Spatial and Temporal Regulation of Gene Expression During Hyphal Growth in Candida albicans

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Candida albicans is both a commensal organism and an opportunistic pathogen capable of surviving and proliferating across diverse host niches. This adaptability is driven by its remarkable morphological plasticity, which enables growth as yeast, pseudohyphae, or hyphae. The yeast-to-hypha transition is among the best-characterized features of *C. albicans* biology, owing to its strong association with fungal virulence and its more recently recognized role in commensalism through enhanced competitive fitness within host environments. Hyphal growth is induced by host-associated cues and supported by a well-defined transcriptional program. However, despite the identification of key regulatory factors, the molecular mechanisms governing hyphal growth remain poorly understood. In particular, how polarized growth is regulated within multinucleated hyphae, and how local environmental cues and host interactions shape gene expression dynamics at the cellular and subcellular level, remain largely unexplored.

To address these questions, we developed single-cell and single-molecule mRNA imaging and quantification approaches to investigate growth and gene expression in morphologically intact *C. albicans* cells. Using these tools, we analyzed cells exposed to hyphal-inducing conditions and during interaction with the mammalian host. Our results reveal that the expression of hyphal virulence factors and host-response genes is spatially regulated at both the cellular and subcellular levels. Together, these findings support the existence of a previously unappreciated spatial dimension of gene regulation that underpins *C. albicans* morphological plasticity and host adaptation.