Physiologically relevant alternative carbon sources modulate biofilm formation, cell wall architecture and antifungal resistance of Candida glabrata

ABSTRACT

Flexibility in carbon metabolism is pivotal for the survival and propagation of many human fungal pathogens within host niches. Indeed, flexible carbon assimilation enhances pathogenicity and affects the immunogenicity of Candida albicans. Over the last decade, Candida glabrata has emerged as one of the most common and problematic causes of invasive candidiasis. Despite this, the links between carbon metabolism, fitness, and pathogenicity in C. glabrata are largely unexplored. Therefore, this study has investigated the impact of alternative carbon metabolism on the fitness and pathogenic attributes of C. glabrata. We confirm our previous observation that growth on carbon sources other than glucose, namely acetate, lactate, ethanol, or oleate, attenuates both the planktonic and biofilm growth of C. glabrata, but that biofilms are not significantly affected by growth on glycerol. We extend this by showing that C. glabrata cells grown on these alternative carbon sources undergo cell wall remodeling, which reduces the thickness of their β-glucan and chitin inner layer while increasing their outer mannan layer. Furthermore, alternative carbon sources modulated the oxidative stress resistance of C. glabrata as well as the resistance of C. glabrata to an antifungal drug. In short, key fitness and pathogenic attributes of C. glabrata are shown to be dependent on carbon source. This reaffirms the perspective that the nature of the carbon sources available within specific host niches is crucial for C. glabrata pathogenicity during infection.

Keyword: Candida glabrata; Biofilms; Cell wall; Antifungal resistance; Metabolic adaptation; Metabolism; Alternative carbon metabolism; Pathogenicity