About the thioredoxin system The thioredoxin system and glutathione/glutaredoxin system help maintain the reduced environment of the cell and play a significant role in defending the cell against oxidative stress. They also have been proposed to play a role in purine and pyrimidine biosynthesis as required for DNA synthesis, protein folding and regulation, and sulfur metabolism.Thioredoxins and glutaredoxins are small heat-stable proteins with redox-active cysteines that facilitate the reduction of other proteins by catalyzing cysteine thiol-disulfide exchange reactions. Thioredoxins contain two conserved cysteines that exist in either a reduced form as in thioredoxin-2) or in an oxidized form as in thioredoxin-S2) when they form an intramolecular disulfide bridge. Thioredoxins donate electrons from their active center dithiol to protein disulfide bondsthat are then reduced to dithiols2). The resulting oxidized thioredoxin disulfide is reduced directly by thioredoxin reductase with electrons donated by NADPH. Hence the thioredoxin reduction system consists of thioredoxin, thioredoxin reductase, and NADPH. Oxidized glutaredoxins, on the other hand, are reduced by the tripeptide glutathioneusing electrons donated by NADPH. Hence the glutathione/glutaredoxin system consists of glutaredoxin, glutathione, glutathione reductase and NADPH.S. cerevisiae contains a cytoplasmic thioredoxin system comprised of the thioredoxins Trx1p and Trx2p and the thioredoxin reductase Trr1p, and a complete mitochondrial thioredoxin system comprised of the thioredoxin Trx3p and the thioredoxin reductase Trr2p. Evidence suggests that the cytoplasmic thioredoxin system may have overlapping function with the glutathione/glutaredoxin system. The mitochondrial thioredoxin system, on the other hand, does not appear to be able to substitute for either the cytoplasmic thioredoxin or glutathione/glutaredoxin systems. Instead, the mitochondrial thioredoxn proteins, thioredoxinand thioredoxin reductasehave been implicated in the defense against oxidative stress generated during respiratory metabolism.The two cytoplasmic thioredoxinsare believed to supply reducing equivalents to the enzymes ribonucleotide reductaseand 3'-phosphoadenosine 5'-phosphosulfatereductase. Deletion of either TRX1 or TRX2 has no effect on cell growth or morphology, but, deletion of both genes affects the cell cycle, and makes the cells auxotrophic for methionine/cysteine. Deletion of the single gene TRX2 does result in extreme sensitivity to H2O2 and is thereby believed to be involved in the response against H2O2. The expression of TRX2 and TRR1 are regulated by the transcription factors Yap1p and Skn7p in response to H2O2.