Editorial: The dark side of yeast biology

Yeast species provide tractable systems to study many aspects of fundamental biology and remain model organisms for studying higher eukaryotes. In addition, yeasts are the work horses of industrial biotechnology and provide us with some of our favourite consumer products. However, not all yeasts are beneficial to mankind. Some yeast species have turned to the dark side, have evolved to live on and inside the human host, and are important pathogens with a significant negative impact on global health.

This thematic issue pulls together mini-reviews from world leaders studying human fungal pathogens. Many of these fungal species are opportunistic pathogens. They are often part of the normal microbiota, but cause disease when an individual becomes immunocompromised or has an underlying defect in a component of the innate immunity response that defends us from invading pathogens. Under these conditions, the yeast can escape from its normal niche, invade the body and/or initiate hyper-immune stimulation, which contributes to the pathobiology of the infection.

Here, I have kept the topics broad to provide a taste of molecular medical mycology and to reflect the vibrant and dynamic community investigating human fungal pathogens. The issue begins with a perspective by Professor Judy Berman on the impact of ploidy plasticity on the ability of *Candida albicans* to adapt to stresses, including exposure to antifungal drugs (Berman 2016). Using a range of complimentary approaches, Judy has shown that *C. albicans* cells respond to severe stress by altering the total number of chromosomes, i.e. creating aneuploidy. Aneuploidy provides the cells with a selective advantage and can result in, for example, resistance to antifungal drugs such as fluconazole.

The remainder of this thematic issue is composed of a series of mini-reviews highlighting our current understanding of fungal commensalism and pathogenicity, the ability to colonize and invade the host and the contribution of yeast pathogens to the human microbiota. Examples include the important traits that contribute to *C. albicans* pathobiology, such as how this pathogen overcomes nutritional immunity, i.e. the sequestration of trace nutrients by the host. In particular, the mechanisms involved in uptake of iron and zinc micronutrients are explored (Crawford and Wilson 2015). The importance of mitochondrial function to fungal virulence is described through the influence of mitochondria on metabolism, stress responses and regulation of signalling pathways that impact on fitness, morphogenesis and antifungal drug susceptibility (Calderone, Li and Traven 2015). We then turn to *C. albicans* as an important but often over-looked member of the human microbiota. One virulence trait of *C. albicans* and other *Candida* species is their ability to form drug-resistant biofilms on implanted medical devices, catheters and dentures. In the oral cavity, *C. albicans* exists in a biofilm community in association with other microbes. Interactions between microbes have become a hot topic of research as microorganisms very rarely exist in isolation. O’Donnell et al. (2015) explore polymicrobial biofilms in the context of oral disease and their influence on clinical outcome. Importantly, the authors highlight how little we know about microbial interactions in specific host niches and how this knowledge may help us design better therapeutic regimens to counteract mixed species infections. Turning to another host niche, *C. albicans* commensalism in the gastrointestinal tract is discussed (Neville, d’Enfert and Bougnoux 2015). This mini-review describes recent advances in our understanding of *C. albicans* gut colonization, including approaches used to study this in animal models. The application of these models has led to the identification of genes and phenotypes that enable *C. albicans* to exist in the gut in competition with resident microbiota, as well as the important innate immune components that prevent dissemination of and subsequent host invasion by this fungal pathogen.

*Pneumocystis* species are important lung pathogens with strict host specificities and are thought to be obligate biotrophs. *Pneumocystis* pneumonia was a common secondary infection of AIDS patients in the 1980s prior to antiretroviral therapies. Culture of these species *ex vivo* is challenging and has hampered research into these organisms. In this thematic issue, Skalski, Kottom and Limper (2015) describe key features of *Pneumocystis* pathobiology with a specific focus on the life cycle, cell wall and signalling pathways.

*Cryptococcus* species are also important human pathogens, gaining entry into the body by inhalation of infectious propagules. Bielska and May (2016) outline what is known about the pathogenicity of *C. gattii*, the encapsulated basidiomycete species responsible for the outbreak of cryptococcal disease in the Pacific Northwest. This species has a propensity to cause lung infections in immunocompetent hosts.

In Latin America, sporotrichosis is the most prevalent subcultural fungal infection caused by several pathogenic species of the *Sporothrix schenckii* complex. Comparative genomics is now beginning to facilitate the association of genotypes with virulence. Mora-Montes et al. (2015) report on recent advances in our understanding of the *S. schenckii* complex, covering strain variation, insights from genome sequencing and the development of new tools to study these important pathogens at the molecular level.
In general, the field of molecular medical mycology is still building the tools and generating resources to enable us to perform high throughput screens and phenotyping. In many species, the methods for transformation and creating even single gene disruptions have not yet been developed or remain challenging. Many pathogenic yeast are genetically intractable; one exception is *C. glabrata*, which is more closely related to *Saccharomyces cerevisiae* than to other pathogenic *Candida* species. Ho and Haynes (2015) present recent advances in the toolkit available to study *C. glabrata* virulence, including libraries of gene knockout strains and Gateway plasmids. With an eye to the future, the CRISPR-Cas9 system has great potential to expand this toolkit further. The continuing expansion of the molecular tools and mutant libraries available to study yeast pathogens will provide the community with a route to gain a deeper understanding of the genes and pathways important for growth, commensalism, stress-adaptation, drug resistance and virulence, opening the door to the design of better therapeutics. In addition, we hope it will encourage others in the yeast community to take up the challenge of working with currently understudied human pathogenic species that have a significant global impact on human health.

The Dark Side of Yeast Biology can be found online at [http://femsyr.oxfordjournals.org/content/thematic-issue-dark-side-yeast-biology](http://femsyr.oxfordjournals.org/content/thematic-issue-dark-side-yeast-biology)

**REFERENCES**


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