VMA2 encodes the B subunit of the yeast V-ATPase V1 domain. Vacuolar-ATPasesare ATP-dependent proton pumps that acidify intracellular vacuolar compartments. Vacuolar acidification is important for many cellular processes, including endocytosis, targeting of newly synthesized lysosomal enzymes, and other molecular targeting processes. The V-ATPase consists of two separable domains. The V1 domain has eight known subunits, is peripherally associated with the vacuolar membrane, and catalyzes ATP hydrolysis. The V0 domain is an integral membrane structure of five subunits, and transports protons across the membrane. The structure, function, and assembly of V-ATPases are reviewed in references 6, 8, 9 and 10. The B subunitof the V-ATPase contains nucleotide binding sites, but does not catalyze ATP hydrolysis. Some vma2 point mutations reduce the ATPase and proton transport activities of the V-ATPase holoenzyme, suggesting that ATP binding to the noncatalytic sites may regulate V-ATPase activity.26 PH,PR,CC, The vma2 null mutation is synthetically lethal with mutations that cause defects in endocytosis. V-ATPases have been identified in numerous eukaryotes; the vma2 null phenotype can be fully complemented by expression of the Candida tropicalis V-ATPase B subunit, and partially complemented by the bovine B subunit.