

***Candida albicans* adhesion to central venous catheters: Impact of blood plasma-driven germ tube formation and pathogen-derived adhesins.**

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Abstract

Candida albicans-related bloodstream infections are often associated with infected central venous catheters (CVC) triggered by microbial adhesion and biofilm formation. We utilized single-cell force spectroscopy (SCFS) and flow chamber models to investigate the adhesion behavior of *C. albicans* yeast cells and germinated cells to naïve and human blood plasma (HBP)-coated CVC tubing. Germinated cells demonstrated up to 56.8-fold increased adhesion forces to CVC surfaces when compared to yeast cells. Coating of CVCs with HBP significantly increased the adhesion of 60-min germinated cells but not of yeast cells and 30-min germinated cells. Under flow conditions comparable to those in major human veins, germinated cells displayed a flow directional-orientated adhesion pattern to HBP-coated CVC material, suggesting the germ tip to serve as the

major adhesive region. None of the above-reported phenotypes were observed with germinated cells of an *als3Δ* deletion mutant, which displayed similar adhesion forces to CVC surfaces as the isogenic yeast cells. Germinated cells of the *als3Δ* mutant also lacked a clear flow directional-orientated adhesion pattern on HBP-coated CVC material, indicating a central role for Als3 in the adhesion of germinated *C. albicans* cells to blood exposed CVC surfaces. In the common model of *C. albicans*, biofilm formation is thought to be mediated primarily by yeast cells, followed by surface-triggered the formation of hyphae. We suggest an extension of this model in which *C. albicans* germ tubes promote the initial adhesion to blood-exposed implanted medical devices via the germ tube-associated adhesion protein Als3.

Involved units

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