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Suppression of the pathogenicity of *Candida albicans* by the quorum-sensing molecules farnesol and tryptophol

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This study examines the ability of the quorum-sensing molecules (QSMs) farnesol and tryptophol to induce programmed cell death of the pathogenic fungus *Candida albicans*, to alter the expression of apoptosis-related genes, and to reduce the pathogenicity and virulence of *C. albicans* in *Galleria mellonella*. Our results showed that both farnesol and tryptophol inhibited *C. albicans* germ tube formation. In the QSM-treated group, the expression levels of the apoptosis genes increased, whereas the expression level of the anti-apoptosis gene decreased. Further, pretreatment of *C. albicans* with tryptophol or farnesol prior to *G. mellonella* larval infection significantly enhanced host survival compared with larvae infected with untreated *C. albicans*. Thus, farnesol and tryptophol may trigger apoptosis of *C. albicans in vitro* and reduce the virulence of *C. albicans in vivo*. Although further study is needed to identify the precise mechanisms underlying the antifungal properties of farnesol and tryptophol, these results suggest that QSMs may be effective agents for controlling fungal infection.

Key Words: *Candida albicans*; *Galleria mellonella*; germ tube; quorum-sensing molecules; tryptophol

Introduction

Candida albicans is a dimorphic fungus that grows as both yeast and in filamentous forms. It is present as normal flora in various organisms, such as the oral, vaginal, and genital tracts of warm-blooded animals, including humans. However, *C. albicans* is also an important opportunistic pathogen in immunocompromised hosts (Alangaden, 2011; Armstrong, 1993; Odds, 1996; Wenzel, 1995). One of the crucial factors for the virulence of *C. albicans* is its ability to switch from yeast to hyphae (Lo et al., 1997; Mayer et al., 2013; Mitchell, 1998) because the hyphal form can adhere and penetrate tissues more readily than the yeast form (Brennan, 2002; Grubb et al., 2008; Hornby et al., 2004; Shen et al., 2008; Wang and Lin, 2012). The first stage in this transition is the formation of a germ tube, which is triggered by interaction with the host cell and is dependent on factors, such as serum, pH, temperature, and quorum-sensing molecules (QSMs) (Grubb et al., 2008; Wang and Lin, 2012).

QS is a mode of microbial cell-cell communication that depends on cell density and serves to regulate fungal behaviors, such as biofilm formation, competence, and bioluminescence (Grubb et al., 2008; Shen et al., 2008; Wang and Lin, 2012). At the molecular level, these changes require the release of hormone-like QSMs (Nealson and Hastings, 1979). QSMs have been the subject of studies dating back to the 1960s and 1970s on bacteria, such as *Streptococcus pneumoniae* and bioluminescent marine *Vibrio* species, respectively (Hastings and Nealson, 1977; McMillan et al., 2015; Nealson and Hastings, 1979). In eukaryotes, the QSM farnesol (FOH) was first isolated from *C. albicans*. In addition, other QSMs have been found in *C. albicans*, such as tyrosol, phenylethanol, and tryptophol (TOH). In fungi, QSMs are important regulators of morphogenesis, biofilm development, and cell population density control (Alem et al., 2006; Lindsay et al., 2012; Wongsuk et al., 2016). The QSM FOH has been

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