Aldehyde dehydrogenases play a critical role in the conversion of acetaldehyde to acetyl-CoA during growth on non-fermentable carbon sources and in the breakdown of toxic aldehydes accumulated under stress conditions. Acetaldehyde arises during the metabolism of pyruvate to acetate by the cytoplasmic pyruvate dehydrogenase bypasspathway, which involves the enzymatic activities pyruvate decarboxylase, acetaldehyde dehydrogenase, and acetyl-CoA synthetase. In an alternate mitochondrial pyruvate dehydrogenase bypass pathway, pyruvate is first decarboxylated to acetaldehyde in the cytosol by pyruvate decarboxylase and is then converted to acetate by the mitochondrial acetaldehyde dehydrogenases. In the yeast genome, there are five genes known to encode aldehyde dehydrogenases, as well as an additional gene with sequence similarity. Ald2p and Ald3p are cytosolic enzymes which use only NAD+ as cofactor. Both genes are induced in response to ethanol or stress and repressed by glucose. Ald4p and Ald5p are mitochondrial, use NAD and NADP as cofactors, and are K+ dependent. Ald4p, the major isoform, is glucose repressed and ald4 mutants do not grow on ethanol, while Ald5p, the minor isoform, is constitutively expressed. ALD6 encodes the Mg2+ activated cytosolic enzyme, which uses NADP+ as cofactor and is constitutively expressed. HFD1 has been predicted to encode a fatty aldehyde dehydrogenase.Expression of ALD4 is regulated by several different proteins. The transcription factor Stb5p induces transcription of ALD4, while the transcription repressors Nrg1p and Nrg2p decrease it.Aldehyde dehydrogenases are conserved across many species and are key enzymes in metabolic pathways, some of which function to detoxify harmful chemical intermediates. In humans, mutations in aldehyde dehydrogenase genesare associated with alcoholism and carcinogenesis. In plants, these enzymes play important roles in fertility and in fruit ripening.