URE2 encodes a bifunctional protein that is involved in both nitrogen catabolite repressionand oxidative stress response. When optimal sources of nitrogen are available, Ure2p acts as a transcriptional corepressor and downregulates the expression of many genes involved in nitrogen utilization by inhibiting the GATA transcriptional activators Gln3p and Gat1p. Ure2p, which localizes to the cytosol, binds to the phosphorylated forms of Gln3p and Gat1p and prevents them from entering the nucleus. URE2 may have an additional role in protecting the cell from oxidative stress. Ure2p, which forms a homodimer by dimerizing through its C-terminal region, binds glutathione with high affinityand has been shown to exhibit glutathione peroxidase activity in vitro. The crystal structure of Ure2p also shows that it has structural similarity to glutathione S-transferases.Ure2p enzyme activity is repressed by the pleiotropic regulatory protein Mks1p. URE2 does not appear to be regulated, but the URE2 mRNA contains an internal ribosome entry sitefrom which translation is repressed by YGR054W, the yeast homolog of the mammalian protein Eukaryotic Initiation Factor 2A. IRES-mediated translation leads to an N-terminally truncated form of the protein that retains regulatory activity but is unable to drive prion formation.S. cerevisiae cells lacking functional Ure2p no longer respond to NCR and can thus utilize poor nitrogen sources even in the presence of optimal ones. This condition results in improved alcoholic fermentation of fruit juices and grape musts. ure2 mutant strains are also hypersensitive to growth inhibition by rapamycinand to the toxic effects of many oxidative agents and heavy metals. However, ure2 mutations do lead to improved ion tolerance in calcineurin cnb1 single and cna1 cmp2 double mutants.[URE3] is a yeast prion formed by the autocatalytic conversion of Ure2p into infectious, protease-resistant, amyloid fibrils. The Ure2p prion domain spans amino acids 1-89 and is rich in asparagines and glutamines, and it has been shown that [URE3] formation is driven primarily by prion domain amino acid composition as opposed to primary sequence. The N-terminal prion domain polymerizes to form an amyloid filament backbone surrounded by the C-terminal nitrogen regulatory domains. The regulatory domains retain their native conformation but are sterically inactivated.Conversion of Ure2p to [URE3] can be induced by overexpression of either the full-length Ure2p or just the prion domain, 27). However, in cells already infected with [URE3], overexpression of the prion domain can cure the cells. Other conditions that either clear or prevent [URE3] generation/propagation include: the presence of glutamate, growth in medium containing guanidine, overexpression of a Ure2-GFP fusion protein, expression of truncated Ure2p from the URE2 mRNA IRES, loss of the Ure2p repressor Mks1p, overexpression of the HSP70 family member Ssa1p, expression of a P395L mutant of Ssa2p, loss of the protein chaperon Hsp104p, or overproduction of the protein chaperone Ydj1p.Although the Ure2p regulatory domain is evolutionarily conserved across several yeast genera, the prion domain is not conserved even among related Saccharomyces species. [URE3] is being studied as a model for human amyloid diseases such as Alzheimer's disease, non-insulin-dependent diabetes mellitus, and transmissible spongiform encephalopathyand as a target to screen anti-prion drugs.