URA3 encodes orotidine 5-phosphate decarboxylase, an enzyme involved in the de novo synthesis of pyrimidine ribonucleotides. ODCase, which is responsible for catalyzing the decarboxylation of orotidine 5-phosphateto uridylic acid, is one of the most proficient enzymes in nature. Not only does it function in the absence of cofactors, ODCase enhances the reaction rate by an unusually large magnitude, reducing a reaction half-time of 78 million years to 18 milliseconds. Crystallography experiments and studies of the human and mammalian homologs suggest that the active yeast ODCase functions as a dimer. In mammals, OMP conversion to UMP is mediated by the UMP synthase, which catalyzes both this step in the pathway and the one preceding it. S. cerevisiae ODCase shares ~54% sequence similarity with the ODCase domain of the mammalian UMP synthase. Mutations in the human homolog UMP synthase lead to the only known human disease of the de novo pyrimidine biosynthetic pathway, orotic aciduria I and II.Loss of ODCase activity leads to a lack of cell growth unless uracil or uridine is added to the media. In addition, ODCase can convert 5-FOA into the toxic compound 5-fluorouracil. Since URA3 allows for both positive and negative selection, it has been developed as a genetic marker for DNA transformations and other genetic techniques in bacteria and many fungal species.Uracil starvation or increased levels of the pyrimidine biosynthesis pathway intermediate dihydoorotic acidcan induce URA3 expression 3-5 fold. This regulation is mediated by the transcriptional activator Ppr1p, which binds to the UASURA sitein the promoters of URA1, URA3, and URA4. DNA-bound Ppr1p is transcriptionally inactive, but the addition of DHO converts Ppr1p to an active state that interacts with RNA polymerase II, leading to increased expression of the URA genes.