

## Yeast Yak1 Kinase, a Bridge between PKA and Stress-Responsive Transcription Factors, Hsf1 and Msn2/Msn4

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Hsf1 and Msn2/Msn4 transcription factors in *Saccharomyces cerevisiae* play important roles in cellular homeostasis by activating gene expression in response to multiple stresses including heat shock, oxidative stress, and nutrient starvation. Although it has been known that nuclear import of Msn2 is inhibited by PKA-dependent phosphorylation, the mechanism for PKA-dependent regulation of Hsf1 is not well understood. Here we demonstrate that Yak1 kinase, which is under the negative control of PKA, activates both Hsf1 and Msn2 by phosphorylation when PKA activity is lowered by glucose depletion or by overexpressing Pde2 that hydrolyses cAMP. We show that Yak1 directly phosphorylates Hsf1 *in vitro*, leading to an increase in DNA binding activity of Hsf1. We also demonstrate that Yak1 phosphorylates Msn2 *in vitro*, but does not affect DNA binding activity of Msn2 or nuclear localization of Msn2 upon glucose depletion. These results suggest a central role for Yak1 in mediating PKA-dependent inhibition of Hsf1 and Msn2/Msn4.

### References

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