TITLE: THE GENE *FKS1* IS INVOLVED IN THE ADAPTIVE RESPONSE TO STRESS CAUSED BY ANTIFUNGAL AGENTS IN THE DERMATOPHYTE *TRICHOPHYTON RUBRUM*

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ABSTRACT

Trichophyton rubrum is a prevalent dermatophyte in skin superficial infections in Brazil and worldwide. Currently, commercial antifungal drugs have main targets in the fungal cell: ergosterol and its biosynthesis, nucleic acids and the cell wall. The cell wall is essential for fungal viability, and it is absent in mammalian cell, which makes it an attractive antifungal target. Among the antifungals that act on cell wall are the echinocandins that inhibit the beta (1,3) -D-glycan synthase enzyme, which is related to polymerization of the cell wall. In this context, *fsk1* is the encoding gene of protein involved in synthesis of catalytic subunit of beta (1,3) -D-glycan synthase. In addition, literature reports showed that in some fungi the gene *fks1* modulates the susceptibility to drugs that act on the cell wall, and it is also involved in the cell wall integrity (CWI) pathway. On the other hand , little is known about the role of *fks1* in physiology of dermatophytes. Recently, data from our research group obtained from a high throughput expression assay of *T. rubrum* challenged by the natural compound *trans*-chalcone, showed a *cross-talking* between pathways related to cell wall integrity as an adaptive response to the stress caused by this compound, with a remarkable modulation of the gene *fks1*. In this context, the objective of this work was to analyze the expression of gene *fks1* after the *T. rubrum* exposure to sublethal concentrations of antifungal compounds that act on cell wall and ergosterol. The gene expression was analyzed by quantitative PCR using Sybr Green, after exposure of *T.rubrum* conidia for 1h to sub inhibitory concentrations of Congo Red, *trans*-chalcone, fluconazole and terbinafine. The results showed an expressive up-regulation of gene *fks1* by *trans*-chalcone, and its slightly induction after congo red exposure, while terbinafine and fluconazole caused a decrease in fks1 transcript levels. Therefore, the data suggest that the gene *fks1* is differently modulated in response to the stress caused by commercial and natural compounds that act on the cell wall and cell membrane (ergosterol), and also contributes to wide the knowledge about *trans*-chalcone mode of action.

Keywords: *Trichophyton rubrum*, cell wall, *fks1*, *trans*-chalcone

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