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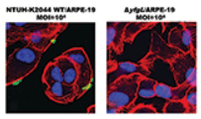

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EDITORIAL

New insights into the antimicrobial blue light inactivation of *Candida albicans*

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The incidence of superficial and deep-seated fungal infections has increased considerably in recent years.[1] They are coincident with the rising number of immunocompromised patients, the wide development of organ transplantation, tracheal intubation and endoscopic techniques, and the extensive application of broad-spectrum antibiotics, immunosuppressants and corticosteroids. Patients with HIV infection, neutropenia, burns, and pancreatitis are also susceptible to fungal infection. Thus, they represent an exponentially growing threat for human health because a combination of difficult diagnosis and a shortage of effective antifungal drugs. Candidiasis is an opportunist fungal infection usually caused by *Candida albicans*. This yeast is commensal and a constituent of the normal gut flora comprising microorganisms that live in the human mouth and gastrointestinal tract. The identification of specific metabolic or structural antimicrobial targets for fungi is difficult due to the common eukaryotic nature of fungal and human cells.[2] Thus, the different composition of cholesterol in humans and ergosterol in fungi render the cytoplasmic membrane of *Candida* a suitable target for the action of antifungals. Triazoles are inhibitors of the cytochrome P450 14α-sterol demethylase (CYP51), an essential enzyme in the biosynthesis of ergosterol. However, patient responses to these antifungal drugs tend to be slow with a high risk of reinfection. In particular, fluconazole has been widely used in clinical practice due to its efficacy and reduced toxicity. However, inadequate dosing has contributed to treatment failure and the emergence of antifungal-resistant *C. albicans* strains.[3] Despite the discovery of new molecules and formulations to reduce the toxicity and increase bioavailability, the search for antifungal agents and the characterization of novel targets are a continued need. In this sense, new therapies are also being searched for treating fungal infections. An interesting alternative is represented by photodynamic inactivation (PDI) of microorganisms.[4] PDI involves the addition of a phototherapeutic agent, which is rapidly bound to cells. The aerobic irradiation of the infection with visible light produces highly reactive oxygen species (ROS), which rapidly react with a variety of substrates inducing damage in biomolecules. These reactions induce a loss of biological functionality leading to cell inactivation. Experimental investigations have demonstrated that yeasts can be effectively photoinactivated *in vitro* by several photosensitizers.[5,6]

Moreover, an innovative light-based antimicrobial approach, antimicrobial blue light (aBL), has attracted increasing attention due to its intrinsic ability to inactivate pathogens without the involvement of exogenous photosensitizers.[7] Many microbial cells are highly sensitive to killing by blue light (400–470 nm) due to accumulation of naturally occurring photosensitizers such as porphyrins and flavins. The ideal wavelength range of blue light should be the one that is selectively absorbed by the chromophores in pathogenic bacteria but not those in host cells. The lethality of blue light for bacteria has been demonstrated both *in vitro* and *in vivo* which can produce a broad-spectrum bactericidal effect on both Gram-negative and Gram-positive bacteria.[8] The precise mechanism of the antimicrobial effect of blue light is not fully elucidated. In general, accepted hypothesis is that blue light excites endogenous intracellular porphyrins to act as photosensitizers, and this photon absorption sequentially leads to energy transfer and ultimately, the production of highly cytotoxic ROS.[7] A disadvantage in light-based therapy is the limitation of light

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penetration in tissue. Penetration depth of blue light in tissue is lower than that of red light, which is commonly employed in photodynamic therapy. However, this is not a limitation for the treatment by aBL of superficial infections.

In this issue of *Virulence*, Zhang *et al.*[9] investigated the effectiveness of aBL for inactivation of *C. albicans in vitro* and in infected mouse burns. These studies demonstrated that *C. albicans* was much more susceptible to aBL than human keratinocytes. The results indicated an approximately 42-fold faster inactivation rate of *C. albicans* by aBL than keratinocytes. The results obtained from the studies demonstrated that *C. albicans* was approximately 42-fold more susceptible to aBL than human keratinocytes. After a low aBL After an exposure of 35.1 J/cm^2 aBL, transmission electron microscopy images showed disruption of inner organelles with a deformed cell wall in some *C. albicans* cells. However, complete decomposition of inner organelles with disrupted cell walls was observed using 70.2 J/cm^2 blue light irradiation.

Fluorescence spectroscopic measurements suggested that C. albicans contains both endogenous porphyrins and flavins. As 415-nm wavelength is close to the absorption peak of porphyrins, authors hypothesize that the inactivation of *C. albicans* was due to the photo-excitation of endogenous porphyrins.

Authors observed a tendency of reduced aBL susceptibility of *C. albicans* with the numbers of passages of *C. albicans* on aBL exposure. However, statistical analysis revealed no significant difference in aBL inactivation extent between the first and the last passage. Moreover, the *in vivo* study indicated that a single exposure of aBL at 432 J/cm^2 significantly reduced the fungal burden in infected mouse burns. Even though reoccurrence of fungal infection was observed during the following days in the aBL-treated mouse burn, the fungal load in the untreated mouse burn was always more than 10-fold higher than that of the aBL-treated mouse. Therefore, the results found by Zhang and colleagues demonstrate that aBL is a potential therapeutic approach for *C. albicans* infections.

Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

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