SL807 Transcriptional Regulation of a DNA Repair Gene in *Saccharomyces cerevisiae*

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In *Saccharomyces cerevisiae* UV irradiation and a variety of chemical DNA-damaging agents induce the transcription of specific genes, including several involved in DNA repair. One of the best characterized of DNA-damage inducible genes is *PHR1*, which encodes the apoenzyme for DNA photolyase. Basal-level and damage-induced expression of *PHR1* require an upstream activation sequence, UAS_{PHR1}. Here we report the identification of the *UME6* gene of *S. cerevisiae* as a regulator of UAS_{PHR1} activity. Surprisingly, the effect of deletion of *UME6* is growth phase dependent. In wild-type cells *PHR1* is induced in late exponential phase, concomitant with the initiation of glycogen accumulation that precedes the diauxic shift. Deletion of *UME6* abolishes this induction, decreases the steady-state concentration of photolyase molecules and *PHR1* mRNA, and increases the UV sensitivity of a *rad2* mutant. The results suggest that *UME6* contributes to the regulated expression of a subset of damage-responsive genes in yeast. Furthermore, the upstream repression sequence, URS_{PHR1}, is required for repression and damage-induced expression of PHR1. Here we show identification of YER169W and YDR096W as putative regulators acting through URS_{PHR1}. These open reading frames were designated as *RPH1* (YER169W) and *RPH2* (YDR096W) indicating regulator of *PHR1*. Simultaneous disruption of both genes showed a synergistic effect, producing a four-fold increase in basal level expression and a similar decrease in the induction ratio following treatment of methyl methanesulfonate(MMS). Mutation of the sequence (AG_4) bound by Rph1p rendered the promoter of *PHR1* insensitive to changes in *RPH1* or *RPH2* status. The data suggest that *RPH1* and *RPH2* act as damage-responsive negative regulators of *PHR1*. Surprisingly, the sequence bound by Rph1p *in vitro* is found to be AG_4 which is identical to the consensus binding site for the regulators Msn2p and Msn4p involved in stress-induced expression. Deletion of *MSN2* and *MSN4* has little effect on the induction ratio following DNA damage. However, all deletions led to a significant decrease in basal-level and induced expression of *PHR1*. These results imply that *MSN2* and *MSN4* are positive regulators of *PHR1* but are not required for DNA damage repression. [Supported by grant from NIH]