VMA6 encodes the d subunit of the yeast V-ATPase V0 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 1, 3, 4 and 5. The vma6 null mutant is viable but shows a growth defect at neutral pH and is sensitive to calcium. In the absence of Vma6p, the remaining V0 subunits are destabilized and the V1 domain does not assemble onto the vacuolar membrane. V-ATPases have been identified in numerous eukaryotes; Vma6p homologs have been identified in red beet and Arabidopsis.