Drug resistance and adhesion: a closer look into the dark side of the wall.

Hélène Martin-Yken, Cécile Formosa, Marion Schiavone, Jean Marie François, Etienne Dague

Drug resistance and adhesion: a closer look into the dark side of the wall.

Hélène Martin-Yken, Cécile Formosa, Marion Schiavone, François Jean-Marie and Etienne Dague.

Stress conditions and presence of drugs or antifungal compounds induce significant changes in yeast and fungi cell wall composition. The molecular architecture of the cell wall is also modified in these conditions, particularly the nature, repartition and attachment of cell wall proteins to the cell surface. Atomic Force Microscopy (AFM) is a powerful tool for studying the morphology, nanomechanical and adhesive properties of live microorganisms under physiological conditions. We took advantage of the most recent AFM technological developments to image and measure the biophysical consequences of these various stresses on *C. albicans* cell morphology at the nanoscale, focusing on changes in cell surface aspect and characteristics: roughness, elasticity, and adhesive properties. We notably explored the effects of the antifungal drug caspofungin used in human health[1]. Our investigation revealed a deep cell wall remodeling induced by this drug, evidenced by a dramatic increase in chitin and decrease in beta-glucan content. Remarkably, a low dose of caspofungin (*i.e.*, 0.5 × MIC) also leads to a characteristic expression of adhesins on *C. albicans* cell surface.

Moreover, in order to get a better understanding of *C. albicans* adhesion mechanisms, we performed Single Molecule Force Spectroscopy (SMFS) experiments to visualize the organization of adhesins and quantify the adhesion forces. We were able to map the adhesins at the cell surface and to distinguish between hydrophobic and specific affinity interactions[2]. Combined with molecular biology tools, this approach also enabled us to further unravel the particular contribution of previously uncharacterized proteins (PGA22 and

PGA59) to *C. albicans* adhesion mechanism[3]. In the future we will focus on new approaches using Single Cell Force Spectroscopy with AFM and Optical Tweezers as well as Sheer-Stress Flow Chamber to study adhesion from the molecule scale to the population scale.

1. Formosa C. et al., 2013. Nanoscale effects of caspofungin against two yeast species; Saccharomyces cerevisiae and Candida albicans, Antimicrobial Agents and Chemotherapy, 57. 3498-3506.
2. Formosa C. et al., Multiparametric Imaging of Adhesive Nanodomains at the Surface of Candida Albicans by Atomic Force Microscopy. Nanomedicine NBM, 11, 57-65.
3. Cabral V. et al., Targeted changes of the cell wall proteome influence Candida albicans ability to form single- and multi-strain biofilms. PloS Pathogens.