STRATEGY OF TRANSCRIPTION REGULATION IN YEAST SUBJECTED TO OXIDATIVE AND CADMIUM STRESS

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Yeast possesses a complex program of gene expression when exposed to a plethora of environmental cues. HSF and Msn2p/Msn4p are transcription factors that regulate gene expression during stress. However, the two basic leucine-zipper (b-ZIP) transcription factors, Yap1p and Yap2p, along with six newly identified proteins, form a family of trans-regulators that have been implicated in various forms of stress response. Yap1p plays a major role in the regulation of enzymes that protect against oxidative stress provoked by H_2O_2 and by thiol-reactive agents whereas Yap2 was shown to be involved in cadmium adaptation. C-terminus of these proteins contains several cysteines which depending on the oxidative stress inducer are either involved in the formation of an intramolecular disulphide bond (C303/C598) or the drug directly binds the Yap1 molecule via the residues C598/C620/C629 and for Yap2, Cd^{++} binds either C391/C387 or C391/C356. These modifications disrupt the interaction of Crm1, the exportin responsible for nuclear-cytoplasmic shuttling and thus leading to nuclear accumulation. *yap1* mutant has a sensitivity phenotype to cadmium in contrast to *yap2*. However, replacement of the Yap1 cCRD by the homologous Yap2 domain preserved the response to Cd^{++} but not to H_2O_2, confirming the equivalency of cCRDs domains in cadmium sensing functions and demonstrating that the built-in specificity of the Yap1 cCRD towards H_2O_2 is not conserved in the homologous Yap2 domain. A *bona-fide* target of Yap2, Frm2, was found leading us to postulate that Yap2 exerts under Cd^{++} a specific function independent of Yap1 as Frm2 seems to function in lipid metabolism. The potential cross-talk between the various Yaps will be discussed.

Keywords: Yap, oxidative stress, cadmium