TITLE: EVALUATION OF *Galleria mellonella* LARVAE IMMUNE RESPONSE TO INFECTION WITH SWITCHED PHENOTYPIC VARIANTS OF *Candida tropicalis*

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ABSTRACT:

Among *Candida* putative virulence factors, phenotypic switching is associated with fungal adaptability to environmental changes during invasion of host organism. We previously showed that switching affect *Candida tropicalis* virulence using the *Galleria mellonella* model. In the present study we evaluate the effect of switching on modulation of *G. mellonella* immune responses. We employed strains of the switching system 49.07 comprised of five morphotypes (parental, crepe variant, rough variant, crepe revertant and rough revertant), and evaluate larvae melanization following infection with phenotypes and the expression of antimicrobial peptides by the larvae. In addition to the humoral response, the cellular response mediated by hemocytes was also evaluated. Infection of *G. mellonella* with *C. tropicalis* morphotypes ($5x10^5$ cells/larvae) induced larvae melanization. After 24 hours of infection, larvae infected with switching strains (variants and revertants) showed higher melanization compared to larvae infected with the parental morphotype, revealing distinct levels of host humoral response. After two hours of infection, larvae infected with the crepe variant resulted in lower expression of the peptide galiomycin compared to that observed following infection with the parental strain. However, the peptide expression was increased after 4 hours of infection with the crepe morphotype (the most virulent strain), showing that the production of galiomycin in response to infection with crepe variant probably occurs at latter stages which may favor the virulence of this switch variant against *G. mellonella* larvae. *G. mellonella* hemocytes phagocytose all *C. tropicalis* morphotypes. The crepe variant and its revertent exhibited higher susceptibility to phagocytosis compared to the parental strain. On the other hand, the rough variant showed susceptibility to phagocytosis at same extent as observed for the parental strain. The susceptibility to phagocytosis exhibited by the crepe variant does not guarantee success in its elimination, since this strain may have mechanisms of escape of the immune system, including the filamentation capacity. Based on the data obtained in the present work, it can be concluded that interactions between the host *G. mellonella* and the phenotypic strains of *C. tropicalis* are diverse. We conclude that susceptibility to phagocytosis by cells of the innate immune system is an important distinction between switched strains of *C. tropicalis*.

Keywords: *Candida tropicalis,* phenotypic switching, *Galleria mellonella*

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