The Snf1-activating kinase Sak1 is a key regulator of metabolic adaptation and *in vivo* fitness of *Candida albicans*.

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Details

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Abstract

The metabolic flexibility of the opportunistic fungal pathogen Candida albicans is important for colonisation and infection of different host niches. Complex regulatory networks, in which protein kinases play central roles, link metabolism and other virulence-associated traits, such as filamentous growth and stress resistance, and thereby control commensalism and pathogenicity. By screening a protein kinase deletion mutant library that was generated in the present work using an improved SAT1 flipper cassette, we found that the previously uncharacterised kinase Sak1 is a key upstream activator of the protein kinase Snf1, a highly conserved regulator of nutrient stress responses that is essential for viability in C. albicans. The sak1Δ mutants failed to grow on many alternative carbon sources and were hypersensitive to cell wall/membrane stress. These phenotypes were mirrored in mutants lacking other subunits of the SNF1 complex and partially compensated by a hyperactive form of Snf1. Transcriptional profiling of sak1Δ mutants showed that Sak1 ensures basal expression of glyoxylate cycle and gluconeogenesis genes even in

glucose-rich media and thereby contributes to the metabolic plasticity of C. albicans. In a mouse model of gastrointestinal colonisation, sak1Δ mutants were rapidly outcompeted by wild-type cells, demonstrating that Sak1 is essential for the in vivo fitness of C. albicans.

Involved units

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