

TITLE: EXPRESSION OF VIRULENCE TRAITS BY SWITCHING PHENOTYPIC VARIANTS OF *Candida tropicalis* USING *Galleria mellonella* MODEL

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ABSTRACT:

According to recent epidemiological surveys, *Candida tropicalis* has emerged as clinically important pathogen of bloodstream infections. The epigenetic event of phenotypic switching was previously described for this species where switched morphological variants of *C. tropicalis* showed differentiated virulence in *G. mellonella* larvae model. The aim of the present study was to evaluate possible virulence mechanisms associated with phenotypic switching in *C. tropicalis*. For this, we employed strains of the system 49.07 comprised of five morphotypes (parental, crepe variant, rough variant, crepe revertant and rough revertant), and evaluate hemocytes density after larvae infection, strains survival following co-cultivation with larvae hemocytes and the expression of *Efg1* and *Bcr1* genes (related to the cell wall dynamics and yeast morphogenesis). Larvae infected with *C. tropicalis* morphotypes (5×10^5 cells/larvae) showed reduced number of hemocytes from hemolymph compared to control larvae (inoculated with PBS buffer). Infection with the crepe variant resulted in higher reduction of hemocytes density compared to the parental strain (isolate 49.07). This variant also exhibited higher virulence in *G. mellonella* larvae. On the other hand, infection with the revertant of rough resulted in low reduction of hemocytes density after two hours of infection. In addition to the ability to induce reduction of hemocytes, all phenotypic variants were viable after co-cultivation with *G. mellonella* hemocytes. The variants crepe and rough as well as the revertant of crepe showed higher viability (CFU counting) compared to the parental phenotype, whereas the rough revertant had reduced growth. The expression of *Efg1* and *Bcr1* genes was up-regulated in the switched morphological variants compared to that observed for the parental strain after 4 hours of larvae infection. Considering that these genes may possibly be related with yeast escape factors against the larvae immune system, this data corroborates with the higher viability observed for the switched strains. Taking together, our results suggest that the event of switching is associated with higher fitness of *C. tropicalis* strains. Although virulence is a multifactorial event, virulence traits differently expressed by distinct epigenetic strains may lead to a better knowledge of the role of phenotypic switching in virulence.

Keywords: Phenotypic switching, *Candida tropicalis*, *Galleria mellonella*.

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