

Ahr1 and Tup1 contribute to the transcriptional control of virulence-associated genes in *Candida albicans*.

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Abstract

The capacity of *Candida albicans* to reversibly change its morphology between yeast and filamentous stages is crucial for its virulence. Formation of hyphae correlates with the upregulation of genes ALS3 and ECE1, which are involved in pathogenicity processes such as invasion, iron acquisition, and host cell damage. The global repressor Tup1 and its cofactor Nrg1 are considered to be the main antagonists of hyphal development in *C. albicans*. However, our experiments revealed that Tup1, but not Nrg1, was required for full expression of ALS3 and ECE1. In contrast to NRG1, overexpression of TUP1 was found to inhibit neither filamentous growth nor transcription of ALS3 and ECE1. In addition, we identified the transcription factor Ahr1 as being required for full expression of both genes. A hyperactive version of Ahr1 bound directly to the promoters of ALS3

and ECE1 and induced their transcription even in the absence of environmental stimuli. This regulation worked even in the absence of the crucial hyphal growth regulators Cph1 and Efg1 but was dependent on the presence of Tup1. Overall, our results show that Ahr1 and Tup1 are key contributors in the complex regulation of virulence-associated genes in the different *C. albicans* morphologies. **IMPORTANCE** *Candida albicans* is a major human fungal pathogen and the leading cause of systemic Candida infections. In recent years, Als3 and Ece1 were identified as important factors for fungal virulence. Transcription of both corresponding genes is closely associated with hyphal growth. Here, we describe how Tup1, normally a global repressor of gene expression as well as of filamentation, and the transcription factor Ahr1 contribute to full expression of ALS3 and ECE1 in *C. albicans* hyphae. Both regulators are required for high mRNA amounts of the two genes to ensure functional relevant protein synthesis and localization. These observations identified a new aspect of regulation in the complex transcriptional control of virulence-associated genes in *C. albicans*.

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