VMA13 encodes the H 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 2, 4, 5 and 6. In a vma13 null mutant, the remaining V1 subunits associate with the vacuolar membrane, but the complex is inactive and less stable than the wild type complex, suggesting that Vma13p is required for activity but not assembly of the V-ATPase. Free cytosolic V1 domains normally exist in a dynamic equilibrium with fully assembled V-ATPase complexes but are inactive; loss of Vma13p results in some ATPase activity in free V1 domains. Mutations in several V-ATPase subunits, including Vma13p, can cause calcium sensitivity due to loss of ATP-dependent Ca2 uptake. V-ATPases have been identified in numerous eukaryotes, and the genes encoding bovine and porcine V-ATPase H subunits have been cloned.