Yfh1p is a mitochondrial matrix proteinthat functions as an iron chaperone. Yfh1p binds ferrous ironand couples protein assembly with iron oxidation and storage. Yfh1p is specifically involved in the biosynthesis of iron-sulfurclusters, a prosthetic group required for the function of mitochondrial respiratory chain complexes, aconitase of the citric acid cycle, proteins involved in cofactor biosynthesis and many others. YFH1 interacts with several genesinvolved in either the synthesis of the Fe/S scaffold or its subsequent transfer to apoprotein targets. There are also ferrous iron regulated physical interactions between Yfh1p and the core Fe/S assembly complex. Yfh1p is essential for de novo Fe/S cluster assembly on Isu1p, suggesting a direct role in the incorporation of iron into Fe/S clusters.YFH1, the yeast frataxinhomolog, was originally identified based on its similarity to the human FRDA gene. Mutations in the human gene result in Friedreich's ataxia, a disease characterized by neurodegeneration, cardiomyopathy, and diabetes. Frataxin is evolutionarily conserved with similar genes in worms, flies and mammals.Deletion of YFH1 results in yeast strains with severe mitochondrial defects including the inability to grow on non-fermentable carbon sources, constitutive induction of high-affinity iron uptake, and an increase in both mitochondrialand cellulariron content that results in hypersensitivity to oxidative stress. Increased oxidative stress results in mitochondrial DNA damage and loss, nuclear DNA damage, increased sensitivity to DNA damaging agentsand lifespan reduction. Multiple Fe/S-dependent enzyme deficiencies have been observedin null mutants. Many of these defects are shared by cells derived from Friedreich's ataxia patients. In addition, defects associated with yfh1 null mutants can be rescued by expression of either the full-length human geneor chimeric constructs containing the YFH1-homologous domain, but not disease-associated missense constructs, suggesting conservation of function.