

Lewis L.E., Bain J.M., Lowes C., Gillespie C., Rudkin F., Gow N.A.R., Erwig, L-P. (2012). Stage specific assessment of *Candida albicans* phagocytosis by macrophages identifies cell wall composition and morphogenesis as key determinants. *PLoS Pathogens* 8(3): e1002578.

Candida albicans is a major life-threatening human fungal pathogen. Host defence against systemic *Candida* infection relies mainly on phagocytosis of fungal cells by cells of the innate immune system. In this study, we have employed video microscopy, coupled with sophisticated image analysis tools, to assess the contribution of distinct *C. albicans* cell wall components and yeast-hypha morphogenesis to specific stages of phagocytosis by macrophages. We show that macrophage migration towards *C. albicans* was dependent on the glycosylation status of the fungal cell wall, but not cell viability or morphogenic switching from yeast to hyphal forms. This was not a consequence of differences in maximal macrophage track velocity, but stems from a greater percentage of macrophages pursuing glycosylation deficient *C. albicans* during the first hour of the phagocytosis assay. The rate of engulfment of *C. albicans* attached to the macrophage surface was significantly delayed for glycosylation and yeast-locked morphogenetic mutant strains, but enhanced for non-viable cells. Hyphal cells were engulfed at a slower rate than yeast cells, especially those with hyphae in excess of 20 μm , but there was no correlation between hyphal length and the rate of engulfment below this threshold. We show that spatial orientation of the hypha and whether hyphal *C. albicans* attached to the macrophage via the yeast or hyphal end were also important determinants of the rate of engulfment. Breaking down the overall phagocytic process into its individual components revealed novel insights into what determines the speed and effectiveness of *C. albicans* phagocytosis by macrophages.