Downstream functions of the Sty1 MAPK pathway in *S. pombe*

ABSTRACT

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MAP kinase pathways are involved in the response to environmental changes in eukaryotic cells regulating transcriptional and translational events. In *S. pombe*, the major stress activated MAP kinase, Sty1, is activated by a vast number of stresses hereby regulating the transcriptional response through its downstream target, transcription factor Atf1.

We identified two MAPK activated kinases, Mkp1 and Mkp2, both found to interact with Sty1 in exponentially growing cells. Phosphorylation of Mkp1 is Sty1-dependent and this modification disappears upon nitrogen starvation. Overexpression of *mkp1*$^{+}$ leads to severely elongated cells and a delay in mating and sporulation whereas *mkp1*$^{-}$ cells showed an enhanced rate of mating and entry into meiosis. Both kinases are cytoplasmatic, with a distinct sub-localization of Mkp2 to septa in actively dividing cells.

The MAP kinase Sty1 is required for the translational adaptation after oxidative, hyperosmotic stress and after nitrogen starvation. The transcription factor Atf1 contributes to the recovery of translation after hyperosmotic stress, but not oxidative or nutrient stress. We found Sty1 to interact with translation factors eIF3a and eEF2. The Sty1-eEF2 interaction reaches a maximum shortly after nitrogen withdrawal and thereafter decreases. The Sty1-eIF3a interaction decreases after oxidative, hyperosmotic stress and upon nitrogen withdrawal. The eIF3a protein disappears upon nitrogen starvation at the time of polysomal re-initiation. The protein levels of eIF3a are reduced in *sty1*$^{-}$ cells.

In a whole genome mRNA stability analysis, we find that there is a strong trend for mRNAs that are transcriptionally upregulated to also become stabilized after oxidative stress. This early, temporary change in stability of functional subgroups of mRNAs is largely Sty1-dependent. Transcripts involved in ribosome biogenesis and assembly have a stability defect in *sty1*$^{-}$ cells.

Keywords: *S.pombe*, MAPK, Sty1, Mkp1, oxidative stress, translation, mRNA stability
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