MAPK signaling pathways mediate acetic acid-induced cell death in *Saccharomyces cerevisiae*

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Mitogenic Activated Protein Kinase (MAPK) cascades are important signaling pathways that allow yeast cells to swiftly adapt to a changing environment. These pathways regulate various important processes, from proliferation and differentiation to cell death. MAPK cascades normally contain three protein kinases that act in sequence: a MAP kinase kinase kinase (MAPKKK, MAP3K, MEKK or MKKK), a MAP kinase kinase (MAPKK, MAP2K, MEKor MKK) and a MAP kinase (MAPK). *Saccharomyces cerevisiae* contains five MAPKs (Fus3p, Kss1p, Hog1p, Mpk1p, Smk1p) on five functionally distinct cascades, associated with mating, invasive growth/pseudohyphal development and cell wall integrity, high osmolarity, and sporulation. It has been shown that deletion of the MAPK Hog1p leads to impaired growth of *S. cerevisiae* on solid medium containing acetic acid. Hog1p directly phosphorylates the aquaglyceroporin channel Fps1p, targeting it for endocytosis and degradation in the vacuole. Accordingly, *fps1*Δ mutant cells grow better than wild type cells on solid medium containing acetic acid. However, it is still not known what role other MAPK pathways play in signaling acetic-acid induced apoptosis.

In the present work, we describe the involvement of MAPK pathways in acetic acid-induced cell death. Several mutants deleted for components of these pathways were constructed and screened for altered phenotypes after incubation with acetic acid. We show there is a decreased sensitivity to acetic acid-induced cell death in the *ste20*Δ, *wsc2*Δ and *wsc3*Δ mutant strains. These results correlated with decreased production of reactive oxygen species and increased cell membrane integrity, assessed by flow cytometry. The data obtained suggested a relationship between MAPK pathways and cell death mediated by acetic acid.

This work was funded by FEDER through the program “Programa Operacional Factores de Competitividade-COMPETE” and by FCT through the projects Pest-C/BIA/UI4050/2011 and FCOMP-01-0124-FEDER-007047. F.A. was supported by an FCT fellowship (FCOMP-01-0124-FEDER-007047).