Role of Rck2 in metal and oxidative stress response

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ABSTRACT

Yeast cells respond to rapid and drastic changes in their environment by activating signal transduction cascades that perform specific functions depending on the type of stress caused. MAP kinase pathways are one such network of protein kinases that result in the induction of transcription factors and a plethora of transcriptional and translational events leading to stress response.

In *Saccharomyces cerevisiae*, the MAPK activated protein kinase Rck2 functions downstream of the MAPK Hog1, regulating a subset of events in response to stress. Upon oxidative stress, Hog1 is activated by a Pbs2-dependent phosphorylation event and thereafter relocates to the nucleus. Rck2 is also phosphorylated in response to oxidative stress. Rck2 and its homolog Rck1 interact with several stress response proteins among which, genetic and biochemical interactions between Rck1 and Yap2, Rck2 and Zrc1 are verified. This relay of events connects the Hog1 MAPK with effectors of oxidative stress response.

Exposure of cells to Zn^{2+} concentrations above 5 mM leads to rapid degradation of Rck2, which is otherwise a stable protein. Degradation of Rck2 is not a result of general protein turnover but is a targeted event. Rck2 degradation occurs through the vacuolar protein degradation pathway in response to excess zinc conditions.

Cells over-expressing a catalytically inactive allele of *RCK2*, *rck2-kd*, are sensitive to oxidative stress. In wild type and *rck2Δ* cells, oxidative stress results in a general down-regulation of translational events. However, in cells over expressing *rck2-kd*, dissociation of polysomes is greatly delayed and does not correlate with the rate of protein synthesis. Microarray analysis using total and polysomal mRNAs resulted in the identification of two groups of mRNAs that are regulated by Rck2: those encoding cytoplasmic ribosomal protein mRNAs and nucleolar proteins. Rck2 may regulate translation elongation by mediating the ribosomal association with mRNAs. Interference with this association compromises the efficiency of response to stress.

Keywords: *Saccharomyces cerevisiae*, *RCK2*, MAPKAP kinase, oxidative stress, metal stress, stress response, polysomal association
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