Candida albicans pathogenesis caused by cyclic mechanical deformation

Julia Kurylec[1], Carolina Montoya[1], Divyashri Baraniya[1], Sumant Puri[1], Santiago Orrego[1,2]

[1]Department of Oral Health Sciences, Kornberg School of Dentistry, Temple University. Philadelphia, PA.
[2]Bioengineering Department, College of Engineering, Temple University. Philadelphia, PA.

Statement of Purpose: Biofilms are surface-attached microbial communities that pose significant problems in clinical procedures. Biofilms form on most medical devices and implants such as catheters, mechanical heart valves, pacemakers, prosthetic joints, and contact lenses, posing a critical medical problem.

Candida albicans is a dimorphic yeast, existing in a yeast or hyphal phases[1]. *C. albicans* constitute the most common fungal specie in the oral cavity and is isolated in over 80% of oral lesions[1]. Oral fungal-associated infections such as prosthetic stomatitis affect more than 70% of patients wearing complete dentures[2]. These disorders pose a significant threat to immunocompromised individuals and can lead to adverse long-term effects if left untreated[3].

Microbe adhesion and biofilm formation are complex processes controlled by the interplay between physicochemical and biological phenomena. Microbe-biomaterial interactions are controlled by different surface properties including, wettability, charge density, stiffness, roughness, topography, chemistry, and the combination of thereof[4]. Thus, understanding microbe-surface interactions is essential for biofilm control and the prevention of infections. The goal of this work is to explore the effect of cyclic deformation of biomaterials on the pathogenesis of *C. albicans* biofilms. For the first time, our preliminary indicates that cyclic forces (i.e., mastication) enables increased biofilm formation and pathogenesis of *C.albicans.*

Methods: PMMA beams were fabricated following a standard protocol[5]. Samples were simultaneously subjected to a fungal liquid culture and cyclic mechanical deformation for 24 hours mimicking mastication patterns. Biofilms were grown on material surfaces using liquid cultures *C. albicans* in RPMI 1640 medium. During the experiment, two levels of mechanical strain were evaluated including ε=0% (static), and ε=0.25% (cyclic loading). After incubation, cell viability, metabolism, and biofilm biomass were evaluated using colony-forming units (CFU), MTT assays, and Crystal Violet (CV), respectively. The yeast-to-hyphae transition was monitored under a light microscope after 4 h of biofilm growth under cyclic mechanical deformation.

Results: For the first time, our results showed that cyclic mechanical deformation promotes a significantly increased biofilm formation compared to the static PMMA (**Figure 1a**). This increase was evidenced by higher biofilm biomass, metabolic activity, and number of viable cells in the mechanically stimulated PMMA.

Moreover, microscopic examination of the cell's morphology showed fully developed and robust hyphae in the loaded PMMA while spherical/oval cells predominated in the static PMMA (**Figure 1b**). Quantification of the yeast-to-hyphae transition showed that 88% of the cells on the loaded PMMA were transformed, while only 20% was observed for the static PMMA.

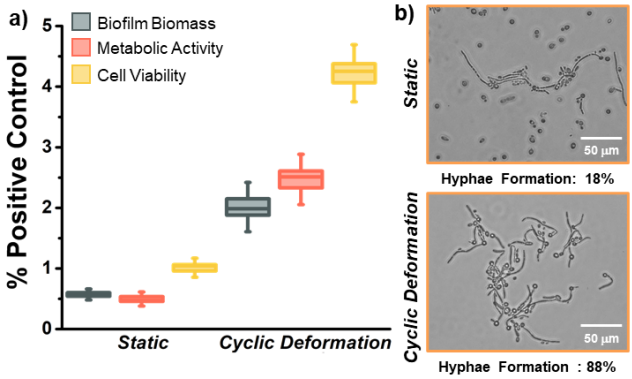

Figure 1. Biofilm–biomaterial evaluations for *C. albicans* biofilms cultured on PMMA substrates. a) Effect of cyclic deformation on biofilm biomass, metabolic activity and number of viable cells. b) Micrographs showing the morphology of *C. albicans* when in contact with static PMMA and PMMA with a repetitive cyclic deformation (0.25%).

Conclusion: For the first time, our results showed that cyclic mechanical deformation is an environmental factor that affects biofilm growth and morphology of *C. albicans* biofilms. Our results indicate that cyclic deformation of PMMA triggers the hypha formation and contributes to biofilms with augmented biomass and number of viable cells. These findings open a new need for designing antifungal dental composites that halt and further prevent biofilm formation and transition into the mycelial stage due to mastication forces.

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