candida* immunogenicity and pathogenicity at multiple levels. *Trends in Microbiology* 22: 614–622.

Brown, A.J., Odds, F.C. and Gow, N.A. (2007). Infection-related gene expression in *Candida albicans*. *Current Opinion in Microbiology* 10: 307–313.

Brown, G.D., Herre, J., Williams, D.L., Willment, J.A., Marshall, A.S., Gordon, S. (2003). Dectin-1 mediates the biological effects of beta-glucans. *Journal of Experimental Medicine* 197: 1119–1124.

Brown, N.A., Dos Reis, T.F., Goinski, A.B., Savoldi, M., Menino, J., Almeida, M.T., Rodrigues, F., Goldman, G.H. (2014b). The *Aspergillus nidulans* signalling mucin MsbA regulates starvation responses, adhesion and affects cellulase secretion in response to environmental cues. *Molecular Microbiology* 94: 1103–1120.

Brunke, S. and Hube, B. (2013). Two unlike cousins: *Candida albicans* and *Candida glabrata* infection strategies. *Cellular Microbiology* 15: 701–708.

Butler, G. (2010). Fungal sex and pathogenesis. *Clinical Microbiology Reviews* 23: 140–159.

Butler, G., Rasmussen, M.D., Lin, M.F., Santos, M.A., Sakthikumar, S., Munro, C.A., Rheinbay, E., Grabherr, M., Forche, A., Reedy, J.L., Agrafioti, I., Arnaud, M.B., Bates, S., Brown, A.J., Brunke, S., Costanzo, M.C., Fitzpatrick, D.A., de Groot, P.W., Harris, D., Hoyer, L.L., Hube, B., Klis, F.M., Kodira, C., Lennard, N., Logue, M.E., Martin, R., Neiman, A.M., Nikolaou, E., Quail, M.A., Quinn, J., Santos, M.C., Schmitzberger, F.F., Sherlock, G., Shah, P., Silverstein, K.A., Skrzypek, M.S., Soll, D., Staggs, R., Stansfield, I., Stumpf, M.P., Sudbery, P.E., Srikantha, T., Zeng, Q., Berman, J., Berriman, M., Heitman, J., Gow, N.A., Lorenz, M.C., Birren, B.W., Kellis, M., Cuomo, C.A. (2009). Evolution of pathogenicity and sexual reproduction in eight *Candida* genomes. *Nature* 459: 657–662.

Calandra, T., Roberts, J.A., Antonelli, M., Bassetti, M., Vincent, J.L. (2016). Diagnosis and management of invasive candidiasis in the ICU: an updated approach to an old enemy. *Critical Care* 20: 125.

Calcagno, A.M., Bignell, E., Rogers, T.R., Canedo, M., Mühlschlegel, F.A., Haynes, K. (2004). *Candida glabrata* Ste20 is involved in maintaining cell wall integrity and adaptation to hypertonic stress, and is required for wild-type levels of virulence. *Yeast* 21: 557-568.

Calcagno, A.M., Bignell, E., Rogers, T.R., Jones, M.D., Mühlschlegel, F.A., Haynes, K. (2005). *Candida glabrata* Ste11 is involved in adaptation to hypertonic stress, maintenance of wild-type levels of filamentation and plays a role in virulence. *Medical Mycology* 43: 355-364.

Calcagno, A.M., Bignell, E., Warn, P., Jones, M.D., Denning, D.W., Mühlschlegel, F.A., Rogers, T.R., Haynes, K. (2003). *Candida glabrata STE12* is required for wild-type levels of virulence and nitrogen starvation induced filamentation. *Molecular Microbiology* 50: 1309–1318.

Campbell, J.J., Smith, R.A. and Eagles, B.A. (1953). A deviation from the conventional tricarboxylic acid cycle in *Pseudomonas aeruginosa*. *Biochimica et Biophysica Acta* 11: 594.

Casal, M., Paiva, S., Andrade, R.P., Gancedo, C., Leão, C. (1999). The lactate-proton symport of *Saccharomyces cerevisiae* is encoded by *JEN1*. *Journal of Bacteriology* 181: 2620–2623.

Casal, M., Paiva, S., Queirós, O., Soares-Silva, I. (2008). Transport of carboxylic acids in yeasts. *FEMS Microbiology Reviews* 32: 974–994.

Cavalheiro, M. and Teixeira, M.C. (2018). *Candida* biofilms: threats, challenges, and promising strategies. *Frontiers in Medicine* 13: 28.

Cheah, H.L., Lim, V. and Sandai, D. (2014). Inhibitors of the glyoxylate cycle enzyme *ICL1* in *Candida albicans* for potential use as antifungal agents. *PLOS One* 9: e95951.

Chen, Y., Toffaletti, D.L., Tenor, J.L., Litvintseva, A.P., Fang, C., Mitchell, T.G., McDonald, T.R., Nielsen, K., Boulware, D.R., Bicanic, T., Perfect, J.R. (2014). The *Cryptococcus neoformans* transcriptome at the site of human meningitis. *mBio* 5: e01087–13.

Childers, D.S., Raziunaite, I., Mol Avelar, G., Mackie, J., Budge, S., Stead, D., Gow, N.A., Lenardon, M.D., Ballou, E.R., MacCallum, D.M., Brown, A.J. (2016). The rewiring of ubiquitination targets in a pathogenic yeast promotes metabolic flexibility, host colonization and virulence. *PLOS Pathogens* 12: e1005566.

Chowdhary, A., Sharma, C. and Meis, J.F. (2017). *Candida auris*: a rapidly emerging cause of hospital-acquired multidrug-resistant fungal infections globally. *PLOS Pathogens* 13: e1006290.

Citiulo, F., Jacobsen, I.D., Miramón, P., Schild, L., Brunke, S., Zipfel, P., Brock, M., Hube, B., Wilson, D. (2012). *Candida albicans* scavenges host zinc via Pra1 during endothelial invasion. *PLOS Pathogens* 8: e1002777.

Collart, M.A. and Oliviero, S. (1993). Preparation of yeast RNA. P. 13.12.1 – 13.12.5. In Ausubel, F.M., Brent, R., Kingston, R.E., Moore, D.D., Seidman, J.G., Smith, J.A., Struhl, K. (ed.), *Current Protocols in Molecular Biology*. John Wiley and Sons, New York, N.Y.

Cormack, B.P., Ghori, N. and Falkow, S. (1999). An adhesin of the yeast pathogen *Candida glabrata* mediating adherence to human epithelial cells. *Science* 285: 578–582.

Costa, C., Henriques, A., Pires, C., Nunes, J., Ohno, M., Chibana, H., Sá-Correia, I., Teixeira, M.C. (2013b). The dual role of *Candida glabrata* drug:H+ antiporter CgAqr1 (ORF CAGL0J09944g) in antifungal drug and acetic acid resistance. *Frontiers in Microbiology* 4: 170.

Costa, C., Nunes, J., Henriques, A., Mira, N.P., Nakayama, H., Chibana, H., Teixeira, M.C. (2014). *Candida glabrata* drug:H+ antiporter CgTpo3 (ORF CAGL0I10384g): role in azole drug resistance and polyamine homeostasis. *Journal of Antimicrobial Chemotherapy* 69: 1767–1776.

Costa, C., Pires, C., Cabrito, T.R., Renaudin, A., Ohno, M., Chibana, H., Sá-Correia, I., Teixeira, M.C. (2013a). *Candida glabrata* drug:H+ antiporter CgQdr2 confers imidazole drug resistance, being activated by transcription factor CgPdr1. *Antimicrobial Agents and Chemotherapy* 57: 3159–3167.

Cota, J.M., Grabinski, J.L., Talbert, R.L., Burgess, D.S., Rogers, P.D., Edlind, T.D., Wiederhold, N.P. (2008). Increases in *SLT2* expression and chitin content are associated with incomplete killing of *Candida glabrata* by caspofungin. *Antimicrobial Agents and Chemotherapy* 52: 1144-1146.

Cowen, L.E., Sanglard, D., Howard, S.J., Rogers, P.D., Perlin, D.S. (2014). Mechanisms of antifungal drug resistance. *Cold Spring Harbor Perspectives in Medicine* 5: a019752.

Cuéllar-Cruz, M., Briones-Martin-del-Campo, M., Cañas-Villamar, I., Montalvo-Arredondo, J., Riego-Ruiz, L., Castaño, I., De Las Peñas, A. (2008). High resistance to oxidative stress in the fungal pathogen *Candida glabrata* is mediated by a single catalase, Cta1p, and is controlled by the transcription factors Yap1p, Skn7p, Msn2p, and Msn4p. *Eukaryotic Cell* 7: 814–825.

Cullen, P.J., Schultz, J., Horecka, J., Stevenson, B.J., Jigami, Y., Sprague, G.F. Jr. (2000). Defects in protein glycosylation cause *SHO1*-dependent activation of a *STE12* signaling pathway in yeast. *Genetics* 155:1005-1018.

Cunha, D.V., Salazar, S.B., Lopes, M.M., Mira, N.P. (2017). Mechanistic insights underlying tolerance to acetic acid stress in vaginal *Candida glabrata* clinical isolates. *Frontiers in Microbiology* 8: 259.

Dai, W., Chen, Q., Wang, Q., White, R.R., Liu, J., Liu, H. (2017). Complementary transcriptomic and proteomic analyses reveal regulatory mechanisms of milk protein production in dairy cows consuming different forages. *Scientific Reports* 7: 44234.

Davies, D. (2003). Understanding biofilm resistance to antibacterial agents. *Nature Reviews Drug Discovery* 2: 114–122.

De Groot, P.W., Kraneveld, E.A., Yin, Q.Y., Dekker, H.L., Gross, U., Crielaard, W., de Koster, C.G., Bader, O., Klis, F.M., Weig, M. (2008). The cell wall of the human pathogen *Candida glabrata*: differential incorporation of novel adhesin-like wall proteins. *Eukaryotic Cell* 7: 1951–1964.

De Paula, R.G., Antoniêto, A.C.C., Carraro, C.B., Lopes, D.C.B., Persinoti, G.F., Peres, N.T.A., Martinez-Rossi, N.M., Silva-Rocha, R., Silva, R.N. (2018). The duality of the MAPK signalling pathway in the control of metabolic processes and cellulase production in *Trichoderma reesei*. *Scientific Reports* 8: 14931.

Delaloye, J. and Calandras, T. (2014). Invasive candidiasis as a cause of sepsis in the critically ill patient. *Virulence* 5: 161–169.

DeMattei, R.C., Feigelson, R.S. and Weber, P.C. (1992). Factors affecting the morphology of isocitrate lyase crystals. *Journal of Crystal Growth* 122: 152–160.

Denning, D.W., Kneale, M., Sobel, J.D., Rautemaa-Richardson, R. (2018). Global burden of recurrent vulvovaginal candidiasis: a systematic review. *The Lancet Infectious Diseases* 18: e339–347.

Derengowski, L.S., Tavares, A.H., Silva, S., Procópio, L.S., Felipe, M.S., Silva-Pereira, I. (2008). Upregulation of glyoxylate cycle genes upon *Paracoccidioides brasiliensis* internalization by murine macrophages and *in vitro* nutritional stress condition. *Medical Mycology* 46: 125–134.

Desai, J.V., Bruno, V.M., Ganguly, S., Stamper, R.J., Mitchell, K.F., Solis, N., Hill, E.M., Xu, W., Filler, S.G., Andes, D.R., Fanning, S., Lanni, F., Mitchell, A. P. (2013). Regulatory role of glycerol in *Candida albicans* biofilm formation. *mBio* 4: e00637–e12.

Dexter, J.P., Xu, P., Gunawardena, J., McClean, M.N. (2015). Robust network structure of the Sln1-Ypd1-Ssk1 three-component phospho-relay prevents unintended activation of the HOG MAPK pathway in *Saccharomyces cerevisiae*. *BMC Systems Biology* 9:17.

Donlan, R.M. and Costerton, J.W. (2002). Biofilms: survival mechanisms of clinically relevant microorganisms. *Clinical Microbiology Reviews* 15: 167–193.

Du, H., Zheng, Q., Bing, J., Bennett, R.J., Huang, G. (2018). A coupled process of same- and opposite-sex mating generates polyploidy and genetic diversity in *Candida tropicalis*. *PLOS Genetics* 14: e1007377.

Duggan, S., Essig, F., Hünniger, K., Mokhtari, Z., Bauer, L., Lehnert, T., Brandes, S., Häder, A., Jacobsen, I.D., Martin, R., Figge, M.T., Kurzai, O. (2015). Neutrophil activation by *Candida glabrata* but not *Candida albicans* promotes fungal uptake by monocytes. *Cell Microbiology* 17: 1259–1276.

Dujon, B., Sherman, D., Fischer, G., Durrens, P., Casaregola, S., Lafontaine, I., De Montigny, J., Marck, C., Neuveglise, C., Talla, E., Goffard, N., Frangeul, L., Aigle, M., Anthouard, V., Babour, A., Barbe, V., Barnay, S., Blanchin, S., Beckerich, J.M., Beyne, E., Bleykasten, C., Boisramé, A., Boyer, J., Cattolico, L., Confanioleri, F., De Daruvar, A., Despons, L., Fabre, E., Fairhead, C., Ferry-Dumazet, H., Groppi, A., Hantraye, F., Hennequin, C., Jauniaux, N., Joyet, P., Kachouri, R., Kerrest, A., Koszul, R., Lemaire, M., Lesur, I., Ma, L., Muller, H., Nicaud, J.M., Nikolski, M., Oztas, S., Ozier-Kalogeropoulos, O., Pellenz, S., Potier, S., Richard, G.F., Straub, M.L., Suleau, A., Swennen, D., Tekaia, F., Wésolowski-Louvel, M., Westhof, E., Wirth, B., Zeniou-Meyer, M., Zivanovic, I., Bolotin-Fukuhara, M., Thierry, A., Bouchier, C., Caudron, B., Scarpelli, C., Gaillardin, C., Weissenbach, J., Wincker, P. & Souciet, J.L. (2004). Genome evolution in yeasts. *Nature* 430: 35–44.

Dunn, M. F., Ramírez-Trujillo, J. A. and Hernández-Lucas, I. (2009). Major roles of isocitrate lyase and malate synthase in bacterial and fungal pathogenesis. *Microbiology* 155: 3166–3175.

Eastmond, P.J., Germain, V., Lange, P.R., Bryce, J.H., Smith, S.M., Graham, I.A. (2000). Postgerminative growth and lipid catabolism in oilseeds lacking the glyoxylate cycle. *Proceedings of the National Academy of Sciences of the United States of America* 97: 5669–5674.

Ebel, F., Schwienbacher, M., Beyer, J., Heesemann, J., Brakhage, A.A., Brock, M. (2006). Analysis of the regulation, expression, and localisation of the isocitrate lyase from *Aspergillus fumigatus*, a potential target for antifungal drug development. *Fungal Genetics and Biology* 43: 476–489.

Ehrström, S., Yu, A. and Rylander, E. (2006). Glucose in vaginal secretions before and after oral glucose tolerance testing in women with and without recurrent vulvovaginal candidiasis. *Obstetrics and Gynecology* 108: 1432–1437.

Ene, I.V. and Bennett, R.J. (2014). The cryptic sexual strategies of human fungal pathogens. *Nature Reviews Microbiology* 12: 239–251.

Ene, I.V., Adya, A.K., Wehmeier, S., Brand, A.C., MacCallum, D.M., Gow, N.A., Brown, A.J. (2012a). Host carbon sources modulate cell wall architecture, drug resistance and virulence in a fungal pathogen. *Cellular Microbiology* 14: 1319–1335.

Ene, I.V., Brunke, S., Brown, A.J., Hube, B. (2014). Metabolism in fungal pathogenesis. *Cold Spring Harbor Perspectives in Medicine* 4: a019695.

Ene, I.V., Cheng, S.C., Netea, M.G., Brown, A.J. (2013). Growth of *Candida albicans* cells on the physiologically relevant carbon source lactate affects their recognition and phagocytosis by immune cells. *Infection and Immunity* 81: 238–248.

Ene, I.V., Heilmann, C.J., Sorgo, A.G., Walker, L.A., de Koster, C.G., Munro, C.A., Klis, F.M., Brown, A.J. (2012b). Carbon source-induced reprogramming of the cell wall proteome and secretome modulates the adherence and drug resistance of the fungal pathogen *Candida albicans*. *Proteomics* 12: 3164–3179.

Ene, I.V., Walker, L.A., Schiavone, M., Lee, K.K., Martin-Yken, H., Dague, E., Gow, N.A., Munro, C.A., Brown, A.J. (2015). Cell wall remodelling enzymes modulate fungal cell wall elasticity and osmotic stress resistance. *mBio* 6: e00986.

Eschrich, D., Kötter, P. and Entian, K.D. (2002). Gluconeogenesis in *Candida albicans*. *FEMS Yeast Research* 2: 315–325.

Fairlamb, A.H., Gow, N.A., Matthews, K.R., Waters, A.P. (2016). Drug resistance in eukaryotic microorganisms. *Nature Microbiology* 1: 16092.

Falcone, M., Concia, E., Iori, I., Lo Cascio, G., Mazzone, A., Pea, F., Violi, F., Venditti, M. (2014). Identification and management of invasive mycoses in internal medicine: a road-map for physicians. *Internal and Emergency Medicine* 9: 501–511.

Fan, W., Kraus, P.R., Boily, M.J., Heitman, J. (2005). *Cryptococcus neoformans* gene expression during murine macrophage infection. *Eukaryotic Cell* 4: 1420–1433.

Fang, F.C., Libby, S.J., Castor, M.E., Fung, A.M. (2005). Isocitrate lyase (AceA) is required for *Salmonella* persistence but not for acute lethal infection in mice. *Infection and Immunity* 73: 2547–2549.

Fernández-Arenas, E., Cabezón, V., Bermejo, C., Arroyo, J., Nombela, C., Diez-Orejas, R., Gil, C. (2007). Integrated proteomics and genomics strategies bring new insight into *Candida albicans* response upon macrophage interaction. *Molecular and Cellular Proteomics* 6: 460–478.

Fidel, P.L. Jr., Vazquez, J.A. and Sobel, J.D. (1999). *Candida glabrata*: review of epidemiology, pathogenesis, and clinical disease with comparison to *Candida albicans. Clinical Microbiology Reviews* 12: 80–96.

Fisher, J.F., Kavanagh, K., Sobel, J.D., Kauffman, C.A., Newman, C.A. (2011). *Candida* urinary tract infection: pathogenesis. *Clinical Infectious Diseases* 52: 437–451.

Fitzpatrick, D.A., Logue, M.E., Stajich, J.E., Butler, G. (2006). A fungal phylogeny based on 42 complete genomes derived from supertree and combined gene analysis. *BMC Evolutionary Biology* 22: 99.

Fradin, C., Kretschmar, M., Nichterlein, T., Gaillardin, C., d'Enfert, C., Hube, B. (2003). Stage-specific gene expression of *Candida albicans* in human blood. *Molecular Microbiology* 47: 1523–1543.

Fujita, S.I., Senda, Y., Nakaguchi, S., Hashimoto, T. (2001). Multiplex PCR using internal transcribed spacer 1 and 2 regions for rapid detection and identification of yeast strains. *Journal of Clinical Microbiology* 39: 3617–3622.

Fukuda, Y., Tsai, H.F., Myers, T.G., Bennett, J.E. (2013). Transcriptional profiling of *Candida glabrata* during phagocytosis by neutrophils and in the infected mouse spleen. *Infection and Immunity* 81: 1325–1333.

Garcia-Cuesta, C., Sarrion-Pérez, M.G. and Bagán, J.V. (2014). Current treatment of oral candidiasis: a literature review. *Journal of Clinical and Experimental Dentistry* 6: e576–582.

Garcia-Effron, G., Lee, S., Park, S., Cleary, J.D., Perlin, D.S. (2009). Effect of *Candida glabrata FKS1* and *FKS2* mutations on echinocandin sensitivity and kinetics of 1,3-beta-D-glucan synthase: implication for the existing susceptibility breakpoint. *Antimicrobial Agents and Chemotherapy* 53: 3690–3699.

Garreau, H., Hasan, R.N., Renault, G., Estruch, F., Boy-Marcotte, E., Jacquet, M. (2000). Hyperphosphorylation of Msn2p and Msn4p in response to heat shock and the diauxic shift is inhibited by cAMP in *Saccharomyces cerevisiae*. *Microbiology* 146: 2113–2120.

Gasch, A.P., Spellman, P.T., Kao, C.M., Carmel-Harel, O., Eisen, M.B., Storz, G., Botstein, D., Brown, P.O. (2000). Genomic expression programs in the response of yeast cells to environmental changes. *Molecular Biology of the* Cell 11: 4241–4257.

Gilbert, A.S., Wheeler, R.T. and May, R.C. (2015). Fungal pathogens: survival and replication within macrophages. *Cold Spring Harbor Perspectives in Medicine* 5: a019661.

Goodwin, S., McPherson, J.D. and McCombie, W.R. (2016). Coming of age: ten years of next-generation sequencing technologies. *Nature Reviews Genetics* 17: 333–351.

Gorner, W., Durchschlag, E., Martinez-Pastor, M.T., Estruch, F., Ammerer, G., Hamilton, B., Ruis, Helmut., Schüller, C. (1998). Nuclear localization of the C_2H_2 zinc finger protein Msn2p is regulated by stress and protein kinase A activity. *Genes and Developments* 12: 586–597.

Goswami, D., Goswami, R., Banerjee, U., Dadhwal, V., Miglani, S., Lattif, A.A., Kochupillai, N. (2006). Pattern of *Candida* species isolated from patients with diabetes mellitus and vulvovaginal candidiasis and their response to single dose oral fluconazole therapy. *The Journal of Infection* 52: 111–117.

Hadley, S., Lee, W.W., Ruthazer, R., Nasraway, S.A. Jr. (2002). Candidemia as a cause of septic shock and multiple organ failure in non-immunocompromised patients. *Critical Care Medicine* 30: 1808–1814.

Harriott, M.M., Lilly, E.A., Rodriguez, T.E., Fidel, P.L., Noverr, M.C. (2010). *Candida albicans* forms biofilms on the vaginal mucosa. *Microbiology* 156: 3635–3644.

Havlickova, B., Czaika, V.A. and Friedrich, M. (2008). Epidemiological trends in skin mycoses worldwide. Mycoses 51: 2–5.

Heymann, P., Gerads, M., Schaller, M., Dromer, F., Winkelmann, G., Ernst, J.F. (2002). The siderophore iron transporter of *Candida albicans* (Sit1p/Arn1p) mediates uptake of ferrichrome-type siderophores and is required for epithelial invasion. *Infection and Immunity* 70: 5246–5255.

Hiesinger, M., Roth, S., Meissner, E., Schüller, H.J. (2001). Contribution of Cat8 and Sip4 to the transcriptional activation of yeast gluconeogenic genes by carbon source-responsive elements. *Current Genetics* 39: 68–76.

Hinnebusch, A.G. (2005). Translational regulation of *GCN4* and the general amino acid control of yeast. *Annual Review of Microbiology* 59: 407–450.

Hohmann, S. (2002). Osmotic stress signalling and osmoadaptation in yeasts. *Microbiology and Molecular Biology Reviews* 66: 300–372.

Honer Zu Bentrup, K., Miczak, A., Swenson, D. L., Russell, D. G. (1999). Characterization of activity and expression of isocitrate lyase in *Mycobacterium avium* and *Mycobacterium tuberculosis*. *Journal of Bacteriology* 181: 7161–7167.

Hood, M.I. and Skaar, E.P. (2012). Nutritional immunity: transition metals at the pathogen-host interface. *Nature Reviews Microbiology* 10: 525–537.

Huang, D.W., Sherman, B.T. and Lempicki, R.A. (2008). Systematic and integrative analysis of large gene lists using DAVID bioinformatics resources. *Nature Protocols* 4: 44–57.

Huang, G. (2012). Regulation of phenotypic transitions in the fungal pathogen *Candida albicans*. *Virulence* 3: 251–261.

Hull, C.M. and Johnson, A.D. (1999). Identification of a mating type-like locus in the asexual pathogenic yeast *Candida albicans*. Science 285: 1271-1275.

Hull, C.M., Bader, O., Parker, J.E., Weig, M., Gross, U., Warrilow, A.G., Kelly, D.E., Kelly, S.L. (2012). Two clinical isolates of *Candida glabrata* exhibiting reduced sensitivity to amphotericin B both harbor mutations in ERG2. *Antimicrobial Agents and Chemotherapy* 56: 6417–6421.

Idnurm, A. and Howlett, B. J. (2002). Isocitrate lyase is essential for pathogenicity of the fungus *Leptosphaeria maculans* to canola (*Brassica napus*). *Eukaryotic Cell* 1: 719–724.

Iraqui, I., Garcia-Sanchez, S., Aubert, S., Dromer, F., Ghigo, J.M., d'Enfert, C., Janbon, G. (2005). The Yak1p kinase controls expression of adhesins and biofilm formation in *Candida glabrata* in a Sir4p-dependent pathway. *Molecular Microbiology* 55: 1259–1271.

Ishola, O.A., Ting, S.Y., Tabana, Y.M., Ahmed, M.A., Yunus, M.A., Mohamed, R., Than, L.T., Sandai, D. (2016). The role of isocitrate lyase (ICL1) in the metabolic adaptation of *Candida albicans* biofilms. *Jundishapur Journal of Microbiology* 9: e38031.

Jacobsen, I.D., Brunke, S., Seider, K., Schwarzmüller, T., Firon, A., d'Enfért, C., Kuchler, K., Hube, B. (2010). *Candida glabrata* persistence in mice does not depend on host immunosuppression and is unaffected by fungal amino acid auxotrophy. *Infection and Immunity* 78: 1066–1077.

Jain, R., Valiante, V., Remme, N., Docimo, T., Heinekamp, T., Hertweck, C., Gershenzon, J., Haas, H., Brakhage, A.A. (2011). The MAP kinase MpkA controls cell wall integrity, oxidative stress response, gliotoxin production and iron adaptation in *Aspergillus fumigatus*. *Molecular microbiology* 82: 39–53.

Jeffery-Smith, A., Taori, S.K., Schelenz, S., Jeffery, K., Johnson, E.M., Borman, A., *Candida auris* Incident Management Team, Manuel, R., Brown, C.S. (2017). *Candida auris*: a review of the literature. *Clinical Microbiology Reviews* 31: e00029–17.

Kasper, L., Seider, K. and Hube, B. (2015). Intracellular survival of *Candida glabrata* in macrophages: immune evasion and persistence. *FEMS Yeast Research* 15: fov042.

Kasper, L., Seider, K., Gerwien, F., Allert, S., Brunke, S., Schwarzmüller, T., Ames, L., Zubiria-Barrera, C., Mansour, M.K., Becken, U., Barz, D., Vyas, J.M., Reiling, N., Haas, A., Haynes, K., Kuchler, K., Hube, B. (2014). Identification of *Candida glabrata* genes involved in pH modulation and modification of the phagosomal environment in macrophages. *PLOS One* 9: e96015.

Kastora, S.L., Herrero-de-Dios, C., Avelar, G.M., Munro, C.A., Brown, A.J.P. (2017). Sfp1 and Rtg3 reciprocally modulate carbon source-conditional stress adaptation in the pathogenic yeast *Candida albicans*. *Molecular Microbiology* 105: 620–636.

Kaur, R., Domergue, R., Zupancic, M.L., Cormack, B.P. (2005). A yeast by any other name: *Candida glabrata* and its interaction with the host. *Current Opinion in Microbiology* 8: 378–384.

Kaur, R., Ma, B. and Cormack, B. P. (2007). A family of glycosylphosphatidylinositol-linked aspartyl proteases is required for virulence of *Candida glabrata*. *Proceedings of the National Academy of Sciences of the United States of America* 104: 7628–7633.

Ketela, T., Green, R., Bussey, H. (1999). *Saccharomyces cerevisiae* mid2p is a potential cell wall stress sensor and upstream activator of the *PKC1-MPK1* cell integrity pathway. *Journal of Bacteriology* 181: 3330-3340.

Klimova, N., Yeung, R., Kachurina, N., Turcotte, B. (2014). Phenotypic analysis of a family of transcriptional regulators, the zinc cluster proteins, in the human fungal pathogen *Candida glabrata*. *G3: Genes, Genomes, Genetics* 4: 931–940.

Klotz, S.A., Chasin, B.S., Powell, B., Gaur, N.K., Lipke, P.N. (2007) Polymicrobial bloodstream infections involving *Candida* species: analysis of patients and review of the literature. *Diagnostic Microbiology and Infectious Disease* 59: 401–406.

Knowles, S.E., Jarrett, I.G., Filsell, O.H., Ballard, F.J. (1974). Production and utilization of acetate in mammals. *The Biochemical Journal* 142: 401–411.

Ko, Y.H. and McFadden, B.A. (1990). Alkylation of isocitrate lyase from *Escherichia coli* by 3-bromopyruvate. *Archives of Biochemistry and Biophysics* 278: 373–380.

Köhler, J.R., Casadevall, A. and Perfect, J. (2014). The spectrum of fungi that infects humans. *Cold Spring Harbor Perspectives in Medicine* 5: a019273.

Kołaczkowska, A. and Kołaczkowski, M. (2016). Drug resistance mechanisms and their regulation in non-*albicans Candida* species. *Journal of Antimicrobial Chemotherapy* 71: 1438–1450.

Kondrashov, F.A., Koonin, E.V., Morgunov, I.G., Finogenova, T.V., Kondrashova, M.N. (2006). Evolution of glyoxylate cycle enzymes in Metazoa: evidence of multiple horizontal transfer events and pseudogene formation. *Biology Direct* 1: 31.

Kornberg, H.L. (1966). The role and control of the glyoxylate cycle in *Escherichia coli*. *Biochemical Journal* 99: 1–11.

Kruppa, M., Greene, R.R., Noss, I., Lowman, D.W., Williams, D.L. (2011). *Candida albicans* increases cell wall mannoprotein, but not mannan, in response to blood, serum and cultivation at physiological temperature. *Glycobiology* 21: 1173–1180.

Kucharíková, S., Neirinck, B., Sharma, N., Vleugels, J., Lagrou, K., Van Dijck, P. (2015). *In vivo Candida glabrata* biofilm development on foreign bodies in a rat subcutaneous model. *Journal of Antimicrobial Chemotherapy* 70: 846–856.

Kühbacher, A., Burger-Kentischer, A. and Rupp, S. (2017). Interaction of *Candida* species with the skin. *Microorganisms* 5: E32.

Kullberg, B.J. and Arendrup, M.C. (2015). Invasive candidiasis. *The New England Journal of Medicine* 373: 1445–1456.

Kunze, M. and Hartig, A. (2013). Permeability of the peroxisomal membrane: lessons from the glyoxylate cycle. *Frontiers in Physiology* 4: 204.

Kunze, M., Pracharoenwattana, I., Smith, S.M., Hartig, A. (2006). A central role for the peroxisomal membrane in glyoxylate cycle function. *Biochimica et Biophysica Acta* 1763: 1441–1452.

Kuo, M.H., Nadeau, E.T., Grayhack, E.J. (1997). Multiple phosphorylated forms of the *Saccharomyces cerevisiae* Mcm1 protein include an isoform induced in response to high salt concentrations. *Molecular and Cellular Biology* 17: 819-832.

Laity, J.H., Lee, B.M. and Wright, P.E. (2001). Zinc finger proteins: new insights into structural and functional diversity. *Current Opinion in Structural Biology* 11: 39–46.

Lamoth, F., Lockhart, S.R., Berkow, E.L., Calandra, T. (2018). Changes in the epidemiological landscape of invasive candidiasis. *Journal of Antimicrobial Chemotherapy* 73: i4–i13.

Larone, D. (2002). Medically important fungi: A guide to identification. Washington, DC: ASM Press.

Latosinska, A., Vougas, K., Makridakis, M., Klein, J., Mullen, W., Abbas, M., Stravodimos, K., Katafigiotis, I., Merseburger, A.S., Zoidakis, J., Mischak, H., Vlahou, A., Jankowski, V. (2015). Comparative analysis of label-free and 8-Plex iTRAQ approach for quantitative tissue proteomic analysis. *PLOS One* 10: e0137048.

Lau, B.Y., Clerens, S., Morton, J.D., Dyer, J.M., Deb-Choudhury, S., Ramli, U. (2016). Application of a mass spectrometric approach to detect the presence of fatty acid biosynthetic phosphopeptides. *The Protein Journal* 35: 163–170.

Lee, B.N. and Elion, E,A. (1999). The MAPKKK Ste11 regulates vegetative growth through a kinase cascade of shared signaling components. *Proceedings of the National Academy of Sciences of the United States of America* 96:12679-12684.

Lee, I., Fishman, N.O., Zaoutis, T.E., Morales, K.H., Weiner, M.G., Synnestvedt, M., Nachamkin, I., Lautenbach, E. (2009). Risk factors for fluconazole-resistant *Candida glabrata* bloodstream infections. *Archives of Internal Medicine* 169: 379–383.

Lee, K.K., Maccallum, D.M., Jacobsen, M.D., Walker, L.A., Odds, F.C., Gow, N.A., Munro, C.A. (2012). Elevated cell wall chitin in *Candida albicans* confers echinocandin resistance *in vivo*. *Antimicrobial Agents and Chemotherapy* 56: 208–217.

Lee, S.H., Won, T.H., Kim, H., Ahn, C.H., Shin, J., Oh, K.B. (2014). Suvanine sesterterpenes from a tropical sponge *Coscinoderma* sp. inhibit isocitrate lyase in the glyoxylate cycle. *Marine Drugs* 12: 5148–5159.

Lee, Y.V., Wahab, H.A. and Choong, Y.S. (2015). Potential inhibitors for isocitrate lyase of *Mycobacterium tuberculosis* and non-*M. tuberculosis*: a summary. *Biomed Research International* 2015: 895453.

Lima, P., Casaletti, L., Bailão, A.M., de Vasconcelos, A.T., Fernandes, G., Soares, C.M. (2014). Transcriptional and proteomic responses to carbon starvation in *Paracoccidioides*. *PLOS Neglected Tropical Diseases* 8: e2855.

Lindsey, T.L., Hagins, J.M., Sokol, P.A., Silo-Suh, L.A. (2008). Virulence determinants from a cystic fibrosis isolate of *Pseudomonas aeruginosa* include isocitrate lyase. *Microbiology* 154: 1616–1627.

Lodi, T. and Ferrero, I. (1993). Isolation of the *DLD* gene of *Saccharomyces cerevisiae* encoding the mitochondrial enzyme D-lactate ferricytochrome c oxidoreductase. *Molecular and General Genetics* 238: 315–324.

Lodi, T., Diffels, J., Goffeau, A., Baret, P.V. (2007). Evolution of the carboxylate Jen transporters in fungi. *FEMS Yeast Research* 7: 646–656.

Lorenz, M.C. and Fink, G.R. (2001). The glyoxylate cycle is required for fungal virulence. *Nature* 412(6842): 83–86.

Lorenz, M.C. and Fink, G.R. (2002). Life and death in a macrophage: role of the glyoxylate cycle in virulence. *Eukaryotic cell* 1: 657–662.

Lorenz, M.C., Bender, J.A. and Fink, G.R. (2004). Transcriptional response of *Candida albicans* upon internalization by macrophages. *Eukaryotic Cell* 3: 1076–1087.

Lowman, D.W., Ensley, H.E., Greene, R.R., Knagge, K.J., Williams, D.L., Kruppa, M.D. (2011). Mannan structural complexity is decreased when *Candida albicans* is cultivated in blood or serum at physiological temperature. *Carbohydrate Research* 346: 2752–2759.

Lyu, X., Zhao, C., Yan, Z.M., Hua, H. (2016). Efficacy of nystatin for the treatment of oral candidiasis: A systematic review and meta-analysis. *Drug Design, Development and Therapy* 16: 1161–1171.

MacPherson, S., Larochelle, M. and Turcotte, B. (2006). A fungal family of transcriptional regulators: the zinc cluster proteins. *Microbiology and Molecular Biology Reviews* 70: 583–604.

Magee, B.B. and Magee, P.T. (2000). Induction of mating in *Candida albicans* by construction of MTLa and MTLalpha strains. *Science* 289: 310–313.

Maicas, S., Moreno, I., Nieto, A., Gómez, M., Sentandreu, R., Valentín, E. (2005). *In silico* analysis for transcription factors with Zn (II)(2)C(6) binuclear cluster DNA-binding domains in *Candida albicans*. *Comparative and Functional Genomics* 6: 345–356.

Martchenko, M., Levitin, A., Hogues, H., Nantel, A., Whiteway, M. (2007). Transcriptional rewiring of fungal galactose-metabolism circuitry. *Current Biology* 17: 1007–1013.

Mayer, F.L., Wilson, D. and Hube, B. (2013). *Candida albicans* pathogenicity mechanisms. *Virulence* 4: 119–128.

McFadden, B.A. and Purohit, S. (1977). Itaconate, an isocitrate lyase-directed inhibitor in *Pseudomonas indigofera*. *Journal of Bacteriology* 31: 136–144.

Messer, S.A., Jones, R.N. and Fritsche, T.R. (2006). International surveillance of *Candida* spp. and *Aspergillus* spp.: report from the SENTRY Antimicrobial Surveillance Program (2003). *Journal of Clinical Microbiology* 44: 1782–1787.

Messer, S.A., Moet, G.J., Kirby, J.T., Jones, R.N. (2009). Activity of contemporary antifungal agents, including the novel echinocandin anidulafungin, tested against *Candida* spp., *Cryptococcus* spp., and *Aspergillus* spp.: report from the SENTRY Antimicrobial Surveillance Program (2006 to 2007). *Journal of Clinical Microbiology* 47: 1942–1946.

Miller, M.G. and Johnson, A.D. (2002). White-opaque switching in *Candida albicans* is controlled by mating-type locus homeodomain proteins and allows efficient mating. *Cell* 110: 293–302.

Miramón, P. and Lorenz, M.C. (2017). A feast for *Candida*: Metabolic plasticity confers an edge for virulence. *PLOS Pathogens* 13(2): e1006144.

Miyazaki, T., Inamine, T., Yamauchi, S., Nagayoshi, Y., Saijo, T., Izumikawa, K., Seki, M., Kakeya, H., Yamamoto, Y., Yanagihara, K., Miyazaki, Y., Kohno, S. (2010). Role of the Slt2 mitogen-activated protein kinase pathway in cell wall integrity and virulence in *Candida glabrata*. *FEMS Yeast Research* 10: 343-352.

Mohd Tap, R., Lim, T.C., Kamarudin, N.A., Ginsapu, S.J., Abd Razak, M.F., Ahmad, N., Amran, F. (2018). A fatal case of *Candida auris* and *Candida tropicalis* candidemia in neutropenic patient. *Mycopathologia* 183: 559–564.

Monge, R.A., Román, E., Nombela, C., Pla, J. (2006). The MAP kinase signal transduction network in *Candida albicans*. *Microbiology* 152: 905–912.

Moran, C., Grussemeyer, C.A., Spalding, J.R., Benjamin, D.K. Jr, Reed, S.D. (2010). Comparison of costs, length of stay, and mortality associated with *Candida glabrata* and *Candida albicans* bloodstream infections. *American Journal of Infection Control* 38: 78–80.

Morio, F., Loge, C., Besse, B., Hennequin, C., Le Pape, P. (2010). Screening for amino acid substitutions in the *Candida albicans* Erg11 protein of azole-susceptible and azole-resistant clinical isolates: new substitutions and a review of the literature. *Diagnostic Microbiology and Infectious Disease* 66: 373–384.

Morschhäuser, J. (2010a). Regulation of white-opaque switching in *Candida albicans*. *Medical Microbiology and Immunology* 199: 165–172.

Morschhäuser, J. (2010b). Regulation of multidrug resistance in pathogenic fungi. *Fungal Genetics and Biology* 47: 94–106.

Mota, S., Alves, R., Carneiro, C., Silva, S., Brown, A.J., Istel, F., Kuchler, K., Sampaio, P., Casal, M., Henriques, M., Paiva, S. (2015). *Candida glabrata* susceptibility to antifungals and phagocytosis is modulated by acetate. *Frontiers in Microbiology* 6: 919.

Moyes, D.L., Wilson, D., Richardson, J.P., Mogavero, S., Tang, S.X., Wernecke, J., Höfs, S., Gratacap, R.L., Robbins, J., Runglall, M., Murciano, C., Blagojevic, M., Thavaraj, S., Förster, T.M., Hebecker, B., Kasper, L., Vizcay, G., Iancu, S.I., Kichik, N., Häder, A., Kurzai, O., Luo, T., Krüger, T., Kniemeyer, O., Cota, E., Bader, O., Wheeler, R.T., Gutsmann, T., Hube, B., Naglik, J.R. (2016). Candidalysin is a fungal peptide toxin critical for mucosal infection. *Nature* 532: 64–68.

Mühlhausen, S. and Kollmar, M. (2014). Molecular phylogeny of sequenced *Saccharomycetes* reveals polyphyly of the alternative yeast codon usage. *Genome Biology and Evolution* 6: 3222–3237.

Muller, H., Hennequin, C., Gallaud, J., Dujon, B., Fairhead, C. (2008). The asexual yeast *Candida glabrata* maintains distinct a and alpha haploid mating types. *Eukaryotic Cell* 7: 848–858.

Munoz-Duarte, A.R., Castrejon-Jimenez, N.S., Baltierra-Uribe, S.L., Perez-Rangel, S.J., Carapia-Minero, N., Castaneda-Sanchez, J.I., Luna-Herrera, J., Lopez-Santiago, R., Rodriguez-Tovar, A.V., Garcia-Perez, B.E. (2016). *Candida glabrata* survives and replicates in human osteoblasts. *Pathogens and Disease* 74: ftw030.

Muñoz-Elías, E. J. and McKinney, J. D. (2005). *Mycobacterium tuberculosis* isocitrate lyases 1 and 2 are jointly required for *in vivo* growth and virulence. *Nature Medicine* 11: 638–644.

Munro, C.A., Selvaggini, S., de Bruijn, I., Walker, L., Lenardon, M.D., Gerssen, B., Milne, S., Brown, A. J., Gow, N. A. (2007). The PKC, HOG and Ca2+ signalling pathways co-ordinately regulate chitin synthesis in *Candida albicans*. *Molecular Microbiology* 63: 1399–1413.

Nagalakshmi, U., Wang, Z., Waern, K., Shou, C., Raha, D., Gerstein, M., Snyder, M. (2008). The transcriptional landscape of the yeast genome defined by RNA sequencing. *Science* 320: 1344–1349.

Nagayoshi, Y., Miyazaki, T., Minematsu, A., Yamauchi, S., Takazono, T., Nakamura, S., Imamura, Y., Izumikawa, K., Kakeya, H., Yanagihara, K., Kohno, S. (2014). Contribution of the Slt2-regulated transcription factors to echinocandin tolerance in *Candida glabrata*. *FEMS Yeast Research* 14: 1128-1131.

Neilson, K.A., Ali, N.A., Muralidharan, S., Mirzaei, M., Mariani, M., Assadourian, G., Lee, A., van Sluyter, S.C., Haynes, P.A. (2011). Less label, more free: approaches in label-free quantitative mass spectrometry. *Proteomics* 11: 535–553.

Nevitt, T. and Thiele, D.J. (2011). Host iron withholding demands siderophore utilization for *Candida glabrata* to survive macrophage killing. *PLOS Pathogens* 7: e1001322.

Ng, T.S., Chew, S.Y., Rangasamy, P., Mohd Desa, M.N., Sandai, D., Chong, P.P., Than, L.T.L (2015). *SNF3* as high affinity glucose sensor and its function in supporting the viability of *Candida glabrata* under glucose-limited environment. *Frontiers in Microbiology* 6: 1334.

Nielsen, K. and Heitman, J. (2007). Sex and virulence of human pathogenic fungi. *Advances in Genetics* 57: 143–173.

Niimi, K., Maki, K., Ikeda, F., Holmes, A.R., Lamping, E., Niimi, M., Monk, B.C., Cannon, R.D. (2006). Overexpression of *Candida albicans CDR1*, *CDR2*, or *MDR1* does not produce significant changes in echinocandin susceptibility. *Antimicrobial Agents and Chemotherapy* 50: 1148–1155.

Nikolaou, E., Agrafioti, I., Stumpf, M., Quinn, J., Stansfield, I., Brown, A.J. (2009). Phylogenetic diversity of stress signalling pathways in fungi. *BMC Evolutionary Biology* 21: 44.

Noble, S.M. and Johnson, A.D. (2005). Strains and strategies for large-scale gene deletion studies of the diploid human fungal pathogen *Candida albicans*. *Eukaryotic Cell* 4: 298–309.

O'Brien, H.E., Parrent, J.L., Jackson, J.A., Moncalvo, J., Vilgalys, R. (2005). Fungal community analysis by large-scale sequencing of environmental samples. *Applied and Environmental Microbiology* 71: 5544–5550.

Odds, F.C. and Bernaerts, R. (1994). CHROMagar *Candida*, a new differential isolation medium for presumptive identification of clinically important *Candida* species. *Journal of Clinical Microbiology* 32: 1923–1929.

Okawa, Y. and Goto, K. (2006). Antigenicity of cell wall mannans of *Candida albicans* and *Candida stellatoidea* cultured at high temperatures in BACTEC medium. *Biological and Pharmaceutical Bulletin* 29: 1723–1727.

Orlean, P. (2012). Architecture and biosynthesis of the *Saccharomyces cerevisiae* cell wall. *Genetics* 192: 775–818.

Paiva, S., Devaux, F., Barbosa, S., Jacq, C., Casal, M (2004). Ady2p is essential for the acetate permease activity in the yeast *Saccharomyces cerevisiae*. *Yeast* 21: 201–210.

Papon, N., Courdavault, V., Clastre, M., Bennett, R.J. (2013). Emerging and emerged pathogenic *Candida* species: beyond the *Candida albicans* paradigm. *PLOS Pathogens* 9: e1003550.

Pappas, P.G., Kauffman, C.A., Andes, D.R., Clancy, C.J., Marr, K.A., Ostrosky-Zeichner, L., Reboli, A.C., Schuster, M.G., Vazquez, J.A., Walsh, T.J., Zaoutis, T.E., Sobel, J.D. (2016). Clinical practice guideline for the management of candidiasis: 2016 update by the Infectious Diseases Society of America. *Clinical Infectious Diseases* 62: e1–50.

Pappas, P.G., Lionakis, M.S., Arendrup, M.C., Ostrosky-Zeichner, L., Kullberg, B.J. (2018). Invasive candidiasis. *Nature Reviews Disease Primers* 11: 18026.

Pemmaraju, S.C., Pruthi, P.A., Prasad, R., Pruthi, V. (2016). Modulation of *Candida albicans* biofilm by different carbon sources. *Mycopathologia* 181: 341–352.

Perlin, D.S. (2015). Echinocandin Resistance in *Candida*. *Clinical Infectious Diseases* 61: S612–S617.

Perlin, D.S., Rautemaa-Richardson, R., Alastruey-Izquierdo, A. (2017). The global problem of antifungal resistance: prevalence, mechanisms, and management. *The Lancet. Infectious Diseases* 17: e383–e392.

Pfaller, M.A. and Diekema, D.J. (2007). Epidemiology of invasive candidiasis: a persistent public health problem. *Clinical Microbiology Reviews* 20: 133–163.

Pfaller, M.A., Andes, D.R., Diekema, D.J., Horn, D.L., Reboli, A.C., Rotstein, C., Franks, B., Azie, N.E. (2014). Epidemiology and outcomes of invasive candidiasis due to non-*albicans* species of *Candida* in 2,496 patients: data from the Prospective Antifungal Therapy (PATH) registry 2004–2008. *PLOS One* 9: e101510.

Pfaller, M.A., Castanheira, M., Lockhart, S.R., Ahlquist, A.M., Messer, S.A., Jones, R.N. (2012). Frequency of decreased susceptibility and resistance to echinocandins among fluconazole-resistant bloodstream isolates of *Candida glabrata*. *Journal of Clinical Microbiology* 50: 1199–1203.

Pfaller, M.A., Diekema, D.J., Gibbs, D.L., Newell, V.A., Ellis, D., Tullio, V., Rodloff, A., Fu, W., Ling, T.A. (2010). Results from the ARTEMIS DISK Global Antifungal Surveillance Study, 1997 to 2007: a 10.5-year analysis of susceptibilities of *Candida* Species to fluconazole and voriconazole as determined by CLSI standardized disk diffusion. *Journal of Clinical Microbiology* 48: 1366–1377.

Piekarska, K., Hardy, G., Mol, E., van den Burg, J., Strijbis, K., van Roermund, C., van den Berg, M., Distel, B. (2008). The activity of the glyoxylate cycle in peroxisomes of *Candida albicans* depends on a functional beta-oxidation pathway: evidence for reduced metabolite transport across the peroxisomal membrane. *Microbiology* 54: 3061–3072.

Piekarska, K., Mol, E., van den Berg, M,. Hardy, G., van den Burg, J., van Roermund, C., MacCallum, D., Odds, F., Distel, B. (2006). Peroxisomal fatty acid beta-oxidation is not essential for virulence of *Candida albicans*. *Eukaryotic Cell* 5: 1847–1856.

Pierce, C.G., Uppuluri, P., Tristan, A.R., Wormley, F.L.Jr, Mowat, E., Ramage, G., Lopez-Ribot, J.L. (2008). A simple and reproducible 96-well plate-based method for the formation of fungal biofilms and its application to antifungal susceptibility testing. *Nature Protocols* 3: 1494–1500.

Potrykus, J., Ballou, E.R., Childers, D.S., Brown, A.J. (2014). Conflicting interests in the pathogen-host tug of war: fungal micronutrient scavenging versus mammalian nutritional immunity. *PLOS Pathogens* 10: e1003910.

Pradhan, A., Avelar, G.M., Bain, J.M., Childers, D.S., Larcombe, D.E., Netea, M.G., Shekhova, E., Munro, C.A., Brown, G.D., Erwig, L.P., Gow, N.A.R., Brown, A.J.P. (2018). Hypoxia promotes immune evasion by triggering β-glucan masking on the *Candida albicans* cell surface via mitochondrial and cAMP-protein kinase A signaling. *mBio* 9: e01318.

Pulimood, S., Ganesan, L., Alangaden, G., Chandrasekar, P. (2002). Polymicrobial candidemia. *Diagnostic Microbiology and Infectious Disease* 44: 353–357.

Rai, M.N., Balusu, S., Gorityala, N., Dandu, L., Kaur, R. (2012). Functional genomic analysis of *Candida glabrata*-macrophage interaction: role of chromatin remodelling in virulence. *PLOS Pathogens* 8: e1002863.

Rai, M.N., Sharma, V., Balusu, S., Kaur, R. (2015). An essential role for phosphatidylinositol 3-kinase in the inhibition of phagosomal maturation, intracellular survival and virulence in *Candida glabrata*. *Cellular Microbiology* 17: 269–287.

Ram, A.F., Kapteyn, J.C., Montijn, R.C., Caro, L.H., Douwes, J.E., Baginsky, W., Mazur, P., van den Ende, H., Klis, F. M. (1998). Loss of the plasma membrane-bound protein Gas1p in *Saccharomyces cerevisiae* results in the release of beta 1, 3-glucan into the medium and induces a compensation mechanism to ensure cell wall integrity. *Journal of Bacteriology* 180: 1418–1424.

Ramírez, M.A. and Lorenz, M.C. (2007). Mutations in alternative carbon utilization pathways in *Candida albicans* attenuate virulence and confer pleiotropic phenotypes. *Eukaryotic Cell* 6: 280–290.

Ramírez, M.A. and Lorenz, M.C. (2009). The transcription factor homolog *CTF1* regulates beta-oxidation in *Candida albicans*. *Eukaryotic Cell* 8: 1604–1614.

Ray, D., Goswami, R., Banerjee, U., Dadhwal, V., Goswami, D., Mandal, P., Sreenivas, V., Kochupillai, N. (2007). Prevalence of *Candida glabrata* and its response to boric acid vaginal suppositories in comparison with oral fluconazole in patients with diabetes and vulvovaginal candidiasis. *Diabetes Care* 30: 312–317.

Reuß, O., Vik, Å., Kolter, R., Morschhäuser, J. (2004). The *SAT1* flipper, an optimized tool for gene disruption in *Candida albicans*. *Gene* 341: 119–127.

Rodaki, A., Bohovych, I.M., Enjalbert, B., Young, T., Odds, F.C., Gow, N., Brown, A. (2009). Glucose promotes stress resistance in the fungal pathogen *Candida albicans*. *Molecular Biology of the Cell* 20: 4845–4855.

Rodrigues, C.F., Silva, S. and Henriques, M. (2014). *Candida glabrata*: a review of its features and resistance. European *Journal of Clinical Microbiology and Infectious Diseases* 33: 673–688.

Rodrigues, M.L. and Albuquerque, P.C. (2018). Searching for a change: The need for increased support for public health and research on fungal diseases. *PLOS Neglected Tropical Diseases* 12: e0006479.

Roetzer, A., Gratz, N., Kovarik, P., Schüller, C. (2010). Autophagy supports *Candida glabrata* survival during phagocytosis. *Cellular Microbiology* 12: 199–216.

Roetzer, A., Gregori, C., Jennings, A.M., Quintin, J., Ferrandon, D., Butler, G., Kuchler, K., Ammerer, G., Schüller, C. (2008). *Candida glabrata* environmental stress response involves *Saccharomyces cerevisiae* Msn2/4 orthologous transcription factors. *Molecular Microbiology* 69: 603–620.

Roth, S., Kumme, J. and Schüller, H.J. (2004). Transcriptional activators Cat8 and Sip4 discriminate between sequence variants of the carbon source-responsive promoter element in the yeast *Saccharomyces cerevisiae*. *Current Genetics* 45: 121–128.

Rude, T.H., Toffaletti, D.L., Cox, G.M., Perfect, J.R. (2003). Relationship of the glyoxylate pathway to the pathogenesis of *Cryptococcus neoformans*. *Infection and Immunity* 70: 5684–5694.

Sabina, J. and Brown, V. (2009). Glucose sensing network in *Candida albicans*: a sweet spot for fungal morphogenesis. *Eukaryotic Cell* 8: 1314–1320.

Sadeghi, G., Ebrahimi-Rad, M., Mousavi, S.F., Shams-Ghahfarokhi, M., Razzaghi-Abyaneh, M. (2018). Emergence of non-*Candida albicans* species: epidemiology, phylogeny and fluconazole susceptibility profile. *Journal de Mycologie Médicale* 28: 51–58.

Sandai, D., Yin, Z., Selway, L., Stead, D., Walker, J., Leach, M.D., Bohovych, I., Ene, I.V., Kastora, S., Budge, S., Munro, C.A., Odds, F.C., Gow, N.A., Brown, A.J. (2012). The evolutionary rewiring of ubiquitination targets has reprogrammed the regulation of carbon assimilation in the pathogenic yeast *Candida albicans*. *mBio* 3: e00495–12.

Sanglard, D., Ischer, F. and Bille, J. (2001). Role of ATP-binding-cassette transporter genes in high-frequency acquisition of resistance to azole antifungals in *Candida glabrata*. *Antimicrobial Agents and Chemotherapy* 45: 1174–1183.

Sanglard, D., Ischer, F., Calabrese, D., Majcherczyk, P.A., Bille, J. (1999). The ATP binding cassette transporter gene *CgCDR1* from *Candida glabrata* is involved in the resistance of clinical isolates to azole antifungal agents. *Antimicrobial Agents and Chemotherapy* 43: 2753–2765.

Sanguinetti, M., Posteraro, B., Fiori, B., Ranno, S., Torelli, R., Fadda, G. (2005). Mechanisms of azole resistance in clinical isolates of *Candida glabrata* collected during a hospital survey of antifungal resistance. *Antimicrobial Agents and Chemotherapy* 49: 668–679.

Saraste, M (1999). Oxidative phosphorylation at the fin de siècle. Science 283: 1488–1493.

Sardi, J.C., Scorzoni, L., Bernardi, T., Fusco-Almeida, A.M., Mendes Giannini, M.J. (2013). *Candida* species: current epidemiology, pathogenicity, biofilm formation, natural antifungal products and new therapeutic options. *Journal of Medical Microbiology* 62: 10–24.

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. *Microbiology and Immunology* 53: 41–44.

Schloss, J.V. and Cleland, W.W. (1982). Inhibition of isocitrate lyase by 3-nitropropionate, a reaction-intermediate analogue. *Biochemistry* 21: 4420–4427.

Schöbel, F., Ibrahim-Granet, O., Avé, P., Latgé, J.P., Brakhage, A.A., Brock, M. (2007). *Aspergillus fumigatus* does not require fatty acid metabolism via isocitrate lyase for development of invasive aspergillosis. *Infection and Immunity* 75: 1237–1244.

Schöler, A. and Schüller, H.J. (1994). A carbon source-responsive promoter element necessary for activation of the isocitrate lyase gene *ICL1* is common to genes of the gluconeogenic pathway in the yeast *Saccharomyces cerevisiae*. *Molecular and Cellular Biology* 14: 3613–3622.

Schrettl, M. and Haas, H. (2011). Iron homeostasis - Achilles' heel of *Aspergillus fumigatus*? *Current Opinion in Microbiology* 14: 400–405.

Schwarzmüller, T., Ma, B., Hiller, E., Istel, F., Tscherner, M., Brunke, S., Ames, L., Firon, A., Green, B., Cabral, V., Marcet-Houben, M., Jacobsen, I.D., Quintin, J., Seider, K., Frohner, I., Glaser, W., Jungwirth, H., Bachellier-Bassi, S., Chauvel, M., Zeidler, U., Ferrandon, D., Gabaldón, T., Hube, B., d'Enfert, C., Rupp, S., Cormack, B., Haynes, K., Kuchler, K. (2014). Systematic phenotyping of a large-scale *Candida glabrata* deletion collection reveals novel antifungal tolerance genes. *PLOS Pathogens* 10: e1004211.

Seider, K., Brunke, S., Schild, L., Jablonowski, N., Wilson, D., Majer, O., Barz, D., Haas, A., Kuchler, K., Schaller, M., Hube, B. (2011). The facultative intracellular pathogen *Candida glabrata* subverts macrophage cytokine production and phagolysosome maturation. *Journal of Immunology* 187: 3072–3086.

Seider, K., Gerwien, F., Kasper, L., Allert, S., Brunke, S., Jablonowski, N., Schwarzmüller, T., Barz, D., Rupp, S., Kuchler, K., Hube, B. (2014). Immune evasion, stress resistance, and efficient nutrient acquisition are crucial for intracellular survival of *Candida glabrata* within macrophages. *Eukaryotic Cell* 13: 170–183.

Seider, K., Heyken, A., Lüttich, A., Miramón, P., Hube, B. (2010). Interaction of pathogenic yeasts with phagocytes: survival, persistence and escape. *Current Opinion in Microbiology* 13: 392–400.

Selmecki, A., Forche, A. and Berman, J. (2006). Aneuploidy and isochromosome formation in drug-resistant *Candida albicans*. *Science* 313: 367–370.

Sharma, V., Sharma, S., Hoener zu Bentrup, K., McKinney, J.D., Russell, D.G., Jacobs, W.R. Jr, Sacchettini, J.C. (2000). Structure of isocitrate lyase, a persistence factor of *Mycobacterium tuberculosis*. *Nature Structural Biology* 7: 663–668.

Shen, X.X., Zhou, X., Kominek, J., Kurtzman, C.P., Hittinger, C.T., Rokas, A. (2016). Reconstructing the backbone of the Saccharomycotina yeast phylogeny using genome-scale data. *G3: Genes, Genomes, Genetics* 6: 3927–3939.

Sherman, F. (1991). Getting started with yeast. *Methods in Enzymology* 194: 3–21.

Sherrington, S. L., Sorsby, E., Mahtey, N., Kumwenda, P., Lenardon, M.D., Brown, I., Ballou, E. R., MacCallum, D.M., Hall, R. A. (2017). Adaptation of *Candida albicans* to environmental pH induces cell wall remodelling and enhances innate immune recognition. *PLOS Pathogens* 13: e1006403.

Shimamura, S., Miyazaki, T., Tashiro, M., Takazono, T., Saijo, T., Yamamoto, K., Imamura, Y., Izumikawa, K., Yanagihara, K., Kohno, S., Mukae, H. (2019). Autophagy-inducing factor Atg1 Is required for virulence in the pathogenic fungus *Candida glabrata*. *Frontiers in Microbiology* 10: 27.

Silva, S., Henriques, M., Martins, A., Oliveira, R., Williams, D., Azeredo, J. (2009). Biofilms of non-*Candida albicans Candida* species: quantification, structure and matrix composition. *Medical Mycology* 47: 681–689.

Silva, S., Negri, M., Henriques, M., Oliveira, R., Williams, D.W., Azeredo, J. (2012). *Candida glabrata*, *Candida parapsilosis* and *Candida tropicalis*: biology, epidemiology, pathogenicity and antifungal resistance. *FEMS Microbiology Reviews* 36: 288–305.

Simpson-Lavy, K. and Kupiec, M. (2019). Carbon catabolite repression in yeast is not limited to glucose. *Scientific Reports* 9: 6491.

Slutsky, B., Staebell, M., Anderson, J., Risen, L., Pfaller, M., Soll, D.R. (1987). "White-opaque transition": a second high-frequency switching system in *Candida albicans*. *Journal of Bacteriology* 169:189–197.

Sobel, J.D. (2006). The emergence of non-*albicans Candida* species as causes of invasive candidiasis and candidemia. *Current Infectious Disease Reports* 8: 427–433.

Solomon, P.S., Lee, R.C., Wilson, T.J., Oliver, R.P. (2004). Pathogenicity of *Stagonospora nodorum* requires malate synthase. *Molecular Microbiology* 53: 1065–1073.

Soontorngun, N., Larochelle, M., Drouin, S., Robert, F., Turcotte, B. (2007). Regulation of gluconeogenesis in *Saccharomyces cerevisiae* is mediated by activator and repressor functions of Rds2. *Molecular and Cellular Biology* 27: 7895–7905.

Sosinska, G.J., de Groot, P.W.J., Teixeira de Mattos, M.J., Dekker, H.L., de Koster, C.G., Hellingwerf, K.J., Klis, F.M. (2008). Hypoxic conditions and iron restriction affect the cell-wall proteome of *Candida albicans* grown under vagina-simulative conditions. *Microbiology* 154: 510–520.

Strollo, S., Lionakis, M.S., Adjemian, J., Steiner, C.A., Prevots, D.R. (2017). Epidemiology of hospitalizations associated with invasive candidiasis, United States, 2002-2012. *Emerging Infectious Diseases* 23: 7–13.

Taimur, S. (2018). Yeast infections in solid organ transplantation. *Infectious Disease Clinics of North America* 32: 651–666.

Tam, P., Gee, K., Piechocinski, M., Macreadie, I. (2015). *Candida glabrata*, friend and foe. *Journal of Fungi* 1: 277–292.

Tamir-Ariel, D., Navon, N. and Burdman, S. (2007). Identification of genes in *Xanthomonas campestris* pv. vesicatoria induced during its interaction with tomato. *Journal of Bacteriology* 189: 6359–6371.

Thirach, S., Cooper, C.R. Jr. and Vanittanakom, N. (2008). Molecular analysis of the *Penicillium marneffei* glyceraldehyde-3-phosphate dehydrogenase-encoding gene (gpdA) and differential expression of gpdA and the isocitrate lyase-encoding gene (acuD) upon internalization by murine macrophages. *Journal of Medical Microbiology* 57: 1322–1328.

Thompson, D.S., Carlisle, P.L. and Kadosh, D. (2011). Coevolution of morphology and virulence in *Candida* species. *Eukaryotic Cell* 10: 1173–1182.

Thompson, G.R. 3rd., Patel, P.K., Kirkpatrick, W.R., Westbrook, S.D., Berg, D., Erlandsen, J., Redding, S.W., Patterson, T.F. (2010). Oropharyngeal candidiasis in the era of antiretroviral therapy. *Oral Surgery, Oral Medicine, Oral Pathology, and Oral Radiology* 109: 488–495.

Timmermans, B., De Las Peñas A., Castaño, I., Van Dijck, P. (2018). Adhesins in *Candida glabrata. Journal of Fungi* 4: E60.

Torelli, R., Posteraro, B., Ferrari, S., La Sorda, M., Fadda, G., Sanglard, D., Sanguinetti, M. (2008). The ATP-binding cassette transporter-encoding gene *CgSNQ2* is contributing to the *CgPDR1*-dependent azole resistance of *Candida glabrata*. *Molecular Microbiology* 68: 186–201.

Trinh, H.V., Grossmann, J., Gehrig, P., Roschitzki, B., Schlapbach, R., Greber, U.F., Hemmi, S. (2013). iTRAQ-based and label-free proteomics approaches for studies of human adenovirus Infections. *International Journal of Proteomics* 2013: 581862.

Tsai, H.F., Krol, A.A., Sarti, K.E., Bennett, J.E. (2006). *Candida glabrata PDR1*, a transcriptional regulator of a pleiotropic drug resistance network, mediates azole resistance in clinical isolates and petite mutants. *Antimicrobial Agents and Chemotherapy* 50: 1384–1392.

Turcotte, B., Liang, X.B., Robert, F., Soontorngun, N. (2010). Transcriptional regulation of nonfermentable carbon utilization in budding yeast. *FEMS Yeast Research* 10: 2–13.

Turner, S.A. and Butler, G. (2014). The *Candida* pathogenic species complex. *Cold Spring Harbor Perspectives in Medicine* 4: a019778.

Ueno, K., Matsumoto, Y., Uno, J., Sasamoto, K., Sekimizu, K., Kinjo, Y., Chibana, H. (2011). Intestinal resident yeast *Candida glabrata* requires Cyb2p-mediated lactate assimilation to adapt in mouse intestine. *PLOS One* 6: e24759.

Uppuluri, P. and Lopez-Ribot, J.L. (2016). Go forth and colonize: dispersal from clinically important microbial biofilms. *PLOS Pathogens* 12: e1005397.

Uppuluri, P., Chaturvedi, A.K., Srinivasan, A., Banerjee, M., Ramasubramaniam, A.K., Köhler, J.R., Kadosh, D., Lopez-Ribot, J.L. (2010). Dispersion as an important step in the *Candida albicans* biofilm developmental cycle. *PLOS Pathogens* 6: e1000828.

Uppuluri, P., Khan, A. and Edwards, J.E. (2017). Current trends in candidiasis. In Prasad, R (Ed.). *Candida albicans: Cellular and Molecular Biology* (pp.6), Switzerland: Springer International Publishing AG. ISBN 978-3-319-50408-7.

Vale-Silva, L.A. and Sanglard, D. (2015). Tipping the balance both ways: drug resistance and virulence in *Candida glabrata*. *FEMS Yeast Research* 15: fov025.

Van de Veerdonk, F.L., Kullberg, B.J., Netea, M.G. (2010). Pathogenesis of invasive candidiasis. *Current Opinion in Critical Care* 16: 453–459.

Vanni, P., Giachetti, E., Pinzauti, G., McFadden, B.A. (1990). Comparative structure, function and regulation of isocitrate lyase, an important assimilatory enzyme. *Comparative Biochemistry and Physiology B* 95: 431–458.

Velayuthan, R.D., Samudi, C., Lakhbeer Singh, H.K., Ng, K.P., Shankar, E.M., Denning, D.W. (2018). Estimation of the burden of serious human fungal infections in Malaysia. Journal of Fungi 4: E38.

Vereecke, D., Cornelis, K., Temmerman, W., Jaziri, M., Van Montagu, M., Holsters, M., Goethals, K. (2002). Chromosomal locus that affects pathogenicity of *Rhodococcus fascians*. *Journal of Bacteriology* 184: 1112–1120.

Vermitsky, J.P. and Edlind, T.D. (2004). Azole resistance in *Candida glabrata*: coordinate upregulation of multidrug transporters and evidence for a Pdr1-like transcription factor. *Antimicrobial Agents and Chemotherapy* 48: 3773–3781.

Vermitsky, J.P., Earhart, K.D., Smith, W.L., Homayouni, R., Edlind, T.D., Rogers, P.D. (2006). Pdr1 regulates multidrug resistance in *Candida glabrata*: gene disruption and genome-wide expression studies. *Molecular Microbiology* 61: 704–722.

Vieira, N., Casal, M., Johansson, B., MacCallum, D.M., Brown, A.J., Paiva, S. (2010). Functional specialization and differential regulation of short-chain carboxylic acid transporters in the pathogen *Candida albicans*. *Molecular Microbiology* 75: 1337–1354.

Vincent, O. and Carlson, M. (1998). Sip4, a Snf1 kinase-dependent transcriptional activator, binds to the carbon source-responsive element of gluconeogenic genes. *The EMBO Journal* 17: 7002–7008.

Wächtler, B., Citiulo, F., Jablonowski, N., Förster, S., Dalle, F., Schaller, M., Wilson, D., Hube, B. (2012). *Candida albicans*-epithelial interactions: Dissecting the roles of active penetration, induced endocytosis and host factors on the infection process. *PLOS One* 7: e36952.

Walker, L.A., Munro, C.A., de Bruijn, I., Lenardon, M.D., McKinnon, A., Gow, N. A. (2008). Stimulation of chitin synthesis rescues *Candida albicans* from echinocandins. *PLOS Pathogens* 4: e1000040.

Wall, D.M., Duffy, P.S., Dupont, C., Prescott, J.F., Meijer, W. G. (2005). Isocitrate lyase activity is required for virulence of the intracellular pathogen *Rhodococcus equi*. *Infection and Immunity* 73: 6736–6741.

Wang, M., Zhao, Q., Yang, J., Jiang, B., Wang, F., Liu, K., Fang, X. (2013). A mitogen-activated protein kinase Tmk3 participates in high osmolarity resistance, cell wall integrity maintenance and cellulase production regulation in *Trichoderma reesei*. *PLOS One* 8: e72189.

Wang, T., Xiu, J., Zhang, Y., Wu, J., Ma, X., Wang, Y., Guo, G., Shang, X. (2017). Transcriptional responses of *Candida albicans* to antimicrobial peptide MAF-1A. *Frontiers in Microbiology* 8: 894.

Wang, X., Liu, Q. and Zhang, B. (2014). Leveraging the complementary nature of RNA-Seq and shotgun proteomics data. *Proteomics* 14: 2676–2687.

Wang, Z., Gerstein, M. and Snyder, M. (2009). RNA-Seq: a revolutionary tool for transcriptomics. *Nature Reviews Genetics* 10: 57–63.

Wang, Z.Y., Thornton, C.R., Kershaw, M.J., Debao, L., Talbot, N.J. (2003). The glyoxylate cycle is required for temporal regulation of virulence by the plant pathogenic fungus *Magnaporthe grisea*. *Molecular Microbiology* 47: 1601–1612.

Werner, M., Feller, A., Messenguy, F., Piérard, A. (1987). The leader peptide of yeast gene *CPA1* is essential for the translational repression of its expression. *Cell* 49: 805–813.

Wilson, D., Thewes, S., Zakikhany, K., Fradin, C., Albrecht, A., Almeida, R., Brunke, S., Grosse, K., Martin, R., Mayer, F., Leonhardt, I., Schild, L., Seider, K., Skibbe, M., Slesiona, S., Waechtler, B., Jacobsen, I., Hube, B. (2009). Identifying infection-associated genes of *Candida albicans* in the postgenomic era. *FEMS Yeast Research* 9: 688–700.

Workowski, K.A., Bolan, G.A. and Centers for Disease Control and Prevention (2015). Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recommendations and Reports* 64: 1–137.

Yamaguchi, N., Sonoyama, K., Kikuchi, H., Nagura, T., Aritsuka, T., Kawabata, J. (2005). Gastric colonization of *Candida albicans* differs in mice fed commercial and purified diets. *The Journal of Nutrition* 135: 109–115.

Yapar, N. (2014). Epidemiology and risk factors for invasive candidiasis. *Therapeutics and Clinical Risk Management* 13: 95–105.

Yarrow, D. and Meyer, S.A. (1978). Proposal for amendment of the diagnosis of the genus *Candida* Berkhout nom. cons. *International Journal of Systematic Bacteriology* 28: 611–615.

Zaoutis, T.E., Argon, J., Chu, J., Berlin, J.A., Walsh, T.J., Feudtner, C. (2005). The epidemiology and attributable outcomes of candidemia in adults and children hospitalized in the United States: a propensity analysis. *Clinical Infectious Diseases* 41: 1232–1239.

Zhang, Y.J. and Rubin, E.J. (2013). Feast or famine: the host-pathogen battle over amino acids. *Cellular Microbiology* 15: 1079–1087.