The oxidative and osmotic stress responses of *S. cerevisiae*

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Abstract

The yeast Hog1 is a stress responsive mitogen activated protein kinase (MAPK) similar to mammalian p38 and JNK. Rck2 is a protein kinase downstream of Hog1. The Hog1 pathway was previously implicated exclusively in the response to osmotic stress.

This thesis investigates the role of the Hog1 MAPK signalling pathway in global post-transcriptional regulation and survival during environmental stress. We have shown that mutations in Hog1 pathway components make cells sensitive to oxidative and heavy metal stress and that Hog1 and Rck2 are activated during these stress conditions. Putative downstream components involved in oxidative stress resistance are identified.

Rck2 has a profound effect on the translational apparatus. During stress, Rck2 prevents polysome levels from falling too low. A kinase-dead allele of Rck2 confers stress sensitivity, and causes inactive polysomes to persist bound to mRNA during stress. Transcripts encoding translational components are deregulated in *rck2* mutants.

In response to osmotic stress, the Hog1 pathway affects mRNA levels of several hundred genes. This is accomplished to a large extent by regulation of mRNA stability, which is fast, widespread, and specific for several large groups of genes. Regulation of mRNA stability is dynamic throughout the response and precedes accumulation as well as decline of transcript levels. Unexpectedly, Rck2 has a larger effect on transcript levels than on stability, indicating a role in transcription.

A comparison between two large scale studies reveals a positive global correlation between changes in polysomal association and mRNA stability in the adaptation phase. No global correlation was found in the early response. Among genes annotated as stress responsive, two groups were found which differed in their regulation at the polysomal level early in the response, and these were used to discover new genes with a characteristic post-transcriptional behavior after stress. Transcripts encoding components of the cytoplasmic translational apparatus were divided into three separate groups with a characteristic behavior. A group of genes shown to be translationally upregulated was shown to also be stabilized in response to stress.

Keywords: Hog1, Rck2, MAPK pathway, stress signaling, mRNA decay, polysome association, translation, microarray

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