

EDITORIAL

Fungi to the Fore: The Emerging Importance of Fungi in Human Health

Opportunistic infections caused by fungi have become an important and substantial threat to human health, mainly due to increased numbers of immunocompromised individuals. Most at risk from invasive fungal infections are people suffering from cancer and HIV, as well as those undergoing major surgery and organ transplants. The mortality rate from invasive fungal infections is extremely high (commonly ~30-50%) and the associated burden on health care systems is substantial.

Understanding the biology of pathogenic fungi and the mechanisms of virulence has remained obscure, predominantly because their impact on human health has been under-appreciated; for example, numerous instances of misdiagnosis exist in the literature. This contrasts markedly with the well-understood economic implications of plant disease and crop loss due to fungal pathogens. Over the last ten years, this has changed dramatically, as has the ability to genetically manipulate these organisms and the availability of molecular, genetic and biochemical tools. Recent completion of genome sequences of several human fungal pathogens and draft genome sequences of many others has fostered the development of new molecular tools and opened a new chapter in fungal pathogen research in this 'post-genomic' era.

The Australian groups working on the molecular biology of human fungal pathogens cover a range of organisms. *Cryptococcus neoformans* is the main pathogen affecting HIV patients, causing often-fatal meningoencephalitis, and is endemic to Australia. *Penicillium marneffei* is a dimorphic fungal pathogen (i.e., exists in two morphological forms – non-pathogenic multicellular filaments and pathogenic unicellular yeast cells), which is endemic to South-East Asia and causes life-threatening illness in AIDS patients. The commensal

yeast *Candida albicans* causes serious illness in cancer and HIV patients. *Candida* is also a main pathogen in hospital-acquired infections related to the use of implanted medical devices because of its ability to form biofilms – communities of fungal cells that are highly resistant to antifungal drugs – on the device. Currently, there are no efficient ways to treat biofilm-related infections. Moreover, the arsenal of anti-fungal drugs available for treatment is small, partly due to the evolutionary relatedness of fungi to animals, making fungal-specific drug targets difficult to identify.

The research on human fungal pathogens in Australia spans diverse biological questions, aimed at understanding molecular mechanisms that underpin the ability of these fungi to be successful pathogens. The research topics include molecular mechanisms enabling the switch between yeast and filamentous morphologies, deciphering pathways that enable secretion of virulence factors and remodelling of cell walls and membranes, understanding the epidemiology of fungal infections, and elucidating how the pathogen changes its genetic makeup during infection in the host to enable a selective advantage.

The four reviews in this Showcase on Research cover some of these topics and are a sampling of the high quality of research on fungal pathogens in Australia. Julianne Djordjevic reviews what is known about the roles of phospholipases in virulence of *C. neoformans*. Eve Chow and James Fraser write about 'microevolution' or how *C. neoformans* rearranges its genome in the host, and the potential relevance of this in pathogenesis. Wieland Meyer presents an updated account of the epidemiology of *Cryptococcus*, while Nathalie Uwamahoro and Ana Traven review the morphological changes in *C. albicans* and what is known about biofilms and their high drug resistance.

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Cover Illustration

J774 mouse macrophage cell with four *Penicillium marneffei* yeast cells growing internally. Merged image shows the J774 and *P. marneffei* cell outlines using DIC imaging and calcofluor white labelled *P. marneffei* cells using fluorescence imaging. Magnification is 100x.

Image courtesy of Kylie Boyce and Alex Andrianopoulos, Department of Genetics, University of Melbourne.

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Australian Biochemist – Editor Rebecca Lew, Editorial Officer Liana Friedman

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