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Characterizing C. albicans Morphogenesis Regulation in the Context of Host Macrophages

Candida albicans is the most clinically relevant fungal pathogen. Because existing treatment options are limited and exhibit poor efficacy, rigorous mechanistic work characterizing the virulence of this microorganism is crucial in order to develop new treatments that improve clinical outcomes. Innate immune cells such as macrophages are the primary defense against invading fungal cells and serve as a robust model *ex vivo* for understanding virulence mechanisms. *C. albicans* undergoes a morphological transition after macrophage engulfment, which allows the fungus to rupture the immune cell and escape the compartment designated for microbial killing. The molecular signals that trigger the morphological change of *C. albicans* in this context are unknown, although several have been implicated. In this study, we have tested the hypothesis that either CO_2 or alkaline transformation of the phagolysosome/fungal cytosol serve as the primary hyphal inducing signal within the macrophage. *C. albicans* mutants deficient in components of the CO_2-sensing pathway (a null mutant of the Nce103 carbonic anhydrase and a bicarbonate-insensitive point mutant of the Cyr1 adenylyl cyclase) were evaluated in their ability to change morphology once engulfed by host macrophages. These mutants do not exhibit significant morphological defects inside of the macrophage compared to the wild-type strain. Further, using the pH sensor pHluorin, we have demonstrated that the cytosolic pH of *C. albicans* is unchanged during morphogenesis, and others have recently shown that phagolysosomal pH does not contribute to hyphal formation. Thus, neither CO_2 sensing nor pH changes are required for the induction of morphogenesis in this context. Work is ongoing to reveal the signal(s) driving this process.