The role of Isocitrate Lyase (ICL1) in the metabolic adaptation of Candida albicans biofilms

ABSTRACT

Background
A major characteristic of Candida biofilm cells that differentiates them from free-floating cells is their high tolerance to antifungal drugs. This high resistance is attributed to particular biofilm properties, including the accumulation of extrapolymeric substances, morphogenetic switching, and metabolic flexibility.

Objectives
This study evaluated the roles of metabolic processes (in particular the glyoxylate cycle) on biofilm formation, antifungal drug resistance, morphology, and cell wall components.

Methods
Growth, adhesion, biofilm formation, and cell wall carbohydrate composition were quantified for isogenic Candida albicans ICL1/ICL1, ICL1/icl1, and icl1/icl1 strains. The morphology and topography of these strains were compared by light microscopy and scanning electron microscopy. FKS1 (glucan synthase), ERG11 (14-α-demethylase), and CDR2 (efflux pump) mRNA levels were quantified using qRT-PCR.

Results
The ICL1/icl1 and icl1/icl1 strains formed similar biofilms and exhibited analogous drug-tolerance levels to the control ICL1/ICL1 strains. Furthermore, the drug sequestration ability of β-1, 3-glucan, a major carbohydrate component of the extracellular matrix, was not impaired. However, the inactivation of ICL1 did impair morphogenesis. ICL1 deletion also had a considerable effect on the expression of the FKS1, ERG11, and CDR2 genes. FKS1 and ERG11 were upregulated in ICL1/icl1 and icl1/icl1 cells throughout the biofilm developmental stages, and CDR2 was upregulated at the early phase. However, their expression was downregulated compared to the control ICL1/ICL1 strain.

Conclusions
We conclude that the glyoxylate cycle is not a specific determinant of biofilm drug resistance.

Keyword: Biofilms; Isocitrate Lyase (ICL1); Resistance; Candida albicans