ADE4 encodes 5-phosphoribosyl-1-pyrophosphate amidotransferase, also known as amidophosphoribosyltransferase or PRPPAT, which catalyzes the first step of the de novo purine nucleotide biosynthetic pathway. Expression of ADE4, and of other genes in the yeast ADE regulon, is repressed by the presence of purine bases and derepressed in the absence of purines through the action of transcription factors such as Bas1p, Pho2p, and Gcn4p. Bas1p binds several ADE promotersand DNA-bound Bas1p recruits Pho2p to activate ADE genes in S. cerevisiae. Gcn4p also regulates the expression of these genes. There are three Gcn4p responsive elementsin the 5'-flanking region of ADE4. Two GCREs are essential to synergistically activate ADE4 transcription by binding Gcn4p. The distal GCRE1 is also required for basal transcription of ADE4. Ade4p forms cytoplasmic foci in the absence of adenine, and cycling between punctate and diffuse cellular distribution can be controlled by adenine subtraction and addition. ade4 null mutants exhibit adenine auxotrophy, decreased resistance to ethanol, and slow growth. Cisplatin resistance is conferred either by an ADE4 activation mutation, which causes constitutive AMP synthesis and hypoxanthine excretion, or by overexpression of ADE4, which increases de novo synthesis of purine nucleotides. Mutations in ADE4 are epistatic with mutations in ADE2, which encodes encodes aminoimidazole ribonucleotide-carboxylase, an enzyme catalyzing the sixth step of purine nucleotide biosynthesis, and with mutations in ADE13, which encodes adenylosuccinate lyase, an enzyme catalyzing steps 8 and 12 of the de novo purine pathway. Orthologs of Ade4p have been identified in Bacillus subtilis, Escherichia coli, Ashbya gossypii, Schizosaccharomyces pombe, Gallus gallus, Rattus rattus, and Homo sapiens. The human PRPPAT cDNA complements the S. cerevisiae ade4 null mutant.