

Zinc limitation induces a hyper-adherent goliath phenotype in *Candida albicans*.

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Abstract

Pathogenic microorganisms often face acute micronutrient limitation during infection due to the action of host-mediated nutritional immunity. The human fungal pathogen *Candida albicans* is polymorphic and its morphological plasticity is one of its most widely recognized pathogenicity attributes. Here we investigated the effect of zinc, iron, manganese, and copper limitation on *C. albicans* morphology. Restriction of zinc specifically resulted in the formation of enlarged, spherical yeasts, a phenotype which we term Goliath cells. This cellular response to zinc restriction was conserved in *C. albicans*, *C. dubliniensis* and *C. tropicalis*, but not in *C. parapsilosis*, *C. lusitanae* or *Debaryomyces hansenii*, suggesting that it may have emerged in the last common ancestor of these related pathogenic species. Cell wall analysis revealed proportionally more chitin exposure on the Goliath cell surface. Importantly, these cells were hyper-adherent, suggesting a possible role in pathogenicity. Interestingly, the zincophore-encoding gene *PRA1* was expressed by Goliath cells in zinc limited media and lack of *Pra1* inhibited both cellular enlargement and adhesion.

Goliath cells represent a further layer of Candida phenotypic plasticity.

Involved units

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Leibniz-HKI-Authors



Bernhard Hube

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Elisabeth Weiß

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Duncan Wilson

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