

BioFrontiers - Biology Seminar

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Mapping Metabolic Pathways to Uncover New Targets in a Human Fungal Pathogen

Histoplasma capsulatum is a human fungal pathogen capable of surviving and replicating within macrophages, presenting a unique challenge for host defense and therapeutic intervention. To better understand the metabolic strategies that support intracellular survival, we applied a multi-omics approach combining metabolomics, transcriptomics, and ¹³C-based metabolic flux analysis (a.k.a. fluxomics). This systems-level approach enables the quantitative mapping of central carbon metabolism and the identification of metabolic adaptations that occur during infection.

Mass spectrometry-based metabolomics was used to profile levels of intracellular and extracellular metabolites under varying carbon sources, while transcriptomic data provided complementary insights into gene expression. To quantify *in vivo* reaction rates and carbon flow, we applied ¹³C-stable isotope labeling and computational flux modeling, revealing key features of *Histoplasma*'s metabolism.

By combining these techniques, we aim to uncover regulatory nodes and metabolic bottlenecks that are critical for fungal survival and proliferation within host cells. This integrative strategy not only advances our understanding of fungal pathogenesis but also provides a foundation for rational therapeutic design, demonstrating how engineering principles can be applied to dissect and potentially disrupt infection-enabling metabolism.

