PDR1 and PDR3 encode zinc finger transcription factors that are regulators of the pleiotropic drug response in S. cerevisiae. Pdr1p and Pdr3p are 36% identical in amino acid compositionand can form homodimers or heterodimers. Pdr1p and Pdr3p serve as both transcriptional activators and repressors by binding to pleiotropic drug response elementspresent in the promoters of target genes involved in multidrug resistance. A key feature of the PDRE consensus sequence, 5'-TCCGCGGA-3', is the presence of CGG triplets in an everted repeat orientationand both Pdr1p and Pdr3p constitutively occupy both perfect and degenerate PDREs. These two factors have overlapping but not identical sets of target genes and the individual effect on any given shared target gene can also differ. This variation in regulatory ability may be due either to differences in post-translational modification or heterodimer formation with other transcriptional factors such as Rdr1p and Stb5p. Targets include the ABC transporters encoded by PDR5, PDR10, PDR15, SNQ2, and YOR1, the hexose transporter genes HXT9 and HXT11, and sphingolipid biosynthetic genes such as IPT1. Pdr3p also participates in other processes that do not involve Pdr1p, such as retrograde response signaling, as well as regulating the DNA damage-inducible genes MAG1 and DDI1. Loss of either PDR1 or PDR3 results in differential drug tolerance, and loss of both pdr1 and pdr3 results in severe drug hypersensitivity. Single pdr1 null mutants are markedly decreased in their resistance to different drugs while the affect of a single pdr3 null mutation is less severe. Hyperactive mutants of Pdr1p and Pdr3p often lead to enhanced drug resistance due to an increase in drug transporters, but only about 10% of the roughly 200 genes containing a PDRE-like element in their promoters respond transcriptionally to the hyperactive forms of Pdr1p and Pdr3p, indicating that factors beyond the presence of a PDRE may be necessary for transcriptional activation by Pdr1p and Pdr3p.Pdr3p positively autoregulates its own transcription through two PDREs present in the PDR3 promoter. These PDREs are also recognized and regulated by Pdr1p. PDR3 expression is also downregulated in the absence of cell growth brought on by glucose or nitrogen limitation or when cells approach stationary phase. In cells which have lost their mitochondrial genome, PDR3 expression varies depending on both strain background and carbon source. Cell stress is another regulator of PDR3 transcription through the action of the heat shock transcription factor Hsf1p. The heat shock HSP70 protein Ssa1p is able to bind to Pdr3p and may post-translationally negatively regulate Pdr3p activity.