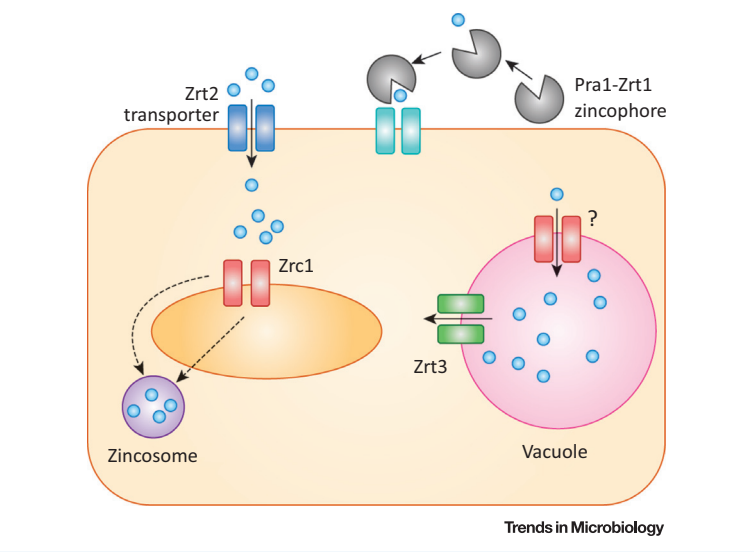
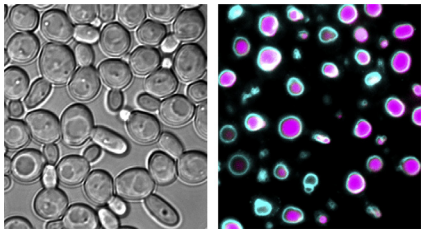
Candida albicans

Duncan Wilson[1,*]

[1]Medical Research Council Centre for Medical Mycology at the University of Aberdeen, Aberdeen Fungal Group, Institute of Medical Sciences, Foresterhill, Aberdeen, UK



Pathogens often face zinc restriction due to the action of nutritional immunity – host processes which restrict microbial access to key micronutrients such as zinc and iron. *Candida albicans* scavenges environmental zinc via two pathways. The plasma membrane transporter Zrt2 is essential for zinc uptake and growth in acidic environments. Neutralisation to pH 7 severely decreases the solubility of ionic Zn^{2+}; this increase in pH triggers expression and activity of a second zinc scavenging system, the zincophore. This fungus-specific system consists of a secreted zinc-binding protein, Pra1, which captures zinc and returns to the cell via a syntenically expressed receptor, Zrt1. If present in excess, zinc is detoxified via a Zrc1-dependent mechanism. In *C. albicans* Zrc1 plays an important role in the generation of zincosomes. *C. albicans* faces both low and high zinc bottlenecks *in vivo* as Zrt2 and Zrc1 are required for kidney and liver colonisation, respectively, in a murine infection model.



KEY FACTS:

A normal member of the human gastrointestinal microbiota (mycobiota).

A polymorphic fungus – it grows as unicellular yeasts, filamentous hyphae, or pseudohyphae, and forms chlamydospores, Goliath cells; it undergoes yeast-phase phenotypic switching, for example, the white–opaque switch.

Hypha formation is important as it allows tissue invasion; the expression of important virulence factors is coregulated with hypha formation.

Virulence factors: it expresses a range of adhesins and invasins, secreted hydrolases, and a cytolytic toxin, candidalysin.

Fitness attributes: it requires effective nutrient acquisition, robust metabolic, and environmental stress responses for pathogenicity.

DISEASE FACTS:

In the genus *Candida*, *C. albicans* is the most common causal agent of candidiasis.

Superficial infections, like oral and vaginal candidiasis (thrush), are extremely common – vaginal candidiasis (thrush) affects 75 million women per year.

For invasive candidiasis there are conservative estimates of 250 000 cases and at least 50 000 deaths per year.

TAXONOMIC AND CLASSIFICATION INFORMATION:

KINGDOM: Fungi
PHYLUM: Ascomycete
CLASS: Saccharomycetes
ORDER: Saccharomycetales
FAMILY: Saccharomycetaceae
GENUS: *Candida*
SPECIES: *albicans*

*Correspondence:
Duncan.Wilson@abdn.ac.uk (D. Wilson).

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Literature

1. Crawford, A.C. *et al.* (2018) Biphasic zinc compartmentalisation in a human fungal pathogen. *PLoS Pathog.* 14, e1007013
2. Łoboda, D. and Rowińska-Żyrek, M. (2017) Zinc binding sites in Pra1, a zincophore from *Candida albicans*. *Dalton Trans.* 46, 13695–13703
3. Citiulo, F. *et al.* (2012) *Candida albicans* scavenges host zinc via Pra1 during endothelial invasion. *PLoS Pathog.* 8, e1002777
4. Crawford, A. and Wilson, D. (2015) Essential metals at the host–pathogen interface: nutritional immunity and micronutrient assimilation by human fungal pathogens. *FEMS Yeast Res.* 15, fov071
5. Mayer, F.L. *et al.* (2013) *Candida albicans* pathogenicity mechanisms. *Virulence* 4, 119–128
6. Brown, G.D. *et al.* (2012) Hidden killers: human fungal infections. *Sci. Transl. Med.* 4 (165), rv113
7. Kullberg, B.J. and Arendrup, M.C. (2015) Invasive candidiasis. *N. Engl. J. Med.* 373, 1445–1456

  https://doi.org/10.1016/j.tim.2018.10.010