ANALYSIS

SCIENCE AND MEDICINE

Light as a defence against fungal infection

Fungi love the dark, and one day we may be able to turn this fact against them to fight fungal infections. New research suggests that the way in which the fungus *Cryptococcus neoformans* detects light plays a role in its virulence. Two genes controlling light responses in *C. neoformans* were recently discovered by Alexander Idnurm and Joseph Heitman, who found that deleting either gene reduced the virulence of the fungus.[1] The finding suggests that light-based therapies may have a role in treating fungal infections.

Virulence factors

C. neoformans is a well-known opportunistic pathogen. It normally infects people with compromised immune systems, such as organ transplant recipients and AIDS patients. In fact, it is endemic in Africa and Southeast Asia, infecting upward of 30% of AIDS patients.[2] The fungus has a number of virulence factors (e.g., a polysaccharide capsule, melanin synthesis, various enzymes); when the genes encoding these factors are mutated, virulence is diminished.

Idnurm and Heitman have now identified *C. neoformans*' light-sensing proteins as another virulence factor. A pair of proteins that sense blue light have been well studied in the fungus *Neurospora crassa*.[3] Idnurm and Heitman identified genes in *C. neoformans*, named *BWC1* and *BWC2*, that produce similar proteins; mutation of these genes allowed the pathogen to mate in the presence of light (Fig. 1). As well, they found that organisms with mutated *BWC1* were also sensitive to ultraviolet light, whereas wild-type strains were not.

Interestingly, the researchers also demonstrated that *C. neoformans* strains with mutations in either *BWC1* or *BWC2* gene were less virulent. For instance, mice inoculated with wild-type *C. neoformans* died within 30 days; however, mice inoculated with strains lacking either of the 2 light-sensing genes survived an average of 44 days. The finding suggests that the light-sensing proteins, although not essential for virulence, influence the speed with which the pathogen kills its host.

DOI:10.1503/cmaj.050365

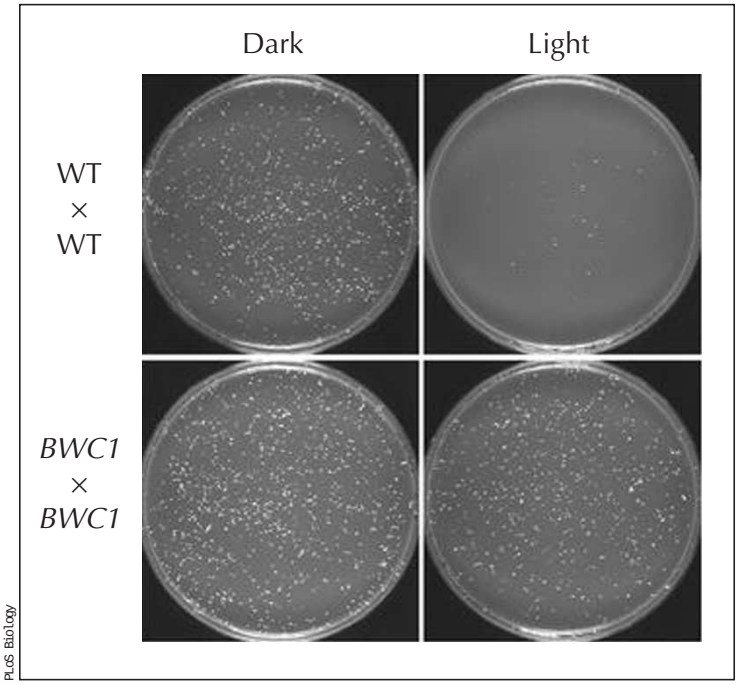

Fig. 1: The effect of exposure to blue light on fusion rates of wild-type (WT) and *BWC1*-mutated *Cryptococcus neoformans* cells. Light inhibited fusion in wild-type strains but not in *BWC1* mutant strains.[1]

Light therapy for fungal infections?

Idnurm and Heitman suggest a teleological rationale for *BWC1* and *BWC2*: the ability to sense darkness in an animal host may induce virulence factors that allow the pathogen to colonize the host. This hypothesis is still far from being confirmed, but it does suggest that the effects of light on other *C. neoformans* virulence factors, such as its polysaccharide capsule, should be studied further.

Idnurm and Heitman's work also brings up the intriguing possibility of using light therapy for the treatment of fungal infections. Light therapy already has some uses in clinical settings: vitiligo is commonly treated with ultraviolet radiation to repigment the skin. In recent years targeted phototherapy systems, which deliver light only to affected regions, have been developed.[4] If light is found to generally inhibit the virulence of pathogenic fungi, a combination of targeted light therapy and antifungal drugs could be a promising new treatment for fungal skin and nail infections. — *David Secko*, Vancouver

References

1. Idnurm A, Heitman J. Light controls growth and development via a conserved pathway in the fungal kingdom. *PLoS Biol* 2005;3(4):e95
2. Steenbergen JN, Casadevall A. The origin and maintenance of virulence for the human pathogenic fungus *Cryptococcus neoformans*. *Microbes Infect* 2003;5(7):667-75.
3. Liu Y, He Q, Cheng P. Photoreception in *Neurospora*: a tale of two white collar proteins. *Cell Mol Life Sci* 2003; 60(10):2131-8.
4. Grimes PE. New insights and new therapies in vitiligo. *JAMA* 2005;293 (6):730-5.