LEU4 and LEU9 encode alpha-isopropylmalate synthase, the enzyme that catalyzes the conversion of 2-keto-isovalerate into alpha-isopropylmalate. This reaction is the first step in leucine biosynthesis. Leu4p and Leu9p are 83% identical; Leu4p is the major isozyme, accounting for about 80% of total alpha-isopropylmalate synthase activity in wild-type cells.Leu9p is localized to the mitochondrial matrix, where the majority of alpha-isopropylmalate synthesis occurs. The enzyme is less sensitive to feedback inhibition by leucine than Leu4p which is most likely due to amino acid differences in the 39-amino acid C-terminal regulatory region of the two proteins. leu9 deletion strains are still able to grow in the absence of leucine due to redundant Leu4p activity, but cells lacking both enzymes are leucine auxotrophs. In contrast to Leu4p, the presence of Leu9p is not required for normal growth on non-fermentable carbon sources.