The fifth step in the pathway of de novo synthesis of pyrimidine ribonucleotidesis the conversion of orotate to orotidine- 5'-monophosphate, which is catalyzed by orotate phosphoribosyl transferase. S. cerevisiae has two genes that encode for OPRTase, URA5 and URA10. These two gene products share greater than 75% amino acid similarity. Ura5p contributes most of the OPRTase activity found in yeast cells and is not regulated by any product or intermediate of the pyrimidine biosynthesis pathway.. In contrast, Ura10p is responsible for 20% of the total OPRTase activity and URA10 expression is upregulated by the pyrimidine intermediate dihydoorotic acidvia Ppr1p. Ppr1p is a transcriptional activator that binds to the UASURA motif CGGN6CCG in gene promoters. 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 Ppr1p-regulated genes.Unrelated to pathway intermediates, URA5 transcription is downregulated by DMSO, but URA10 expression is upregulated under the same conditions. URA10 is also upregulated by zinc depletion through Zap1p activity, downregulated by inositol and choline in a Opi1p-dependent manner, and upregulated by the presence of lithium.In higher eukaryotes, orotate conversion to OMP is mediated by a bifunctional enzyme that catalyzes both this and the following step in the pyrimidine biosynthesis pathway. S. cerevisiae OPRTase shares ~30% sequence similarity with the OPRTase domain of the homologous Arabidopsis thaliana protein. Mutations in the human homolog, UMP synthase, lead to the only known human disease of the de novo pyrimidine biosynthetic pathway, orotic aciduria.