

TITLE: PHENOTYPIC SWITCHING ALTERS ADHERENCE TO VERO CELLS IN BLOOD *Candida tropicalis* ISOLATES

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ABSTRACT:

Candida tropicalis is the third leading cause of candidemia in Brazil, and is one of the most recurrent species in invasive infections in kidney transplanted patients. Adhesion ability is a prerequisite for the establishment of *Candida* infections. In *C. tropicalis* the event of phenotypic switching has impact on several virulence attributes. In this study, we investigated the effect of switching on adhesion to Vero cells. For this, *C. tropicalis* blood isolates 100.10 (Is100.10) and 335.07 (Is335.07), and their switch variant strains (crepe-C and irregular center-IC) and revertant strains that switched back to the original isolate phenotype (crepe revert-CR and irregular center revertant) were used to evaluate adhesion to Vero cells (ATCC CCL81). 1×10^7 yeasts/mL in DMEM medium was added to Vero cell monolayer (>80% confluence) in 24-well plates with 5% CO₂ at 37°C for 2h. Adhesion was determined by total biomass (crystal violet method), and directly counting of 300 Vero cells under a light microscope, with two parameters: (1) Percentage of Vero cells with adhered yeasts; (2) Mean of yeast adhered per Vero cell. All *C. tropicalis* strains were able to infect Vero cells monolayers, and phenotypic switching affected this ability. The crepe revertant (OD 0.596±0.097) exhibited higher adhesion than its parental isolate counterpart Is100.10 (OD 0.426±0.0226) ($p < 0.05$). Other switch strains exhibited lower adhesion than their parental counterparts (T-paired test $p < 0.05$), including the Irregular center variant (OD 0.285±0.086) vs Is335.07 (OD 0.414±0.104), and the Crepe variant (OD 0.272±0.0287) vs Is100.10 (OD 0.426±0.0226). The mean of adhered yeasts per Vero cell was also lower for the Crepe variant (2.22±0.056) and Crepe revertant (3.45±0.33) ($p < 0.05$) compared to their Is100.10 parental counterpart (2.88±0.32). Similar profile was evidenced for the percentage of Vero cells with adhered yeasts, where Crepe revertant (93.5±0.3) > Is100.10 (83.6±0.9) > Crepe (72.1±1.4) ($p < 0.05$). In conclusion, this study shows that adhesion of *C. tropicalis* was significantly altered depending on its phenotypic state.

Keywords: Adhesion, Vero cells, *Candida tropicalis*, switch states.

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