Zwf1p is a cytoplasmic glucose-6-phosphate dehydrogenasethat catalyzes the first step, which is irreversible and rate-limiting, of the pentose phosphate pathway, which regenerates NADPH from NADP+ through an oxidation/reduction reaction. Zwf1p is important for maintaining cytosolic levels of NADPH but has little effect on mitochondrial levels. Zwf1p is also involved in protecting yeast against oxidative stress. Although Zwf1p expression in yeast is essentially constitutive, Zwf1p activity is inhibited by NADPH such that processes that decrease the cytosolic levels of NADPH stimulate the oxidative branch of the pentose phosphate pathway. Null mutants in zwf1 are viable, but display decreased sporulation, reduced aerobic growth on medium lacking lysine, increased sensitivity to oxidative stress, and increased sensitivity to the fermentation inhibitor furfural. Null mutants require an organic sulfur sourceand display methionine auxotrophy when grown on glucose. Double null mutants in ald6 and zwf1 are inviable under standard conditionsbut may be isolated and propagated on nonfermentable carbon sources, and idp2 zwf1 double nulls exhibit a rapid loss of viability when transferred to medium containing oleate as the carbon source. Zwf1p is of industrial interest because its deletion from recombinant Saccharomyces cerevisiae strains engineered to ferment xylose to ethanolresults in increased ethanol production and decreased xylitol production. Zwf1p also influences sensitivity to furfural, which is an inhibitory byproduct of xylose fermentation. Zwf1p is of medical interest because of its homology to human glucose-6-phosphate dehydrogenase, which is highly polymorphic with over 130 mutations identified thus far. Complete loss of G6PD in humans is fatal, while partial loss of function can result in neonatal jaundice and hemolytic anemia. Zwf1p also displays similarity to the glucose-6-phosphate dehydrogenase proteins in Drosophila and rats.