# 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